

Cephalalgia

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PRESIDENTIAL SYMPOSIUM

Presidential symposium: Pain and inflammatory mechanisms

PS-1

Sensory innervation of the skull: possible role in the pathophysiology of migraine headache

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Background Migraine pain is perceived as exploding headache (intracranial pressure), imploding headache (extracranial pressure) or ocular headache (pressure behind the eyeball). Having found that only imploding and ocular headaches are suppressible by Botulinum Toxin Type-A injections to pericranial muscles, we ask whether this effect is achieved through blockade of nerve fibers that cross the skull?

Objective To map sensory innervation of the skull.

Methods Serial sections of whole-head preparations of postnatal mice were processed using immunohistochemistry for markers of small-diameter sensory axons (CGRP and peripherin) and large-diameter myelinated axons (neurofilament).

Results Each of the 3 immunostaining markers revealed rich innervation in the occipital, parietal, temporal and frontal bones of the skull. We observed large nerve bundles running in the galea aponeurotica, on the surface of the periosteum, which appeared to send collateral branches that crossed the osteum transversely and terminate in the dura and pia. We also observed large nerve bundles running in the dura, which appeared to send collateral branches that cross the osteum transversely. In addition to bone-crossing pain fibers, there were pain fibers that run front to back and top to bottom within the endosteum.

Conclusion The findings suggest that pain fibers may arrive at the meninges not only intracranially, but also extracranially. Unlike the prevailing view that migraine headache is a referred pain driven by central trigeminovascular neurons, it is tempting to speculate that it may also be, at least in some patients, a primary pain directly driven by bone-crossing pain fibers.

PS-2

Cortical spreading depression – a critical link in migraine pathogenesis

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This presentation will review the importance of cortical spreading depression (CSD) to migraine pathogenesis and its potential as a target for treatment. A number of investigators have implicated cortical spreading depression in migraine pathogenesis, particularly migraine with aura. Studies by

Milner, Leao, Olesen, and Lauritzen, Woods and Mazziotta, Welch and more recently, Hadjikhani, and Strong and colleagues provided imaging and electrophysiological data indicating that CSD can develop in human cortex. This presentation will review a few of the ways in which CSD may impact migraine pathogenesis. For example, studies by Bolay and colleagues established that cortical spreading depression is noxious and activates the trigeminovascular system. Studies first published by Ayata and more recently, van den Maagdenberg and colleagues provided convincing evidence that changes in CSD susceptibility provide an important phenotype in mice expressing point mutations in genes implicated in Familial Hemiplegic Migraine. Haerter and colleagues more recently found that female mice are more susceptible than male mice in this regard. In 2006, Ayata and colleagues provided the first evidence that cortical spreading depression is suppressed by the chronic administration of topiramate, valproate, amitriptyline, propranolol and methysergide. Acute administration was ineffective and longer treatment appeared to confer greater resistance. These pharmacological findings raise intriguing questions about whether CSD may be important in migraine with and without aura.

Taken together, the observations outlined above support the notion that: (1) susceptibility to CSD is modified by mutations in specific genes, (2) CSD may cause pain by discharging trigeminovascular afferents, (3) female hormones may modulate the susceptibility to CSD, and (4) CSD provides a target for prophylactic treatment of migraine.

PS-3

Links between cortical spreading depression and migraine pain

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A key unresolved question regarding the pathophysiology of migraine is the relationship between its cortical phenomena and pain. Some migraine symptoms are clearly caused by changes in cortical activity, and propagated changes in cortical blood flow and brain activity have been observed with functional imaging studies in migraine patients. Cortical spreading depression has been shown in elegant studies to activate trigeminal nociceptive pathways in animal models. These and other observations support the hypothesis that cortical processes are a primary event in migraine that may be a trigger for pain. However, the fact that the majority of migraine occurs without associated aura symptoms raises questions about how changes in cortical activity could be a primary event in migraine. How could cortical processes cause migraine pain in the absence of cortical symptoms? One explanation could be the involvement of glial and vascular, as well as neuronal mechanisms in propagated cortical waves associated with migraine. Intercellular calcium waves in

astrocytes spread over long distances with temporal and spatial characteristics that are remarkably similar to those of cortical spreading depression. Cortical surface blood vessels also appear to have intrinsic mechanisms for propagated vasodilation. These glial and vascular mechanisms could produce propagated cortical waves that are distinct from classical spreading depression, thereby resulting in spreading changes in cortical activity and blood flow without aura. Astrocyte calcium waves are associated with significant active release of neurotransmitters and neuromodulators that could activate nociceptive pathways. For example, astrocytes release substantial quantities of ATP, which is known to play important roles in pain transmission via activation of purinergic receptors. Both astrocytes and vascular cells are also capable of releasing nitric oxide, another potentially important modulator of pain transmission. These non-neuronal mechanisms will be discussed along with neuronal mechanisms that may represent links between cortical phenomena and pain in migraine.

PS-4**The sensory neurogenic component: microvascular mechanisms and links with inflammatory mediators**

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Neurogenic vasodilatation occurs when sensory nerves, principally C and A fibres release neuropeptides such as CGRP. These sensory nerves are also involved in hyperalgesic signalling, important in pain processing, and inflammation. The exact mechanisms involved are unclear. However, there is an increasing understanding from the study of inflammatory diseases of the impact of some of the sensory nerve activating systems on inflammatory mediator generation and of possible mediator interactions. This talk will discuss some of these with emphasis on TRPV1-activating mechanisms.

SCIENTIFIC SESSION

Scientific session 1: Genetics and co-morbidity

ScS1-1

The first genome-wide interpopulation study of migraine families points to a locus on chromosome 10q22

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Objectives Several genetic loci have been linked to common forms of migraine, though consistency between different studies remains a problem. To address some of the analytical challenges involved in combining information from different scans and populations, we performed a joint analysis of two new, large, well-characterized study samples from Finland and Australia. We hypothesized that study harmonization would lead to more consistent results.

Methods 400 genome-wide microsatellite markers were genotyped in 1344 study subjects from 58 independent Finnish multigenerational and 125 independent Australian nuclear families. Phenotype data was collected using migraine-specific questionnaires. Parametric and non-parametric linkage analyses were performed using the end-point diagnosis and phenotypes from the trait component analysis and the latent class analysis.

Results The most encouraging finding is the linkage observed to chromosome 10q22 (highest NPL score 3.7). This locus is now detected in five separate genome-wide scans and provides thus the best consistency for any locus in common forms of migraine so far. In addition, preliminary results show suggestive or nominal evidence of linkage with at least one trait to six previously detected loci, on 4q24, 4q31, 5q21, 13q14, 17p13, and 18q12.

Conclusions The locus on 10q22 has now been linked to migraine in three different populations and five genome-wide scans. In addition, we were able to confirm six previously identified loci. This study also confirms the strength of the trait component and the latent class analyses in locus identification of migraine related traits especially in situations where different study samples need to be jointly analyzed.

ScS1-2

Association of dopamine beta-hydroxylase (DBH) functional variants with migraine

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Migraine is a common and debilitating neurological disorder with a significant genetic component. Although a number of linkage and association studies have been undertaken the number and identity of all migraine genes has yet to be defined. The existence of dopaminergic hypersensitivity in migraine has been recognised on a pharmacological basis and some studies have reported genetic association between migraine and variants within dopamine receptor genes. Our laboratory has previously reported association of migraine in case-controls and families, with a promoter STR marker in the DBH gene¹. In the present study, we analysed two additional DBH markers in a population of 275 cases and 275 matched controls. Results showed a significant association between a tested promoter insertion/deletion variant and disease ($\chi^2 = 8.92$, $P = 0.011$), in particular in migraine with aura ($\chi^2 = 11.53$, $P = 0.003$) and also showed that male individuals with the homozygous deletion had three times the risk of developing migraine, compared to females². In addition, a functional diallelic DBH promoter variant tested in the same population also showed a significant association with migraine ($P = 0.005$ in total migraine; $P = 0.012$ in MA). Varying DBH activity levels have been postulated as being involved in the migraine process with an increase of dopamine, resulting from a lower DBH activity shown to be positively correlated with migraine severity. Both DBH polymorphisms are in linkage disequilibrium with the previously reported migraine associated DBH microsatellite and both polymorphisms are functional, significantly affecting DBH enzyme activity. It is thus plausible that these functional variants may contribute to the migraine disorder.

ScS1-3

Is the FHM3 gene SCN1A implicated in migraine?

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Objective To determine if SCN1A gene is associated with migraine.

Methods First, we performed a family-based association study with the rs2298771 SNP. A total of 564 subjects (124 families; 388 migraineurs and 176 healthy individuals) were genotyped. The TDT-STDT Spielman method was used to test for association. Second, a case-control study was carried out with

704 sex and age matched subjects (346 cases – 193 MA, and 358 controls) and a set of 6 SNPs spanning the SCN1A gene. Genotypic and allelic association were performed using Chi² (corrected for multiple testing). Haplotype trend regression analyses were performed using the Power Marker v.3.2 program.

Results Family study. Some 58 families were suitable for TDT study. Allele 2 was transmitted 58 times and not transmitted 50 times ($p = ns$). The sTDT statistic was computed in 103 families. The allelic differences among sibs with and without migraine were significant for allele 2 ($z = 3.334$, $p = 0.001$; combined scores $z' = 2.813$, $p = 0.01$, corrected).

Case-control study. No single SNP was associated with migraine. Only rs557222 showed some differences between MA and controls ($p = 0.036$, ns after correction). Haplotypic trend regression analysis disclosed a significant association of the SCN1A gene using the six SNPs ($p = 0.026$, after 100,000 permutations).

Conclusions Our family and case-control association study suggests that SCN1A gene might be implicated in migraine. Study supported by: FISS PI 050388; Pfizer Grant 2005-0847; IFIMAV api/22/05.

ScS1-4

Prevalence of patent foramen ovale and MRI white matter lesions in migraine with aura

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Background High prevalence of patent foramen ovale (PFO) (41–53%) was reported in migraine with aura (MA) patients. White matter lesions (WML) on T2-MRI are also more prevalent in MA. It is not known if these abnormalities are causally related nor if PFO closure is useful in MA.

Objectives To search prospectively for PFO and WML in MA patients and for a correlation between them.

Methods 84 MA patients were recruited up to now. 67 (age range: 13–66 yrs) underwent both cerebral MRI and either transthoracic echocardiography (TTE) ($n = 48$) or transcranial Doppler (TCD) ($n = 19$) or both ($n = 5$).

Results PFO was detected overall in 13% (9/67): TTE 10% (5/48), TCD 21% (4/19; 2 small, 2 medium shunts). Among the patients with both tests, 1 out of 2 with a positive TCD also had a positive TTE. WML were found in 27% of all patients (18/67): 16% in the TCD group (3/19), 31% in the TTE group (15/48). The number of WML ranged from 1 to more

than 10; no infarcts were found. There was no correlation between the PFO and WML; only 2 out the 18 patients with WML (11%) had a PFO. We found no correlations with attack frequency.

Conclusions TTE may not have sufficient sensitivity for the detection of PFO in MA. TCD seems more sensitive, but our results suggest that PFO prevalence in MA patients may be overestimated. We also found a low prevalence of white matter lesions and no correlation with PFO.

ScS1-5

Quality of sleep, fatigue and daytime sleepiness in migraine – a controlled study

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Objectives To evaluate whether the quality of sleep, and the degree of fatigue and daytime sleepiness are related to migraine.

Methods We investigated 489 subjects comprising 240 patients with >4 migraine attacks per month, 130 patients with 1–4 attacks per month and 119 migraine-free controls with <6 headache days per year. The patients were recruited via articles in newspapers not stressing the subject of the study. All participants underwent a semistructured interview and completed the Pittsburgh Sleep Quality Index (PSQI), the Fatigue Severity Scale (FSS), the Epworth Sleepiness Scale (ESS), the Self-rating Depression Scale and the Self-rating Anxiety Scale. Kruskal-Wallis tests were used for statistical analysis and Bonferroni correction was applied for multiple testing.

Results The PSQI total score was highest in patients with frequent migraine and lowest in controls (5.7 ± 2.7 vs 5.4 ± 2.8 vs 4.3 ± 2.5 , $p < 0.001$). Five subscores of the PSQI showed similar statistically significant differences. The FSS total score was also highest in patients with frequent migraine (32.7 ± 11.5 vs 30.0 ± 10.4 vs 28.6 ± 9.7 ; $p = 0.013$), but after Bonferroni correction this difference was statistically not significant. The ESS score was similar in the three study groups. After excluding patients with depression and/or anxiety, the difference in the PSQI total score and in three subscores remained statistically significant.

Conclusion In patients with migraine, quality of sleep is decreased, fatigue tends to be increased and daytime sleepiness does not differ from healthy controls. The decreased quality of sleep is a consequence of migraine and cannot be explained by comorbidity with depression or anxiety.

LUNCH SEMINARS

LS1

Lunch seminar: intractable headache

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Objective Despite our best intentions, many migraine sufferers remain refractory to medical care. This lunchtime symposia will explore the various reasons for treatment failure.

Methods This symposium will consist of two parts; a brief lecture highlighting the common causes of treatment failure and a series of case studies of patients with medically refractory headaches. Audience participation is encouraged.

Results At the conclusion of this symposium attendees will have a complete understanding of why treatment fails and will be able to identify and avoid the common pitfalls that lead to refractory headaches.

Conclusions Although many options exist to treat our patients who suffer from headache, many patients remain resistant to therapy. By identifying the common causes of treatment failure, healthcare providers can increase the likelihood of a successful outcome.

LS2

Interesting cases from headache clinics

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General comments It is assumed the attendees will have knowledge of general concepts of headache diagnosis, including primary and secondary headache disorders and treatment of such, as well as most pertinent laboratory tests and imaging tests used in headache medicine.

This course is intended for neurologists, headache specialists, residents and other health care professional dealing with difficult headache disorders.

Goal of the course Following the course the attendee should have comprehensive overview of interesting clinic headache cases. This will be achieved by way cases highlights to solidify clinical knowledge in this important area.

Objectives At the end of the course the attendee should:

- Have an overview of interesting clinic headache cases, including some rare primary and secondary disorders.
- Have knowledge of the most important laboratory and imaging techniques used to assess patients presenting with these interesting headache disorders.
- Have an evidence-based approach to usual and new therapies for interesting clinic headache disorders.

LS3

Seminar: history of headache

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Objectives To put important milestones in the history of headache against the background of important discoveries in the history of medicine.

Methods Going through the centuries, we will study the work of a number of physicians, who published on headache. Important movements in medicine will be discussed by selecting the work of Aretaeus, Galen, Willis, Van Swieten, Dubois Reymond, Woakes and Wolff. Case reports on patients and physician-patients will be presented.

Results Pathophysiology and treatment of headache followed contemporary medical insights, including the humoral theories that dominated up to the 19th century. The transition to solid pathology at the end of the 18th and the introduction in medicine of the scientific method in the 19th century resulted in new models, including the vasomotor theory, which was also applied to the study and treatment of migraine. Neurogenic theories became popular around the same period. Both theories remained current throughout the 20th century when further insights were discovered.

Conclusion The history of headache is a sequence of contemporary medical theories and paradigms applied to observations on headache. It should put our current work into perspective and make us realise that future generations of headache researchers may smile at present discoveries. Today's scientific truth may be tomorrow's lie.

POSTER

Poster session 1

A001

Gender differences in symptoms comorbid with headache in a rural North American population

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Objective To evaluate gender differences in symptoms comorbid with headache in a population of rural U.S. patients who screened positive for the presence of multiple physical and psychological symptoms.

Methods Out of a group of 1061 patients (347 men, 714 women) who screened positive for the presence of multiple physical or psychological symptoms logistic regression was run separately for each gender on multiple self-reported symptoms to ascertain conditions that were statistically comorbid with headache.

Results In these patients both genders reported increased rates of fatigue ($P = 0.005$ for men, $P = 0.02$ for women). In men the only other symptom that was comorbid with headache was back pain ($P = 0.003$) while in women menstrual complaints ($P = 0.002$), dizziness ($P = 0.003$) and insomnia ($P = 0.02$) were also comorbid with headache. Arm and leg pain, stomach pain, chest pain, faintness, heart problems, bowel difficulties, dyspnea, self assessment of overall health, depression, anxiety, worry, panic attacks, marital status and education level all failed to correlate with headache.

Conclusion We conclude that in this older rural population for both genders fatigue may be a marker of mild debility or may be caused by headache disorders as has been documented in migraine post-drome. Men with the complaint of headache tend to have less comorbidity with this diagnosis and their symptoms are more physical in character. Women have more associated comorbidity with headache some of which could be attributable to the association of migraine and hormonal fluctuations while the other comorbid symptoms of dizziness and insomnia are more nonspecific in character.

A002

Endothelial function in migraine

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Migraine is associated with cardiovascular disorders. Endothelial dysfunction may be a mechanism underlying this association. The present study tested the hypothesis that endothelium-dependent vasodilation, basal endothelial nitric oxide release and stimulated endothelial tissue plasminogen

activator (t-PA) release are impaired in migraine patients. Graded doses of sodium nitroprusside (SNP, 0.2 to 0.8 $\mu\text{g min}^{-1} \text{dL}^{-1}$ forearm), substance P (0.2 to 0.8 pmol $\text{min}^{-1} \text{dL}^{-1}$ forearm) and NG monomethyl-L-arginine (L-NMMA, 0.1 to 0.4 $\mu\text{mol min}^{-1} \text{dL}^{-1}$ forearm) were infused into the brachial artery of 16 migraine patients with or without aura during headache-free intervals and 16 age- and sex-matched subjects without a history of migraine. Forearm blood flow (FBF) was measured by strain-gauge venous occlusion plethysmography. Local forearm release of tissue plasminogen activator (t-PA) in response to substance P was measured using the arteriovenous plasma concentration gradient. In both migraine patients and control subjects, SNP and substance P caused a dose-dependent increase, and L-NMMA a dose-dependent decrease in FBF ($P < 0.001$ for all responses). In both groups, substance P caused a significant increase in t-PA release ($P < 0.001$). FBF responses and t-PA release were comparable between migraine patients and control subjects. We could not demonstrate the presence of endothelial dysfunction in forearm resistance vessels of migraine patients.

A003

Fibromyalgia comorbidity in primary headaches

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Aims To test the frequency of fibromyalgia and its influence on clinical outcome in a cohort of primary headache outpatients, compared with a population of healthy non-headache suffering subjects.

Methods Two hundreds consecutive primary headache outpatients were enrolled at the Headache Center of our Department. The frequency of fibromyalgia was evaluated (Wolf et al, 1990), and compared with 200 age and sex matched non headache suffering healthy subjects. In addition, in all patients Total Tenderness score (TTS), anxiety and depression scales (SAS and SDS by Zung), MIDAS score, allodynia questionnaire, Short Form 36 Health Survey (SF36), MOS (Medical Outcomes Study-Sleep Scale) and MAF (Multidimensional Assessment of Fatigue) were evaluated.

Results The forty-two per cent of headache patients presented fibromyalgic symptoms, in respect with 5.5% of non headache people (chi square test: $p < 0.001$). The tension type headache prevailed in patients with concomitant fibromyalgia, in respect with migraine and other forms of primary headaches (chi square test $p < 0.01$). The TTS and allodynia were more severe in patients with fibromyalgia, while the MIDAS, SAS and SDS scores were similar across headache patients.

Conclusions Primary headache is a risk factor for fibromyalgia, which prevails in patients with tension-type headache in

respect with migraine patients. Fibromyalgia is not associated with a more severe outcome of headache, though its comorbidity influences higher levels of pericranial muscular tenderness in both tension type headache and migraine patients and allodynia in migraine patients. Primary headaches and fibromyalgia may share a common disorder of pain modulation system.

A004

Prevalence and characteristics of migraine in Japanese nurses

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Objectives To determine prevalence and characteristics of migraine in Japanese nurses, and to investigate use of medical care and whether food preference is associated with risk of migraine.

Methods Structured questionnaires were given to 634 nurses (28 men and 606 women) in Toho University Omori Medical Center. A board-certified neurologist (O.K.) examined and interviewed headache history and migraine was diagnosed according to the criteria of the International Classification of Headache Disorders.

Results Prevalence of migraine was 12.2% (migraine with aura, 2.0% and without aura, 12.1%). The highest prevalence of migraine was assistant senior staff members (15.1%) among chiefs (5.1%), senior staff (9.3%), junior staff (9.5%) and assistant junior staff (7.7%). At different section of job, out-patient clinic was the highest (15.0%) among in-patient clinic (8.5%), operating room (10.0%), intensive and cardiac care unit (9.5%) and laboratory room (14.6%). Of 11.4% migraineurs were absent from job and 84.3% decreased to 50% performance of their job during a attack. Main trigger factors were general fatigue (78.8%), shoulder stiffness (68.9%), lack of sleep (67.1%), mental stress (67.1%), eyestrain (52.7%) and menstruation (40.5%). Past experience of physician consultation of headache was 31.4%. Migraineurs (53.9%) took over-the-counter medicine whereas they did not have information of tryptans. Food preference and migraine are under analysis now.

Conclusion Only a few migraineurs receive benefits of tryptans on migraine in nurse. Physicians and medical staffs should pay more attention for adequate headache medication.

A005

A case-control study on excessive daytime sleepiness in episodic migraine

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Sleepiness is often complained by migraine patients both during and outside the attack and may reduce the quality of life, leading to potential harmful situations such as loss of attention and sleep attacks. Excessive daytime somnolence (EDS), defined as difficulty in maintaining a desired level of

wakefulness, has been reported in a very high percentage of migraineurs in an uncontrolled study and has been considered as potentially mediated by the hypothalamus. We therefore investigated EDS in a case-control study on 100 patients with episodic migraine (M/F: 16/84; mean age 36.9 + 12.1 yrs; MWA/MA: 86/8, MWA+MA: 6) and 100 age- and sex-matched healthy controls screening factors which may interfere with sleep-awake cycle (coffee, alcohol, smoke, type of work, BMI, restless leg syndrome, drugs, anxiety, depression and other concomitant diseases). Restless leg syndrome, anxiety, depression and use of psychoactive drugs were more frequent among patients ($p < 0.01$). We found that EDS was more frequent in migraineurs than controls (14% vs 5%; OR = 3.1 (CI 95% = 1.1–8.9), but its impact was less pronounced than previously reported and correlated with migraine disability, sleep problems and anxiety. In addition, EDS did not correlate with the presence of somnolence during the attack, feature that probably clinically identifies at least some of the 'hypothalamic migraineurs'. Consequently, our data suggest that EDS in migraine is not mediated by the hypothalamus but is probably a consequence of the complex clinical burden of the disease, stemming from the full headache-sleep-affective symptom constellation.

A006

Migraine in adolescents: association with socioeconomic status and family history

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Objective The influence of the socioeconomic status on the prevalence of migraine is unknown in adolescents. Accordingly, we investigated the prevalence of migraine in a large sample of adolescents by sociodemographic features.

Methods A validated headache questionnaire was mailed to 120,000 households representative of the U.S. population. All individuals in the household were interviewed (probands and their parents). We calculated sex-specific prevalence estimates of migraine in adolescents derived by demographics and parental status of migraine, using log-linear models.

Results A total of 32,015 adolescents were identified. Surveys were returned by 18,714 of them (58.4% response rate). The one-year prevalence of migraine was 6.3% (5.0% in boys and 7.7% in girls). The prevalence was higher in girls than in boys older than 12 and in Caucasians than African Americans. In families with an annual income lower than 22,500, the adjusted prevalence of migraine in adolescents without a parental history of migraine was 4.4%; in families earning 90,000 or more, it was 2.9% (OR = 0.49, 95% CI 0.38–0.63). In adolescents with a parental history of migraine, the prevalence in the lower vs the higher income group was 8.6% vs. 8.4% (OR = 0.97, 0.81–1.15).

Conclusions In adolescents with family history of migraine, household income does not have a significant effect. This suggests the social causation hypothesis rather than the social

selection hypothesis, highlighting the need for exploration of environmental risk factors related to low income and migraine and the search for specific comorbidities and stressors in this group.

A007

Clinical markers of cardiovascular risk in migraine: association with weight change

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Objectives To estimate the influence of weight change in the clinical markers of cardiovascular risk (CVR), and headache response in subjects participating in a clinical trial.

Methods Subjects were randomized to receive TPM 100 mg/d or AMI 100 mg/d for 26 weeks. Based on weight change, they were stratified into three groups: major loss (>5% reduction), major gain (>5% increase), and no major change (<5% change). Pooling treatment groups, we determined if major weight changes were associated with changes in migraine frequency, blood pressure (BP), heart-rate (HR), glycosylated hemoglobin (HbA1C), cholesterol (CHOL), triglycerides (TG), and C-reactive protein (hs-CRP).

Results From 331 subjects, 56 (17%) experienced major weight loss and 52 (16%) experienced major weight gain. Both subjects with major weight gain and major weight loss responded similarly to preventive therapy in regard to reduction in mean frequency of monthly migraine episodes (-2.7 vs. 3.3, respectively; $p = 0.110$). However, subjects with major weight gain experienced elevations in mean diastolic BP (+2.5 vs. -1.3, $p < 0.001$), HR (+7.6 vs. -1.3, $p < 0.001$), HbA1C (+0.09 vs. -0.04, $p = 0.048$), CHOL (+6.4 vs. -6.3, $p = 0.017$), TG (+15.3 vs. -10.4, $p = 0.025$), and hs-CRP (+1.8 vs. -1.9, $p = 0.102$). Of subjects experiencing major weight gain, 87% received AMI. For the major weight loss group, 91% received TPM.

Conclusions The effectiveness of preventive therapy is not influenced by change in weight during treatment. Migraineurs who gained weight experienced increases in markers of risk for cardiovascular disease. Given that migraine is itself a risk factor for cardiovascular events, avoiding weight gain might be particularly important.

A008

Transformed migraine – report of 4 cases

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Objectives In studying EEG aspects of migraine, there appears to be a close relationship between migraine and epilepsy. Presented here are 4 patients who developed epilepsy after a long history of migraine.

Patients

Case I: 41 female (Migraine without aura), Migraine at 11 yrs, Epilepsy at 40 yrs, Interval between two: 29 yrs, petit mal type.

Case II: 34 female (M. with aura), M. at 20 yrs, E. at 34 yrs, Interval: 14 yrs, sudden onset of right hand weakness with subsequent numbness & right hemiparesis.

Case III: 27 female (M. without aura), M. at 23 yrs, E. at 27 yrs, Interval: 4 yrs, psychomotor type.

Case IV: 23 female (M. without aura), M. at 21 yrs, E. at 23 yrs, Interval: 2 yrs, grand mal type.

Methods Each patient was examined by CT, TCD, and EEG. One patient was also examined with SPECT (Tc HMPAO).

Results

1. CT findings included small ventricles & shallow Sylvian fissures being observed in all of the patients.
2. TCD demonstrated the increased blood flow velocity in all of the patients.
3. EEG in the rest revealed multiple sharp wave or theta wave bursts in three patients. The remaining one (case I) had added megimide activation.
4. SPECT was used to one patient (case III), which revealed hypoperfusion in the right temporal lobe.

Conclusion Both migraine and epilepsy may be caused by the excessive excitability of the same group of neurons. These four cases reported here strongly support my speculation that migraine and epilepsy share a similar category of pathogenesis.

Keywords: migraine epilepsy, transformation, epileptic discharge

A009

Migraine and sleep-wakefulness cycle: relation to the quality of life and comorbidity

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Objectives Although the triggering role of sleep in migraine (M) is well known, the relation between sleep-wakefulness cycle and the quality of life (QL) in M is not determined. Our study was aimed to compare clinical-psychological characteristics and the quality of life in patients with M attacks occurring during wakefulness (Day-time M-DM) and night sleep (Sleep M-SM).

Methods From 320 M patients examined in our Clinic in 1999–2001 (mean age – 37.9, F – 85%, M – 15%) 60% had only day-time attacks, 25% – both D and S attacks, while 15% didn't have D attacks at all and complained of pure S attacks (M pain evoked patients during night sleep or was present at the moment of awakening). Methods: detailed interview, focused on the patients state during pain-free interval, The West Haven-Yale Multidimensional Pain Inventory, Sleep Quality and Life Quality Inventories, STAI for anxiety, BDI for depression, total tenderness score of pericranial muscles based on manual palpation.

Results Compared to DM group subjects with SM had significantly ($p < 0.03$) more frequent disturbances in pain-free interval (panic attacks, dysfunction of pericranial muscles, persistent sleep disturbances even out of SM attacks), more high levels of depression and anxiety and severely impaired QL.

Conclusion Patients with Sleep M attacks are characterized by more frequent comorbid conditions in pain-free interval (depression, anxiety, autonomic disorders, dysfunction of pericranial muscles, dyssomnia) which determine low quality of life in Sleep M. It was suggested that depression is the main comorbidity responsible for transformation of Day-time M into Sleep M, for persistent sleep disturbances and low quality of life in M.

A010

Tolosa Hunt syndrome in a patient with a history of episodic cluster headache

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Introduction Tolosa-Hunt syndrome (THS) is defined as painful ophthalmoplegia caused by inflammation of the cavernous sinus or superior orbital fissure. Cluster headache (CH) is an idiopathic syndrome consisting of recurrent brief attacks of sudden, severe, unilateral, periorbital pain with ipsilateral autonomic phenomena of the face.

A case is presented where THS appeared shortly after a CH attack.

Case Report The patient is a 59 year old man having CH attacks once yearly for the past 40 years. Upon presentation his familiar attack occurred lasting for 20 days. This time 2 weeks of strong periorbital left sided constant pain followed. One day before admission he presented diplopia due to paresis of VI cranial nerve.

On Neurological Examination he had no other pathological findings. Complete Blood Count, biochemistry, immunology and other lab examinations were all normal.

Brain CT, MRI, Magnetic Resonance Angiography, cervical blood vessel (triplex) Ultrasound Scan showed no relevant pathological findings.

The patient was treated with corticosteroids. Significant pain relief was achieved within 24 hours. 3 months later, ophthalmoparesis has improved but was not resolved completely.

Discussion A case is described in which THS appeared immediately after an attack of CH.

The differential diagnosis of CH includes THS but only one case has been described in bibliography suffering from cluster headache before the THS started.

There is similarity in the symptoms as well as in lab findings between these two entities. It has been suggested that THS and CH may have the same etiology.

A011

Prevalence of primary and associated headaches in people with multiple sclerosis

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Objectives Headache is not considered a common symptom of Multiple Sclerosis (MS). Recent data though show a high incidence of headache in MS.

We aimed to describe the prevalence of primary and secondary headache (diagnosis using ICHD-II criteria) in our patients with MS using various parameters described below.

Methods In this prospective study, a group of 66 patients suffering from definite MS was given a questionnaire in order to obtain information about headache frequency, duration, quality, intensity, localization and its possible association with MS or disease modifying therapy (DMT) for MS.

Results The prevalence of all headache types in patients with MS was 36.36% (24 out of 66 patients). Headache was migraine in 5 cases (20.8%), tension-type in 16 (66.6%) and secondary to MS or DMT in 5 (20.8%). Among patients who were on disease modifying therapy with interferon, 3 were suffering from migraine, 12 from tension type and 26 were free of headache.

Conclusion In our study we used no control group made of people without MS but, a previous study with the prevalence of primary headache among the general population in our region exists. According to that previous study, prevalence was found 46% for migraine and 36% for tension type headache.

In contrast, among patients with MS, we estimated migraine prevalence 20.8% (approximately twice less than that among general population). Tension-type headache prevalence in patients with MS was 66.6% (about twice of that found among general population).

A012

Family migraine headache presence importance for children migraine syndrome appearance

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The aim of this research is to determine heritability of the migraine syndrome.

Heredity of the migraine syndrome was investigated among 24,828 children aged 3 to 16 years, in Vojvodina, during 16 years. The presence of headaches was compared among all the members of the family within three generations.

Positive family anamnesis of the recurrent headaches was detected among 98.6% children with migraine headaches, 64.7% among children with primary recurrent non migraine headaches, and 32.4% among children without recurrent headaches. The family as a whole is the most significant for migraine syndrome heritability with the correlation quotient

(r12) 0.9653, and determination quotient (r212) 93.17%. The highest migraine syndrome heritability comes from a mother (r12 0.900, r212 81%), father's father r12 0.98000, r12 96.04%), mother's father (r12 0.9834, r212 96.71%), father's mother (r12 0.9780, r212 65.65%), mother's mother (r12 0.9472, r212 89.72%), mother's brother daughter (r12 0.8479, r212 71.89%), father's sister (r12 0.7041, r212 49.58%), father's sister daughter (r12 0.5771, r212 33.30%). The relation among the members of the nuclear family with the contingency quotient 0.429, is significantly stronger than the relation to the members of wider family, with the contingency quotient 0.338.

Conclusion The probability of a child having the migraine and not the non-migraine headache, is 0.664 for mother, 0.644 for father, 0.411 father's mother, 0.175 mother's mother, 0.165 mother's father, and 0.102 for father's father.

Keywords: headache, migraine, heritability

A013

Hereditity of headaches and migraine syndrome in children – twin study

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Hereditity of headaches and migraine syndrome was investigated by analyzing 396 twin pairs aged 3 to 27 years (42.4% monozygotic and 57.6% dizygotic).

Heritability quotient (0.3882) confirms the significance of heritability as well of environmental factors effect on recurrent headaches appearance as. The heritability quotient 0.2286 of the non-migraine headaches clearly shows that the external factors are more significant than heredity for non-migraine headache appearance. Migraine syndrome with heritability quotient 0.8598 clearly shows the heredity of the migraine syndrome.

The probability that one of the twins will not have recurrent headaches if the other one also does not have them is 0.72 for monozygotic twins, and 0.50 for dizygotic ones. If one of the twins does not have the migraine syndrome, the probability of the other one also not having them is 0.91 for monozygotic and 0.77 for dizygotic ones. The probability that the child whose twin sibling does not have the non-migraine headaches would also not have non-migraine headaches is 0.81 for monozygotic and 0.68 for dizygotic twins.

Both correlation and determination quotient of the migraine syndrome of all the twins (r12 0.7498; r212 56.12%), monozygotic (r12 0.8458; r212 1.54%) and dizygotic (r12 0.6342; r212 40.22%), clearly show high degree of dependence of the migraine syndrome of one twin on the migraine syndrome of the other twin sibling, and higher dependence and significance of the difference with monozygotic twins.

Keywords: children, twins, headache, migraine, heritability

A014

A dopamine D4 receptor exon 3 VNTR allele protecting against migraine without aura

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Objectives As dopamine plays an important role in the pathophysiology of migraine and anti-migraine drugs have an effect on the dopamine system, we examined the dopamine D4 receptor gene (DRD4) for involvement in the aetiology of migraine.

Methods We tested a variable number of tandem repeats (VNTR) polymorphism in the DRD4 gene, the exon 3 VNTR, in a sample of 190 family trios each with a proband with childhood migraine by using transmission disequilibrium tests (TDT).

Results We found a trend for transmission distortion of this marker in migraine, with the common seven repeat allele of the VNTR transmitted 58 times and not transmitted 82 times (global LRS = 12.27, DF = 6, p = 0.06; for the 7 repeat allele, chisq 5.1, p = 0.02). This effect came only from migraine without aura (MO, 145 trios), with the seven repeat allele transmitted 45 times and not transmitted 69 times (global LRS = 15.18, DF = 6 p = 0.019; for the 7 repeat allele chisq 6.4, p = 0.01; OR 0.47), whereas in migraine with aura (MA, 45 trios) there was no transmission distortion of the seven repeat allele.

Conclusion We conclude that the seven repeat allele of the DRD4 VNTR is a protective factor for MO. Since migraine is a common disorder, this protective effect may have contributed to the positive selection acting on the DRD4 exon 3 VNTR seven repeat allele in recent human history. We speculate that dopamine function in the lateral parabrachial nucleus is involved in MO.

A015

First case of compound heterozygosity in familial hemiplegic migraine: two mutations in Na,K-ATPase gene ATP1A2

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Objectives Familial hemiplegic migraine (FHM) is a rare autosomal dominantly inherited subtype of migraine, in which attacks are associated by hemiparesis. FHM has been associated with mutations in three genes, including ATP1A2, encoding the $\alpha 2$ subunit of the Na,K-ATPase pump (FHM2). In our department genetic testing of the three known FHM genes (CACNA1A, ATP1A2 and SCN1A) is performed. As part of our ongoing genetic screening, the involvement of ATP1A2 FHM2 gene in a FHM family was studied.

Methods Mutation analysis of the *ATP1A2* gene was performed by direct sequencing of all exons and flanking intronic regions, using genomic DNA of the proband. Functional consequences of the mutations were analyzed by cellular survival assays.

Results The proband suffered from hemiplegic migraine attacks that started at age 8 after minor head injury. Her attacks continued on a monthly basis and lasted from 2 hours to 9 days. Severe attacks were associated with drowsiness and confusion. Several family members suffered from FHM or common migraine. In the proband two novel *ATP1A2* mutations, I286T and T415M, were identified. Each parent was carrier of one of the mutations, in line with compound heterozygosity in the proband. Functional analysis of I286T and T415M mutant pumps in cellular survival assays revealed functional abnormalities for both mutants.

Conclusions We report on a unique FHM family of which the proband has two missense *ATP1A2* FHM2 mutations. Cellular survival assays showed that both mutations are disease-causative. This is the first report of compound heterozygosity for FHM.

A016

Novel *CACNA1A* mutation: genetic evidence for shared etiology of AHC and FHM

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Objectives Familial hemiplegic migraine (FHM) and alternating hemiplegia of childhood (AHC) are both severe neurological disorders that share clinical features. Therefore, FHM genes are candidate genes for AHC. Here we further establish the possible genetic relationship between the two disorders by mutation analysis of FHM1 *CACNA1A* gene in a monozygotic twin pair with a severe complex phenotype of hemiplegia, early onset ataxia, epilepsy and mental retardation. The phenotype partially overlaps with both AHC and FHM.

Methods In our Department we scan patients with FHM and FHM-related phenotypes for the three known FHM genes (*CACNA1A*, *ATP1A2* and *SCN1A*). We performed a mutations analysis in the FHM1 *CACNA1A* gene, using direct sequencing in a monozygotic twin pair that was referred to us.

Results A novel *CACNA1A* mutation, V1696P, was identified in both twins with the severe complex phenotype reminiscent of both AHC and FHM. V1696P occurred *de novo*, since it was not present in both healthy parents.

Conclusion Here we report the first FHM1 *CACNA1A* mutation associated with a phenotype that is a combination of features associated with AHC and FHM. Our results further strengthen a shared genetic etiology for AHC and FHM.

A017

Clinical and immunological correlates of migraine and atopic disorders: a multicenter controlled attack study

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Activation of resident immune cells such as macrophages and mast cells, which are a prominent feature of the intracranial meninges, is likely to serve as a critical step in promoting the enhanced excitability of meningeal nociceptors in migraine as well as bronchial epithelial cells in asthma. Although there are some supportive data about migraine and atopic disorder association both of clinical and epidemiological based, none of them evaluated the mast cell activation during attacks in human studies. In order to evaluate the abnormalities relating to mast cell activation during migraine attacks and compare with tension type headache (TTH) patients and matched healthy controls, we performed this multicenter (9 headache center from different area of our country) study. After the evaluation of inclusion criteria, proportionally distributed 213 subjects included in this study. Of all 67.8% were composed from migraineous subjects, 19.4% were TTH patients and others were healthy controls. All of the subjects included in the study were matched according to age, sex and headache subgroups. Patients with migraine showed high ratios of family history for headache, positive history of atopic disorders both of the sufferers and families. Immunological screening showed that significantly high ratio of IL-1 beta, IL-2, IL-6 and TNF- α in migraine group compared to TTH sufferers and healthy controls. However none of the subjects showed IL-10 abnormalities. Approximately 20% of the headache subjects showed immunoglobulin abnormalities with various ratios and IgG predominance. Our data suggested a pathophysiological based association between migraine and atopic disorders, as completing previous data.

A018

Gender differences in clinical features of migraine

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Background and objective The prevalence of migraine is higher in women than in men. The author investigated about gender differences in clinical features of migraine.

Methods 510 patients (358 women and 152 men) visited the headache clinic over 12 months. All patients were investigated by questionnaires and interview. Diagnosis of headache was based on the ICHD-2.

Results Among 510 patients, 288 (57 men and 231 women) had migraine. The prevalence of migraine was 64.5% in women and 37.5% in men. The onset of migraine was typically during 10s and 20s in both men and women. Men were

more likely than women to have their first migraine attack under 10 years of age (6.7% vs. 1.8%). The severity, frequency and disability of migraine were similar in men and women. Mental stress and computer working were common triggers of migraine attacks in both men and women. Women reported neck/shoulder stiffness (67.5%), lack of sleep or oversleeping (45.0%), weather changes (36.4%), crowded places (35.6%) as triggers of migraine attacks more than men. Men reported eyestrain (47.4%) and alcohol (21.1%) more than women. Women had more family history of headache than men (60.6% vs. 43.9%).

Conclusions The trigger factors of migraine were different between men and women. Women may be more affected by endogenous and exogenous factors than men.

A019

Characteristics of the mood disorder of chronic daily headache in Japanese patients

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Objectives Chronic daily headache (CDH) is clinically defined as a headache that occurs for at least 15 days per month and for at least 4 hours each day. This classification encompasses the primary headache disorders, including chronic migraine, chronic tension type headache, new daily persistent headache, and hemicrania continua based on ICHD-II. Each of these forms of CDH can occur with or without the overuse of medications.

The aim of this study was to analyze the mood disorder in patients with CDH in Japanese patients.

Methods This study included 20 patients (mean age: 41.6 ± 15.7 [$\pm SD$], range: 26–71 years) representing all those admitted consecutively to Dokkyo Medical University Hospital (Department of Neurology) for CDH. Psychiatric comorbidities were checked with the Mini International Neuropsychiatric Interview (MINI), scores of the Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Scale (HAM-A) and Apathy scale.

Results The prevalence of depression was 65% and panic disorder was 30% in the CDH. This prevalence was higher than the depression in other disorders. In addition, in CDH more of suicide and feeling of guilt were seen compared with the other organic depression. This findings suggest that pathophysiology of CDH may be more associated with endogenous depression.

Conclusion Our data suggest that prevalence of mood disorder of CDH is higher and this fact must be important for its treatment.

A020

The prevalence of syncope in migraine

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Objectives Some reports suggest that there might be a comorbidity between migraine and syncope. A recently

published population-based study demonstrated an elevated prevalence of syncope in migraineurs, ranging from 35% for males to 50% for females, with a median of 46%.

Methods We examined 1200 consecutive migraine patients referred to our Headache Centre, investigating specifically the possible occurrence of syncopal episodes. The diagnosis of syncope was made according to the criteria established by the Task Force of the European Society of Cardiology, published in 2004.

Results We could identify 10 patients, all females, constituting 0.8% of our population, who presented at least one certain, rigorously defined syncope. All the subjects suffered from migraine without aura and had neurally-mediated syncopes. In all the cases baseline ECG, Holter monitoring, echocardiogram, tilt testing, EEG and MRI of the head were performed. The median age of patients at first observation was 36.6 ± 10.5 , and the median age of onset was 21.8 ± 4.6 for migraine and 20.3 ± 9.4 for syncope, respectively. We did not find any correlation between the migraine severity and the occurrence of syncope.

Conclusion The prevalence of syncope in our clinic-based study is far lower than reported in a population-based survey. Notwithstanding the different study design, our data do not support the hypothesis of a possible comorbidity between migraine and syncope. Further studies are warranted to clarify this aspect, but we believe that strict international consensus guidelines for the diagnosis of syncope must be used to obtain reliable conclusions.

A021

Insertion/deletion polymorphism of the angiotensin I-converting enzyme gene in migraine patients

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Introduction Recently, in Literature has been reported that the ACE-DD polymorphism may play an important role in the determinism and in the frequency of migraine attacks.

Objective The aim of our study was to determine the incidence of ACE polymorphism in a consecutive series of migraineous patients and of patients affected by myocardial infarction.

Materials We studied a series of 58 migraineous patients aged $35.5 \text{ years} \pm 14.8$ (ICHD-II-2004 criteria) come at our observation in the period 2005–2006. The control group was composed by 58 patients affected by Acute Myocardial Infarction in the same period. The analysis was based on Polymerase Chain Reaction and on reverse-hybridization.

Results 22 (38%) migraineous patients and 32 (56%) cardiopathy patients had an ID genotype; 28 (48%) migraineurs and 20 (34%) cardiopaths had a DD genotype.

Conclusions The results of our study confirm the high incidence the ACE I/D genetic polymorphism in migraine and in the patients affected by myocardial infarction. This gives evidence of a strong relationship between migraine and major

vascular diseases and let us hypothesize an important role of ACE system in the pathogenetic model of migraine for its capability to interfere with the endothelial regulation tone. Once an effective role in the genesis of migraine and in the increased risk of migraineous patients to evolve into an ischemic pathology has been obviously assigned to this genetic mutation, future researches must aim through wider and more controlled casistics.

A022

Multilocus analyses of estrogen-related genes reveal involvement of the ESR1, FSHR, and PR genes in migraine

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Objective To examine whether polymorphisms within ESR1, FSHR, CYP19A1, NRIP1, and PR genes are susceptible factors for migraine and to test the joint effects of these genes.

Methods Genetic association study on migraine, using both single-gene and multilocus (set association method implemented in SUMSTAT program) approaches with 834 matched subjects (416 with migraine).

Results We observed that only ESR1 and FSHR genes showed genotypic ($\chi^2 = 7.015$, $p = 0.029$, and $\chi^2 = 8.087$, $p = 0.017$, respectively) and allelic ($\chi^2 = 4.036$, $p = 0.045$, and $\chi^2 = 4.115$, $p = 0.044$, respectively) association with migraine in the two-point study. In the set association approach, allowing for gene-gene interactions, only the model constructed with ESR1-FSHR-PR genes was significantly associated with migraine (minimum $p = 0.004$; final $p = 0.010$, after 50,000 permutations).

Conclusions (1) We observed individual association of ESR1 and FSHR polymorphisms with migraine. (2) Our set association study supports further evidence that estrogen hormone metabolism is implicated in migraine. (3) NRIP1 and CYP19A1 polymorphisms were discarded as migraine factors. Granted by FISS PI050388 and IFIMAV PSG01/06.

A023

Temperament evaluation in patients with migraine

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Previous studies have shown a significant comorbidity of migraine and psychiatric disorders such as depression and anxiety disorders. Furthermore, it has been tried to define a specific migraine personality without reliable results. Recently, the modern concept of temperament characteristics according to the classification by Akiskal has been established. We applied the respective TEMPS-A scale to a sample of migraine patients ($N = 75$) without any psychiatric comorbidity and compared the results to patients with major depression

and without migraine ($N = 37$), to patients with tension-type headache ($N = 18$) and to healthy controls ($N = 130$). Migraine patients showed significantly higher depressive, cyclothymic, and phobic scores than healthy controls and significantly lower depressive and cyclothymic but higher hyperthymic and phobic scores than patients with major depression and without migraine. Patients with tension-type headache showed similar results as healthy controls. Most scores of the TEMPS-A scale were significantly correlated to the Beck Depression Inventory score and to the impairment by migraine as measured by the Headache Disability Inventory and by migraine attack duration. We conclude that migraine is associated with a depressive, cyclothymic, and phobic temperament as measured by the TEMPS-A scale independently from a comorbidity with major depression. This temperament might, however, be a risk factor for the known comorbidity of migraine with depression and anxiety disorders. There were no specific temperament pattern in patients with tension-type headache.

A024

Comorbidity of migraine and restless legs syndrome – a case-control study

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In order to evaluate a possible association between migraine and restless legs syndrome (RLS), we performed a case-control study on the comorbidity of RLS and migraine. 411 patients with migraine and 411 sex- and age-matched control subjects were included. Migraine was diagnosed according to IHS criteria, RLS according to the criteria of the International Restless Legs Syndrome Study Group. Furthermore, all patients had to fill out a self-assessment test performance on depression (Beck's Depression Inventory, BDI). RLS frequency was significantly higher in migraine patients than in control subjects (17.3% versus 5.6%, $p < 0.001$; OR = 3.5, CI = 2.2–5.8). In our sample, there was no significant association between migraine and depression as defined by the BDI (9.6% in migraine versus 4.0% in control subjects, $p = 0.190$). Depression was, however not statistically significant, more frequent in migraine patients with RLS (13.6%) than in migraine patients without RLS (8.7%). In addition, migraine patients with RLS had a significantly higher BDI score. RLS features, in particular the RLS severity scale score, did not differ significantly between migraine patients with RLS and control subjects with RLS. We conclude that there is an association between RLS and migraine and, in addition, a co-association with depression. The underlying mechanism, however, remains undetermined and might be related to a dysfunction of dopaminergic metabolism in migraine.

A025**Lack of association of migraine and idiopathic intracranial hypertension (pseudotumor cerebri)**

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Previous studies suggested a pathophysiological link between migraine and idiopathic intracranial hypertension. These observations were based on patients with sinus venous thrombosis or on patients with intracranial hypertension without papilledema. We evaluated a possible association between migraine and idiopathic intracranial hypertension (pseudotumor cerebri) in a multicentre case-control study on the epidemiological comorbidity of pseudotumor cerebri and migraine. In total, 100 patients with pseudotumor cerebri (CSF pressure above 20 and normal brain imaging) were enrolled and compared to 37 control subjects with proven normal CSF pressure. The migraine life time prevalence in the patients and in the control group was 24.0% and 24.3%, respectively ($p = 0.940$). The migraine features did not differ significantly between both groups. There was a significantly higher prevalence of smokers ($p < 0.004$) including an increased number of pack years ($p < 0.001$), an increased number of patients with arterial hypertension ($p < 0.001$), and an increased number of obese patients as assessed by BMI ($p < 0.001$) in the patient group as compared to the control group. We conclude that there is no significant epidemiological association between migraine and elevated CSF pressure as observed in the clinical syndrome of idiopathic intracranial hypertension.

Members of the DMKG study group are (alphabetical order): Stefan Evers (Münster), Charly Gaul (Halle/Saale), Astrid Gendolla (Essen), Karsten Henkel (Ulm), Vera Hösing (Münster), Martin Marziniak (Homburg/Saar), Michael Teeper (Marburg).

A026**The prevalence of right-to-left shunt in cluster headache**

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Patients with migraine with aura have been suggested to have a significantly higher prevalence of patent foramen ovale (PFO) than normal controls. Similar results were found in three studies of small groups of cluster headache (CH) patients detecting PFO prevalence of 36.8% to 42.5%. The link of these findings to the pathomechanism of trigeminal pain perception remains however unclear. We were interested in the prevalence rate of right-to-left shunts in patients with cluster headache. In our ongoing study, we examined CH patients ($N = 15$) by contrast enhanced transcranial Doppler sonography (cTCD) of the middle cerebral artery (MCA) for presence of a right-to-left shunt. The diagnosis of CH was made according to the IHS criteria. The mean age of the subjects enrolled was 47 years. A right-to-left shunt was detected only in two of the patients (13% overall prevalence). In both patients, the underlying mechanism was a PFO. In conclusion, we found no higher prevalence of PFO in CH patients

compared to general population. This result contrasts with previous studies and is to be proven by enrolling more subjects into our ongoing study.

A027**Comorbidity of migraine and headache associated with sexual activity**

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Headache associated with sexual activity (HSA) is a primary headache disorder with specific features. However, an increased prevalence of migraine among patients with this type of headache has been described in some studies. The prevalence of HSA in patients with migraine has not been investigated to date. We performed a case-control-study based on migraine patients in order to elucidate the epidemiological association between these two headache types. By means of a questionnaire and a personal interview, 100 patients with migraine according to the IHS criteria and 100 age- and sex-matched healthy subjects without any history of migraine were interviewed regarding a diagnosis of HSA, in 95 patients we received reliable answers. In five subjects from the migraine group (5.3%) versus none from the control-group, a diagnosis of HSA could be established ($p = 0.021$, Fisher's exact test) suggesting an increased risk of HSA among migraine patients. Previous studies that have demonstrated a comorbidity of migraine and HSA were all based on HSA patients. Thus, it can now be concluded that the association between the two headache disorders is bilateral. It might be that both headache types share a common pathophysiological background.

A028**Personality in migraineurs in the age of 50 – results of the ILSE-study**

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Introduction With the Interdisciplinary Long-Term Study of Adulthood and Aging (ILSE) individual, social and economic determinants of a healthy, self-determined and satisfied ageing can be identified. Aim of the present study is to determine differences in personality between migraine patients and healthy controls in the age of 46–50 years.

Methods 299 subjects were examined medically and psychologically. Out of these 14 patients with episodic migraine (without aura) according to the revised IHS-criteria were identified. Personality structure was recorded by NEO-FFI and Self-rating Depression Scale (SDS) and compared by non-parametric tests.

Results Episodic migraine patients showed a lower score in extraversion ($p < 0.001$), and higher scores in neuroticism ($p < 0.01$) and mild depression ($p < 0.02$). No patient suffered from medication overuse headache.

Discussion Migraine patients in the age of 50 show a pronounced depressive and neuroticism state. There is evidence

that especially mild depression is a cause for transition of episodic into chronic migraine. Therefore these two personality traits may be prerequisites for later chronic migraine in elderly subjects. The study implies to treat not only migraine itself but also the underlying mild depression to prevent chronic migraine.

A029

Affective temperament characteristics of patients with migraine

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Objectives Comorbidity of affective disorders with migraine may influence the clinical features of the disease and suggests that migraine may be a part of the bipolar spectrum disorders. The aim of the study to determine the affective temperament characteristics of the migraineurs.

Methods 65 migraine patients and 50 healthy subjects included in this study. Turkish version of The Temperament Evaluation of Memphis, Pisa, Paris and San Diego (TEMPS-A) and Hospital Anxiety and Depression Scale (HAD) applied to all participants.

Results 92% (60) of the patients are female and 8% (5) of the patients are male. Patients mean age was found 42.03 ± 11.07 , average headache length was 19.6 ± 7.3 years. According to TEMPS-A, total 14 patients had depressive, anxious, irritable or cyclothymic temperament and rest of the patients had sub-threshold scores for affective temperaments. All patients who had affective temperament scored high level of depression and/or anxiety on HAD: In control group only 2 person have depressive and anxious temperament and the others scores were lower than the patients.

Conclusion Despite affective temperament does not fulfill the all characteristics of any disorder, it has been accepted as an inherited situation and some authors suggested that affective temperaments form the basis of the bipolar disorders. In patients with migraine, affective temperaments are frequently seen and it is thought that both have same pathophysiological mechanisms.

A030

Temperament and character profiles of migraine patients

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Objectives Temperament and character features are accepted among the factors which may increase the possibility of having migraine headache and complicate its treatment. The aim of this study was to determine the temperament and character profiles of the migraineurs and to explore the relationship between these characteristics and depression and/or anxiety levels of the patients.

Methods 65 migraine patients and 50 healthy subjects included in this study. Temperament and Character Inventory (TCI) and Hospital Anxiety and Depression Scale (HAD) was applied to all participants.

Results 92% (60) of the patients are female and 8% (5) of the patients are male. Patients mean age was found 42.03 ± 11.07 , average headache length was 19.6 ± 7.3 years. Frequency of the migraine episodes was 5.4 ± 3.2 per month and 23% (15) of the patients had migraine aura. According to HAD scale, 44% (28) of the patients had depression and 33% (22) of them had anxiety. For control group these rates were by turn 6 (9.2%) and 9 (13.8%). According to TCI, patients novelty seeking (NS) scores were lower and harm avoidance (HA) scores were higher than the control group.

Conclusion Serotonergic system has an important role for the etiology of both depression and migraine. Also according to Cloninger's psychobiologic personality model, temperament components have close relationship with the neurotransmitter systems. If we consider all these together, its possible to say that, temperament and character features of migraineurs originate from the same pathological mechanisms and this comorbidity can facilitate the development of psychiatric disorders in migraine patients.

A031

Markers of oxidative stress in healthy female migraineurs. Relationship with von Willebrand factor activity

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Objectives To evaluate, in young healthy women with migraine, the relationship of von Willebrand factor (vWF), a marker of endothelial dysfunction (ED) and stroke risk, with: (1) the angiotensin-converting enzyme gene deletion polymorphism (ACE DD) and (2) a marker of oxidative stress, the nitrate/nitrite (NOx) concentration. Both vWF activity, a marker of ED and stroke risk, and ACE DD have been shown to be elevated in migraineurs. Associations have been demonstrated in hypertensive populations.

Methods Women 18–50 y.o. with ICHD-II defined migraine were enrolled during the interictal period. Laboratory tests included: plasma vWF activity, and urinary NOx concentrations (calorimetric assay). Genomic DNA was isolated from blood and ACE insertion/deletion genotypes were detected by polymerase chain reaction.

Results In 125 women with migraine (mean age 37 yrs, 48% with aura), levels of vWF activity showed significant negative correlation with NOx ($p = 0.02$). In regression analyses, adjusting for age, body mass index, serum total cholesterol, history of hypertension, current smoking, and hormone replacement/contraceptive use, vWF activity levels significantly predicted NOx levels ($p = 0.02$). The ACE genotypic frequencies were: DD 35%, ID 42%, II 23%. Mean values of vWF activity (in %) across the genotypes was DD 152, ID 129, II 119, $p = 0.005$.

Conclusions vWF, an endothelial dysfunction marker, is associated with genotypic (ACE DD) and phenotypic (NOx) markers of oxidative stress, and may be important in the increased stroke risk in female migraineurs.

A032**Von Willebrand factor activity is a marker of endothelial dysfunction in migraine**

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Objective To examine, in young healthy women with migraine, the relationship of von Willebrand factor (vWF) to known downstream markers of endothelial dysfunction (ED). This platelet-binding glycoprotein is a marker of endothelial dysfunction and stroke risk, and has been shown to be elevated in migraineurs.

Methods Women 18 to 50 y.o. with ICHD-II defined migraine and without known vascular disease were enrolled during the interictal period. Laboratory tests included plasma vWF activity and markers of hemostasis (platelet activation: PF4; platelet aggregation: PFA-100 closure time [CT] with collagen-epinephrine [CEPI] and collagen-ADP [CADP]; fibrinolysis: tPA antigen [Ag]; inflammation: hsCRP). Transcranial Doppler (TCD) was done to measure cerebrovascular reactivity (breath-holding index).

Results In 125 women with migraine (mean age 37 yrs, 48% with aura) levels of vWF activity showed negative correlation with CEPI CT ($p < 0.001$) and CADP CT ($p < 0.001$), and % Δ mean flow velocity (MV) ($p = 0.001$), and positive correlation with tPA Ag ($p = 0.02$), and hsCRP ($p = 0.09$). There was no relationship with PF4. In regression analyses, adjusting for age, body mass index, serum total cholesterol, history of hypertension, current smoking, and hormone replacement/contraceptive use, vWF activity levels significantly predicted the markers for platelet aggregation (CEPI $p = 0.002$, CADP $p < 0.001$), fibrinolysis (tPA Ag $p = 0.03$), inflammation (hsCRP $p = 0.02$) and vascular reactivity (% Δ MV $p = 0.005$).

Conclusions vWF is a robust marker of endothelial dysfunction in young women with migraine, and may contribute to the migraine-stroke association in this population.

A033**Search for correlations between the therapeutic response to riboflavin and migraine mitochondrial abnormalities**

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Background The effectiveness of riboflavin in migraine prophylaxis has been attributed to its beneficial effects on mitochondrial metabolism. The classical mitochondrial DNA (mtDNA) mutations have not been found in the common forms of migraine.

Objectives We have therefore compared the prevalence of mutations in the total mtDNA and the clinical response to riboflavin.

Methods Twenty patients suffering from migraine (15 without and 5 with aura) were treated with riboflavin 400

mg/day for 4 months. Therapeutic effectiveness was monitored with diary cards; subjects having a $\geq 50\%$ decrease in attack frequency in month 4 compared to month 1 were considered 'responders'. Blood samples for genetic analyses were obtained during the first screening visit. The entire mtDNA was amplified by PCR, purified and sequenced.

Results Twelve migraine patients (4 with [MA] and 8 without aura [MO]) were considered as 'responders', and 8 (1 with and 7 without aura) as 'non-responders'. There was a higher amino-acidic mutation rate in responders compared to non-responders (6.1 ± 3.9 vs 4.1 ± 1.8 , $p = 0.213$), and nucleotidic substitutions both in the coding (22.4 ± 14.9 vs 14.2 ± 7.9 , $p = 0.142$) and non-coding mtDNA regions (10.6 ± 5.9 vs 8.5 ± 3.5 , $p = 0.439$). These differences were not statistically significant. However, a significantly higher number of nucleotidic mutations was observed in the coding region in MA compared to MO patients (26.6 ± 2.8 vs 16.7 ± 14.1 , $p = 0.01$).

Conclusion These preliminary results suggest that mtDNA mutations are more prevalent in migraine with aura, but not in migraineurs who respond to riboflavin treatment. Further studies on a larger group of patients are however necessary.

A034**Effects of *Helicobacter pylori* eradication on migraine**

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Helicobacter pylori (*H. pylori*) infection, though confined to the gastric mucosa and non-invasive, has been shown to alter systemic inflammatory mediators' levels, therefore playing a role in some vascular functional disturbances, among them migraine. This last association is still controversial. Aim of the study was to ascertain whether *H. pylori* eradication might improve migraine clinical features (frequency, duration, intensity and associated symptoms of the attacks). Twenty-seven patients (6 men, 21 women, mean age 37.41 ± 10.39 years) suffering from migraine according to ICHD-II criteria, referring to the Turin University Headache Centre and positive to the infection, underwent eradication, following the 'triple therapy' scheme. All of them recorded their migraine attacks on a specific diary, for a 2 months' period both before and after the end of the treatment. *H. pylori* infection was assessed through C13 urea breath test and the presence of specific IgG antibodies against the bacterium, detected through ELISA test. To assess the eradication, the same tests were repeated one month after the end of the treatment. Statistical analysis was performed using student T test and χ^2 test. Fourteen patients (51.85%) resulted eradicated, while 13 (48.15%) were still infected. After the eradication therapy clinical features of the attacks did not show meaningful differences in both groups. These data indicate that *H. pylori* eradication do not improve migraine, at least in a short period, and this could be a further indication in favour of the hypothesis that *H. pylori* infection does not play a specific role in the pathogenesis of migraine.

A035

Relationship between body weight and primary headache

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An increasing percentage of the population worldwide is overweight or obese. Recently a high incidence of migraine with aura was observed among morbidly obese women and obesity was identified as a risk factor for transformed migraine. These observations indicate a possible link between obesity and headache. In order to further explore this association the incidence of weight variations was evaluated in a group of headache sufferers so as the clinical aspects of their headache. A group of 212 (153 females and 59 males, age range 18–65 yrs, mean age 40.69 ± 11.63 yrs) attending for the first time at the Turin University Headache Center in the period 01.01.2006–30.06.2006, suffering from primary headaches, according to ICHD-II criteria, was examined. Subjects were divided in four groups based on BMI, underweight (<18.5), normal weight (18.5 to 24.9), overweight (25 to 29.9), obese (>30). The prevalence and clinical aspects of the different primary headaches were assessed. 10 patients resulted underweight, 133 had normal weight, 40 were overweight and 24 obese. Migraine without aura appears to be almost equal in the four groups, while migraine with aura and chronic migraine are much more frequent in overweight and obese patients than in normal weight ones ($p < 0.05$). On the contrary, patients suffering from migraine without aura and episodic tension type headache were more frequently underweight ($p < 0.05$). In migraine patients the clinical aspects of migraine attacks did not show any difference. Many different hypotheses try to explain the above mentioned link. Further studies are needed to clarify it.

A036

Animal models for Familial hemiplegic migraine type 2

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Objectives Familial Hemiplegic Migraine type 2 (FHM2) is due to mutations of the ATP1A2 gene encoding the $\alpha 2$ subunit of Na,K ATPase. In order to clarify the pathogenetic mechanisms of leading to FHM2, we generated two mouse models: an Atp1a2 knock-in mouse carrying the FHM2 W887R mutation and an Atp1a2 conditional knock-out mouse, still in preparation.

Methods Knockin heterozygotes are under phenotypic characterization. In particular, we are assessing susceptibility to cortical spreading depression, a short-lasting depolarization wave that moves across the cortex and contributes to the initiation of migraine attacks. Moreover, we are presently testing Atp1a2 conditional knock-out chimeras for germline transmission by backcrossing them to C57Bl/6 mice.

Results The knockin mouse model is now available. Homozygotes for the mutation (Atp1a2R887/R887) show a lethal phenotype soon after birth.

Conclusion The knock-in mouse model will be central to explore the role of the ATP1A2 mutation in the pathological mechanisms underlying the migraine aura. The expression pattern of the $\alpha 2$ isoform in different neural cell types suggests an important role in the modulation of neuronal activity in the first days after birth. Indeed the $\alpha 2$ subunit is widely expressed in neurons during late gestation, while in adult brain it is primarily expressed in astrocytes. The conditional knock-out mouse will allow to study the cell-specific effects on the pathogenesis of this form of migraine. Results from these studies might be relevant for more frequent forms of migraine.

A037

The comorbidity of headache with psychiatric and chronic pain syndromes

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Objectives to investigate the comorbidity between headache, other chronic pain and psychiatric syndromes.

Method Several chronic pain syndromes, medical disease and psychiatric syndromes were investigated. A semi-structured interview for DSM IV criteria was used for assessment psychiatric disorder: Mini International Neuropsychiatric Interview (MINI) (Lecrubier et al., 1997).

Results Two hundred and thirty four chronic pain patients were recruited, 78 (33.33%) headache, 64 (27.58%) fibromyalgia, 4 (1.75%) complex regional pain syndrome (CRPS), 55 (24.22%) arthrosis, 18 (7.75%) Irritable bowel syndrome, 3 (1.31%) vasculopathy, 6 (2.64%) Arthritis, 7 (3.08%) Post herpetic neuralgia, 13 (5.67%) facial pain, 4 (2.3%) genital pain, 9 (3.94%) neck pain, 50 (20.67%) cancer pain, 16 (6.95%) other pain syndromes.

More positive association between headache and: fibromyalgia ($c2 = 56.58$; $p < 0.0001$); irritable bowel syndrome ($c2 = 17.95$; $p < 0.0001$) and more negative association between headache and: arthrosis ($c2 = 14.51$; $p = 0.0001$), cancer pain ($c2 = 20.38$; $p < 0.0001$) than other pain syndromes was found. An increase prevalence rate of lifetime psychiatric disorders in: Headache ($p = 0.0005$), Fibromyalgia ($p = 0.003$), facial pain ($p = 0.01$), irritable bowel syndrome ($p = 0.03$) than in other chronic pain syndromes, and the lowest in the cancer pain ($p < 0.0001$) was found.

No difference in the prevalence of current Mood disorders was found between pain syndromes instead of current Anxiety disorders was more prevalent in the Headache ($p = 0.01$), Facial Pain ($p = 0.01$) and irritable bowel syndrome ($p = 0.04$) than in other pain syndromes.

Conclusion Mood disorders are present in same prevalence in all chronic pain syndromes. Anxiety disorders is more associated with headache than other pain syndromes.

Reference

Lecrubier et al., 1997.

A038**FHM1 S218L mutation associated with trauma triggered delayed cerebral coma and seizures in sporadic cases**

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Objectives The *CACNA1A* gene is associated with a spectrum of neurological diseases, including familial hemiplegic migraine. Previously, the FHM1 S218L mutation was described in two families and in one sporadic case where patients showed severe atypical attacks with delayed cerebral oedema triggered by trivial head trauma. The objective of this study was to further explore the genotype-phenotype correlation in patients carrying the S218L mutation.

Methods In two sporadic patients with trauma triggered coma direct sequencing of the *CACNA1A* gene was performed.

Results In both patients a de novo S218L mutation was identified. Clinical symptoms included trauma triggered delayed cerebral coma with seizures, mild ataxia and in one patient also hemiplegic migraine attacks occurred independently of the coma.

Conclusion In patients with unexplained episodes of delayed trauma triggered coma with seizures screening for the FHM1 S218L mutation should be considered even if there is no family history of hemiplegic migraine. Notably, a recently generated homozygous *Cacna1a* S218L knockin mouse showed ataxia and mild head trauma induced mortality preceded by epileptic seizures. The S218L mouse model provides a valuable tool for studying pathophysiological mechanisms and exploring novel treatment options.

A039**Possible involvement of the genetic locus Chr1q31 in migraine with aura: a large study of the *cacna1e* gene**

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Objectives Familial Hemiplegic Migraine is associated to mutations on the *CACNA1A* gene (Chrom 19p13), on the *ATP1A2* gene (Chrom 1q23) and on the *SCN1A* gene (Chrom 2q24). Another FHM locus has been identified on chromosome 1q31, which contains the *CACNA1E* gene, coding for R-type Ca^{2+} channels, similar to the P/Q-type encoded by the *CACNA1A* gene. A linkage to this locus has been suggested also for common forms of migraine.

Methods We searched for variations in *CACNA1E* gene in a large group of migraineurs ($N = 111$) and in a control group ($N = 104$). Screening was performed by direct sequencing on blood genomic DNA.

Results We identified a novel single nucleotide polymorphism (D840E) in exon 19 of the *CACNA1E* gene. It was present in 14.4% of control subjects and in 18% of migraineurs, but it was significantly more represented in FHM, SHM and Basilar-type migraine patients (34.6%) than in migraineurs with typical aura (8.9%, $p = 0.01$) and control subjects ($p = 0.03$).

Conclusion We report a novel polymorphism in the *CACNA1E* gene (D840E), particularly represented in some subtypes of migraine with aura. Abnormalities on the locus 1q31 and particularly on the *CACNA1E* gene may thus play a role in some subforms of migraine with aura.

A040**Vascular risk modifies the association between migraine and cardiovascular disease**

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Objectives We aimed to evaluate the association between migraine with aura (MA) and incident cardiovascular disease (CVD) in women stratified by the Framingham Risk Score (FRS) for coronary heart disease.

Methods We used prospective data from 27,519 women participating in the Women's Health Study who were free of CVD at baseline and had information on lipid levels and MA status. We stratified participants based on FRS-estimated 10-year risk.

Results At baseline, 3577 (13.0%) women reported active migraine; 39.7% indicated MA. After 11 years of follow-up, 665 CVD events occurred. Compared to non-migraineurs, women with MA had age-adjusted hazard ratios (HRs [95% CI]) of 2.01 (1.51–2.67) for major CVD, 1.74 (1.09–2.79) for ischemic stroke (IS), and 2.01 (1.30–3.09) for myocardial infarction (MI). When stratified by FRS, the association between MA and major CVD was strongest in the low FRS-risk group. However, the association pattern differed for ischemic stroke (IS) and myocardial infarction (MI). Compared to non-migraineurs, women who reported MA in the low FRS-risk group had HR of 4.48 (2.13–9.44) for IS and 0.98 (0.23–4.10) for MI. Women with MA in the highest FRS risk group had hazard ratios of 0.54 (0.07–3.91) for IS and 3.41 (1.52–7.63) for MI. Women with migraine without aura did not have increased risk of CVD in any of the FRS risk groups.

Conclusion Our data indicate that the association between MA and CVD varies by vascular risk status. The different pattern for IS and MI may suggest different biological mechanisms.

A041

Cluster analysis of Finnish migraine families suggests new methods for experimental disease classification

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Objectives In this study we applied a statistical method, called cluster analysis, to a large Finnish migraine family sample. This method uses an automated, unsupervised division of individuals into subgroups based on data obtained using a validated migraine questionnaire. Our hypothesis is that this clustering method might provide a new tool to identify traits more relevant for underlying gene and pathway identification than clinical diagnoses.

Methods We performed the analysis on roughly 6000 Finnish migraine patients and their close relatives, collected from neurological clinics based on a high prevalence of migraine with aura within the family. Each patient was questioned on over 200 variables. The data was clustered using the naïve Bayesian model and the Expectation-Maximization algorithm, selecting the number of clusters with 10-fold cross-validation over the number of clusters, with our own implementation in the Matlab software.

Results We found that the unsupervised clustering reaches an optimal solution at eight clusters. These clusters represent patient groups where variables describing attack symptomatology as well as those describing known co-morbidity are similar. For example, patients suffering from migraine without aura are divided into two distinct groups.

Conclusions The findings of this study suggest that novel subgroups within the migraine diagnoses can be identified using unsupervised clustering strategies. Identification of genes and pathways behind migraine might require novel classification on symptoms and measurable traits that are more directly associated with the underlying biology. Non-supervised clustering represents a possible method to detecting such subgroups and will be used in our genetic studies.

A042

Psychiatric co-morbidity in transformed migraine: impact on treatment response – a prospective study

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Background and objectives Anxiety and depression are common in transformed migraineurs (TM) and may play a role on treatment outcome. This study evaluated the impact on treatment in transformed migraineurs with different degrees of anxiety and depression.

Methods One hundred patients with TM were divided in two groups (Silberstein et al., 1996) and prospectively studied. Group 1 had moderate or severe (M-S) scores in Hamilton Anxiety (HA) and Depression (HD) scales. Group 2 had mild

or no scores (N-M). All patients were preventively treated with atenolol (60 mg/day) + nortriptyline (20 mg/day) + flunarizine (3 mg/day). After 6 and 14 weeks the headache frequency (HF) was evaluated.

Results Sixty-five women and 15 men completed the study. In baseline, 19 (23.7%) patients for HA and 9 (11.3%) for HD were in group 1. Group 2 had 61 (76.3%) patients in HA and 71 (88.7%) in the HD. At 6 weeks, 36.9% of group 1 (7 patients) (HA) and 39.4% of group 2 (24 patients) (HA) had greater than 50% HF reduction. Among those from HD, two patients of group 1 and 40.8% of group 2 (29 patients) presented greater than 50% HF reduction ($p < 0.001$). At 14 weeks, 15 (79%) of group 1 (HA) and 49 (80.3%) of group 2 (HA) presented headache reduction >50%, which occurred in seven patients of group 1 (HD) and 57 (80.3%) of group 2 (HD). Twenty patients didn't return. Nine (HA) and 12 (HD) had M-S scores.

Conclusions Both groups responded similarly to the treatment after 14 weeks suggesting that anxiety and depression were not predictive of non-response. Further studies are necessary to confirm these observations.

Reference

Silberstein et al., 1996.

A043

Chronology of onset of headache, anxiety and depression in patients from a tertiary headache centre

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Introduction Breslau et al. (2003) showed that over a 2-year period, having baseline depression increased the risk of incident migraine but not the risk of other severe headache; in addition, the risk of incident depression was higher in those with baseline migraine. Merikangas et al (1990) had suggested that anxiety might precede the headache onset and that headache in turn might be followed by depression. The aim of this study was to evaluate the possibility of a preferential order of onset of psychiatric symptoms/disorders in relation to headache and the influence on headache chronicization.

Methods A broad sample of headache sufferers consecutively referring to the Headache Disorders Centre of Bari and receiving a diagnosis of primary headache according to diagnostic criteria of the International Classification of Headache Disorders (2003) were included. A detailed personal and familial medical history was collected. Data concerning the natural history of headache, of possible psychopathologic features and therapies were collected.

Results In about 70% of cases with psychiatric comorbidity, headache onset preceded the occurrence of psychopathological symptoms. In about 10% of cases, headache, anxiety and depression onset were concomitant. In most of patients with anxiety and depression both disorders occurred at once, after the headache onset.

Conclusion The results of this study don't confirm the chronology of onset described in previous studies on general population but seem to indicate that headache is in most cases the first disorder to occur. If headache may represent a predisposing condition to psychopathology remains a priority for future research.

A044

Disease progression to chronic migraine: onset of symptoms of headaches, anxiety and mood disorders

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Objectives In order to evaluate the role of psychiatric disorders in migraine progression, we analyzed the temporal profile of migraine, mood and anxiety disorders onset of symptoms in chronic migraine patients (CM).

Methods Fifty patients with CM diagnosed according to the ICHD-II were enrolled in the study. All patients were interviewed with the SCID-I/P, for psychiatric assessment. The study protocol was approved by the local Ethics Committee, all patients gave written consent.

Results Forty-two patients (84%) met lifetime diagnostic criteria for any mental disorders, 38 (76%) presented any anxiety disorder, 25 (50%) presented any mood disorder, 22 (44%) presented mixed anxiety and mood disorder. The profile of migraine onset and comorbidities is the following: the mean onset of anxiety disorders was significantly longer than migraine (27.1 + 16.9 vs 20.5 + 11.1 years, $p = 0.016$), mood disorders (6.8 + 1.9 years, $p < 0.001$) and CM (4.6 + 2.8 years, $p < 0.001$). Migraine onset was significantly longer than mood disorders and CM, $p < 0.001$, as mood disorders onset compared to daily headaches onset ($p < 0.01$).

Conclusion Anxiety disorders preceded the onset of episodic migraine, which was usually succeeded by depression and finally CM. Moreover, anxiety disorders usually start in childhood or in young adults. The data suggests that anxiety disorders may be an important risk factor for latter migraine and that both anxiety and mood disorders play important role in migraine progression to CM. Thus, the early treatment of anxiety disorder and/or episodic migraine may prevent long term complications, such as depression and CM.

A045

Primary headaches in generalized anxiety disorder patients

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Objectives Anxiety disorders and headaches are comorbid conditions, but the prevalence of primary headaches has

never been studied in generalized anxiety disorders (GAD) patients. The study aim is to analyze the lifetime prevalence of primary headaches in patients with and without generalized anxiety disorder.

Methods Sixty participants were enrolled in the study, 30 GAD patients diagnosed according to the DSM-IV were compared to 30 healthy control subjects. Primary headaches were diagnosed according to the ICHD-II with a structured interview.

Results Eighty six percent of generalized anxiety disorder patients met diagnostic criteria for any primary headache, 60% met criteria for migraine, 16.6% chronic migraine (without aura 6.6%, with aura 10%), 43.3% episodic migraine (without aura 26.7%, with aura 16.6%), 6.6% probable migraine without aura, 20% tension-type headache (10% frequent episodic, 6.6% infrequent episodic and 3.3% chronic). Forty seven percent of control subjects met diagnostic criteria for any primary headache, 10% episodic migraine (3.3% with aura, 6.6% without aura), 23.3% infrequent episodic tension-type headache, 10% frequent episodic tension-type headache and 3.3% probable migraine without aura.

Conclusion Primary headaches overall, chronic migraine, episodic migraine, migraine with and without aura are significantly more common in GAD patients than controls. Frequent episodic tension-type headache is equally common in both groups, infrequent is more common in controls and chronic TTH more common in GAD patients. Primary headache diagnosis is important to be done in anxiety disorders patients, specially GAD, the correct assessment may implicate in a better patient management and clinical outcomes in GAD patients.

A046

Psychiatric comorbidities decrease quality of life in chronic migraine patients

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Objectives Psychiatric comorbidity is an important issue in the management of primary headache disorders. Anxiety and mood disorders are common in chronic migraine (CM) but little is known about their impact in patient's quality of life. The aim of this study was to evaluate psychiatric comorbidities impact in CM patient's quality of life.

Methods Fifty patients with chronic migraine diagnosed according to the International Headache Society, ICHD-II (2004) were enrolled. All were evaluated by a structured interview (SCID-I/P) for mental disorders diagnosis, based on DSM-IV, and were evaluated by the SF-36 Health Survey questionnaire. Patients were divided in the following groups: CM with both mood and anxiety disorders, CM with only anxiety disorders, CM with generalized anxiety disorder, CM with only a mood disorder, and CM without psychopathology. The scores in the group without psychopathology were compared with the other groups. All eight domains of the SF-36 scale were compared in those groups.

Results CM comorbid with psychiatric conditions had significantly lower quality of life scores in all comorbidity groups, in all eight SF-36 domains ($p < 0.05$), except for general health status, in all groups and physical aspects in anxiety disorders.

Conclusion Chronic migraine comorbidity with mental disorders is a significant factor in patient's quality of life.

A047

Hamilton anxiety and depression scales evolution after treatment in transformed migraine: a prospective study

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Objectives To evaluate the evolution of the Hamilton Scales scores for Anxiety (HA) and Depression (HD) after treatment in transformed migraineurs.

Methods One hundred patients with transformed migraine (Silberstein et al., 1996) were prospectively studied. Hamilton Anxiety (HA) and Depression (HD) scales were applied in baseline. All patients were evaluated after 6 and 14 weeks after withdrawal of symptomatic medications and same prophylaxis.

Results Sixty-five W and 15 M presented in baseline moderate or severe scores (M-S) (19 (23.7%) patients for HA and 9 (11.3%) for HD) and mild scores or no alterations (N-M) (61 (76.3%) patients in HA and 71 (88.7%) in the HD). At 6 weeks, the number of patients who presented moderate or severe (M-S) scores respectively in HA and HD, decreased to 12 (14%) and 6 (7.5%). At 14 weeks, 7 (8.7%) in the HA and 7 (8.5%) in the HD revealed moderate or severe scores. In the group who had (M-S) scores during baseline for HA and HD, 36.9% and 22.2% presented headache frequency reduction >50% (HFR > 50%) at 6 weeks whereas 79% and 77.8% at 14 weeks. In those who had (N-M) scores at baseline, HFR > 50% was achieved, respectively after 6 and 14 weeks, in 39.4% and 80.3% for HA and in 40.8% and 80.3% of the patients.

Conclusions The scores in HA and HD scales improved with the treatment but not related to headache frequency reduction. Both groups responded well and similarly to the treatment after 14 weeks. Controlled further studies are necessary.

Reference

Silberstein et al., 1996.

A048

Comorbidities and clinical aspects affecting melatonin secretion in chronic and episodic migraine

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Objectives Substantial evidence points to melatonin as playing a role in the regulation of circadian rhythms, sleep,

and headache. An interictal decrease in the levels of nocturnal plasma melatonin and an alteration of the urinary 6-sulphatoxymelatonin (aMT6s) excretion throughout the ovarian cycle have been described in migraine patients, but chronic and episodic migraine patients levels have never been studied as the factors influencing the melatonin secretion. The aim of our study was to investigate aMT6s levels in patients with chronic (CM) and episodic migraine (EM), compared with controls, and factors influencing its secretion.

Methods Quantitative determination of aMT6s with a capture antibody technique (ELISA test). A total of 220 urinary samples (73 patients with CM, 73 patients with EM and 74 controls) were tested. The headache diagnosis was established according to the International Headache Society diagnostic criteria and the urinary samples were collected in a 12-hour period (from 8:00 pm to 8:00 am). Comorbidity and headache characteristics were ascertained.

Results Lower levels of aMT6s were found in patients with EM and EE, when compared with controls. Furthermore, aMT6s levels were significantly lower during migraine attacks. Anxiety and bodily pain affected melatonin secretion, decreasing aMT6s levels. Headache during the day the urinary sample was collected is the most important factor in decreasing melatonin secretion.

Conclusion Melatonin levels are lower in both CM and EM. Headache attack, anxiety and bodily pain affected melatonin secretion.

A049

Headache prevalence related to diabetes mellitus. The Head-HUNT Study

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Objectives To investigate a possible association between headache and diabetes mellitus (DM) in a large population based cross-sectional population-based health study.

Methods Diagnoses of headache were based on 13 questions in the second of two questionnaires covering a wide range of topics. Migraine was diagnosed according to a modified version of the migraine criteria in the first international classification of headache disorders (IHC-1). Headaches that did not fulfil the criteria for migraine were diagnosed as non-migrainous headache. The diagnoses were mutually exclusive. The diagnoses of DM were based on information from questionnaires and fasting blood samples with serum glucose, anti-GAD and C-peptide. Associations were assessed in multivariate analyses, estimating prevalence odds ratios (ORs) with 95% confidence intervals (CIs).

Results Information on both headache and self-reported DM were available in 51 249 participants, whereof 1499 had self-reported DM and 1097 had fasting blood samples. Prevalence OR of migraine was lower among persons with DM compared to those without DM, the OR being 0.4 (95% CI 0.2–0.9) for type 1 DM and 0.7 (95% CI 0.5–0.9) for type 2 DM. OR of headache were lower among those with duration of DM ≥ 13

years compared to those who had got DM the last 3 years, OR 0.6 (95% CI 0.4–0.9). The analyses revealed no clear associations between non-migrainous headache and DM.

Conclusion The reason for the inverse relationship between migraine and DM is unknown, but might be related to pathophysiological abnormalities, e.g. autonomic discrete neuropathy in patients with DM that protect against migraine.

A050

Headache prevalence related to asthma, hay fever and chronic bronchitis. The Head-HUNT Study

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Objectives To examine the relationship between headache and asthma, hay fever, and chronic bronchitis in a large cross-sectional population-based study.

Methods Diagnoses of headache were based on 13 questions in the second of two questionnaires covering a wide range of topics. Migraine was diagnosed according to a modified version of the migraine criteria in the first international classification of headache disorders (IHC-D-1). Headaches that did not fulfil the criteria for migraine were diagnosed as non-migrainous headache. The diagnoses were mutually exclusive. Diagnoses of asthma, hay fever and chronic bronchitis were based on the same questions as used in most epidemiologic studies on respiratory symptoms. Associations were assessed in multivariate analyses, estimating prevalence odds ratios (ORs) with 95% confidence intervals (CI).

Results Among the 51 383 subjects who answered the headache questions 98.1% also answered the questions about asthma and chronic bronchitis, and 91.5% answered the question about hay fever. Both migraine and non-migrainous headache were approximately 1.5 times more likely among those with current asthma, asthma related symptoms, hay fever, and chronic bronchitis than among those without. The strength of the association increased with increasing headache frequency.

Conclusions This large questionnaire-based study confirms that migraine and other headaches are associated with respiratory and allergic disorders. Headache frequency seems to have a greater impact on the association with respiratory or allergic conditions than headache diagnoses. Whether this represents a causal relationship is uncertain, but the results underline the importance of considering comorbid disorders among patients with frequent headache.

A051

Depression as comorbidity in different types of headache. What is the effect of headache frequency?

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Background Depression and headache frequency are strong predictors of quality of life.

Objective To measure depression in different headache types and frequency of headache in the multicultural population of Luxembourg using the PHQ9 scale.

Method A self administered questionnaire (BURMIG), including PHQ9 was used in a population based study on headache sufferers. It is categorised to determine severity of the depression as 1–4 minimal depression, 5–9 mild depression, 10–14 moderate depression, 15–19 moderately severe depression and 20–27 severe depression.

Results In our sample of 731 headache sufferers (41 ± 12 years, 69.5% female, 64% economic workers), 79% reported a headache frequency of 1–9 days/month. 46% were identified as having migraine (MIG), (88% with 1–9 days/month), 47% as having non-migrainous headache (NMIG) (78% with 1–9 days/month) and 7% as having chronic headache (CH, >15 days/month).

10% of the studied population was suffering a moderately to severe depression. Depression scores were lower in NMIG (46% minimal, 29% mild) than in MIG (27% minimal, 40% mild, 19% moderate) and highest in CH (35% mild, 19% moderate, 23% moderately severe). Severe depression was more prevalent in CH (12.5%) than in the NMIG or MIG (2% and 3%).

Conclusion Our population based study indicates that also in patients who do not see a physician for headache there might be a clinically significant comorbidity with depression, with higher severity of depression associated with high headache frequency.

A052

Influences of WFS1, BDNF, and DRD4 genotypes on monthly drug consumption in MOH

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Objectives Medication overuse headache (MOH), a chronic headache condition due to symptomatic drug overuse, is a borderline disease between severe headache and substance dependence disorder. This study investigated likely influence in MOH drug use of socio-demographic and clinical factors, and three genetic polymorphisms, involved in dependence behavior.

Methods In 82 MOH patients (79.27% women; mean ± SD age: 46.90 ± 11.45 years) clinical data were obtained. A psychiatric assessment was also performed. Subjects were genotyped for three polymorphisms: wolframin (WFS1) H611R (R/R and non-R/R), BDNF G196A (G/G and non-G/G), and DRD4 120bp tandem duplication (L/L and non-L/L).

Results Monthly drug consumption was different in non-R/R vs. R/R ($t = -3.705$; $p < 0.0004$), and in G/G vs. non-G/G ($t = -2.561$; $p = 0.01$), but not in L/L vs. non-L/L ($t = 0.006$; $p = 0.99$). In ANCOVA (covariate: age) there was no 'WFS1 ×

BDNF' interaction effect on monthly drug number ($F_{1,77} = 1.184$; $p = 0.28$). Finally, a General Regression Model ($F_{2,79} = 9.136$; $p = 0.00027$; adjusted $R^2 = 0.167$) showed WFS1 ($t = -3.302$; $\beta = -0.342$; $p = 0.001$) and BDNF ($t = -2.007$; $\beta = -0.208$; $p = 0.04$) as significant predictors of drug use.

Conclusion WFS1 and BDNF polymorphisms, but not DRD4, influence monthly drug consumption in MOH subjects. These preliminary findings are coherent with the hypothesized role of dependence behavior in MOH clinical features.

A053

Intracerebral lesions detected on MRI migraine patients

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Objective Migraine has been considered as an episodic, neurovascular disorder. A possible association between migraine and ischemic brain lesions has been suggested in western patients. We investigated the incidence of intracerebral lesions in Japanese patients with migraine, and assessed the risk factors for cerebrovascular disorders in each patient.

Methods We had 395 patients with migraine (88 with aura and 307 without aura). They comprised 101 males and 294 females and their mean age was 31 years. Intracerebral lesions were assessed by MRI, with special attention to migrainous infarct and periventricular white matter and deep white matter lesions. We also examined risk factors for stroke, such as hypertension, diabetes mellitus, hyperlipidemia and atrial fibrillation.

Results Migrainous infarct was not found in any of the patients. Silent white matter lesions were found in 39 of the 395 patients (9.9%). There was no difference in the prevalence of silent white matter lesions between patients with and without aura. Regarding lesions of vascular territories, 38 lesions were located in the anterior circulation and only one in the posterior circulation. This finding is different from that reported in western patients. The incidence of risk factors for stroke (11%) was lower than that in normal subjects of the same age.

Conclusion White matter lesion located in the anterior circulation was common in Japanese migraine patients. Cerebral arteriosclerosis did not appear to contribute to the development of white matter lesions. Rather, their development could be related to factor(s) derived from migraine proper

B001

Visual evoked potential in migraineurs – effect of age and disease duration

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Migraine headache is one of the commonest presentations at a Neurology clinic. The chronic disorder is often associated with visual disturbances (blurring, aura) and photophobia.

Objective In this study, the visual system of migraineurs was analyzed by visual evoked potentials (VEP) to find the

possible influence of certain parameters like age, duration of disease, etc.

Methods Detailed history was taken and interictal pattern reversal VEP assessment was done in the patients diagnosed with migraine according to the International Headache Society (IHS) criteria.

Results Patients aged more than 20 years were more likely to have increased P100 latencies (mean increase of 25 ms) than patients aged less than 20 years. The effect was statistically significant ($p < 0.05$). Patients with a self-reported disease duration of more than 5 years were more likely to have increased P100 latency ($p < 0.10$). A subset of patients with longer disease duration had decreased P100 amplitude.

Conclusions The neural firing patterns, as reflected by latency of waves in VEP, show that in migraineurs older than 20 years, P100 latency is greater.

B002

Eletriptan effects differently 5-HT synthesis in migraine patients than those in normal subjects as measured by PET

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Background and aims Triptans efficacy in migraine has been ascribed to cerebrovascular 5-HT1B and/or 5-HT1D/1F receptors on trigeminovascular afferents. We investigated influence of eletriptan, a potent lipophilic 5-HT1B/1D receptor agonist on brain 5-HT synthesis in patients suffering from migraine headache and normal controls.

Methods Seven female patients (32.1 ± 9.3 years; migraine without aura – IHS diagnostic criteria) and eight normal female subjects (25.4 ± 4.9 years) had two PET scans. Patients and controls had: Scan-1 at least 3 days without headache (for patients) and scan-2 60 minutes after taking orally a 40 mg tablet of eletriptan. Sixty minutes dynamic PET scans were taken with venous blood sampling after an injection of about 10 mCi of α -[11C]methyl-L-tryptophan. Images of the brain trapping constant (K^*) were colocalized with individual MRI in 3-D. Twenty-two regions of interest were selected including periaqueductal gray, limbic, frontal, parietal, visual and sensorimotor cortices. Two-way RMANOVA (Fisher LSD post-hoc); $p < 0.05$ was taken as significant.

Results Plasma tryptophan levels were similar for all scans. The mean (\pm SEM) values of K^* were in patients 5.46 ± 0.33 (scan-1) and 4.52 ± 0.25 (scan-2), and 5.34 ± 0.30 (scan-1) and $6.36 \pm 0.51 \mu\text{L/g/min}$ in controls. The global K^* in scan-1 was significantly ($p < 0.05$) different from scan-2; in patients was greater while in controls is reverse. Synthesis in scan-2 was lower than in scan-1 in patients but reverse was in controls. No difference in the synthesis between patients and controls at the base line (scan-1).

Conclusions Data suggest that 5-HT synthesis is differently controlled/modulated in migraine sufferers than controls. Supported by Pfizer Canada Inc.

B003**Mast cell degranulation activates a pain pathway underlying migraine headache**Dan Levy¹, V Kainz², AM Strassman¹¹BIDMC, ²Anesthesia, Harvard Medical School, USA

It is generally accepted that intracranial headaches such as migraine are initiated by activation of meningeal nociceptors, but the mechanisms responsible for triggering this neuronal event are poorly understood. In this study, we examined whether meningeal nociceptors can be activated locally through a neuroimmune interaction with resident mast cells in vivo in the rat. Degranulation of meningeal mast cells using intraperitoneal administration of the basic secretagogue agent compound 48/80 (2 mg/kg) induced a prolonged state of excitation in meningeal nociceptors together with increased expression of the phosphorylated form of the extracellular signal-regulated kinase (pERK), an anatomical marker for nociceptor activation. Such mast cell – nociceptor interaction was also associated with downstream activation of the spinal trigeminal nucleus. Our findings provide evidence linking meningeal mast cell degranulation to activation of the trigeminal pain pathway believed to underlie intracranial headaches such as that of migraine. Targeting mast cell activation or their mediators could serve as a new approach for migraine prophylaxis.

B004**Change in brain blood flow noted in patients with headache**Marina Koreshkina¹, M.I. Koreshkina², A.A. Strelnikov³¹Neurological, MD, PhD, ²Nerological, International Clinic and Hospital MEDEM, ³Medical Director, MD, Prof, Russia

Purpose Because migraines are a highly prevalent and disabling illness that remains largely under-diagnosed and inadequately treated in the primary care setting we used the ultrasound dopplerography as a diagnostic test to distinguish migraines from other kinds of headache.

Methods 68 female and 54 male (17–45 ages) participated in the study. The study protocol included a neurological examination, answering a questionnaire, rating the strength of the headaches and disabling on a scale, MRI of the brain (for excluding secondary headache disorders), ultrasound dopplerography of vessels. We have three groups: 1. Migraine patients – 49; 2. Patients with Tension type headache – 35; 3. Health people – 38. The ultrasound dopplerography was made in all vessel regions of the brain (carotids and vertebral).

Results In the migraine cases there was an expressed hyperperfusion in the MCA in all cases. In our study of migraine patients, through examination by transcranial ultrasound dopplerography it was shown that unilateral headache is associated with a marked dilation of the middle cerebral artery on the headache side. The dopplerography of patients with tension type headache showed vessels' spasm in 28 cases, and normal blood flow in 7. The data of blood circulation of health people was normal in 100%.

Conclusion 1. Measuring the difference in blood flow in the MCA using ultrasound dopplerography, gives the practitioner an objective diagnostic method for headache patients. 2. The changes of blood flow in the middle cerebral arteries are directly connected with pathogenesis of migraine attack.

B005**Cortical atrophy and memory deficits in 4 clusters of chronic migraine sufferers: a 6 years' observation**Maria Nicolodi¹, F Fanfani², MG Spillantini³, A Torrini⁴¹Prevention Therapy Headache, ²Prevention Therapy Headache, Interuniversity Headache Centre, Italy, and ³MRC, UK, and ⁴Prevention and Therapy Headache, Italy

Objectives It seems that gray matter atrophy increases in sufferers from chronic migraine without aura paralleling severity of superuse of antimigraine abortive drugs.

Background Neurotrophins regulate growth, survival of neural cells. NGF stimulates release of SP, CGRP; NMDA up-regulates NGF. Analgesics superuse should be mirrored by CNS changes.

Method Observation regarded: (A) neuroimaging by means of 3-T MRI analyzed with VBM, (B) memory function investigated by using Randt Memory Battery, Short Story Test, Attentional Matrices, Trial Making Test, (C) NGF, SP, CGRP levels in saliva evaluated by using ELISA and HPLC, respectively. We enrolled 650 chronic migraine sufferers (380 females) and a matched group of exempt subjects. They all were clustered according to age: 18–25, 25–35, 35–45, 45–55 years. Inclusion criteria: Chronic migraine without aura. Exclusion criteria: Psychiatric disorders, vascular/heart diseases, hypertension, major systemic, neurological diseases. Observation lasted 6 years. Neuroimaging was performed once every two years, memory/attention explored once a year. Peptides and NGF were measured in 40 randomly chosen chronic migraine and a matched group of exempts.

Results More than 65% of the migraine sufferers had memory/attention problems. Peak value was in the interval 37–45 years. Gray matter rarefaction was evident in 15% of the subjects, peak is lowering in the time: nowadays 38–42 years. SP and CGRP were three times higher than in exempts, NGF have a sinusoid pattern: often undetectable. Memory/attention did not differ ($p > 0.5$) in subjects with gray matter abnormalities.

Conclusion Analgesics super-use can counteract positive/negative neurotrophins action.

B006**Enhanced expression of neuropeptides in rat trigeminal ganglion neurons during culture**Aniko Kuris¹, C.B. Xu², M.F. Zhou², J. Tajti³, R. Uddman⁴, L. Edvinsson¹¹Experimental Vascular Research, IHC, Sweden, and ²Neurology, IHC, Hungary, and ³Otorhinolaryngology, ⁴Experimental Vascular Research, Sweden

Objectives The sensory innervation of intracranial vessels originates in the trigeminal ganglion with calcitonin gene-

related peptide (CGRP), substance P (SP) and pituitary adenylate cyclase activating peptide (PACAP) as frequent neuronal messenger peptides. The present study was designed to compare the expression of neuropeptides in cultured rat trigeminal ganglion neuron cells to organ culture of sections of rat trigeminal ganglia.

Methods Rat ganglion neuron cells were isolated and cultured in serum free DMEM supplied with nerve growth factor, organ culture of ganglia were performed by incubation in serum free DMEM. The axon growth and the expression of the neuropeptides CGRP, SP and PACAP were assessed by immunocytochemistry and real-time PCR.

Results The length of axons growing in peripheral direction increased up to 48 hours. Immunocytochemistry revealed that cultured neurons and axons were CGRP, SP and PACAP immunoreactive (-ir). In addition, the cell bodies showed increased expression of CGRP at 24 hours and SP immunoreaction at 24–48 hours, whereas cell culture did not affect PACAP-ir. A significant elevation of CGRP mRNA was seen 12 hours before the increase of CGRP-ir. Organ culture of trigeminal ganglia revealed an increased expression of CGRP up to 48 hours.

Conclusions Neurons of rat trigeminal ganglia alter their expression of neuropeptides during cell and organ culture. The culture method provides a basis for studying underlying molecular mechanisms responsible for regulation of neuropeptide expression.

B007

Gaba and glutamate levels in migraine sufferers and controls – a study using magnetic resonance imaging spectroscopy

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Objectives To assess the interictal cortical levels of GABA and Glutamate in migraineurs and controls, using Magnetic Resonance Spectroscopy Imaging (MRS).

Methods Participants had migraine with (MA) or without aura (MO), not using any medications. They were imaged more than 72 h after their last headache. Controls were matched by age and gender. We used a 4.1T MRS. For GABA, acquisition was run in single voxel mode selected in the occipital lobe, 1.5 × 3 × 3 (13.5 cc) and less than 15 min signal averaging. The data was analyzed in the spectral domain. For glutamate, moderate echo adiabatic refocusing sequence was used. The data was analyzed using LCM with rejection if the Cramer-Rao bounds exceeded 0.30. Ratios of GABA and glutamate were developed relative to N-acetyl aspartate (NAA).

Results GABA data was obtained from 10 individuals with MA, 8 with MO and 8 controls. Mean concentration was not different between controls (0.71 + 0.14), MA (0.63 + 0.18) and MO (0.67 + 0.15). Pooling subjects, GABA correlated with number of severe headaches in the month. In those with none, the level was 0.72 + 17, vs. 0.52 + 0.64 in those with 1 or more ($p = 0.03$). For moderate or severe headaches, in those with

0–3/month, it was 0.62 + 0.14, vs 0.72 + 0.18 in those with 4+ ($p = 0.07$). It did not correlate with total headaches. For glutamate, we faced technical limitations and obtained data from just 8 patients. The Glutamate/NAA did not correlate with severe headaches (0.0637 vs. 0.0617).

Conclusions The levels of GABA in the occipital cortex are inversely correlated with the frequency of severe headaches experienced by migraineurs.

B008

Course of migraine during pregnancy: an ERP study

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Objectives The aim of the current study is to investigate the course of migraine attacks during pregnancy in a prospective approach and to analyse cortical stimulus processing by means of measuring the psychobiological parameter of the Contingent Negative Variation.

Methods In the present study, we have observed the incidence of migraine during pregnancy and after delivery by examining the amplitudes of event-related potentials within the paradigm of the Contingent Negative Variation (CNV) in 15 healthy pregnant and 15 pregnant migraine patients. These data were compared to those in non-pregnant women: 13 migraine sufferers and 16 healthy women.

Results The results showed significantly lower habituation in the initial CNV in pregnant women. In the group of pregnant women with migraine, we observed a slower reaction time and amplitudes similar to those in depressive patients, especially during the third trimester and after delivery. The group of responders (without migraine attacks in the 2nd or 3rd trimester) showed higher habituation in the initial CNV, a longer duration of the disease and a higher age at initial manifestation in comparison to non-responders (migraine attacks in 2nd/3rd trimester).

Conclusion Our results show that responders and non-responders differ with respect to the degree of habituation as manifested in iCNV amplitudes, the duration of the disease and the age at its initial manifestation. Responders are characterized by habituation, while non-responders continue to dishabituate. Finally, a model of cortical stimulus processing with respect to migraine in pregnancy is developed and presented.

B009

Total cerebral blood flow response to nitroglycerin is impaired in migraine

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Background Nitroglycerin (NTG) triggers migraine attacks in susceptible patients. The cerebrovascular response to NTG may be impaired in migraine patients, however, previous

studies are inconclusive. In this study we assessed the response of total cerebral blood flow (tCBF) to NTG in migraine.

Methods Migraineurs (n = 32) received NTG (n = 27) IV 0.5 µg/kg/min for 20 min or placebo (n = 5). Healthy volunteers (n = 12) all received NTG. We measured tCBF (defined as the combined blood flow in basilar artery and both internal carotid arteries) at baseline and during infusion of NTG/placebo using 3T phase contrast magnetic resonance angiography. In migraine patients we also measured tCBF during the provoked migraine attack or 6 hours after infusion of NTG/placebo.

Results During infusion of nitroglycerin tCBF decreased 115.9 ml/min in healthy volunteers and 24.9 ml/min in migraine patients ($p = 0.02$). A sub-analysis within migraine patients showed a tCBF decrease of 112.5 ml/min in patients who did not develop a provoked migraine attack after NTG (n = 7) compared to an increase of 7.4 ml/min in patients who developed a provoked migraine attack (n = 20).

Conclusions Migraine patients have significantly less tCBF response to nitroglycerin compared to healthy volunteers, mainly due to an impaired response in patients who developed a provoked migraine attack after several hours. During the provoked attack there was no difference in tCBF change between patients with a provoked attack compared to patients without an attack.

B010

Scalp and forearm pressure pain thresholds in migraine cycle; pressure allodynia during prodrome

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Objectives To measure changes in scalp and forearm pressure pain-threshold (PPT) with a Fischer Algometer, during each phase of a migraine cycle and to compare with non-migrainous controls.

Methods Ten migraine patients and 10 non-migrainous controls entered the study. PPT measurements were made on headache side (HS) and non-headache side (nHS) during different phases of a migraine cycle. PPTs of both forearms were measured during each phase. Scalp and forearm measurements of controls were made on one occasion. Three measurements at each site were averaged and analysis of variance performed. Patient readings totaled 474, 6 lost due to patient declining scalp measurements during headache. Control readings totaled 120. 95% confidence intervals and Alpha level 0.05 were used for statistical significance.

Results (partial) Scalp on HS differed significantly from nHS during each phase of the cycle. On HS, prodrome PPT was significantly lower (more tender) than interictal PPT (used as baseline), indicating presence of pressure allodynia during prodrome. During headache phase, HS forearm PPT was significantly lower than nHS forearm PPT.

Conclusions Scalp pressure allodynia is present on the HS during prodrome, before onset of headache. This differs from

cutaneous allodynia (PPT measured by von Frey hairs), which appears about one hour after onset of headache.

During headache phase, significant differences in scalp and forearm tenderness between HS and nHS could provide early warning of impending headache and a signal to start treatment.

B011

Inhibitory effect of the CGRP receptor blockers BIBN4096BS and CGRP8-37 on perfused rat middle cerebral artery

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Background Calcitonin gene-related peptide (CGRP), a potent vasodilator, is believed to play a pivotal role in the pathogenesis of migraine, by activation of CGRP receptors in the trigeminovascular system. The CGRP-antagonist, BIBN4096BS, has proven effective in treatment of acute migraine attacks; however, the site of its action is unclear.

Methods We have used the luminal perfused rat middle cerebral artery (MCA) in an arteriograph, pressurized to 85 mm Hg, and myograph studies of isolated ring segments of the MCA. The ability of rat α CGRP, β CGRP, adrenomedullin and amylin to induce vasodilatation after luminal or abluminal administration was investigated. Subsequently to this the inhibitory effects of the blockers BIBN4096BS and CGRP8-37 were studied.

Results In myograph studies of isolated ring segments of the MCA, rat α CGRP and β CGRP induced strong concentration-dependent dilatation while adrenomedullin and amylin induced weak dilatation. In the perfusion system only abluminal application of α CGRP and β CGRP caused dilatation (maximum $35 \pm 0.5\%$) of the MCA with pD₂ values of 8.98 ± 0.07 and 8.74 ± 0.12 , respectively, while adrenomedullin and amylin resulted in weak dilatation. In contrast, when given luminally no effects were observed by the peptides. In abluminal perfusion experiments the relaxant response to α CGRP was antagonised by BIBN4096BS and CGRP8-37. The blockers were without effect per se given to MCA in the myograph bath or during either luminal or abluminal application in the doses used. The maximum α CGRP response was reduced from $12.0 \pm 0.8\%$ to $7.7 \pm 0.2\%$ ($p < 0.0001$) by BIBN4096BS when given abluminally. Luminal application of BIBN4096BS had some inhibitory effect in the highest dose ($6.2 \pm 0.9\%$; $p < 0.05$). Similar data were obtained with CGRP8-37. In myograph experiments relaxation induced by α CGRP was significantly blocked by BIBN4096BS (10^{-7} M) and CGRP8-37 (10^{-6} M).

Conclusion The data show that the rat MCA is equipped with the CGRP1 type of receptors, located on the smooth muscle cells. The blood-brain barrier effectively prevented the entry of the CGRP receptor agonists; the CGRP antagonists were prevented from reaching the CGRP receptors by the arterial endothelium.

B012**Comparison of NO and CGRP responses in the human peripheral microcirculation of migraine and control subjects**Marie-Louise Edvinsson¹, L Edvinsson²¹University, ²Internal Medicine, Lund University, Sweden

Background Calcitonin gene-related peptide (CGRP) and nitric oxide (NO) are the two most important agents proposed to have a functional role in the pathogenesis of migraine. Both molecules are released in attacks but it is unclear if there is an altered responsiveness (supersensitivity) to them in migraine subjects. To test this we have studied the skin blood flow with laser Doppler technique and administered the agents by local iontophoresis.

Methods Local blood flow on the dorsal part of an arm was studied with laser Doppler technique and acetylcholine (release of endothelial NO), and sodium nitroprusside (SNP) and CGRP (both smooth muscle cell responses) were administered by iontophoresis. The experiment was carried out in healthy volunteers with or without a history of migraine (having a history of >10 years of migraine with or without aura).

Results All procedures resulted in local vasodilatation. Acetylcholine induced a mean relaxation of 873% (of baseline) in control and 1043% in migraine. The responses were 377% for SNP and 228% for CGRP in control, and 990% for SNP and 555% for CGRP in migraine. The responses to local heating were 2505% in control and 1020% in migraine subjects. The material is based on a limited number of subjects hence the data is not statistically significant.

Conclusion The data show that the local microcirculation responds to the iontophoretic administration of acetylcholine, SNP and CGRP. This material did not reveal a difference in the responses of the human peripheral microcirculation.

B013**Up-regulation of CGRP expression in neurones of trigeminal ganglion via intracellular MAPK ERK1/2 pathways**Aniko Kuris¹, J. Taiti², C.B. Xu³, R. Uddman⁴,
L. Edvinsson⁴¹Experimental Vascular Research, IHC, Sweden, and ²Neurology, IHC, Hungary, and ³Otorhinolaringology, ⁴Experimental Vascular Research, Sweden

Objectives Calcitonin gene-related peptide (CGRP) plays an important role in the pathogenesis of migraine and cluster headache. The present study was designed to investigate involvement of extracellular signal-regulated kinase 1 and 2 (ERK 1/2) of mitogen-activated protein kinase (MAPK) pathways in CGRP expression in rat trigeminal ganglion (TG) neuronal cells during organ culture.

Methods Rat trigeminal ganglia were removed, sectioned and incubated in serum-free DMEM in the presence of the ERK 1/2 inhibitor U0126 (2×10^{-5} M) or DMSO (control) for 24–48 hours. The expression of the neuropeptides CGRP and substance P (SP) was assessed by immunocytochemistry.

Results Organ culture of TG for 24 to 48 hours induced a significant up-regulation of CGRP expression in the neuronal cells; the number of CGRP positive cells increased from $13.4 \pm 0.7\%$ (control, at 0 hour) to $20.2 \pm 1.3\%$ at 24 hours and $23.7 \pm 2.4\%$ at 48 hours. Inhibition of ERK1/2 by U0126 attenuated the enhanced expression of CGRP; the number of CGRP positive cells were diminished ($p < 0.05$), compared to DMSO. However, organ culture of TG in the presence of DMSO or U0126 did not alter SP expression or the number of SP immunoreactive neuronal cells.

Conclusions Our observations suggest that CGRP expression in trigeminal neurons at least in part occur via intracellular ERK1/2 pathways and interaction with this may provide new therapeutic strategy for migraine and cluster headache.

B014**Cephalgia alopecia induced loss of epidermal nerve fibers is reversed by Botulinum toxin treatment**Fred Michael Cutrer¹, P. Sandroni¹, G. Crabb²¹University of Minnesota, ²Neurology, Mayo Clinic, USA

Background We previously reported a case in which following a flu-like illness, a young woman developed severe focal neuralgiform pain followed by hair loss at sites on the scalp (Cutrer et al. 2006). Biopsy of affected areas showed perifollicular infiltration of autoreactive T lymphocytes. The pain and hair loss were refractory to multiple oral treatments and injected steroids. Injection of Botulinum toxin A into symptomatic site resulted in resolution of neuralgiform pain and subsequent hair re-growth which persisted for 5–8 weeks. By 12 weeks post-treatment there was return of pain and subsequent loss of re-grown hair.

Methods After obtaining IRB approved informed consent, we performed biopsies at areas of scalp which were: 1. unaffected by pain or hair loss (site A); 2. affected by pain and hair loss prior to treatment (sites B & C) and 3. six weeks after treatment in areas previously affected by pain and hair loss that had resolution of pain and hair regrowth (site D). Using immunohistochemical fluorescence methods and imaging with montaged confocal microscopy (Kennedy et al.) we quantified the density of epidermal nerve fibers by counting fibers as they passed through the dermal-epidermal basement membrane under each of the sampling conditions.

Results Epidermal Nerve Density (ENFs/mm) was: Site A 105.4; Site B 84.1; Site C 46.6 and Site D 105.2.

Discussion Cephalgia alopecia, presumably through an immune mediated mechanism, is associated with a reduction in perifollicular ENF density which is transiently reversed by injection with Botulinum toxin A.

References

Cutrer. Cephalgia 2006; 26:747–751.
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B015**Development of the allodynia symptom checklist (ASC) in a population study of persons with migraine**

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Objective To measure the prevalence and concomitants of cutaneous allodynia (CA) in migraineurs from the population. **Methods** Migraineurs (11,388) identified in the population screening phase of the AMPP, completed the ASC, comprising 12 questions about the frequency of allodynia symptoms during severe headaches. Response options were never (0), rarely (0), less than half the time (1), half the time or more (2). We used Item Response Theory (IRT) to explore how well each item discriminated the degree of allodynia and examined the relationship of CA to headache features.

Results All 12 questions had excellent item properties. The most discriminating items focused on CA while 'taking a shower' (discrimination = 2.54), wearing a necklace (2.39) or ring (2.31), exposure to heat (2.1) or cold (2.0). Factor analysis revealed three factors corresponding to thermal, mechanical static and mechanical dynamic allodynia. CA severity grades included none (scores 0–2), mild (3–5), moderate (6–8) and severe CA (>9). The prevalence of allodynia was 63.2%. Severe CA occurred in 20.4%. The prevalence of allodynia increased with attack frequency and was higher in migraine with aura than in migraine without aura (OR = 3.5, 95% CI = 3.2–3.8). CA was associated with a 3-fold risk disability as measured by MIDAS.

Conclusion The ASC measures the prevalence, and severity of allodynia overall and in each of 3 domains. Allodynia is common in the general migraine population (63%) confirming clinic based studies. CA is associated with frequency, severity, disability and associated symptoms of migraine.

B016**Prevalence and characteristics of allodynia in headache sufferers**

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Objectives To estimate the prevalence and severity of cutaneous allodynia (CA) in subjects with various types of primary headaches from the general population.

Methods We mailed questionnaires to 24,000 severe headache sufferers identified in the population. We assessed CA with the validated ASC questionnaire, as well as disability and comorbidities. We modeled headache status, as well as frequency of headaches and disability as dependent variables in multivariate analyses.

Results Of 16,577 respondents, 11,388 (68.7%) individuals had migraine, 2,929 (17.67%) had probable migraine (PM), 1,395 (8.52%) had severe episodic tension-type headache (S-ETTH), 655 (3.9%) had transformed migraine (TM) and 165

had other chronic daily headaches (O-CDH) (0.9%). CA scores were higher in TM (68.3% with CA, scores of 5.5 + 5.0) than in migraine (63.3%, 4.6 + 4.5, $p < 0.001$) and in both vs. O-CDH (36.8%, 1.59 + 2.5), PM (46.2%, 0.8 + 1.9) and S-ETTH (36.7%, 2.15 + 2.99) ($p < 0.001$ for all comparisons). In migraineurs, CA was more common in women than men (PR = 1.4, 95% CI 1.28–1.59), in those of longer illness duration (10–19 years vs <10 years; PR = 1.15, 95% CI = 1.06–1.25) and higher disability (MIDAS IV vs I, PR = 1.61, 95% CI = 1.46–1.75). It increased with body mass index and headache frequency and decreased with age. For all headache types, individuals with major depression had higher ASC scores than individuals without depression.

Conclusions CA is more common and severe in TM and migraine than in other primary headaches. Among migraineurs, CA is associated with female gender, headache frequency and disability, obesity and depression.

B017**Enhanced sensitivity of the trigeminal system to glutamic acid during the proestrus stage of the rat estrous cycle**

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Objective To determine if the response of neurons to glutamic acid (GA) varies during the different stages of the rat estrous cycle within the trigeminal system.

Methods Normally cycling female rats were used and the stage of the estrous cycle was determined by vaginal smear. Intracellular recordings were made between 13:30–16:00 hours from neurons within the trigeminal nucleus caudalis and C1–C3 regions that had dural receptor fields. The region of the recordings was perfused with known dosages of GA using a push pull procedure. The dura and sinuses were electrically stimulated and the response magnitude (number of spikes \times duration) was compared between different stages of the rat estrous cycle for each dosage of GA using an ANOVA and paired t-tests.

Results The response magnitude was significantly greater (p values < 0.05) during proestrus ($n = 5$) than diestrus ($n = 5$) and metestrus ($n = 5$) while estrus ($n = 6$) did not differ from the other stages. The response to GA could be partially blocked by NMDA antagonist 5-AP.

Conclusions There is enhanced sensitivity of the trigeminal system to GA during proestrus that may result from 'estrogen withdrawal' as serum estradiol levels abruptly decline during the later part of this stage while estradiol levels gradually rise during metestrus and diestrus. Enhanced glutamatergic tonus could be important to the pathogenesis of menstrual migraine if similar changes occur within the trigeminal system of humans after 'estrogen withdrawal'.

B018**NMDA receptor phosphorylation may play role in low serotonin-induced trigeminal nociceptive facilitation**

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Objective To determine the effect of low serotonin on chemical nociception induced phosphorylation of NMDA receptor subunit 1 (NR1) in trigeminal nucleus caudalis neurons (TNC) and on trigeminal nociception.

Method Adult male Wistar rats were separated into low serotonin and control groups. Serotonin was depleted by peritoneal injection with para-chlorophenylalanine 3 days prior to the experiment. To induce trigeminal nociception, inflammatory soup was applied on exposed dural surface for 30 minutes. Two hours after induction, the brainstems and cervical cords were removed for serine-896 phosphorylated NR1 (pNR1) and Fos immunohistochemical studies.

Results Meningeal inflammation led to the phosphorylation of NR1 subunit as well as activation of trigeminal nociceptive system. There was strong correlation between numbers of pNR1- and Fos-immunoreactive cells in the TNC ($r^2 = 0.76$, $p \leq 0.001$). The processes of nociception induced NR1 receptor phosphorylation and trigeminal nociception were enhanced in the low serotonin condition. The averaged number of pNR1-immunoreactive cells in low serotonin and control groups were 46 ± 11 and 29 ± 4 cells per section respectively ($p = 0.01$). The averaged number of Fos-immunoreactive cells in low serotonin and control groups were 40 ± 13 and 13 ± 4 cells per section respectively ($p = 0.003$).

Conclusion The process of meningeal inflammation induced trigeminal nociception is enhanced in the low serotonin condition. The mechanism of nociceptive facilitation may involve the increase in NR1 receptor phosphorylation. This study further supports the role of serotonin in the control of trigeminal nociception.

B019**Relevance of RNA-Spiegelmer (a novel CGRP-binding compound) to migraine**

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Calcitonin gene-related peptide (CGRP), present in perivascular sensory nerve endings, is a potent endogenous dilator of cerebral and meningeal arteries. CGRP is implicated in migraine pathophysiology due to its migraine provoking effects. A selective antagonist has documented efficiency in the treatment of migraine. Instead of blocking the CGRP-receptor, scavenging CGRP itself might be a new therapeutic principle in migraine.

Objective The RNA-Spiegelmer binds to CGRP molecules with high affinity capable of inhibiting the function of CGRP. The aim of the present study was to investigate the effect of RNA-Spiegelmer in vivo/in vitro on CGRP-induced and electrically evoked vasodilatation of cerebral and meningeal arteries.

Method In vivo we used the closed cranial window model to visualize cerebral and meningeal arteries simultaneously in the same rat, before and after CGRP in the presence and absence of RNA-Spiegelmer. In vitro we used a conventional myograph and perfusion-system to characterize concentration-response curves and effects of the blood-brain barrier.

Results Pretreatment with the RNA-Spiegelmer (1 mg/kg) resulted in a significant inhibition of CGRP-induced (0.3 μ g/kg) vasodilatation of both arteries. This is in agreement with the in vitro studies performed on rat middle cerebral artery. Electrical stimulation (25 V, 10 sec) evokes dilatations of both arteries; however, RNA-Spiegelmer had no inhibiting effect, supporting the result of the in vitro studies where intraluminally administered RNA-Spiegelmer did not inhibit relaxation caused by abluminal CGRP-administration.

Conclusion The RNA-Spiegelmer exerted an inhibiting effect on CGRP-induced vasodilatation of both arteries; however, vasodilatation brought about by electrical stimulation was unaffected by the RNA-Spiegelmer.

B020**CACNA1A mutations of FHM-1 do not confer hypersensitivity to glyceryl trinitrate**

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Aim To test the hypothesis that CACNA1A mutation in patients with familial hemiplegic migraine of type 1 (FHM-1) is associated with hypersensitivity to nitric oxide.

Material and methods We included 8 FHM-1 patients with R583Q and C1369Y mutations and 9 healthy controls. All participants received intravenous infusion of 0.5 μ g/kg/min glyceryl trinitrate (GTN) over 20 min. The following variables were recorded: Headache intensity on a verbal rating scale; mean flow velocity in the middle cerebral artery (Vmean-MCA) by transcranial Doppler; diameter of the superficial temporal artery (STA) by Dermoscan. The primary end-points were differences in incidence of migraine headache (fulfilling the IHS criteria) and area under the curve (AUC) for headache score during an immediate phase (0–120 min) and a delayed phase (2–14 h).

Results One patient reported migraine without aura 5 h after start of infusion. No aura was reported after GTN. The AUC-headache in the immediate phase was more pronounced in patients than in controls ($P = 0.01$). In the 14 h following GTN infusion, there was no difference in the AUCheadache between patients and controls ($P = 0.17$). We found no difference in the AUCVmeanMCA ($P = 0.12$) or AUCSTA ($P = 0.71$) between FHM-1 patients and controls. None of the control persons reported migraine like headache.

Conclusions FHM-1 patients do not show hypersensitivity of the NO-cGMP pathway, as characteristically seen in migraine patients with and without aura. This indicates that the pathophysiological pathways underlying migraine headache in FHM-1 may be different from the common types of migraine.

B021**Sensitisation of TNC neurons to facial air jet, but not meningeal electrical stimulation elicited by CGRP**Philip Robert Holland¹, PJ Goadsby²¹*Neurology, University of San Francisco, USA, and* ²*Headache Group, Institute of Neurology, UK*

Objectives To study the effects of CGRP administration on dural nociceptive and facial mechanical input to the trigeminal nucleus caudalis (TNC).

Methods Rats were anaesthetised with pentobarbitone (60 mg kg⁻¹) and cannulated for measurement of blood pressure, administration of experimental drugs and supplementary anaesthesia. CGRP was given intravenously at either 1 µg kg⁻¹ i.v. bolus or 150 ng kg⁻¹ per minute. Effects on neurons in the TNC in response to facial air jet and dural electrical stimulation combined with middle meningeal artery diameter measurement were examined using electrophysiological and intravital microscopy techniques, respectively.

Results CGRP administration caused a consistent dural vasodilation which was blocked by CGRP₈₋₃₇ (300 µg kg⁻¹) but not sumatriptan (10 mg kg⁻¹). The dural vasodilation was accompanied by sensitisation of TNC second order neurons to facial air jet stimulation in the ophthalmic ($F_{1,8,9,6} = 20.32, P$ $F_{2,4,12,3} = 12.5, P$ $F_{1,8,9,6} = 2.32, P = 0.14$). This effect was reversed by the CGRP receptor antagonist CGRP₈₋₃₇ and sumatriptan ($F_{4,5,15,4} = 0.37, P = 0.7$). Spontaneous activity was not significantly altered in either group.

Conclusions The results demonstrate a clear differential response of TNC neurons to facial mechanical and dural electrical stimulation following CGRP induced dural vasodilation. The data indicate that dural vessel dilation during migraine may sensitise cutaneous inputs, but not dural afferents.

B022**Differences in cortical reorganisation in patients with exploding and imploding migraine**Lars Arendt-Nielsen¹, L Lindhardt Egsgaard¹, L Buchgreitz², R Jensen², Lars Bendtsen²¹*Center for Sensory-Motor Interaction, Aalborg University, ²Danish Headache Center, Copenhagen University, Denmark*

Objective To study cortical reorganisation in patients with exploding and imploding migraine.

Methods 11 patients with migraine and 11 healthy controls were included. Patients were divided into exploding (5 patients) and imploding (6 patients) migraine (Jakubowski et al. 2006).

Painful electrical stimulation was applied to the trapezius muscle and somatosensory evoked potentials (SEP) were recorded with 124-channel EEG during 3 experimental conditions (1) baseline (2) tonic pain induced by glutamate injection in the trapezius muscle and (3) post-baseline. Peak stages around 100, 200 and 300 ms were analysed with topography and equivalent current dipoles (x, y, z coordinates) were superimposed to magnetic resonance imaging slices of a stan-

dard brain to investigate source localization and changes in representational field in the cortex.

Results Tonic pain changes the cortical representation. Migraine patients showed more reorganisation than controls of the z-coordinate (P300 SEP peak) during in tonic pain. Only for the migraine patients the z-coordinate changes from baseline to glutamate.

Significant baseline difference was found in peak latency (P200) between exploding and imploding. Only in exploding migraine patients the x-coordinate of N100 changed from baseline to the tonic pain.

Conclusion In general migraine patients showed more cortical reorganisation than controls and patients with exploding migraine showed more reorganisation than those imploding migraine.

Reference

Jakubowski et al. 2006.

B023**Self-reported cutaneous allodynia vs. objective gauze brushing test in Taiwanese patients during migraine attack**Chi-Hsiang Chou¹, Fuh Jong-Ling², Wang Shuu-Jiun²¹*Neurology, Yuan-Shan Veterans Hospital, ²Neurological Institute, Taipei Veterans General Hospital, Taiwan*

Objectives Cutaneous allodynia is common during migraine attacks. This study was designed to examine the relationship between self-reported cutaneous allodynia and an objective gauze brushing test in Taiwanese patients with migraine.

Methods We recruited consecutive patients who were having an attack of migraine with or without aura in our headache clinic. Patients with chronic daily headache were also included. A history of experience of cutaneous allodynia over the head and hands was queried. In addition, we performed a gauze brushing test over the patients' face and hands during migraine attacks.

Results Eighty-three patients (61 women, 22 men; mean age 39.1 ± 15.3 years) participated in the study. Seven of them had migraine with aura (8%) and 19 (23%) had chronic daily headache. Eighteen patients (22%) reported having experienced cutaneous allodynia during migraine attacks. Twenty-three (28%) patients exhibited brushing allodynia during our tests. The proportions of patients with brushing allodynia did not differ between those with chronic daily headache and episodic migraine (37% vs. 25%, $p = 0.38$). Overall, sensitivity of the questionnaire was 44% and specificity, 87%. The agreement rate was 75%.

Conclusion Compared with previous studies, a low incidence of allodynia was found in our participants. A low percentage of participants with migraine with aura or racial differences should be considered if comparing these results with others. The discrepancy between self reported experience and brushing allodynia warrants further studies.

B024**Stimulation or lesioning of dopaminergic A11 cell group affects neuronal firing in the trigeminal nucleus caudalis**Annabelle Charbit¹, P Holland², PJ Goadsby²¹UCL Institute of Neurology, ²Headache Group, ION, UK

Introduction The A11 nucleus, located in the posterior hypothalamus, provides the only known source of descending dopaminergic innervation for the spinal grey matter. The study aimed to investigate the effect of A11 stimulation and lesioning on trigeminovascular nociceptive transmission in the rat.

Methods Male Sprague-Dawley rats were anaesthetised with propofol (20–25 mg/kg⁻¹/hr⁻¹). Extracellular recordings were made in the trigeminal nucleus caudalis (TNC), in response to electrical stimulation of the middle meningeal artery (MMA, 8–16 v, 0.2–1 ms, 0.5–0.8 Hz). Receptive fields were characterised by mechanical noxious and innocuous stimulation of the ipsilateral ophthalmic dermatome. After recording baseline firing evoked by MMA stimulation (20 sweeps) and receptive field nociceptive or innocuous stimulation (2 s), the A11 was either stimulated (5–50 µA, 0.5 ms, 5–100 Hz; n = 14) or lesioned (200–1000 µA, 0.5 ms, 20–50 Hz for 2–3 minutes; n = 8) and the effect on TNC firing determined.

Results Stimulation of the A11 significantly inhibited MMA ($F_{4,48,5} = 2.59$; P $F_{0,0,108,0} = 4.58$; P n = 5) (MMA: $F_{1,3,8} = 1.65$; P = 0.284; Noxious pinch: $F_{1,32,6} = 2.12$; P = 0.266). Lesioning of the A11 significantly facilitated evoked firing of neurons from the TNC (MMA: $F_{2,3,13,6} = 3.62$; P $F_{3,0,14,9} = 4.60$; P $F_{4,0,23,8} = 2.43$; P

Conclusion Neurons in the A11 may through a dopaminergic mechanism modulate trigeminovascular nociceptive traffic.

B025**Pre- and post-synaptic involvement of GluR5 kainate receptors in trigeminovascular nociceptive processing**Anna Andreou¹, P Holland², P Goadsby²¹Headache group, Institute of Neurology, London, ²Headache Group, Institute of Neurology, UK

Objectives To investigate the possible involvement of kainate receptors carrying the glutamate receptor subunit GluR5 in trigeminovascular nociceptive processing in the trigeminocervical complex (TCC).

Methods Rats were anaesthetised with pentobarbitone (60 mg/kg) and cannulated for measurement of blood pressure and maintenance of anaesthesia. Wide-dynamic-range neurons (n = 30), responding to electrical stimulation of the middle meningeal artery (MMA) and microiontophosphorised L-glutamate, (2S,4R)-4-Methylglutamic acid (SYM2081; kainate receptor agonist), (S)-(-)-5 Iodowillardiine (IWA; specific GluR5 receptor agonist) or the α -amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) receptor agonist (S)-(-)-5-Fluorowillardiine (FWA), were studied. The effect of (S)-1-(2-amino-2-carboxyethyl)-3-(2-carboxybenzyl)pyrimidine-2,4-dione (UBP302), a specific GluR5 receptor, antagonist was also studied.

Results Application of UBP302 significantly inhibited cell firing responses to IWA.

Conclusions The data provides evidence for the presence of GluR5 carrying kainate receptors on second order neurons, particularly in superficial laminae of the TCC. The significant facilitation observed with MMA stimulation responses at high doses of UBP302, suggests the possible involvement of pre-synaptic GluR5 kainate receptors in trigeminovascular nociceptive processing.

B026**Are cortical spreading depression and aura in migraine causally linked?**Julia Wolthausen¹, S Sternberg², C Gerloff¹, A May²¹Neurology, ²Systems Neuroscience, University of Hamburg, Germany

Introduction During the past decades, the pathophysiology of migraine has been discussed controversially. Lately, the underlying mechanisms of cortical spreading depression (CSD) have received strong consideration.

Cases We describe three patients (two of which are first grade relatives), each fulfilling the IHS criteria for migraine with aura. All three patients suffered from more than five headache attacks per month. Two patients (mother and daughter) were treated with Flunarizine and the third patient with Topiramate for the duration of four month. All patients reported that aura symptoms resolved completely, whereas the migraine headache attacks persisted with the same frequency and intensity.

Discussion Recent neuroimaging and magnetoencephalography studies in humans have provided inferential evidence that CSD-like phenomena within the occipital lobe generate visual aura. However, it remains controversial whether or not CSD may cause headache.

In our patients, the migraine prophylactic agents impeded aura symptoms (probably by suppressing CSD) without attenuating the headache. These observations question the theory that CSD (silent or not) is a prerequisite in migraine headache. A lack of causal correlation between CSD and headache would also explain why numerous patients experience migraine with and without aura or even isolated auras and why aura symptoms do not predict the side of the headache.

Conclusions We suggest that in our patients CSD is not a prerequisite for developing a migraine headache. Further investigation is needed to elucidate the question whether migraine headache and aura are causally related.

B027**Interictal cortex excitability in transcranial magnetic stimulation of migraine and chronic tension type headache**Jeongho Han¹, D. E. Kim¹, E. J. Choi²¹Psychiatry, Evergreen Neuropsychiatric Clinic, ²Neurology, Seoul Veterans Hospital, Korea

Objectives The pathophysiology of migraine is only partly understood. Transcranial magnetic stimulation has been

developed to study cortical physiology noninvasively. Chronic tension-type headache has not been studied with transcranial magnetic stimulation. Among other hypotheses, it has been proposed that interictal hypoexcitability could be partly responsible for the migraine.

Methods Patients were divided into three groups: normal subjects ($n = 30$), migraine with ($n = 11$) or without aura ($n = 19$) and chronic tension-type headache ($n = 30$) according to the International Headache Society criteria. We studied cortical excitability between normal subjects and patients with migraine with or without aura and between normal and patients with chronic tension-type headache.

Results The mean amplitude of cortex and spinal cord for normal subjects was 3.76 ± 1.74 mV, 2.03 ± 1.54 mV (abductor digiti minimi muscles, respectively) and 2.99 ± 2.04 mV, 3.88 ± 3.89 mV (abductor hallucis muscles, respectively). The mean amplitude of cortex and spinal cord for migraine with aura or without aura was 2.16 ± 1.21 mV, 0.90 ± 0.80 mV (abductor digiti minimi muscles, respectively) and 1.88 ± 1.23 mV, 2.31 ± 2.25 mV (abductor hallucis muscles, respectively). The mean amplitude of cortex and spinal cord for chronic tension-type headache was 1.61 ± 0.50 mV, 0.72 ± 0.32 mV (abductor digiti minimi muscles, respectively) and 1.54 ± 0.55 mV, 1.51 ± 0.59 mV (abductor hallucis muscles, respectively). The amplitude of motor evoked potentials of cortex and spinal cord in migraine and chronic tension-type headache showed significant decreases compared to normal subjects ($p < 0.001$).

Conclusions These results are explained by cortical and spinal hypoexcitability in migraine and chronic tension-type headache. We suggest that enhanced serotonergic activity could be some rule for cortical hypoexcitability.

B028

Cortical blood flow change in the primary headache: a study using near-infrared spectroscopy

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Objectives To evaluate cortical blood flow change in the patients with the primary headache during attacks.

Methods In the present study, we investigated 8 patients with migraine without aura and 2 tension type headaches by means of multi-channel near-infrared spectroscopy (NIRS) during headache attacks. NIRS was covered over the bilateral parietal lobes. Analysis was performed mainly for the change of oxygenated hemoglobin in 2 minutes.

Results Significant differences of oxygenated hemoglobin between the left and right hemisphere were found in patients with migraine. In addition, increased oxygenated hemoglobin was found in the hemicrania side. However, these changes could not be observed in the patients with tension type headache.

Conclusion NIRS is an optical method, which allows non-invasive *in vivo* measurements of blood flow changes in the brain tissue. Our data suggest that significant differences of blood flow change between the left and right hemisphere can be detected by multi-channel NIRS only in migraine, and

these data may be useful for understanding the pathophysiological mechanism of migraine.

B029

Plasma matrix metalloproteinase-9 levels of migraineurs increase during headache free periods

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Background and objective The cortical spreading depression (CSD) and the neurogenic inflammation have been hypothesized to play essential roles in development of migraine headache.

Recent studies suggested possible association of matrix metalloproteinase-9 (MMP-9) to CSD, inflammation, and cerebral ischemia. MMP-9 (or gelatinase B) has a broad range of specific substrates such as native collagens as well as elastin, fibrillin, and osteonectin. To explore the alteration of MMP-9 in migraine, we investigated plasma MMP-9 levels of migraine sufferers.

Methods Eighty-four subjects (mean age \pm SD; 33.4 ± 13.0 years) with migraine headache and 61 headache free healthy controls (32.5 ± 11.1 years) were participated in this study. Venous blood samples were collected during the headache-free period. Plasma MMP-9 levels were determined by enzyme-linked immunosorbent assay.

Results The mean plasma MMP-9 level in migraineurs was 42.5 ± 4.6 (SE) ng/ml, which was significantly higher than in the controls (25.4 ± 2.7 ng/ml, $p = 0.004$, Student's *t* test). There was no significant difference between migraine with aura and without aura. The MMP-9 levels did not correlate with age, duration of illness, or frequency of migraine headache. In addition, we measured MMP-9 in subjects with tension type headache ($n = 23$, mean age 51.3 ± 18.2). The mean MMP-9 level (24.6 ± 4.8 ng/ml) did not differ from that in the controls.

Conclusions The increased degradation of extracellular matrix with MMP-9 may associate with occurrence and development of migraine attacks. The further studies of MMPs in migraine are necessary.

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B030

Involvement of orexin-A in medication-overuse headache: findings in cerebrospinal fluid

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Background Experimental evidence suggests the involvement of the hypothalamic neuropeptide orexin-A in stress, motivation and reward. Corticotrophin-releasing factor (CRF) has been recognized to be responsible for its relay. A putative role of the CRF/orexin-A system can therefore be hypothesized in medication-overuse headache (MOH).

Patients and methods Twenty-five patients with chronic migraine (CM) and 30 MOH patients were admitted to our hospital to undergo a lumbar puncture. Twenty age-matched subjects who underwent lumbar puncture for diagnostic purposes and for whom CNS or systemic diseases were excluded served as control group. Both orexin-A and CRF were determined by RIA methods.

Results Significantly higher levels of orexin-A and CRF were detected in the CSF of MOH patients and, to a lesser extent in patients with CM without medication overuse (orexin-A = $p < 0.001$ and $p < 0.02$, CRF = $p < 0.002$ and $p < 0.0003$). A trend toward a positive, although not significant, correlation emerged between orexin-A and CRF levels in the CSF of MOH patients. A significantly positive correlation was found in the same group between CSF orexin-A, daily drug intake and Leeds Dependence Questionnaire (LDQ) scores ($r = 0.53$; $p < 0.001$ and $r = 0.48$; $p < 0.002$, respectively).

Discussion These findings support the involvement of the CRF/orexin-A system in the negative motivational state that drives drug dependence in MOH. This is suggested by the correlation between analgesics abused and LDQ scores. The slight but significantly higher levels found in CM without medication overuse can be interpreted as an expression of hypothalamic response to stress due to chronic pain.

B031

Reduced cerebellar inhibition in migraine with aura: a TMS study

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Objectives Several evidences point to the involvement of cerebellum in migraine. Indeed, calcium channels are strongly expressed in cerebellar cortex and subtle clinical cerebellar alterations have been found in migraine with aura. Moreover, abnormalities in visual and motor cortex excitability consistent with a lack of inhibitory efficiency, have been described in migraine and it is known that cerebellum exerts an inhibitory control on motor and non motor areas of cerebral cortex. The aim of the present study was to investigate if impairment of cerebellar activity on motor cortex, i.e. reduced inhibitory control, can be found in migraine.

Methods 7 patients affected by migraine with aura and 8 healthy controls underwent an experimental protocol with transcranial magnetic stimulation (TMS) designed to investigate the cerebellar inhibitory drive on motor cortico-spinal pathways: a conditioning pulse on right cerebellar cortex was delivered 5, 7, 10, 15 msec before a test stimulus on contralateral motor cortex. The cerebellar conditioning stimulus inhibits the size of the motor evoked potential (MEP) produced by the test stimulus by approximately 30–50%. Amplitude of conditioned (cerebellar stimulation) MEP is measured as percentage of amplitude of MEP test alone.

Results Significant inhibition of motor cortex was induced by cerebellar stimulation, in healthy subject. On the contrary, no reduction of MEP test was found after cerebellum conditioning in patients.

Conclusions Cerebellar inhibition is reduced in migraineurs; this could account for the reduced inhibitory efficiency of cerebral cortex showed in previous studies, suggesting a pathophysiological role of cerebellum in migraine.

B032

Saharan desert dust containing atmospheric conditions activate trigeminovascular system

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Objectives Recently it has been noticed that dust originating from Saharan Desert transported to other continents by atmosphere has an influence on public health. The microorganisms present within the dust particles becomes active and releases oxalate and forms bioavailable iron upon contact with cloud water. Thus, the chemical and biological composition of air can be altered significantly during periods when the atmosphere is dominated by air mass originating from desert regions. We aim to evaluate whether the Saharan dust containing weather could trigger trigeminovascular system.

Methods Freely moving rats incubated within simulated atmospheric conditions containing (a) Saharan dust, (b) Co60 treated Saharan dust (sterilized) and (c) dust free air, were investigated for the presence of c-fos expression (immunohistochemically) in trigeminal nucleus caudalis (TNC), and NOx (Griess method) and MDA level in plasma samples. Atmospheric samples were analyzed for microorganisms.

Results Saharan dust containing atmospheric conditions induced c-fos expression in nociceptive neurons within TNC. Number of c-fos positive neurons in lamina I and II was significantly higher in Saharan dust group (30.43 ± 5.2 , $p = 0.0001$) compared to dust free air (11.02 ± 1.8) or Co60 treated Saharan dust group (15.01 ± 2.4). Significant increase in NOx and decrease in MDA levels were detected in plasma samples of rats exposed to Saharan dust containing atmosphere.

Conclusion This study has revealed an unknown environmental factor as possible a triggering factor of headache. It is the first time that, transport of Saharan dust with atmospheric air stream is documented to trigger trigeminovascular system directly or indirectly in animals. Further studies are needed to explore the mechanisms mediating this nociceptive effect to guide for new treatment strategies.

B033

Endocannabinoids and serotonin levels in platelets of medication-overuse headache and chronic migraine patients

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Background Based on experimental evidence of the antinociceptive action of endocannabinoids, a dysfunction of this

system in medication-overuse headache (MOH) and chronic migraine (CM) is hypothesized.

Objective To test this hypothesis, we determined the levels of the endogenous cannabinoid 2-arachidonoylglycerol (2-AG) and arachidonoyl ethanolamide (anandamide, AEA) in platelets of 15 patients with MOH, 15 patients with CM and 15 age-matched control subjects and also related these levels to those of serotonin.

Methods Endogenous cannabinoids were purified from platelet pellets by high-performance liquid chromatography (HPLC), and quantified by isotope dilution gas-chromatography/mass-spectrometry. Platelet serotonin levels were also measured by HPLC.

Results In both patients and controls the content of 2-AG was about 20-fold greater than that of AEA. 2-AG and AEA levels were significantly lower both in MOH and CM patients than in controls ($p < 0.02$ and $p < 0.04$, respectively), without significant differences between the two groups. Serotonin levels were significantly reduced in both patient groups ($p < 0.001$ and $p < 0.002$, respectively) and were significantly correlated with 2-AG and serotonin levels (0.48, $p < 0.01$ and 0.46, $p < 0.02$).

Conclusions The above results may reflect an imbalance in the endocannabinoid system occurring in parallel with serotonergic dysfunction both in CM and MOH. These concur with experimental findings of mutual interaction of 2-AG and 5-HT in modulating different signalling pathways relevant for pain processing. Variations in AEA transporter and AEA hydrolase activity in platelets remain to be established in CM and MOH.

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B034

Infusion of glyceroltrinitrate facilitates CGRP release but not transcription in rat trigeminal ganglia

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Infusion of a nitric oxide (NO) donor has been shown to cause delayed headaches in humans and delayed activation of central trigeminal neurons that process intracranial afferent input in rats (Ashina 2004, Koulchitsky 2004). NO may increase the release or production of calcitonin gene-related peptide (CGRP), a key mediator in primary headaches (Fanciullacci 1995).

Following two hours infusion of the NO donor glyceroltrinitrate (GTN, 500 µg/kg), the NO synthase inhibitor N- ω -nitro-L-arginine-methyl-ester (L-NAME, 60 mg/kg) or saline under isoflurane anaesthesia trigeminal ganglia from adult male Wistar rats were dissected. A reversible increase in immunoreactive CGRP release was evoked by 5 minutes application of inflammatory mediators (pH 6.1; PGE2 10 mM, bradykinin 10 mM, histamine 10 mM, serotonin 10 mM), which was facilitated by preinfusion of GTN by 80% and

suppressed by pretreatment with L-NAME by 40% compared to animals with saline infusion.

In separate experiments total mRNA was extracted from rat trigeminal ganglia 0.5 or 6 hours after GTN (500 µg/kg) or saline infusion over two hours, untreated animals served as control. After reverse transcription a real time PCR for relative quantification of CGRP was performed using the housekeeping genes GAPDH and α -Actin as reference genes for normalisation. No difference between GTN and saline treated groups could be detected at 0.5 or 6 hours after infusion.

The present data suggest that a prolonged increase of NO levels facilitates CGRP release from rat trigeminal ganglion, which is not based on altered CGRP gene transcription.

B035

GluR5 kainate receptor activation inhibits trigeminal neurogenic dural vasodilation

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Objectives To investigate the possible involvement of pre-junctional kainate receptors which carry the glutamate receptor subunit 5 (GluR5) in a model of neurogenic dural vasodilation (NDV).

Methods Rats were anaesthetised with pentobarbitone (60 mg/kg) and cannulated for measurement of blood pressure, experimental drug administration and maintenance of anaesthesia. The effects of the specific GluR5 antagonist (S)-1-(2-Amino-2-carboxyethyl)-3-(2-carboxybenzyl)pyrimidine-2,4-dione (UBP302; 50 mg/kg) and the specific GluR5 agonist (S)-(-)-5 Iodowillardiine (IWA; 10 mg/kg) were investigated on neurogenic and CGRP induced dural vasodilation, using intravital microscopy.

Results Administration of IWA was able to inhibit MMA dilation caused by electrical stimulation ($F_{3,12} = 10.6$; $P F_{2,11} = 0.59$; $P = 0.59$). Administration of the GluR5 antagonist UBP 302 alone had no significant effect on NDV. CGRP (1 mg/kg) induced dural vasodilation, was not inhibited by the GluR5 agonist IWA ($F_{2,9} = 3.2$; $P = 0.08$).

Conclusions The current study demonstrates that activation of the GluR5 kainate receptors with the selective agonist IWA is able to inhibit neurogenic dural vasodilation. This effect is likely to result from inhibition of pre-junctional release of CGRP from trigeminal neurons.

B036

Evidence for a peripheral mechanism of facial allodynia

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Objectives Migraine is much more common in women than in men, and migraineurs often present with allodynia in the

distribution of all three branches of the trigeminal nerve (V1, V2, and V3). Allodynia in the distribution of V2 and V3, i.e. secondary allodynia/hyperalgesia, is thought to be centrally mediated. We used an established model of inflammatory trigeminal pain – injection of Complete Freund's adjuvant (CFA) to the masseter muscle – to study the effect of estrogen treatment on inflammatory secondary hyperalgesia.

Methods Ovariectomized female Sprague-Dawley rats were injected in the masseter with CFA or saline and subcutaneously administered estradiol or vehicle. Withdrawal response to stimulation of the whisker pad using (V2) von Frey filaments was measured.

Results CFA injection to the masseter (V3) in conjunction with estrogen treatment increased withdrawal response compared to CFA alone, indicating an additive effect of CFA and E2 on secondary hyperalgesia. Immunohistochemical labeling of extracellular-signal regulated kinase (ERK), a MAPK involved in inflammatory pain responses, showed increased ERK activation in V2 neurons of ganglia from CFA + E2 treated rats. In order to block ERK activation in the periphery, we stereotactically administered ERK antagonist U0126, or inactive control U0124, to the trigeminal ganglion of CFA + E2-treated rats. Animals treated with U0126 showed a decrease in withdrawal response to von Frey filament stimulation of the whisker pad compared to U0124-treated rats.

Conclusion Allodynia in V2 induced by inflammation in V3 was reduced by antagonizing ERK activation in the ganglion. These data suggest a peripheral component to secondary inflammatory hyperalgesia mediated through activation of ERK.

B037

Reduced threshold for cortical spreading depression in female mice

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Objectives The prevalence of migraine is much greater in females than males. Cortical spreading depression (CSD) is thought to be a fundamental mechanism of migraine, and CSD in rodents is used as a model for migraine. We investigated whether female and male mice have different thresholds for CSD.

Methods We used optical intrinsic signal imaging (OIS) and electrophysiological techniques to investigate CSD threshold in female (n = 13) and male (n = 15) C57Bl/6 mice. In separate groups of experiments, we used controlled release of 1M KCl, and tetanic stimulation, to induce CSD.

Results We found that female mice had a significantly reduced threshold for induction of CSD compared to male mice, using both CSD induction methods. Threshold for CSD induction was $0.34 \pm 0.06 \mu\text{L}$ of KCl in females ($\pm\text{S.E.}$, n = 6 mice) vs. $0.59 \pm 0.09 \mu\text{L}$ of KCl in males (n = 8 mice; $p < 0.03$). In tetanic stimulation experiments, mean threshold for CSD induction was 271 ± 87 vs. 586 ± 94 micro-Coulombs in females (n = 7 animals) vs. males (n = 7 animals; $p < 0.02$). There was no significant difference in amplitude, velocity or

spread of CSD by OIS, nor was there any difference in amplitude of DC shift, between females and males.

Discussion These results suggest an increased cortical excitability in female mice that may be independent of the estrous cycle, and may contribute to the understanding of the increased prevalence of migraine in women.

B038

Effects of topiramate on migraine frequency and cortical excitability in patients with frequent migraine

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We studied the excitability of the visual and motor cortex in 36 patients with frequent migraine without aura (30 females, mean age 38.6 ± 10.0 years) before and after treatment with topiramate (100 mg/day) using transcranial magnetic stimulation.

Topiramate dosage was increased in 25 mg per week until a target dosage of 100 mg/day, which was continued for another 4 weeks. Headache frequency was documented in headache diaries. Phosphene and motor thresholds (on both sides) were assessed before and 8 weeks after treatment.

Treatment with topiramate resulted in reduction of both, headache frequency (11.0 ± 2.7 to 5.6 ± 3.6 migraine days per month; $p = 0.004$) and cortical excitability: motor cortex thresholds increased on the right side from $44.3 \pm 7.1\%$ to $48.1 \pm 8.9\%$ ($p = 0.049$) and on the left side from $44.2 \pm 8.1\%$ to $48.4 \pm 9.5\%$ ($p = 0.047$), phosphene thresholds increased from $57.4 \pm 12.0\%$ to $70.2 \pm 12.3\%$ ($p = 0.0001$). Interestingly, we found an inverse correlation between increase of visual thresholds and reduction of headache frequency (Spearman's rho = -0.55 , $p = 0.002$). No significant correlations were observed between increase of motor thresholds and reduction of headache frequency.

The neurobiology of the preventive effect of topiramate in migraine seems to be very complex and can not be explained simply via inhibition of cortical excitability. Our findings also cast doubts on the usefulness of TMS thresholds as surrogates of migraine disease activity and the role of cortical excitability in migraine vulnerability.

B039

Headache in multiple sclerosis

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Objective To verify the association between headache and Multiple sclerosis. MS is a chronic demyelinating disease of the CNS and headache could be a problem in MS patients. Headache in multiple sclerosis can be classified into 2 diagnostically and therapeutically relevant categories. (1) Headache directly related to MS: Primary headache (diagnoses according to International Headache Society criteria) in

MS could be due to migraine, tension-type headache and cluster headache. The prevalence of migraine-like headache in patients with MS is associated with plaques in the brainstem or in other locations. A linear trend is observed between numbers of lesion locations and migraine-like headaches, so that presence of a midbrain plaque in patients with MS is associated with an increased likelihood of headache with migraine characteristics. (2) Treatment-related headache: It can be occurred as side effect of beta interferons or glatiramer acetate therapy and/or following treatment with under-study drugs, such as Fingolimod (FTY720), and/or Intravenous Immunoglobulin (IVIg). The increase of serum IL-6 level in response to IFN-beta administration was associated with headache, arthralgia, and disability score at the initiation of the therapy. Regarding, the (ICHD-II) has recently recognized that secondary headaches may occur in patients affected by inflammatory diseases of the CNS, classifying them among the headaches attributed to non-vascular intracranial disorders.

Conclusion The aim of this study is to verify the association between headache and MS as an inflammatory disease of the CNS, by a review of the literature data on the topic, integrated by personal cases and data.

B040

Effects of calcitonin gene-related peptide on meningeal afferent activity in vitro

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Calcitonin gene-related peptide (CGRP) is regarded as a key mediator in the generation of headaches. Since CGRP can release migraine attacks in migraineurs, it has been assumed to stimulate the trigeminovascular system. In an *in vitro* preparation of rodent cranial dura mater we examined the effect of CGRP on the activity of primary meningeal afferents.

A hemisected rat skull lined with cranial dura was superfused by physiological solution. Multifiber and single unit recordings were made with glass pipettes attached to the spinosus nerve. Receptive fields in the dura were identified by electrical stimulation and probing with von Frey filaments. The units were characterised by their responses to mechanical stimulation, heating and cooling. The activity of units and the latency to repetitive electrical stimulation were monitored under control conditions and superfusion with CGRP (10^{-7} M) and CGRP8-37 (10^{-6} M).

Seven of 31 slowly conducting units were activated by CGRP superfusion in a delayed manner. The responsiveness to CGRP was not correlated to any functional property of the units like conduction velocity or responses to other stimuli. The responses could not clearly be blocked by CGRP8-37. In a second set of experiments both CGRP and CGRP8-37 reversibly lowered the activity-dependent slowing of conduction velocity during electrical stimulation at 2 Hz in all units.

In conclusion, a small proportion of meningeal afferents is activated by CGRP without preference of the functional types

of units. The effect on the activity-dependent slowing seems to be unspecific.

B041

Sex differences in the trigeminal and peripheral pain perception

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Sex-specific differences in pain perception have been suggested by previous experimental and epidemiological studies. In order to evaluate the physiological sensory and pain thresholds in the trigeminal and peripheral innervation, we enrolled 80 age-matched healthy subjects without any medication except hormonal contraception (43 men, 37 women; mean age of 23.4 ± 5.3). After evaluation of Beck's depression and anxiety inventory and of the pain disability inventory, we applied electrical stimuli in the masseter (i.e., trigeminal) and the tibial (i.e., peripheral) muscle region. We recorded the sensory and pain threshold (in mA), the rating in the visual analogue scale after threefold painful stimulation, and the pain rating after repetitive stimulation within a time interval of 30 seconds. Measurements after trigeminal stimulation revealed a significantly decreased pain threshold in women. All other pain measurements were not significantly different between men and women. After peripheral stimulation, significantly decreased sensory and pain thresholds and significantly increased pain ratings were noted for women (e.g., 9.6 ± 5.2 versus 5.6 ± 4.0 mA for pain threshold; $p < 0.001$). Pain habituation as measured by the difference between first and second repetitive stimulation was significantly lower in women than in men. Healthy women show lower peripheral pain and sensory thresholds as measured by external electrical stimuli. This phenomenon could not be observed after trigeminal stimulation except a decreased pain threshold. Our study confirms previous observations of increased pain sensitivity in women by a biological-physiological approach. However, this phenomenon is much more prominent in the peripheral than in the trigeminal pain perception and does not reflect emotional pain perception.

B042

Sleep apnea in cluster headache – a case-control study

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Cluster headache often occurs in the night and has been associated with an increased rate of obstructive apneas, attacks often start during REM sleep. However, controlled prospective studies are missing to analyse these associations. We enrolled 37 consecutive cluster headache patients in a prospective study on sleep apnea screening. A control group with 37 subjects matched according to age, sex and body mass

index was also investigated. The RDI was significantly higher in cluster headache patients than in controls (5.9 ± 13.6 versus 2.6 ± 2.3 ; $p < 0.01$). The desaturation index was 5.8 ± 10.6 in cluster headache and 1.1 ± 1.4 in controls ($p = 0.004$). The rate of cluster headache patients fulfilling the criteria for obstructive sleep apnea was 30% versus 5% in control subjects ($p < 0.006$). There was a significantly higher rate of central apneas in cluster headache. These results were all obtained only when the patients were in an active cluster headache episode or were chronic cluster headache sufferers. Our data suggest that active cluster headache is associated both with obstructive and with central sleep apnea. The increased BMI of cluster headache patients does not play a role in this association. The increased rate of central sleep apneas suggests an involvement of the hypothalamus in the sleep pathophysiology of cluster headache.

B043

Trigemino-autonomic activation in experimental pain

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Autonomic parasympathetic activation ipsilateral and simultaneously to unilateral trigeminal pain is a hallmark of a group of primary headache disorders called trigemino-autonomic cephalgias (TAC). However, it is not fully understood whether these symptoms are unspecific accompanying features or specific for these disorders. We injected 0.05 ml capsaicin (0.01 percent) into the forehead of 16 healthy volunteers and carefully observed and documented the appearance of autonomic symptoms. All but two exhibited at least one parasympathetic symptom lasting between 2 and 15 minutes. The most frequent symptom was lacrimation, 11 volunteers had additional autonomic symptoms such as miosis, ptosis, conjunctival injection, and nasal congestion. The concomitant pain was rated between 7 and 10 (VAS 0–10). There was no correlation between the occurrence or duration of autonomic symptoms and the intensity of pain. Injection of capsaicin into the third trigeminal branch produced lacrimation in two subjects but no further autonomic symptoms. Our results suggest that strong pain signals in the ophthalmic division of the trigeminal nerve are sufficient to involve the autonomic system via a trigeminal-autonomic reflex regardless whether the pain is a primary headache or an experimental pain. This finding suggests that activation of the superior salivatory nucleus is unspecific.

B044

Migraine and left-handedness are not associated

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Since 1982 an association between migraine and left-handedness has been discussed with controversial results. It has been suggested that both migraine and left-handedness might be established during the same fetal period. In order to investigate the possible association between migraine and left-

handedness, we enrolled 100 patients with a diagnosis of migraine according to the IHS criteria and 100 age- and sex-matched control subjects into a case-control-study. Handedness was determined by a modified version of the Edinburgh Handedness Inventory. There was no significant difference in the frequency of left-handedness between the migraine patients (4%) and the healthy control group (8%). Also, the laterality quotient was not significantly different. This study does not support Geschwind and Behan's hypothesis of an association between migraine and left-handedness. Additionally, we pooled our data with that from five comparable studies, which did, however, not alter the result. We conclude that there is no association between migraine and left-handedness.

B045

CGRP-antibody; a potential therapeutic tool in migraine treatment

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Calcitonin gene-related peptide (CGRP), present in perivascular sensory nerve endings, is a potent endogenous dilator of cerebral and meningeal arteries. For this reason CGRP is implicated in migraine pathophysiology because of its migraine provoking effects. Furthermore, a selective antagonist has documented efficiency in the treatment of migraine attacks. Instead of blocking the CGRP-receptor, scavenging CGRP itself might be a new therapeutic principle in migraine.

Objective To investigate the effect of a monoclonal CGRP-antibody *in vivo/in vitro* on CGRP and neurogenic vasodilatation of cerebral and meningeal arteries.

Method *In vivo* we used the closed cranial window model to visualize cerebral and meningeal arteries simultaneously in the same rat, before and after CGRP-administration and electrical stimulation in the presence and absence of CGRP-antibody. *In vitro* we used a conventional myograph and perfusion-system to characterize concentration-response curves and the effects of the blood-brain barrier.

Results *I.v.* infusion of 0.3 μ g/kg CGRP induced dilatation of the dural and pial artery. Pretreatment with 10 mg/kg of CGRP-antibody resulted in a significant attenuation of the response of the dural artery diameter only. The response by electrical stimulation was not inhibited by the CGRP-antibody. The CGRP-antibody showed partial inhibiting effect (abluminal application only) in the myograph and the perfusion system.

Conclusion The CGRP-antibody significantly inhibited the effect of systemic CGRP-induced vasodilatation of dural artery. The vasodilatation evoked by electrical stimulation was not affected by the CGRP-antibody. In the myograph, CGRP-antibody inhibited relaxation of MCA in a dose-dependent manner while in perfusion-system only abluminal CGRP-antibody administration had an effect.

B046**White matter lesions and migraine**

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Background There is close correlations between subclinical ischaemic strokes and white matter lesions (WML) in migraineurs as shown by imaging studies. T2-weighted images of migraine patients displayed hyperintense lesions in 6–29% of the cases in different studies. It is well known that the presence of migraine, especially migraine with aura, is an important risk factor for ischaemic stroke.

Aim of this study is to investigate the clinical and diagnostic features of migraine patients with and without WML in T2-weighted MR images.

Method Patients, according to the criteria of ICD-II, diagnosed as migraine with and without aura were subjected in this prospective study. Following to obtain informed consents, patients were grouped according to the presence or absence of WML as group 1 and group 2, respectively. Each group has been evaluated considering their demographic data, medical history, physical and neurological findings, the features of headache, hemogram, biochemical analysis and the level of homosistein.

Results When the headache characteristics and demographic data were compared no differences were encountered between two groups. However, mean homosistein level was found to be higher in patient with WML in MRI.

Conclusion Except the higher levels of homosistein, the presence of WML in migraine patient did not differ for the vascular risk factor and other clinical features. Hence, the association between migraine and ischaemic stroke seems to be hypothetical rather than evidence based although there seem to be a proximity between migraine with aura and white matter lesions in our subjects.

B047**Properties of rodent meningeal afferents recorded in an in vitro preparation**

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Functional properties of intracranial trigeminal afferents are relevant with regard to the generation of headaches but there is only limited data from *in vivo* recordings. We have developed an *in vitro* preparation of rat cranial dura mater in which basic properties and the response behavior to various stimuli of primary meningeal afferents can be studied.

The hemisected rat skull lined with cranial dura is used as an organ bath superfused by physiological solution at 34°C. A micropipette is attached to the dissected spinous nerve for multifibre or single unit recordings. Receptive fields in the dura are identified by electrical stimulation and probing with von Frey filaments. The units are characterised by their responses to mechanical stimulation, heating and cooling. A

pulse protocol of electrical stimuli enables measurements of electrical thresholds and activity-dependent conduction velocity slowing under control and stimulation conditions.

Dural afferents showed conduction velocities in the A- and C-fibre range. The activity-dependent slowing was negatively correlated with the conduction velocity and suggests the existence of TTX-resistant sodium channels in the sensory endings. Major proportions of dural afferents responded to heating at various thresholds and to capsaicin, small proportions were activated by cooling and by chemical stimuli like histamine and calcitonin gene-related peptide but not by nitric oxide.

The *in vitro* preparation can be used for extensive characterisation of biophysical and sensory properties of meningeal afferents and will be used in the future for testing the peripheral effects of substances relevant for the generation and the treatment of headaches.

B048**Effect of paracetamol on neurovascular response to cortical spreading depression**

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Objectives To determine the effect of paracetamol on development of cortical spreading depression (CSD), CSD-evoked cortical hyperaemia and trigeminal nociception.

Methods Adult male Wistar rats were separated into paracetamol and controlled groups (8 rats each). The experimented group received paracetamol (200 mg/kg BW, intraperitoneally) 1 hour before CSD induction. Three milligrams of solid potassium chloride was placed on parietal cortex to elicit CSD. Electrocorticogram was recorded and area-under-curve of the wave of depolarisation shift was calculated. Cortical blood flow was monitored with laser Doppler flowmetry and data were reported as percent of baseline value. One hour after CSD induction, rat brains were removed for Fos-immunohistochemistry. Fos-immunoreactive (Fos-IR) neurons in trigeminal nucleus caudalis (TNC) were counted.

Results Application of potassium chloride led to the development of series of depolarization shift, cyclical hyperaemia and induced expression of Fos in TNC neurones. The area-under-curve of total CSD waves recorded in one hour in the paracetamol and control groups were 980.3 + 471.5 and 1220.7 + 304.7 mV min, respectively. Peak amplitudes of CSD-evoked cortical hyperaemic waves were 187.8 + 48.7 and 153.1 + 76.7 percent of baseline for paracetamol and control groups respectively. No statistically significant difference was observed between the two groups. Pretreatment with paracetamol significantly decreased the number of Fos immunoreactive cells in TNC. The numbers of Fos-immunoreactive cells in the paracetamol and control groups were 10 + 3 and 27 + 8 cells per slide, respectively, $p < 0.05$.

Conclusion Modulation of CSD is unlikely to explain the analgesic mechanism of paracetamol in the process of CSD-induced trigeminal nociception.

B049**Dura mater stimulation alters the behaviour of rats**

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Experimental animal models of migraine are often criticized because of the lack of possibilities to assess headache. Therefore, we investigated whether stimulation of rat dura mater with a pro-inflammatory agent causes behavioural changes consistent with the development of pain.

Rats were anaesthetized and the skull was carefully removed above the meningeal vessels. A refilling chamber was embedded in the skull above the exposed dura mater. After 24 hours the animals were again anaesthetized with Isoflurane (1 min), rectal temperature was measured and the chamber was rinsed with saline. A fixed volume of IL-1 β (10 ng/ml) or vehicle was applied to the meninges. Non-operated and sham operated rats were also studied (n = 11/group). Six hours later locomotor activity and exploratory behaviour were assessed in the open field for 10 min. Feeding behaviour was also observed.

Rectal temperature was not stat. different between groups. Rats exposed to IL-1 β moved significantly less in the open field as measured by the number of squares crossed and also showed reduced rearings compared to all other groups (p < 0.05). Food intake in the first hour was significantly reduced in IL1- β treated rats compared to all other groups (p < 0.05). However, there was no difference between all groups in the intake of highly palatable bait (cherry flavoured sweetened agar).

This study shows for the first time, at least to our knowledge, that meningeal stimulation leads to behavioural changes in rats. Our findings point to the possibility that rats are able to develop stimulus induced meningeal pain.

B050**Trigeminal autonomic cephalgias and hemicrania continua: persistent foramen ovale-related disorders?**

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Previous studies have linked persistent foramen ovale (PFO) to migraine and cluster headache, but data on other TACs are yet not available. The objective of the present work was to investigate the prevalence of right-to-left shunt (RLS) in Cluster Headache (CH), Paroxysmal Hemicrania (PH) and Hemicrania Continua (HC). Transcranial doppler cerebral arteries flow recordings following peripheral intravenous microbubbles injection (shaken 9 ml saline with 1 ml room air) were indicative of RLS if at least three microbubbles within 22 s, either at rest and following Valsalva manoeuvre, were present.

One hemicrania continua (HC, female, 20 y-o); 21 Cluster headache (CH, age: 46.6 ± 41.1, males: 90.5%) and 7 paroxysmal hemicrania (PH, age: 53.2 ± 23.5, 3 males) patients have

been examined so far. RLS was present in one HC, 10 (47.6%) CH and 5 (71.4%) PH patients. In contrast, RLS was present in 5 (33.3%) controls (n = 15, age: 30.8 ± 7.0, males: 93.3%). These preliminary data suggest that RLS prevalence in TACs and HC may be higher as n increases.

Data indicate that RLS is not specifically related to migraine. The lack of headache specificity indicates that RLS is probably not the cause of the headache disorders, but rather a trigger factor that generates distinct headache phenotypes depending on the patients' predisposition. It is possible RLS facilitates hitherto unknown right circulation originated trigger agent(s) to reach the brain starting a cascade of pathophysiological events ultimately leading to a particular primary headache.

B051**PDE9A, PDE10A and PDE11A in the rat trigeminovascular system – role in cyclic nucleotide signalling?**

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Objectives Intracellular signalling by cAMP and cGMP is central in modulation of cerebral artery diameter and function of endothelial and smooth muscle cells. Furthermore, it plays an important role in migraine pathophysiology by modulating the trigeminovascular pain signalling system. Cyclic nucleotide signalling is partly controlled through degradation by phosphodiesterases (PDEs). Of the 11 PDE subtypes presently known, we here describe the distribution of the most recently discovered subtypes (9A, 10A and 11A) in cerebral arteries, the dura mater and the trigeminal ganglion.

Methods The middle cerebral and basilar artery, dura, trigeminal ganglion and caudal trigeminal nucleus of male Sprague-Dawley rats were investigated using real-time PCR, Western blot and immunohistochemistry and compared to two peripheral arteries: the aorta and mesenteric artery, as well as the cortex and cerebellum.

Results PDE gene expression is abundant. PDE10A mRNA is present in all tissues and PDE11A mRNA is only absent from the aorta. PDE9A mRNA is found in all tissues except the trigeminal ganglion and the aorta. Protein expression as seen by Western blotting is also widespread. Immunohistochemistry show strong cytosolic immunoreactivity in the cell bodies of the trigeminal ganglion for all three PDEs.

Conclusion We here present, for the first time a characterisation of the expression of the three most recently discovered PDEs in rat cerebral arteries and in structures relevant to migraine. The functional implications are yet unknown but their location indicate that they may represent new targets for investigating cyclic nucleotide signalling in migraine pathophysiology.

B052**Increased between-attack sound sensitivity in episodic migraine – evidence for interictal sensitization?**

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Objectives To compare sound sensitivity in episodic migraine (EM) subjects with that in controls.

Methods Subjects with IHS-defined EM and age- and gender-matched controls were prospectively recruited. Demographic data and data on migraine characteristics were obtained through a structured questionnaire. Sound stimuli were administered in an audiometric booth using an enhanced real-time processor and psychoacoustic software (PSYCHRP). Sound sensitivity thresholds (SSTs) were determined by delivering pure tones (1000 Hz, 4000 Hz and 8000 Hz) at increasing intensity until a bothersome/painful level, or a maximum of 110 dB, was reached. Between-attack SSTs in migraineurs were compared to SSTs in controls. In migraineurs, between-attack SSTs were also compared to SSTs during an acute untreated attack.

Results 24 migraineurs (23 women, 1 man; mean age 30.6 ± 9.8) and 10 controls (7 women, 3 men; mean age 28.1 ± 4.6 years) were included. The median between-attack SSTs of migraineurs were lower than SSTs of controls: 97 vs. 103.8 dB at 1000 Hz ($p = 0.004$), 90.5 vs. 97 dB at 4000 Hz ($p = 0.28$), and 94.5 vs. 108 dB at 8000 Hz ($p = 0.006$). In migraineurs, within-attack median SSTs were lower than SSTs between attacks: 68.5 vs. 97 dB at 1000 Hz ($p = 0.02$), 70.3 vs. 90.5 dB at 4000 Hz ($p = 0.002$) and 73.3 vs. 94.5 dB at 8000 Hz ($p = 0.11$).

Conclusion Compared with controls, migraineurs had a higher baseline sound sensitivity. This sensitivity increased during an acute attack. These data suggest a between-attack auditory sensitization in EM that is heightened during an attack.

B053**Stellate ganglion block can exacerbate cluster headache**

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We report the case of a 46 year old lady who had had cluster headache since the age of 22, in bouts lasting up to 9 weeks, latterly every 6 months. The pains were around the left eye, occurring three times daily, with a continuous dull background pain as well. Drug treatment had proved ineffective, and 2 weeks after the start of the last bout a left stellate ganglion block with local anaesthetic and corticosteroid was performed. This caused a transient Horner's syndrome and some early relief of the background pain, but after about 4 hours the pain became exceptionally severe, and continued without diurnal variation for 6 weeks, gradually resolving thereafter.

There is much evidence of a cranial sympathetic deficit in cluster headache, which is usually considered a consequence of repeated attacks. This case suggests that under some con-

ditions the deficit may contribute to the pathogenesis of the pain; perhaps the periodicity owes something to the balance between sympathetic and parasympathetic influences on facial structures. It would seem easier to reconcile this, rather than potentially cumulative damage, with the stereotyped attacks patients experience from bout to bout, sometimes over many years.

B054**High frequency somatosensory oscillations in patients with migraine**

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Objectives To evaluate high frequency oscillations (HFOs) in patients with migraine during and between attacks.

Methods We recorded HFOs of somatosensory evoked potentials (SEPs) in patients with migraine and control subjects. Electrical stimuli were delivered to the right median nerve at their wrists. EEGs were recorded from C3€™-Fz (C3€™: 2 cm posterior to C3), using a 0.5–2000 Hz frequency filter. For separation of HFOs from the underlying N20, the wide-band signals were bandpass filtered (500–1000 Hz) and averaged. HFOs were divided into early and late phases based on the N20 peak.

Results Thirteen normal subjects and 56 migraineurs (38 migraine without aura, 18 migraine with aura; 30 between attacks, 26 within 3 days of migraine attacks) finished the study. In early-phase HFOs, patients between migraine attacks had significantly higher maximal amplitudes and trend of significance area under curve than those of our normal subjects. In late-phase HFOs, patients between migraine attacks had a significantly higher number of wavelets and of longer duration than those of our normal subjects. In patients within 3 days of migraine attacks, their early-phase HFOs were similar to those of patients between migraine attacks; whereas their late-phase HFOs were similar to those of normal subjects.

Conclusion It is suggest that early HFOs are generated by thalamo-cortical afferents, and late, by inhibitory interneurons in parietal area 3b. Our study implies that between attacks, migraine patients showed counterbalance between subcortical hyperexcitability and cortical inhibition. The inhibition decreased during migraine attacks.

B055**Cyclic brain function in migraine**

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Objectives Neurophysiological studies, mainly using evoked potentials, have earlier found evidence of a fluctuating neural dysfunction in the interval between migraine attacks. Only a few studies have used quantitative EEG (QEEG). Our aim was to estimate pre- and post-ictal brain function change in a blinded paired QEEG study.

Methods 117 EEG recordings from 40 migraineurs were classified as baseline, pre-, or post-ictal. Delta, theta, alpha and beta power, and hemispheric asymmetry, in frontocentral, temporal and occipitoparietal regions were calculated from artefact-free EEG. Power and power asymmetry were calculated for two time-windows: 36 and 72 hours before/after the attack and compared to the baseline values.

Results Frontocentral delta power increased (74% of SD, Wilcoxon $p = 0.03$) while frontocentral theta and alpha power tended to increase (55% and 61% of SD, $p < 0.09$) within 36 hours before the next attack compared to baseline. Occipitoparietal (alpha and theta) and temporal (alpha) power was more asymmetric before the attack compared to baseline ($p < 0.04$). Differences were not apparent in the 72 hours pre-and post-attack time window. Post-attack power and power asymmetry was not significantly different from baseline.

Conclusion Cortical brain activity changed within 36 hours before a migraine attack. A moderately strong symmetric increase in frontocentral delta power was found. Reduced activity in the brainstem nuclei or basal forebrain systems before the attack is hypothesised. Increased occipitoparietal alpha power asymmetry may suggest reduced interhemispheric synchronization in thalamic modulation of visual cortex.

B056

Effects of visual deprivation on visual evoked potentials in migraineurs and healthy subjects

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Background Interictally visual evoked potentials (VEP) are characterised in migraine by a deficient habituation. Among the possible underlying mechanisms, deficient activation of inhibitory interneurons has been postulated. Cortex excitability is known to increase after visual deprivation (VD) which is attributed to an excitability decrease of cortical inhibitory interneurons (Borojerdi et al. 2000).

Objective To study the effect of VD on VEP and its habituation in migraineurs without aura (MO) and healthy volunteers (HV).

Method Six sequential blocks of 100 averaged VEP at 3.1 Hz were recorded before and after 1 hour of visual deprivation in 6 healthy subjects and in 8 migraineurs. We measured N1-P1 amplitudes in each block and its percentage change between the 1st and the 6th block.

Result Before VD VEP clearly habituated in HV ($-13.87 \pm 8.99\%$) but there was, as expected, a potentiation in MO ($14.35 \pm 15.22\%$) ($p = 0.002$). In MO this potentiation was replaced by habituation after VD ($-3.85 \pm 10.05\%$) ($p = 0.01$) and N1-P1 amplitude in the 1st block decreased significantly ($p = 0.006$). Changes induced by VD were more variable and not significant in HV ($1.63 \pm 17.63\%$).

Conclusions These results suggest that reduced activity of cortical inhibitory interneurons is not responsible for the interictal lack of VEP habituation in migraine or that LD has

in migraineurs a paradoxical effect increasing instead of decreasing excitability of these interneurons.

References

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B057

Phosphorylation of extracellular signal-regulated kinase (pERK) following light stimulation in migraine mode

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Objectives Photophobia is an important sign of migraine headache. However, the neuronal mechanisms underlying the photophobia and its relation to migraine are not known. Previously, it was reported that the spinal trigeminal nucleus caudalis (Vc) neurons responded to intense light stimulation of the eye as well as intracranial dura stimulation. Thus, we hypothesized that the Vc neurons were somehow involved in the photophobia in migraine. We examined whether pERK was activated by an inflammation of the intracranial dura and intense light stimulation. Furthermore, the expression of pERK in trigeminal ganglion (TG) neurons was also studied to clarify the source of the activity evoked by light.

Methods A small part of left frontal bone was removed to apply 10% mustard oil to the dura at 3 days before light stimulation in SD rats anesthetized with pentobarbital Na (50 mg/kg, ip). The pERK immunohistochemistry of Vc and TG neurons was carried out in the dura-inflamed or control rats 2 min after intense light stimulation (0.6–2 joule energy) of the eye. The pERK-LI cells were precisely analyzed.

Results The pERK-like immunoreactive (pERK-LI) cells were observed in Vc and TG neurons after intense light stimulation. The number of pERK-LI cells was significantly larger in the rats with dura inflammation compared with those of control in Vc.

Conclusion The present findings suggested that Vc neurons would be involved in the photophobia associated with migraine, and the primary afferents innervating in the eye may be one of the sources of the light stimulation in photophobia.

B058

Vasoactive intestinal peptide causes marked cephalic vasodilatation but does not induce migraine

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Objectives The parasympathetic nervous system may be involved in the initiation and maintenance of migraine attacks. We hypothesized that intravenous infusion of the

parasympathetic transmitter, vasoactive intestinal peptide (VIP), may induce a migraine attack secondary to marked cerebral vasodilatation.

Methods We randomly allocated 12 patients with migraine without aura to receive 8 pmol/kg/min VIP or placebo over 25 min in a randomized, double-blind crossover study. Headache was scored on a verbal rating scale from 0 to 10, mean blood flow velocity in the middle cerebral artery (VmeanMCA) was measured by transcranial Doppler ultrasonography, and diameter of the superficial temporal artery (STA) was examined by a high frequency ultrasound device. The primary end-points were differences in area under the curve for headache score, VmeanMCA and STA diameter between two trial days.

Results During the immediate phase (0–30 min after start of infusion), 10 patients reported very mild headache after VIP versus none after placebo ($P = 0.005$). Three patients reported delayed headache (3–11 hours after start of infusion) after VIP and 2 patients after placebo ($P = 0.893$). None of the patients developed a migraine attack after administration of VIP. VmeanMCA decreased significantly ($P = 0.001$) and the diameter of STA increased significantly after VIP ($P < 0.001$). The dilatation persisted in the post-infusion period ($P < 0.001$).

Conclusion In conclusion, the present study demonstrates that marked dilatation of cranial arteries induced by a parasympathetic transmitter VIP does not trigger migraine attacks in patients with migraine without aura. These data provide further evidence against a purely vascular origin of migraine.

B059

Effects of light deprivation on 5 Hz rTMS motor evoked potentials in migraineurs and healthy subjects

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Background Among the various electrophysiological tests showing that the cerebral cortex is interictally dysexcitable in migraineurs, we have found that, during a rTMS train at 5 Hz, the motor evoked potential (MEP) decreases whereas it increases in healthy volunteers (HV).

Objectives To explore if this finding could be due to hypoexcitability of cortical inhibitory interneurons (CII) by studying the effect of light deprivation (LD) which is known to decrease the activity of CII both in visual and motor cortices.

Methods We averaged 5 trains of MEP elicited by 20 pulses of 5 Hz rTMS at 110% of the motor threshold (MT) before and after 1 h of LD in 7 migraineurs (4 with aura-MA) and 7 HV. We measured MT, mean MEP amplitude over 20 responses and the amplitude ratio between the 1st and the last response.

Results There was no significant difference in MT or initial MEP amplitude before/after LD in either group. As in our previous study, there was an exaggerated global inhibition pattern of 5 Hz rTMS in migraine, but this was not modified by LD. The average MEP amplitude over 20 responses was increased by VD in all groups, more so in MA (ratio after/before = 2.16) than in HS (1.13) ($p = 0.07$).

Conclusion Hyperexcitability of CII is thus not likely to be responsible for the more marked MEP inhibition during 5 Hz rTMS in migraineurs. However, decreased activity of CII after LD might explain the increase in average MEP amplitude and could be more pronounced in migraine.

B060

IL-1b induced CGRP release and PGE2 synthesis in trigeminal ganglion neurons is mediated by a COX-2 dependent pathway

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Trigeminal neurons are crucial for the pathophysiology of headache. In vivo, a host of stimuli leads to the release of neuropeptides e.g. calcitonin gene related peptide (CGRP). CGRP plays an important role in migraine pathophysiology. Serotonin receptor (5HT1B/D) agonists cause significant pain relief in migraine attacks by blocking CGRP release. In addition, cyclooxygenase (COX) inhibitors abort migraine attacks. However, the precise pathophysiological role of COX-2 and its reaction product prostaglandin E2 (PGE2) as well as the source of COX-2 remains to be determined.

We have used a trigeminal ganglia cell culture model to assess whether primary trigeminal ganglia neurons are able to express COX-2 resulting in PGE2 release. For stimulation we used Interleukin-1 beta (IL-1b), a cytokine implicated in the generation of migraine attacks.

Our results show that trigeminal ganglia neurons express COX-2 upon stimulation with IL-1b. COX-2 expression led to significant PGE2 release after 4 hours and delayed CGRP release after 24 hours. PGE2 and CGRP release could be blocked by the nonselective COX inhibitor indomethacin and the selective COX-2 inhibitor parecoxib. Thus, PGE2 and subsequent CGRP release are dependent on COX-2 synthesis. In contrast the 5HT1B/D receptor agonist sumatriptan was without any effect.

In summary, we show that IL-1b induced PGE2 synthesis and CGRP release in trigeminal neurones are mediated by a COX-2 pathway. Our study reveals the source of an enzyme of importance in migraine and a connection between COX-2 and CGRP which may have implications for the acute treatment of migraine headaches especially in a sensitized state.

B061

Interictal habituation deficit of trigemino-facial and trigemino-cervical reflexes in migraine

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Background Migraine patients may complain pain not only in the orbito-frontal region, innervating by the ophthalmic trigeminal branch, but also in the neck (C2-). There are evidence in favour of anatomical and functional coupling between the trigeminal and the cervical system (trigemino-

cervical complex). Sensitization of this complex is considered a fundamental mechanism for the head pain transmission.

Objectives We simultaneously recorded the nociceptive specific blink (nBR) and trigemino-cervical reflexes (TCR) in migraine without aura (MO) patients in order to assess the activity of the trigemino-facial and trigemino-cervical pathways.

Methods Eight healthy volunteers (HV) and 9 MO patients were recorded by stimulating the supraorbital nerve. Habituation was defined as the % change of the R2 and late-onset TCR area under the rectified curve (AUC) between the 1st and the subsequent 2 blocks of 5 responses.

Results Despite a lack of habituation was observed in MO compared to HV both for nBR (MO +9%, HV -13%) and TCR (MO -16%, HV -36%) at the 2nd block, the statistical significance was reached only for the nBR ($p = 0.04$). The AUC of the 1st nBR and TCR block was both reduced when compared to HV.

Conclusion Our results confirm that migraine patients are interictally characterized by a dishabituation of the nBR, and show that the same phenomenon is detectable by TCR recordings. The AUC reduction of the first block both in nBR and TCR suggests that this deficit is not related to central trigeminal sensitization.

B062

Genomic profiles in patients with medication overuse: predicting response

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Background Migraine and chronic migraine (CM) have a strong genetic basis with distinct genomic expression patterns. Medication overuse (MOH) is a frequent contributor to CM. Gene expression changes can be used to elucidate MOH pathophysiology.

Objective To present distinct genomic expression patterns in patients with MOH that respond rapidly to cessation of acute medication (R: >15 headache days/month) compared to continued frequent headaches (NR: 30 days/month) or intermediate response (IR: 15–30 days/month).

Method Blood samples from patients were obtained from CM with MOH and at follow-up evaluation (45.2 ± 16.8 days). RNA was processed on Affymetrix U133 2.0 Plus microarrays and analyzed using GeneSpring and SAM.

Result 61 patients have been enrolled with analysis completed in 29 (R = 11, NR = 10, IR = 8). All patients had 30 headache days/month with $M = 18.7 \pm 9.5$ at 1st follow-up (R: 9.2 ± 4.8 ; NR: 30 ± 0 ; IR: 17.8 ± 2.1). Unique gene expression patterns were identified between R vs NR in 442 genes (FDR < 5%). Gene ontology demonstrated significant differences in the mRNA of G-protein coupled receptor ($p = 0.0106$) and neuroactive ligand-receptor ($p = 0.0294$). IR patients were able to be differentiated by cluster analysis, predicting the degree of MOH contribution.

Conclusions The distinct genomic profiles identified in MOH patients that respond to cessation of analgesic use compared with NR suggests different underlying pathophysiology for CM and MOH. Future studies will determine if it is possible to predict which patients will only require analgesic withdraw for treatment.

B063

Plasticity of trigeminovascular system in low serotonin condition: the complex changes

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Objectives To determine the plastic change in peripheral and central compartment of trigeminovascular system in response to low serotonin condition.

Methods The study comprised a series of experiments. In each experimental, adult male Wistar rats were separated into low serotonin and controlled groups (6–8 rats each). Low serotonin condition was induced by intraperitoneal injection with para-chlorophenylalanine 3 days prior to the experiment. Trigeminovascular nociception was elicited either by cortical spreading depression (CSD) or dural inflammation. Experimental techniques comprised electrocorticography, laser Doppler flowmetry, immunohistochemistry, and electron microscopy. Outcome variables included magnitude of CSD-induced depolarization shift, number of transient receptor potential vanilloid type 1 (TRPV1) immunoreactive neurons in trigeminal ganglia, number of Fos-immunoreactive neurons and phosphorylated NMDA receptor neurons in trigeminal nucleus caudalis (TNC). Ultrastructure of cerebral microvessels was also studied to determine the changes in vascular compartment.

Results Depletion of serotonin induced substantial changes in various compartments of trigeminovascular system. In the cortex, low serotonin rats had significantly increased degree of CSD-induced depolarization shift and CSD-evoked cerebral hyperaemia. Changes in the trigeminal nociceptive pathway included increased nociception-evoked TRPV1 receptor expression in trigeminal ganglia and NMDA receptor phosphorylation and fos expression in the TNC. Ultrastructural study also revealed higher degree of CSD-induced pinocytosis and microvilli formation reflecting an increase in vascular permeability.

Conclusion Depletion of serotonin induces the trigeminovascular system to undergo plastic changes which reflect the cortical hyperactivity, enhanced nociceptive processing, and increased vascular permeability. Such changes may be the pathophysiological mechanism underlying chronic daily headache, the condition in which serotonin is reduced.

B064**Brainstem auditory evoked potential (BAEP) amplitude habituation in migraine**Trond Sand¹, N Zhitnyi², LJ Stovner²¹Dept Neurology and Neurophysiology, St.Olavs Hospital,²Dept of Neurosciences, NTNU, Norway

Objective Increased sensitivity to sensory stimulation in migraine (e.g. phonophobia) may be reflected by the reported reduced habituation in sensory evoked potentials in migraine. It is not known if cortical or subcortical mechanisms are chiefly responsible for hypersensitivity. We intended to estimate habituation effects in BAEP to low (40 dB), medium (55 dB) and high (70 dB) intensity click stimuli.

Methods BAEP was recorded from both ears with Cz reference in four blocks \pm 750 stimuli. Binaural 10.8 Hz rarefaction clicks were applied via headphones on three different days in 41 adult migraine patients (33 without aura) and 28 controls. Wave IV–V amplitude and amplitude stimulus function (ASF) slopes was averaged across days. Clinical data was obtained from a headache diary.

Results Wave IV–V amplitude habituation was found for 70 dB (ANOVA, $p < 0.005$) but not for 55 or 40 dB BAEP. Group difference was neither found for amplitude level nor for amplitude habituation (ANOVA, $p > 0.18$). ASF slope habituation was not observed. For 40 dB clicks we found slight habituation in wave IV–V desynchronisation in controls but not in migraine. Correlations between phonophobia and wave IV–V amplitude, desynchronisation, or ASF slope were not observed.

Conclusion Significant BAEP wave IV–V amplitude habituation was observed only for high stimulus intensity. Migraine patients did not differ from controls in the majority of BAEP habituation parameters except for less pontine desynchronisation to low-intensity clicks. BAEP habituation is of small magnitude and is difficult to use as a measure of pontine excitability in small groups of healthy subjects and migraine patients.

B065**Role of orexin system in the rat cortical spreading depression – possible involvement in migraine pathogenesis**Kenzo Koizumi, J Hamada, M Fukuda, J Yonekura, N Kanazawa, F Sakai
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Objective In order to elucidate the involvement of orexin system in the migraine pathogenesis, particularly of cortical spreading depression (CSD), we investigated the morphological change of orexin-A and orexin-1 receptors in the dura mater, the trigeminovascular system, the hypothalamus, the periaqueductal gray, the medulla oblongata and autonomic ganglia (superior cervical ganglion, otic ganglion, sphenopalatine ganglion) of the CSD evoked rat.

Methods Using anesthetized, tracheotomized and artificially ventilated Sprague-Dawley rats ($n = 6$), CSDs were triggered by topical application of KCl solution through an open

occipital cranial window. First, CSDs were observed for 40 minutes, and then, following orexin-A (0.3 nmol) injection in right lateral ventricle CSDs were triggered again with the same method and observed for 40 minutes. Then, they were perfused with Zamboni's fixative and those specimens were dissected. Immunofluorescence staining method was utilized to examine microscopically whether expressions of orexin-A and orexin-1 receptors, 5HT1B receptors, CGRP were affected by CSD.

Results Immunoreactivity of both orexin-A and orexin-1 receptors was not different in the post-CSD evoked rat brain. In the lateral hypothalamic area, periaqueductal gray and dorsal raphe, the orexin-1 receptor-IR neurons were co-expressed with 5HT1B receptors.

Conclusion In this study, morphological change of orexin system and CGRP and 5HT1B receptors were not observed. Another study by repeated CSD generation animals is needed. On the other hand, 5HT1B receptors were co-expressed with orexin-1 receptors, suggesting that orexin system is likely to be involved in migraine pathogenesis.

B066**Involvement of NO in the trigeminal nociceptive facilitation induced by serotonin depletion**Supang le Grand¹, W Supornsilpchai², P Nuanboonma³, A Srikiatkachorn²¹Faculty of Medicine Chulalongkorn U, ²Department of Pathology,³Department of Physiology, Thailand

Objective To investigate the involvement of nitric oxide in the process of trigeminovascular nociceptive facilitation induced by serotonin depletion.

Methods Male Wistar rats were separated into the control and low serotonin with and without nitric oxide synthase (NOS) inhibitor. Serotonin was depleted by administration of para-chlorophenylalanine. Cortical spreading depression (CSD) was used to activate trigeminal nociception. N-nitro-L-arginine Methyl Ester (L-NAME) was given to the rats in the low serotonin with NOS inhibitor group after the second wave of the CSD. The ultrastructure of cerebral endothelial cells was studied using electron microscope. The cortical activity and the number of Fos-immunoreactive neurons in trigeminal nucleus caudalis were monitored.

Results CSD altered the ultrastructure of cerebral microvessels as characterized by endothelial pinocytosis and microvilli formation. These vascular changes as well as CSD-evoked Fos expression in the TNC were enhanced in low serotonin group. The CSD-induced trigeminovascular nociceptive facilitation caused by PCPA was attenuated by co-administration with NOS inhibitor. The numbers of pinocytic vesicles and microvilli were significant lower in the group receiving PCPA and L-NAME. The number of CSD wave observed in low serotonin rats with and without L-NAME treatment were $9 + 2$ and $13 + 2$ peak/hr, respectively ($p < 0.05$). Treatment with L-NAME also significantly minimized the number of Fos-immunoreactive cells in TNC ($23 + 5$ and $36 + 7$ cells/slide for those with and without L-NAME, respectively, $p < 0.05$).

Conclusion Inhibition of nitric oxide production can attenuate the trigeminovascular nociception induced by serotonin depletion. Therefore, nitric oxide production is likely to involve in the increment of trigeminal nociception in serotonin depleted state.

B067

Role of NF- κ B protein on the nociceptive transmission of migraine attacks in an animal model

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Objective To study nuclear factor-kappa B (NF- κ B) expression in the periaqueductal gray matter (PAG) induced by electrical stimulation of dural matter near the superior sagittal sinus (SSS) of rats and to further elucidate its role in the nociceptive transmission of migraine attacks.

Methods Seventy male Sprague-Dawley rats, were randomly divided into seven groups: blank, sham-operated, stimulated, sumatriptan, normal saline A, flunarizine, normal saline B group. Ten days prior to operation, flunarizine and normal saline were given i.p. separately to the rats of flunarizine and normal saline B groups. The SSS was stimulated with square wave current for 2 hours after the operation in the stimulated groups. The sumatriptan and normal saline were given i.p. separately in sumatriptan and normal saline A groups by intraperitoneal injection after stimulating 30 minutes. The sham-operated group was not stimulated. The rats were sacrificed, brains harvested and coronally sectioned. Standard avidin-biotin immunohistochemistry analysis detected the NF- κ B protein expression of the neurons.

Results The number of NF- κ B positive neurons in the stimulated group was increased compared with that in the blank, sham-operated, sumatriptan and flunarizine group respectively. The number of NF- κ B positive neurons in sumatriptan group and flunarizine group was decreased compared with that in the normal saline groups.

Conclusion The expression of NF- κ B positive neurons in the PAG activated by electric stimulation on the SSS can be accommodated by sumatriptan and flunarizine, which could be involved in the processing of nociceptive signals in migraine attacks.

B068

Regulation of CGRP release from rat trigeminal nucleus caudalis by melatonin

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Objectives Melatonin has been shown to play a role in migraine pathophysiology. Altered melatonin levels in cluster headache and migraine have been documented. Calcitonin gene-related peptide (CGRP) containing primary afferents project primarily to laminae I, II of the rat TNC. CGRP

released from trigeminal primary afferents has been implicated in the pathophysiology of migraine. CGRP can be released in animals after noxious stimulus. The aim of the present work was to analyze CGRP response within the trigeminal nucleus caudalis (TNC) of rats that received melatonin treatment, after intracisternal infusion of capsaicin, used to induce intracranial trigeminovascular stimulation.

Methods Wistar male rats were studied in two different groups. Animals received solution capsaicin prepared with 3.05 mg capsaicin per 1 ml of vehicle (saline-ethanol-Tween 80, 8 : 2 : 1) and diluted 1 : 50 (200 nM) with saline. Intracisternal infusion of 10 microliters of capsaicin was performed via stereotaxic surgery. Group 1 received only capsaicin, group 2 received capsaicin and intraperitoneal melatonin. Animals underwent transcardiac perfusion. Immunohistochemistry was done with a primary polyclonal antibody anti-CGRP (1 : 1000) and the expression analyzed in the TNC (Laminae I e II).

Results The immunoreaction with CGRP was observed in two groups. The group that received only capsaicin had significantly less expression in the TNC than the group that received capsaicin and melatonin.

Conclusion Capsaicin is thus able to influence afferent fibers in the superficial laminae of rat TNC. Melatonin modulates the expression of CGRP and blocks the capsaicin effect in an experimental model of headache.

B069

Gastric stasis occurs in spontaneous, visually induced and interictal migraine

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Objective To evaluate and compare gastric motility and emptying during spontaneous migraine to previous observations from induced migraine.

Background We have previously demonstrated a delay in gastric emptying both during the interictal period and induced migraine. We have now performed nine additional studies as a follow up to ascertain if there is a similar delay during spontaneous migraine.

Methods Gastric scintigraphy using a standard meal was performed in three subjects during spontaneous migraine, induced migraine and in the interictal period.

Results The time to half emptying was delayed during spontaneous migraine (130 minutes), during induced migraine (152 minutes) and during the interictal period migraine (176 minutes) compared to normative values established at our center (112 minutes). Similar gastric slowing was seen in all three groups when a percentage of nuclear material remaining in the stomach at two hours was used as a more stringent endpoint.

Conclusions This study continues to demonstrate gastric stasis during the interictal period of migraine that is less pronounced, but still evident during induced and spontaneous migraine.

B070**Role of anandamide in the modulation of nitroglycerin-induced hyperalgesia: a study in the rat**

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Systemic nitroglycerin (NTG) provokes spontaneous-like migraine attacks in migraine sufferers and induces a condition of hyperalgesia in the rat with a delay of several hours. Recently, it has been reported that anandamide (AEA), a CB(1) receptor agonist, is tonically released to play a modulatory role in the trigeminovascular system, which seems to suggest a contribution of the endocannabinoid system to the pathogenesis of migraine. The aim of this study was to test the possible role for AEA in the mechanisms mediating nitroglycerin-induced hyperalgesia.

The formalin test – a model of tonic pain – was performed in male Sprague-Dawley rats that were injected with AEA (20 mg/kg, i.p.) or saline 30 minutes before NTG or vehicle injection (10 mg/kg, i.p.).

AEA-induced a significant decrease in the nociceptive behavior during both phases of the formalin test in the animals treated with vehicle and it abolished NTG-induced hyperalgesia during phase II of the formalin test.

These results point to a role for the cannabinoid system in NTG-induced hyperalgesia and support the possibility that this class of drugs may be effective in the treatment of migraine and other inflammatory pain states.

B071**Coexisting migraine or tension-type headache disappears during bouts of cluster headache: report on 5 patients**

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Cluster headache (CH) may coexist with other primary headaches, but the possible relationship between the different types of primary headache is obscure.

We report on the temporal relationship of occurrence of cluster headache bouts in 5 patients (4 males and 1 female, mean age: 41.8 ± 1.63 years) suffering also from migraine without aura (MO) and/or tension-type headache (TTH), according to the ICHD-II criteria.

In the woman the associated primary headache was MO with a weekly frequency, one patient suffered from both monthly MO and frequent TTH. The other 3 subjects suffered from frequent TTH. In 3 patients CH began after the onset of the other primary headache. CH pain was always unilateral and recurred on the same side, except for one patient who presented a side-shift in the last cluster bout. In the female patient migraine and cluster attacks occurred on the same side, while migraine attacks were bilateral in the male migraineur and tension-type headache was always bilaterally located.

Patients used triptans for migraine attacks, and analgesics and non-steroidal anti-inflammatory drugs for TTH episodes. Subcutaneous sumatriptan was effective for CH attacks in four patients, while the remaining one used oral eletriptan. In all patients the coexisting primary headache completely disappeared during the CH bouts.

Though based on a very small group of subjects, our observation that CH occurrence is consistently associated with a prompt spontaneous remission of the coexisting primary headache appears intriguing in terms of possible interactions between central nociceptive pathways and control circuits.

B072**The role of cyclooxygenase-2 and prostaglandin-e2 in an animal model of migraine**

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The animal model of migraine based on the systemic administration of nitroglycerin (NTG), a NO donor, has provided interesting insights into the pathogenetic mechanisms of migraine. Cyclooxygenase-2 (COX-2) increases prostaglandin E2 (PGE2) production in central nervous system and contributes to the severity of pain responses in inflammatory pain. PGE2 synthesized in the brain is probably involved in modulating trigeminal nociception. In this study we evaluated the expression of COX-2 and PGE2 levels within neuronal areas relevant for migraine genesis after administration of NTG. Male Sprague-Dawley rats were injected with NTG (10 mg/kg, i.p.) or vehicle and sacrificed 2 and 4 hours later. The hypothalamus and the lower brainstem were dissected out and utilized for the evaluation of COX-2 expression (western blotting) and for the determination of PGE2 levels (ELISA immunoassay). COX-2 expression increased in the hypothalamus at 2 hours and in the lower brainstem at 4 hours. PGE2 levels showed a differentiated pattern of change with a decrease at 2 hours in the hypothalamus and an increase at 4 hours in the lower brainstem. These results show for the first time that NTG is capable of interfering with the COX-2 pathway *in vivo* within specific cerebral areas.

B073**Plasma levels of orexin-A in migraine and cluster headache**

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Introduction Orexins (hypocretins) are recently discovered neuropeptides which are synthesized mainly in lateral and posterior hypothalamus and have a regulatory role on sleep rhythm. Their fibers project widely in the nervous system, suggesting that they are multifunctional. Considering the relationship between sleep and migraine, orexin may be some contribution to the pathogenesis of the headache.

Objective The aim of the present study was to investigate plasma orexin-A levels in migraine and cluster headache.

Methods Human plasma was obtained from 15 healthy controls, and 6 patients with cluster headache, and 27 patients with migraine in the morning fasting. The plasma was separated, immediately frozen and stored at -80 degrees centigrade prior to extraction of peptides. Orexin-A levels were measured with a commercially available radioimmunoassay. **Results** The plasma orexin-A level of cluster headache patients was 6.5 ± 0.7 pg/ml (mean \pm SE), and of migraine with aura patients was 6.3 ± 1.0 pg/ml. These were significantly lower ($P < 0.05$) than the control group (10.2 ± 1.0 pg/ml).

The orexin-A level of migraine without aura, 8.03 ± 3.6 pg/ml, tended to be lower than the control ($P < 0.1$).

Conclusion Orexin-A can be measured in the human plasma. Plasma orexin-A levels are significantly lower in cluster headache and migraine with aura than normal controls.

These results suggest that the orexin may some influence on the pathophysiological mechanism of migraine and cluster headache.

B074

An fMRI time and space spread post-analysis of the visual cortex in migraine with aura: preliminary results

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Objective The neuropathological mechanisms underlying migraine are still under debate. We applied functional Magnetic Resonance Imaging (fMRI), using a time and space spread post-analysis, to the study of the neuropathological aura processes, in particular searching for a correlation between the clinical assessment and the functional activation pattern.

Methods Five patients suffering from migraine aura (MA), five without aura (MO) and ten healthy volunteers (C), matching in age and sex, underwent two block designed fMRI scans using visual stimuli, lasting 12 minutes each, with a Philips Intera 1.5 T Gyroscan. The functional activation pattern was analyzed along an extended period of time (24 minutes for the two scans), studying the time and space gradients in their surroundings, looking for significant inter-group discrepancies. **Results** No patient developed a migraine attack during the fMRI scan. Preliminary results showed a significantly different pattern of activation between patients and C and, moreover, between MA and MO. Specifically, MA and MO patients experienced a growing occipital excitability in spite of abutment, MA patients with a stronger spatial deactivation.

Conclusions These preliminary data suggest that our post-analysis method is sensible to differences in the physiological response to the visual stimulus in time and location and may open a future prospective in the study of the aura pathophysiology.

B075

Binocular rivalry as an indicator cortical excitation and inhibition in migraine

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Objectives When the two eyes are presented simultaneously with very different images, one experiences binocular rivalry: the percept alternates between the two monocular images approximately every 1–2 sec. Rivalry reflects the dynamical balance between recurrent excitatory and recurrent inhibitory processes operating in visual cortex. Based on network models, weakened inhibition is predicted to produce an increase in the rate of alternation of eye dominance.

Methods Binocular rivalry was assessed in 3 age-matched groups (20 M with A, 20 M w/o A, 20 headache-free controls) classified by IHS criteria. The stimuli were left and right tilted sinusoidal grating patches of 2° diameter isolated to the left and right eyes respectively using CrystalEyes™, stereo goggles. Subjects indicated which pattern was visible by depressing the left or right response key or both simultaneously. Three contrast levels were tested. Visual discomfort for gratings and flicker was assessed separately.

Results There were no statistically significant differences in mean dominance intervals between migraine groups and controls; the trend was toward slightly longer intervals in migraine. The migraine groups had larger interocular differences in dominance intervals than the control group, reaching statistical significance for the 30% contrast stimulus ($P = 0.04$) only. We found highly significant differences in discomfort thresholds for both static and flickering stimuli in both migraine groups compared to controls ($P < 0.01$). Rivalry scores were not correlated with discomfort scores or with years with migraine or frequency of migraine episodes.

Conclusions These results provide no support for weakened visual cortical inhibition in migraine, and only weak support for enhanced recurrent excitation.

B076

Alteration of regional cerebral metabolism (RCM) in chronic migraine as assessed by PET

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Introduction Pathophysiology of migraine is not well understood. There is, however, an increasing body of research evidence for the involvement of nociceptive pathways in chronic daily headache and migraine. The first reports came from Raskin and colleagues who observed a migraine-like headache that developed in patients with electrode implantation in the PAG. Recently the rostral brainstem has been identified as being specifically involved in migraine.

Background Neuroimaging with PET has shed light on the genesis of the two most important headache syndromes,

documenting activation in the midbrain and pons in migraine, and in the hypothalamic gray in cluster headache (CH). We studied ten subjects meeting updated 2006 IHS criteria for chronic migraine using PET imaging.

Methods PET scans have been performed on ten chronic migraine patients. Each patient was scanned 3 times, and the average was used for the group analysis.

Results Preliminary results indicated increased metabolism in the pons compared to global cerebral metabolism while the cerebellum exhibited decreased cerebral metabolism.

Conclusions Chronic migraine is associated with activation of the nociceptive pathways in the pons. An apparent inhibition of the cerebellum is now being demonstrated.

B077

Nociceptin and buprenorphine modulate CGRP release from trigeminal neurons *in vitro*

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Objectives To investigate the effect of nociceptin (1–13)NH₂, an agonist to ORL1 (NOC) receptors, and buprenorphine (BUP), an agonist-antagonist to μ opioid receptors which also interacts with, and activates ORL1, on the modulation of CGRP release from trigeminal neurons *in vitro*.

Methods Primary cultures of trigeminal ganglion neurons are prepared from 6–7 days old rats; neurons are seeded on 24-well tissue culture plates, coated with poly-D-lysine 130–150 $\times 10^3$ cells/well and incubated at 37°C in a humidified atmosphere containing 5% CO₂. Plating medium is enriched with 50 ng/mL of 2.5 S murine Nerve Growth Factor. All experiments are performed from 5 to 7 days after dissection. CGRP-LI is performed by radioimmunological assay (RIA).

Results Trigeminal neurons are stimulated to release CGRP by depolarizing agents such as 56 mM KCl and veratridine, as well as by capsaicin. In this experimental paradigm NOC is able to reduce evoked CGRP-LI release from neurons in a concentration-dependent manner; such effect is reverted by a selective and competitive antagonist to ORL1, N(Phe)nociceptin(1–13)NH₂. In preliminary experiments with BUP, the drug was able to increase CGRP-LI release in a concentration-dependent manner, whereas it failed to reduce capsaicin-evoked CGRP-LI release.

Conclusions Nociceptin shows a definite inhibitory profile over CGRP release, whereas further studies are still required to establish the effects of buprenorphine in this paradigm.

B078

Visual evoked potential (VEP) habituation in migraine

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Objectives It is not known if clinical history in migraine correlates with function in different visual subsystems. We

intended to estimate amplitude, habituation and latency for different pattern reversals VEP components to medium and large checks (31' and 62').

Methods Monocular 1.9 Hz pattern reversals were presented in 33 adult migraine patients without aura (MwoA), 8 with aura (MA) and 28 controls. VEP was recorded from Oz with Fz reference in four blocks \times 50 stimuli. N1 (N70), P1 (P100) and N2 (N145) latency and N1P1 and P1N2 amplitude was measured. Clinical data was obtained from a headache diary.

Results MA patients had significantly higher P1N2 amplitude than controls and MwoA and higher N1P1 amplitude for large checks. N1P1 amplitude potentiation was significant but group difference was not found. N145 latency prolongation for 31' checks and P100 latency potentiation for 62' checks was seen in controls and MwoA, but not in MA. Correlation between photophobia and VEP was not observed. P100 latency correlated positively with headache history duration while headache attack duration correlated positively with N145 latency and N1P1 amplitude (31' and 62' checks)

Conclusion VEP amplitude habituation to medium and large checks was not confirmed to be present in control subjects. MA patients differed from MwoA patients and controls in VEP amplitude and latency habituation. The validity of VEP change in migraine is weakened by the lack of correlation with photophobia. Headache history and headache severity seem to be associated with visual cortex function and excitability in migraine patients.

B079

Satellite cells as new targets of migraine therapy

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Objectives The trigeminal ganglion (TG) contains not only neurons, but also Schwann cells and satellite cells (SCs). To investigate the intraganglionic signal transduction pathways involved in the pathomechanisms of migraine, we examined the activation of TG glial cells (a) in organ culture, and (b) *in vivo* following electrical and nitroglycerin (NTG) induced stimulation.

Methods Following (a) organ culture of adult rat and cat TG in serum-free DMEM with or without the presence of the ERK1/2 inhibitor U0126, capsaicin or kynurenic acid, and (b) *in vivo* following electrical and NTG induced TG stimulation we examined with immunohistochemical techniques location and distribution of calcitonin gene-related peptide (CGRP) and substance P (SP).

Results The TG neurons showed CGRP and SP immunoreactivity (-ir), while the SCs expressed only CGRP-ir. Capsaicin treatment *in vitro* did not alter the SCs CGRP-ir, while treatment with extracellular signal-regulated kinase 1/2 (ERK1/2) inhibitor U0126 strongly reduced the CGRP-ir of the SCs. However, the expression of SP-ir was not affected by the ERK1/2 inhibitor. Kynurenic acid treatment did not

alter the SCs activation. Electrical stimulations of the TG or the systemic NTG treatment did not elicit CGRP-ir of the SCs.

Conclusions Our observations indicate that the SCs may participate in the function of the TG, acting to store excess

released CGRP and participate in the long term development of migraine attacks. The use of a mitogen-activated protein kinase (MAPK) ERK1/2 inhibitor may act to reduce elevated production of CGRP and thus putatively as a migraine prophylactic agent.

SCIENTIFIC SESSION

Scientific session 2: Neurobiology

ScS2-1

FHM1 R192Q *Cacna1a* mutant mice show enhanced adjustment to advanced shifts of the light-dark cycle: a molecular basis to chronobiology in migraine?

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Objectives The hypothalamus governs the rhythmicity and timing of many body functions, but also seems to play a crucial role in episodic brain disorders. Within the hypothalamus the suprachiasmatic nucleus (SCN) acts as the biological clock. Periodicity in the attacks of several types of headache suggests that hypothalamic structures are involved in their pathogenesis. A clear molecular understanding of this relationship is lacking. Our objective was to establish whether recently developed transgenic FHM1 mice had abnormal SCN functioning.

Methods FHM1 R192Q *Cacna1a* mutant and wild-type mice were subjected to shifts in the light-dark regime. Ability of the biological clock to readjust (6 hr advance or delay to the normal cycle) was tested behaviorally and complemented by *ex vivo* and *in vivo* electrophysiological analyses of responses in the SCN.

Results FHM1 R192Q *Cacna1a* mutant mice experienced abnormal behavioral adjustment to advanced shifts of the light-dark cycle. SCN recordings did only reveal adjustment abnormalities in *in vivo* analyses, and these changes supported findings from behavioral experiments.

Conclusion Here we report on a detailed behavioral and electrophysiological characterization of the biological clock of FHM1 R192Q *Cacna1a* mutant mice that gave support for extra-SCN involvement through mutated Ca_v2.1 calcium channels in abnormal functioning of the biological clock. Better insights in the biological clock may lead to a better understanding of the neurobiological mechanisms that are involved in episodic brain disorders.

ScS2-2

Genetic enhancement of CGRP actions: a possible migraine model?

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Objective A common theme among current migraine models is involvement of the neuropeptide calcitonin gene-related peptide (CGRP). To address the role and mechanisms of

CGRP action in migraine, we have generated transgenic mice that are sensitized to CGRP actions.

Methods CGRP acts via an unusual G protein coupled receptor that requires a small subunit called RAMP1. We reasoned that RAMP1 overexpression would sensitize mice to CGRP actions. Towards this goal, we generated mice that have elevated RAMP1 in the central and peripheral nervous systems.

Results As a first step, we showed that RAMP1 is functionally rate limiting in cultured trigeminal ganglion neurons and vascular muscle. The effects of CGRP on cAMP production and substance P release were enhanced following RAMP1 adenoviral-mediated gene transfer. Transgenic mice with about 2-fold elevated RAMP1 expression had increased CGRP-evoked plasma extravasation as a measure of neurogenic inflammation. Initial results from a light aversion behavioral assay suggest that the RAMP1 mice prefer the dark compared to littermate controls. In addition to inflammation and light aversion, the mice also had reduced size and body fat levels, which may reflect increased CGRP and/or amylin activities on food intake.

Conclusion While preliminary, these results indicate that RAMP1 can increase CGRP actions in the nervous system. The increased light aversion may be analogous to the photophobia of migraine. In the long term, this mouse model may potentially provide the foundation for mechanism studies and therapeutic strategies for recalcitrant trigeminal-mediated pathologies such as migraine.

ScS2-3

Anatomical evidence that triptans modulate the affective dimension of migraine by inhibiting CGRP in the amygdala

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Triptans have anti-migraine properties through their selective activation of serotonin 1B, 1D, and 1F (5-HT_{1B/1D/1F}) receptors. In addition to the inhibition of "pain" transmission through an action on peripheral afferents, sumatriptan reportedly activates descending inhibitory controls that arise in the midbrain periaqueductal grey. With a view to identifying the individual receptors that contribute to the potentially diverse actions of triptans in the brain, we used a receptor-subtype selective antibody to the 5-HT_{1D} receptor and immunohistochemistry in the rat brain, and noted a dense terminal pattern of immunoreactivity (5HT_{1D}-IR) in the central nucleus of the amygdala. Using double-label immunohistochemistry, we showed that these terminals co-express the peptide neurotransmitter calcitonin-gene related protein (CGRP), but not any of the following: serotonin, acetylcholine, or the monoamines synthesized by tyrosine hydroxylase. We determined the cells of origin of these 5HT_{1D}-IR terminals in

colchicine treated rats, which revealed a small population of 5HT_{1D}-IR neurons within the subparafascicular (SPF) region of the thalamus. These CGRP-containing projections from SPF to the central amygdala are thought to convey auditory, visual, and visceral enteroceptive information. Interestingly, both physiologic and behavioral evidence by Neugebauer and colleagues points toward the role of CGRP in the amygdala in the expression of pain responses. We therefore hypothesize that triptans may additionally play a role in modulating the affective experience of a migraine attack, in particular, through their inhibition of CGRP release in the amygdala.

ScS2-4

Increased serotonin transporter availability in the brainstem of migraineurs

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Objectives For decades, serotonin has been speculated to play a major role in migraine pathophysiology. The CNS serotonergic system is located in the raphe nuclei in the brainstem. ¹⁵O-H₂O-PET studies on migraineurs show a marked increase of regional cerebral blood flow (rCBF) in the mesopontine brainstem, a region which comprises the rostral raphe nuclei. We hypothesized the mesopontine serotonergic system being involved in the pathophysiology of migraine.

Methods We used ¹²³I-ADAM, a highly specific radioligand targeting the serotonin transporter (SERT) and co-registration of MRI and SPECT to investigate the brain serotonergic system in migraineurs *in vivo*. 19 migraine patients and 10 healthy, age- and sex-matched controls were enrolled. SPECT imaging was performed interictally.

Results Region of interest (ROI)-analysis revealed a highly significant increase of ¹²³I-ADAM uptake in the mesopontine brainstem of migraineurs ($p \leq 0.001$). There was a slight, non-significant increase of ¹²³I-ADAM uptake in the thalamus of migraineurs.

Conclusions This is the first study demonstrating a significant increase of brainstem SERT-availability in migraineurs. Our study points to a chronic dysregulation of the brainstem serotonergic system. It remains to be elucidated whether the altered SERT-availability is causally related to migraine pathophysiology or whether it reflects secondary mechanisms of headache chronification.

ScS2-5

The raphe nucleus in familial hemiplegic migraine

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Familial hemiplegic migraine is a rare autosomal dominantly hereditary disorder, which shows paroxysmal headaches

accompanying symptoms of nausea, photophobia, and phonophobia with prodromal hemiplegia. It has been recently reported that migraine generator might be the periaqueductal gray matter including the raphe nucleus. The raphe nucleus consists of serotonergic neurons and a kind of serotonin agonists relieves migraine attacks. We investigate the raphe nucleus in an autopsy case of acute encephalopathy linked familial hemiplegic migraine. The sections (10- μ m-thick) including the dorsal raphe nucleus and the superior central nucleus were stained routinely with hematoxylin-eosin, Klüver-Barrera, Holzer, and Bodian. For immunohistochemical studies, a panel of antibodies against serotonin and tryptophan hydroxylase antigens was employed. We estimated neuronal loss, neuropil sparseness, and gliosis, and then counted immunohistochemical positive neurons in the dorsal raphe nucleus and the superior central nucleus, respectively, of both the familial hemiplegic migraine patient and 9 normal controls without neurological disease. In the dorsal raphe nucleus, anti-tryptophan hydroxylase positive neurons significantly decreased, compared with normal controls. However, anti-tryptophan hydroxylase positive neurons were preserved in the superior central nucleus of our patient. Thus dysfunction of the dorsal raphe nucleus might be associated with migraine attacks of familial hemiplegic migraine patients.

Scientific session 3: Paediatrics

ScS3-Introductory Lecture

Migraine in children and adolescents – state of the art

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During the last few years important studies have been performed regarding genetic, neurophysiological, psychological and behavioural aspects of migraine in children and adolescents as well as epidemiology, diagnosis, classification, prognosis and treatment.

Genetic studies focused on the serotonin and dopamine system and most importantly revealed evidence that the seven repeat allele of the DRD4 VNTR is a protective factor for migraine without aura. In neurophysiological examinations, suggested an altered maturation of visual information processing, a somatosensory disinhibition at different levels of the central nervous system, and a stereotyped pattern of altered topography of the contingent negative variation in young migraineurs. However, the question whether the central nervous system is hyper- or hypoexcitable in migraine and whether migraineurs are hypersensitive is still discussed controversially.

Studies on behaviour and temperament revealed increased scores of behavioural and emotional symptoms in migraineurs compared to healthy controls.

The revised criteria of childhood migraine in ICHD-II have improved the sensitivity for diagnosing childhood migraine. The prognosis of childhood migraine has been examined in

several recent studies demonstrating that approximately 30% become headache-free and an evolution from migraine to tension-type headache is seen frequently.

Finally, the evidence regarding the treatment of migraine in children and adolescents has improved in recent years, even though the high placebo rate remains the major problem. Ibuprofen, zolmitriptan and rizatriptan were superior to placebo in one study each and a pilot study on topiramate showed possible efficacy in childhood migraine.

ScS3-1

Migraine with aura with onset in childhood and adolescence: long-term natural history

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Objectives To describe the long-term natural history of migraine with aura with onset in childhood and adolescence.

Methods We examined the clinical records of all subjects admitted to our Departments between January 1st 1980 and December 31st 1996 and discharged with a diagnosis of migraine with aura. All relevant clinical, demographical and family history data were collected in an ad hoc checklist.

Results From the original sample of 137 subjects we re-evaluated 90 patients (51 females, 39 males) after a mean follow-up period of 13 years \pm 2.8 years (range 5–21 years). We used the same checklist to collect data at follow-up. At follow-up 46 patients (51.1%) were free from headache attacks for at least 2 years. In patients still suffering from headache (n = 44) intensity of pain was lower in 6 patients (13.6%), unchanged in 37 (84.1%) and was higher in 1 patient (2.3%); duration was shorter in 8 patients (18.2%), unchanged in 35 (79.5%) and was longer in 1 patient (2.3%); frequency of attacks decreased in 20 patients (45%), unchanged in 18 (41%) and increased in 2 cases (5%) (missing data in 4 cases, 9%).

Conclusions Our results point to a favourable long term prognosis of migraine with aura in childhood and adolescence. More in detail, the presence of trigger factors and language/speech disturbances during the aura phase, the absence of subjective vertigo and a younger age at first hospitalization for migraine are associated to a higher probability of getting free from pain at follow-up.

ScS3-2

Aura features in 612 children referred to a French paediatric migraine center

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Aura associated with migraine in children are usually poorly recognised or misdiagnosed.

Method Aura characteristics (visual, sensitive, auditory, speech disturbance, motor weakness) were systematically documented at every initial headache consultation.

Results 612 consecutive children were assessed over a period of 9 months (through January 07). Mean age: 10.9 ± 3.1 years; 6.5% under 6 years; 33% over 12 years. Migraine was diagnosed in 95% (n = 581) of the children referred for headache. Migraine with aura was found in 47% of children. Among the migraine group we found: visual aura (VA) 74%; auditory aura (AA) 41%; sensitive aura (SA) 39%; motor weakness (MW) 10%; speech disturbance (SD) 8%. 30% of children have only one aura; 44% have a combination of 2 aura; 15% a combination of 3; 8% a combination of 4. Aura onset occurs during the headache in 80% of the cases. 40% of children with VA; 20% of children with AA; 17% of children with SA; 33% of children with MW; 52% of children with SD declared that the aura occurred 'always' with each attack. 33% of children with AA, described auditory hallucination as a 'voice calling them'; most of time, it was the mother or a familiar voice.

Conclusions Multiple auras are frequent in children with migraine; they should be investigated systematically.

ScS3-3

Seven Dutch children with alternating hemiplegia of childhood (AHC): a video-presentation

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Objective We studied Dutch patients with alternating hemiplegia of childhood (AHC) by asking Dutch pediatric neurologists to refer AHC patients.

Method Patients history was obtained, a semistructured questionnaire and neurological examination were performed. Videos and photographs of attacks were gathered.

Results Seven AHC children, aged 5–13 yrs (mean 8.4 yr) were examined. Diagnosis AHC was made at the age of 7 months till 5 yrs. First paroxysmal event took place at the age of 2 days–1.5 yr and varied from a hemiplegic attack (4/7 patients), ocular disturbances (1 patient), tonic attack (1 patient) or partial epileptic seizure (1 patient). All 7 patients had premonitory signs, hemiplegic attacks (often bilateral) and paroxysmal ataxia. Symptoms disappeared or diminished after sleep in all children. Five children had tonic attacks and 6 had abnormal ocular movements. Autonomic disturbances were seen in 5 patients and the same patients complained about headache (migrainous in 2 and of unspecified origin in 3 of them). Three AHC children had generalized epileptic seizures. With increasing age mental retardation, gross and fine motor problems as well as ataxia were seen in all of them. There was a positive family history of migraine in 6 and of epilepsy in 2. AHC patients were treated with flunarizine (7/7), lamotrigine (4/7), valproic acid (2/7), vigabatrin (2/7) and topiramate (1) with varying success.

Conclusion We evaluated the history and clinical symptoms of 7 Dutch AHC patients. They fulfilled the International criteria of AHC.

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ScS3-4

Influence of maturation on slow cortical potentials in migraine – an eight year follow-up

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Objectives A lot of studies have shown migraine as a central stimulus processing disorder. As demonstrated with event-related potentials, central processing undergoes maturation. Different cross-section studies have revealed evidence for a delay of sensory maturation in migraine. To prove this evidence we performed a longitudinal study over a period of 8 years (1998–2006).

Methods In 2006 we re-investigated 29 children with migraine (64% of the original sample), 16 healthy siblings (44%) and 23 healthy children (47%) using the contingent negative variation (CNV, reaction time paradigm, 40 trials, 3 sec Interstimulus Interval, EOG control, filters: 0.03–35 Hz). Moreover, psychological variables and headache diaries were obtained in each group.

Results All CNV components demonstrated a significant amplitude reduction over time in all groups (effect Time was significant with $p < 0.007$; interaction Time \times Group non-significant). After 8 years the CNV habituation was more pronounced in all groups, although the greater reduction of habituation was observed in the migraine group ($p = 0.05$). The early CNV appeared to be a good predictor for remission: the larger the amplitude in 1998, the more probable the remission in 2006. Psychological variables differentiated better between migraineurs with and without remission than CNV parameters: patients with remission appeared significantly less aggressive, anxious and presented lesser somatization symptoms.

Conclusion The investigation demonstrated a significant maturation of cortical information processing in all children after 8 years, especially distinct in the migraine group. The remission from migraine may be predicted by the early CNV amplitude in the childhood and actual psychological abnormalities.

ScS3-5

Psychiatric comorbidity and headache familial recurrence: a study on 200 children and their parents

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Background The psychiatric comorbidity (Psi-co) in headache arise questions on the likely common etiological mechanism and direction of influence.

Objective To examine the relationship between headache and familial recurrence of psychiatric disorders by estimating the prevalence of mood, sleep and anxiety disorders in children diagnosed with headache compared to their parents' Psi-co.

Methods Headache history and symptomatology have been collected in a clinical sample of 200 patients and their families, using a semi-structured interview which covered all items required for diagnosing headaches according to ICHD-II criteria (2004). The questionnaire was composed by different sections in which we assessed the Psi-co in parents, according to DSM-IV criteria.

Results A Loglinear analysis was computed in order to evaluate main effects and interactions between the following factors: Headache subtypes (migraine/not-migraine) in children, headache (migraine/not-migraine-absent/present) in parents, headache (absent/present) in grandparents and psychiatric comorbidity (absent/present) have been analysed: 94 mothers (47%) and 51 fathers (25.5%) had at least one psychiatric disorder, mainly mood and anxiety disorders. Considering the significant prevalence of Psi-co in children (69.03%; LRChi-square = 15.62; d.f. = 1; $p < 0.0001$), we compared it with the presence of familiarity for headache: a significant interaction has been found (LRChi-square = 5.03; d.f. = 1; $p < 0.05$) showing that higher percentages of psychiatric disorders were in migraineurs with high familial recurrence of headache (74.65%) and oHs children with no familial loading (87.50%).

Conclusion The occurrence of psychiatric disorders is high in children with headache, but a very different pattern seems to characterise migraine (familial co-transmission of migraine and Psi-Co?) if compared to non-migraine headache.

POSTER

Poster session 2

C001

Amitriptyline vs behavioral therapy for juvenile tension-type headache

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Objectives Recurrent headaches are common in children and adolescents. Most current investigations have employed limited modalities (either medication or behavioral) and few have included treatment comparisons.

Methods In this study relaxation training and amitriptyline were compared for juvenile episodic Tension-Type Headache. Patients were treated by behavioral therapy (limited contact group relaxation training) (group A) or by amitriptyline, 10 mg for 3 months (group B).

Results The clinical improvement was significant for both groups at 1 and 2 year follow-up (days of headache/month: group A 14.8 vs 2.6 vs 3.5; group B 18 vs 1.9 vs 1.2).

In group B, 42 patients started treatment, 14 patients achieved the 24 months follow up.

In group A, of the 38 initial patients, 21 achieved the 2 years follow-up. The patients came regularly for the sessions, practiced routinely, appeared to be compliant and accepting of treatment, although we did not assess this formally.

Conclusions Although clinical similar results in both groups, relaxation therapy seems to be more accepted than medication. The limited contact modality seems to be as useful as other behavioral approaches that require a greater investment of time (by patients and therapists), without unpleasant side effects. Because the sample sizes are small, these conclusions are tentative. Data collection will continue on a larger sample of patients.

C002

Magnesium as a treatment for paediatric episodic tension-type headache: results at 1 year follow up

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Objectives To confirm the long-term utility of magnesium salts treatment on a group of young patients suffering from Episodic Tension Type Headache (ETTH).

Methods Setting: Outpatient Headache Center at the National Neurological Institute 'C. Besta,' Milan, Italy.

Patients: 45 children/adolescents with ETTH reporting consecutively for treatment. Interventions: 2.25 g of magnesium pidolate twice per day for 3 months. Medication was not administered during the one year of follow up. No other treatment was provided at any time.

Results Patients revealed significant symptom reduction.

Headache days decreased by 69.9% whereas analgesics consumption was reduced by 65.4%. Overall disability levels improved by the greatest percent – 75.7%. MIDAS subscores improved as well (question A = 58.0%; question B = 22.5%).

Conclusions Although uncontrolled, these findings are encouraging and suggest that further, more well-controlled research investigations are warranted.

C003

Red ear syndrome and juvenile migraine

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Objectives The red ear syndrome (RES) is characterized by uni-bilateral painful attacks to the ears that become red and burning. Several case-reports suggest an association between the RES and primary headaches, especially migraine. Aim of study was to determine the frequency of red ear syndrome and the relationship with other clinical features in a juvenile migraineous population.

Results Medical records of the children admitted for headache between 1 December 2004 and 30 November 2005, were consecutively studied. A questionnaire was used to study the prevalence of the red ear syndrome. We visited 279 children with headache. The range of age was 3–18 years. We classified the migraine in 62.36%, the other primary headaches in 22.6% and the secondary headaches in about 15.05%. The presence of the red ear syndrome was in about 26% (45 subjects) of migraine cases and it was very rare in the other two headache groups. The red ear syndrome was more present in the males, in the children less than 11 years and in the children with bilateral localization of pain.

Discussion Our study shows that the red ear syndrome is not uncommon and very specific in the migraine. Our clinical data suggest that in juvenile migraine the red ear syndrome may probably be related to the brain maturation factors. The red ear syndrome could be an important clinical marker of evolution in the pediatric migraine, but experimental neurophysiological and clinical follow-up studies are warranted.

C004

Biofeedback and Pet Therapy for treating daily chronic headache in growing up age

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Objectives We have been using Pet Therapy (PT) a few years now for treating headache linked to psychosocial malaise.

This therapy uses the animal world as vehicle with the assistance of psychotherapists.

Purpose of this work is to compare PT with Biofeedback-EMG in patients with CDH (headaches occurring more often than 15 days/month exceeding 4 hours/day),

Methods For BFB ten bi-weekly sessions took place of 30 minutes each (5'baseline 5 periods of 5' BFB after 1' of rest). After the fifth session relaxation exercises (M.P. Lair) were included.

For PT twenty weekly sessions took place of one hour each, with patients divided into two groups (pre and post puberty).

Thirteen patients were included in PT group (7f.6m.) mean age 11.8 ± 2.5 range 8/17 years.

Fourteen patients in the BFB group (7f.7m.) mean age 12.6 ± 2.2 range 10/17 years.

Data was controlled at T0 and T20 weeks, for headache frequency and duration, psychological tests, CDI and FABC anxiety scale.

Results Frequency PT (18.7 ± 1.3 – $11.8 \pm 0.8^*$) BFB (19.2 ± 1 – $9.9 \pm 1.7^*$)

Duration PT (6.2 ± 1.2 – $3.5 \pm 0.7^*$) BFB (5.4 ± 0.8 – $2.8 \pm 0.7^*$)

CDI PT (15.3 ± 0.9 – 7.3 ± 0.9) BFB (16.6 ± 7 – $10.3 \pm 1.3^*$)

Anxiety FABC PT (6.2 ± 1.2 – $3.5 \pm 0.7^*$) BFB (5.4 ± 0.8 – $2.8 \pm 0.7^*$) $p < 0.005$.

Conclusion Frequency and intensity of headache decreased in both therapies; psychological features, conversely, were better for better for PT.

Both therapies are able to control childhood headache.

The greater assurance that derives from an integrated men/animals course may undoubtedly be the reason for the better psychological effect of PT.

We consider PT very useful for childhood headache, even though it has a high cost.

C005

Paediatric chronic daily headache associated with school phobia

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Objective We investigated chronic daily headache (CDH) associated with school phobia in children and adolescents.

Methods Our study involved 208 children (115 girls and 93 boys) who visited our paediatric neurology clinic complaining of recurrent headaches. CDH was defined as the occurrence of headache for at least 15 days per month for more than 3months. Their headache types were diagnosed according to ICHD-II. Of 208 children, 50 (24%) were found with CDH. 24 children with CDH and school phobia were studied about their headache types, psychosocial factors and mental disorders.

Results Of 24 children with CDH and school phobia, 19 were girls aged 8–14 years and 5 were boys aged 11–14 years. Of 24, 1 had chronic migraine, 11 had chronic tension-type headache and 12 had both chronic tension-type headache and migraine. Of 24 with CDH and school phobia, 17 were found with adjustment disorder (6 also with depressed mood and 9

also with anxious mood), 5 were found with anxiety disorder and 2 were found with conversion disorder according to DSM-IV-TR. School problems such as bullying and family problems between parents or between parents and child were sometimes big causes of persistent headaches in children with school phobia. They needed not only pharmacological treatment but also counseling.

Conclusion Our study indicated that children with CDH and school phobia had the circumstances such as problems in school and/or family and mental disorders. They should be treated attentively for headache and their problems.

C006

Specific trigger factors of children recurrent headaches and migraine attacks

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Trigger factors induce recurrent non-migraine or migraine headaches in predisposed persons. A certain trigger factors will not induce a non migraine or migraine headache in every person. In a single headache sufferer a trigger factors may not cause a attack every time. It points to the existence of multi-factor triggering mechanism of individual headaches.

The aim of this investigation was to define conditions related to specific trigger factors for developing non migraine or migraine headaches.

Trigger factors of migraine attacks were studied in 30,636 children up to 17 years of age in North Province of Serbia. Recurrent headache was found in 21.47% children (20.8% male and 21.4% female). Migraine syndrome was found in 6.77% children (6.0% male and 7.6% female). During a 16-year period (1988–2004), the most common trigger factors of migraine attacks were: kinetosis (motion sickness) (89.8%), exposure to tobacco smoke (51.3%), alcohol (44.8%) and chronic stress (88.3%). Overexertion and lack of sleep can not be considered as migraine attack trigger factors, because they equally trigger non-migraine recurrent headaches.

Using canonical discriminant analysis, migraine headaches were differentiated from non-migraine headaches. The canonical discriminant coefficient (CDC) for unclear trigger factors (interference with routine daily activities) of migraine attacks was high (0.772), for unpleasant odors – significant (0.541), for various foods – positive (0.428), and it was negative (-0.406) for psychological stress.

Keywords: recurrent headache, migraine, trigger factors, causality

C007

Is Streptococcus a cause of tension-type headache in children?

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Objectives We previously showed that meningismus is a commonly overlooked feature in so-called Tension-type

headache in children and adolescents (IHC 2005, Kyoto). This finding suggests that such headaches may be caused by an otorhinolaryngeal infection rather than psychological factors. This study investigates the relationship between the major cause of otorhinolaryngeal infection, *Streptococcus*, and meningismus in children with Tension-type headache.

Methods Blood antistreptolysin-O titer (ASOT) was determined in 121 patients, aged 4 to 17, presenting with chronic headaches and in whom meningismus was discovered on neurological examination. ASOT >200 IU/ml was considered significant.

Results In 81% cases, a significantly high ASOT was found. A history of prior inflammation was obtained in many cases, although *Streptococcus* was infrequently implicated.

Conclusion Even in severe Streptococcal infections, only 70–80% of patients exhibit an elevated ASOT. The high incidence (~80%) of significantly elevated ASOT in these patients suggests that infection with *Streptococcus* may play a major causative role in headache with meningismus, so-called Tension-type headache. Hence, the syndrome of headache with meningismus may be related to the recently described PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections) syndrome, which refers to a subset of children with Obsessive Compulsive Disorder and/or Tic disorders, including Tourette's syndrome, where the origin appears to be infection with *Streptococcus* rather than psychological stress or tension, as was formerly believed. We suggest that studies, including autoimmune markers, should be carried out in children and adolescents suffering from headache with meningismus to further elucidate the condition, and perhaps provide appropriate therapy.

C008

Headache in children: does age make a difference?

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Objective To compare the learning profile, psychosocial factors, and headache type and clinical features in children of different age groups.

Methods A retrospective records review was conducted on all children presenting to the clinic for primary headache throughout a 1-year period. Charts were reviewed for headache characteristics and diagnosis based on ICHD-I criteria, the child's learning profile, and associated behavioral and social factors. Clinical indications for neuroimaging and their results were also recorded. Patients were divided according to the age of headache presentation to 3 groups: early onset (under 7 years), prepuberty (7–11 years), and adolescence (12–16 years). The above mentioned evaluation was compared between the 3 groups.

Results 108 patients were included at the study. 37 were under 7 years, 41 were between 7–11 years, and 30 were 12–16 years old. The diagnosis of migraine was more common in the adolescence group comparing to early onset, and the prepubertal group (47% vs. 22% and 32%; $p < 0.0014$). No signifi-

cant differences were found between the age groups with regard to headache disability, abnormal neuroimaging results, school performance, associated learning disabilities, or attention deficit disorder. Nevertheless in the early onset group patients had a significantly higher prevalence of behavioral problems (27% vs. 14% and 13%; $p < 0.067$).

Conclusion Our results suggest that the age of headache onset does not predict relentless headache disability or school performance in children. We may reassure parents that early onset headache does not imply a more severe course or etiology of disease, although behavioral problems may be more common in these children.

C009

Topiramate in two children with alternating hemiplegia of childhood (AHC)

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Objective To examine the effect of topiramate as add-on therapy in children with alternating hemiplegia of childhood (AHC).

Method The parents of seven children with AHC that were known in our hospital were informed about the positive results of treatment of AHC with topiramate. One patient already had topiramate with positive effect on attack frequency; two other children had few attacks and two other parents decided not to start with topiramate at this moment. Patients were neurologically examined before starting topiramate (1 mg/kg/day) and had a neuropsychological investigation. A baseline attack calendar was made by the parents during 2 months and in the months using topiramate.

Results Two AHC girls could be included (aged 5 and 11 yrs). The first patient already used flunarizine and had 5–9 hemiplegic attacks and 1 bilateral attack per month. During topiramate add-on treatment she first got less and shorter attacks during 6 weeks but the frequency increased then, especially of bilateral attacks (2–3 per month). Topiramate was discontinued. The second girl already used lamotrigine. With topiramate she got in a few weeks more attacks and developed behaviour problems and less appetite. Topiramate was also discontinued.

Conclusion In contrast to two earlier reports we did not find an improvement of frequency and duration of hemiplegic attacks in AHC children. An international study will be necessary to evaluate the effect of topiramate.

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C010

The high association between limbic circuit disorders and primary headache disordersAynur Ozge¹, Fevzi Toros², Aynur Ozge¹, Ozlem Kucuk²,Ozge Metin², Osman Yalin¹¹*Neurology, 2Child-Adolescent Psychiatry, Mersin University School of Medicine, Turkey*

Migraine headache is triggered by and associated with a variety of hormonal, emotional, nutritional, and physiological changes. Different migraine triggers activate wide variety of brain areas that impinge on parasympathetic neurons innervating the meninges. According to this hypothesis, migraine triggers such as perfume, stress, or awakening activate multiple hypothalamic, limbic, and cortical areas. There are also conflicting data about the association between limbic circuit disorders and primary headache disorders (especially migraine and tension type headache), epilepsy, atopic disorders and cyclic vomiting syndrome (CVS) in children. In the light of our clinical observations, in order to evaluate the association between some psychiatric disorders (obsessive compulsive disorder – OCD, tic disorder – TD, and attention deficit hyperactivity disorder – ADHD) and mentioned neurological and allergic disorders among the children diagnosed by child psychiatry department and their families, we performed this prospective clinical study. Totally 364 proportionally distributed subjects included in the study as following composition; 128 children (35.2%), 126 mothers (34.6%), 110 fathers (30.2%). Comorbid headache disorders reported 27.6% of children, 46.6% of mothers and 25.9% of fathers with TTH predominance. Epileptic disorders reported only 2.2% of the subjects. Atopic disorders reported average 15.6% of subjects. However 25.8% of the subjects reported abdominal pain but only 9.9% of them consisted with CVS criteria. The high comorbidity of migraine and mentioned psychiatric disorders has been reported both of the children and parents. It was concluded that limbic circuit disorders and primary headache disorders, especially migraine, associated with some neurological disturbances and this issue merit broad epidemiological and genetic studies.

C011

The limited value of neuroimaging studies in pediatric headacheJuan Romero-Sanchez¹, AM Leon-Ruiz¹, MI Romero-Sanchez²¹*Pediatric, Hospital Costa Del Sol, ²Medicina De Familia, Universidad De Cordoba, Spain*

Objectives To assess the value of neuroimaging in a series of children with chronic headaches.

Methods A retrospective chart review was conducted of all children referred to the pediatric outpatient clinic for evaluation of headache over a 3-year period. The charts were reviewed for headache characteristics, neuroimaging indications, and imaging results. Special attention was paid to evidence of space-occupying lesions.

Results A total of 160 sequential records were studied, with subjects ranging in age from 4 to 14 years. Most patients were diagnosed as having migraine headaches (60%) or chronic tension headaches (29.5%). Other diagnoses were post-traumatic (6%) and unclassified (4%). Sixty-six patients (41%) had computed tomography imaging performed. In most cases, brain imaging studies were performed because of clinical data (41%) like atypical pattern, sleep-related headache or increase of headache, because of the parents' concerns about brain lesions (38%) and because of an age less than 5 years (14%). Structural changes were found on brain imaging in 4 patients, but none indicated the presence of a treatable space-occupying lesion and all were deemed unrelated to the headache. Our findings of no relevant abnormalities in a series of 66 neuroimaging studies indicate that the maximal rate at which such abnormalities might appear in this population is 4.4%.

Conclusions These results indicate that neuroimaging studies have very limited value in the clinical evaluation of pediatric patients with chronic headache and should be reserved for those patients with clinical evidence suggestive of underlying structural lesion.

C012

Brain tumours and children headache, clinical cases

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We present some cases we observed last year.

Martina, an 8-year-old girl, presented for widespread headache with onset three years before and ever since experienced conflictive parent separation. Anxious and attached to her mother, her symptoms appeared to be psychological. Neurological examination (NE) was negative.

At the hospital she suffered a headache crisis, which did not recede with drugs. NMR revealed a formation in the back cranial fossa. Surgery revealed an adenoma, 2 months later headache disappeared.

Giorgia is 13 and has suffered migraine for 2 years. Very attached to her mother, suffered sleep disturbances and intense headache almost daily for 3 months. She vomited and coughed, but she was on a diet. NE negative; evident family tensions. During hospitalization had slight difficulty climbing stairs. CAT-scan showed a 6cm hypodense formation in the temporal area. Operated for medulloblastoma I°, underwent a cycle of chemotherapy.

Gianluca, a 5-year-old boy complained of intense headache for several months.

Following cranial trauma, headache worsened and 10 days after he complained of violent headache. NE negative. NMR showed a voluminous formation in back cranial fossa. In Neurosurgery, neurological signs began: vomiting, drowsiness, dysmetria, dysarthria. Operated for Medulloblastoma IV°, chemotherapy and radiotherapy followed. He relapsed. Operated again, chemotherapy followed, but death occurred 16 months after diagnosis.

Headache was the only neurological sign. Psychological diagnosis would have been misleading. Long observation of the child's reactions to headache led us to perform

Neuroimaging, which then led to diagnosis. Children with terrible headache should be seen during the crisis.

C013

A case of chronic paroxysmal hemicrania in paediatric age

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Objectives To describe the case of a child with headache non-responsive to most analgesic drugs. Case report. A 7-years old male referred to our Headache Center because of a headache begun 1 year before. Headache attacks were daily and lasted around 30 minutes. Pain was unilateral in the right orbito-frontal region and was associated with photophobia, vomit and right tearing. Brain magnetic resonance imaging (MRI) was normal. Pain was not ameliorated by most analgesic drugs, including acetaminophen, ketoprofen, and aspirin. A prophylactic treatment with amitriptyline was attempted without any clinical improvement. Lastly, the child began a psychological treatment.

Results Indomethacin 25 mg/die led to a significant improvement in headache frequency, reduced to 2–3 attacks per month. Moreover, pain attack was resolved by the assumption of indomethacin 25 mg. After 6 months, the treatment was interrupted, but the headache worsened. Flunarizine 5 mg/die was attempted without any amelioration, while a satisfactory improvement was obtained after the reprise of indomethacin 25 mg/die (frequency: 6–7 attacks per month). A further reduction in frequency of the headache attacks (2–3 per months) was obtained when topiramate was added at the dose of 1.5 mg/kg/die.

Conclusion The clinical characteristics of our child's headache and the positive response to indomethacin led us to propose the diagnosis of 'Chronic Paroxysmal Hemicrania'. Our child, therefore, can be added to the very few cases of this Trigeminal Autonomic Cephalgias described in paediatric age.

C014

Cerebrospinal fluid hypovolemia (intracranial hypotension) in children and adolescents

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Objectives Cerebrospinal fluid (CSF) hypovolemia synonymous with intracranial hypotension is considered rare disease even in adult. Very few papers of child intracranial hypotension were issued. The aim of this study was to evaluate CSF hypovolemia in child patients with chronic refractory headache.

Methods CSF leakage was evaluated by radioisotope (RI) cisternography and CSF hypovolemia was evaluated by cranial gadolinium enhanced magnetic resonance image (MRI). 15 Patients aged 10 to 17 with chronic refractory headache were treated by epidural blood patch (EBP). Male was 5 and females were 10.

Results Causes of CSF hypovolemia were motor vehicle accident: 3, sports: 4 fall: 2 and unknown: 6. Main symptoms were as follows: orthostatic headache and fatigue in all 15 cases, neck pain in 9 cases, and dizziness in 6 cases. RI cisternography was performed in 6 cases. CSF leak was seen in four cases. Decreased CSF detected by cranial MRI was noted in eight cases. EBP was performed in all cases (one EBP in 5 cases, two EBP in 5 cases, more than three EBP in 5 cases) without any serious complications. Outcome was as follows: good recovery in 11 cases, moderate recovery in 4 cases.

Conclusion CSF hypovolemia was seen in cases of children and adolescents with chronic refractory headache. EBP was effective for child patients with CSF hypovolemia. MRI or RI cisternography should be examined in patients with chronic refractory headache.

C015

The new daily persistent headache and viral infections in children

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The NDPH is type of headache more frequent on the children (ICHD-II, 2004). Among various causes precipitating this headache there are viral infections. The aim of study is to verify the role of viral infections on the history of NPDH in children.

Materials and methods Among 150 patients admitted to Pediatric Clinic of University of L'Aquila are selected 25 children, 16 females and 9 males (5.05 to 14.09 years), suffering from CDH (HIS, 2004). We determined: Ab anti CMV, EBV, HV1 (immunoenzymatic method), Neurophysiopathological tests (VEP – pattern reversal, SEP of trigeminus, Blink reflex).

Results Children suffering from CDH are 13% of the patients observed during 1 year. 40% of children are suffering from NPDH. On 42% of children the cause precipitating the headache is the viral infections (persistent fever and laboratory tests Ig M CMV, EBV and varicella). VEP show the latency of wave P100 higher and amplitude reduced in respect to average of controls (Headache, 2001). The SEP values show P19 wave amplitude reduced on the same size of pain on 66% of children. The latency of Blink reflex R2c on the opposite size of pain is raised. The follow up after 1 year confirm that headache disappeared on the 40% of children. Only on 15% of patients the headache showed one period of daily persistency.

Conclusion Viral illness is precipitating cause on 30% of children. The headache remission is more than its persistency (40% vs 20%). The behaviour of VEP, SEP and Blink reflex underline that the headache of this sample is more secondary type than primary headache.

C016

Abdominal migraine in childhood

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Objectives To evaluate the clinical manifestations of abdominal migraine and its treatment in childhood.

Methods A total of 311 patients with recurrent headache or abdominal pain under 15 years old, participated in this study which was conducted for 2.5 years at 2 hospitals. They were diagnosed with ICHD-2 criteria as primary headache.

Results Among the primary headache, patients with abdominal migraine were 27 (8.7%), and 51 (16.4%) of migraine and tension-type headache had a history of abdominal migraine.

On the abdominal migraine, mean age was 6.2 year-old, and male to female ratio was 1:1.15. Seventeen (70.4%) of them had a limitation of motion during the attack, 22 (81.5%) had a recurrent headache, but their chief complain was recurrent abdominal pain, which lasted for about 3.5 hours.

22 (74.1%) had a family history of recurrent headache. Associated symptoms was change of facial color (37.0%, pallor or flushing), nausea (50.0%), vomiting (34.6%). 15 of them were treated with amitriptyline, and 67.7% of them showed good response.

Conclusion Abdominal migraine is important in early childhood, and commonly associated with recurrent headache. Amitriptyline seemed to be effective in abdominal migraine.

C017

Reduced habituation of the MMN and P300 potentials in children with migraine and TTHMassimiliano Valeriani¹, F Galli², S Tarantino³, R Miliucci¹, D Graceffa², E Pignata², F Vigevano¹, V Guidetti⁴

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Objectives To calculate the habituation of the auditory P300 and mismatch-negativity (MMN) responses in children with different types of headache and to compare it with healthy controls.

Materials and methods Eighteen migraineurs (mean age 10.2 years, range 7–14 years; 9 females, 9 males), eight children with tension-type headache (TTH) (mean age 11.5 years, range 8–16 years; 5 females, 3 males), and six healthy children (mean age 11.7 years, range 8–14 years; 4 females, 2 males) were recruited. To evaluate the evoked potential habituation, the P300 and MMN potentials were recorded to auditory stimuli in 3 successive trials, with an inter-trial interval of 5 minutes.

Results No difference in both MMN latency and amplitude was found among the groups of subjects, while the P300 potential was lower in amplitude and slower in latency in both TTH and migraine patients, as compared to healthy controls. While in healthy children the MMN and P300 amplitudes showed a physiological habituation in the third trial, no MMN and P300 amplitude reduction was obtained in both migraine and TTH patients.

Conclusion The abnormal P300 in children with headache might be related to a higher difficulty, as compared to healthy subjects, in keeping their attention focused on target stimuli. Moreover, in paediatric age the well-known phenomenon of the evoked potential reduced habituation cannot differentiate migraine from TTH, which are likely to represent a common disease.

C018

Correlation between reduced P300 habituation and behaviour disorders in children with migraineFederica Galli¹, S Tarantino², R Miliucci³, D Graceffa¹, E Pignata¹, F Vigevano³, G Biondi², V Guidetti⁴, M Valeriani³

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Objectives To assess the correlation between the habituation of the auditory P300 and mismatch-negativity (MMN) responses in children with different types of headache and behavioural disorders.

Materials and methods Eighteen migraineurs (mean age 10.2 years, range 7–14 years; 9 females, 9 males), eight children with tension-type headache (TTH) (mean age 11.5 years, range 8–16 years; 5 females, 3 males), and six healthy children (mean age 11.7 years, range 8–14 years; 4 females, 2 males) were recruited. To evaluate the evoked potential habituation, the P300 and MMN potentials were recorded to auditory stimuli in 3 successive trials, with an inter-trial interval of 5 minutes. The behaviour of patients and healthy controls was assessed by means of the Child Behaviour Checklist (CBCL) administered to the mother.

Results No significant correlation was found between the MMN habituation and the CBCL scores in all groups. A significant positive correlation was found between the reduced P300 habituation and the total CBCL score in migraine children ($P = 0.01$), but not in TTH patients and healthy subjects ($P > 0.05$). In migraineurs, the reduced P300 habituation showed a significant positive correlation with both the internalising ($P = 0.03$) and the externalising ($P = 0.008$) scores.

Conclusion Our preliminary results suggest that in migraine children the reduced P300 habituation may represent a neurophysiological marker of behaviour disorders, it being higher in patients with worse externalising and internalising scores.

C019

A case of migraine with pervasive developmental disordersNaoki Ando, S Kobayashi, A Hattori, T Ishikawa, H Togari
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Introduction The diagnostic category pervasive developmental disorders (PDD) refers to a group of disorders characterized by delays in the development of multiple basic functions including socialization and communication. They frequently complain of physical symptom such as headache. We report a case of migraine headache with PDD.

Case report A 7-year-old Japanese boy had been complained of headache attacks for less than one hour. He had nausea and/or vomiting during frontotemporal throbbing headache. He was diagnosed as migraine without aura. Because the frequency was about ten times per a month, he was missing of school and disabling his daily life. His intelligence quotient was 100 by the 3rd edition of Wechsler Intelligence Scale for Children. He had some troubles at school, mainly socialization and communication. We diagnosed as PDD additionally. We reported that the trigger factors of migraine were lack of sleep and emotional stress at the 12th Congress of the International Headache Society, Kyoto, 2005. The patients who are diagnosed as PDD are tendency to suffer much emotional stress at school. As a result, migraine has occurred by trigger factors such as emotional stress. We should recognize that the patient with PDD has much emotional stress which is one of the many trigger factors of migraine in childhood or adults.

C020

Socioeconomic status of children with headache in Central Greece

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Objectives To study the socioeconomic differences associated with the occurrence of reported headache in children living in Central Greece.

Methods Children with a history of headache evaluated at the Headache Outpatient Clinic of the University Hospital of Larissa in Central Greece were included in the study. The classification of the headaches was according to the criteria of the International Headache Society (1988). Detailed information was collected through questionnaires about annual household income, parents' education level and parents' employment. For comparison reasons, a control group of 151 children, not suffering from headache, was used. Data analysis was carried out using SPSS statistical software. Differences were considered significant at the level p.

C021

Criterion validity of the BDI-II and MMPI-A depression scale in tertiary care adolescent headache patients

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Objectives To evaluate the accuracy of the Beck Depression Inventory-II (BDI-II) and Minnesota Multiphasic Personality Inventory-Adolescent (MMPI-A) Depression scale (A-Dep) in detecting major depressive disorder (MDD), adjustment disorder with depressed mood (ADDM), and dysthymic disorder (DD) in tertiary care adolescent headache patients.

Methods The sample included 104 tertiary care adolescent headache patients treated between 4/2003 and 12/2006. Data abstracted from medical records included headache diagnosis, psychiatric diagnoses, and BDI-II and A-Dep scores.

Receiver operating characteristic (ROC) analysis was used to evaluate the accuracy of the BDI-II and A-Dep in detecting MDD, ADDM, and DD.

Results The prevalence of MDD, ADDM, and DD was 15.4%, 13.5%, and 9.6%, respectively. Areas under the ROC curve (BDI-II vs. A-Dep) were as follows: MDD – 0.779 vs. 0.712, p = 0.405; ADDM – 0.533 vs. 0.608, p = 0.554; and DD – 0.514 vs. 0.567, p = 0.388. The optimal cutoff score, sensitivity, specificity, and positive and negative predictive values were as follows: MDD – BDI-II: 7/8, 0.875, 0.544, 0.280, 0.956 vs. A-Dep: 67/68, 0.625, 0.795, 0.357, 0.921; ADDM – BDI-II: 21/22, 1.000, 0.193, 0.152, 1.000 vs. A-Dep: 73/74, 0.357, 0.867, 0.294, 0.897; and DD – BDI-II: 7/8, 0.556, 0.605, 0.128, 0.929 vs. A-Dep: 69/70, 0.900, 0.287, 0.118, 0.964. The A-Dep performed poorly when using cutoffs that maximized sensitivity. Excluding patients with elevated scores on the MMPI-A validity scales reduced the accuracy of the A-Dep in detecting MDD.

Conclusions We provide appropriate cutoff scores for detecting depression in tertiary care adolescent headache patients. Due to the need for accurate depression detection in this population, preference should be given to the BDI-II.

C022

Prevalences and incidences of primary headache and functional abdominal pain in first graders at primary school

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Objectives Our project allows to determine the prevalences and incidences of primary headache and functional abdominal pain symptoms (according to IHS 2004, Rome-II Criteria), being assessed simultaneously on the basis of repeated population based epidemiological surveys. Does the life-event 'school-entry' have an impact on the frequencies of these pediatric complaints?

Methods The questionnaire FSEKB could be handed out to 674 (78.1%) parents of the 832 officially announced first graders. 375 (51.9%) participated with their children (48.3%♂, 51.7%♀) in the second data-census, which was enforced by middle of January until end of June 2005. Pupils and their parents were questioned separately.

Results The participation rate declined in this data census: 2004: 73.0%; 2005: 51.9%. The prevalences of primary headaches (H) and headaches in combination with abdominal pain (HAP) increased while those for abdominal pain (AP) and no pain (NP) decreased: (2004 vs 2005: H:3.6% vs 6.9%, HAP:51.7% vs 67.9%, AP:31.9% vs 18.3%, NP:12.8%/6.9%). The following incidences were registered for first graders: H = 0.86%, HAP = 12.57%, AP = 4.29%, with enormous fluctuations between the groups. Relative frequencies for the occurrence of headache attacks: 4.7% (1–6 times weekly), 10.7% (1–3 times monthly). Duration of the attacks: 10.3% (>1 hour), 5.5% (1–3 hours), 4.0% (4–24 hours). 3.2% take always medication during headache attacks. Further data for interrelations between headache symptoms and social status, gender and quality of life measures will be reported.

Conclusion School-entry as a life event does increase prevalences and incidences of headaches occurring single or in combinations with abdominal pain.

C023

More empathy for the children's view on daily pain experiences

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Objectives Children do know where 'the shoe pinches'! They are able to communicate their experienced aversive body sensations, but their way and depending on their developmental stage. Our project reserves space for colloquial pain stories of children and reports empirical findings.

Methods 590 pain interviews of children (5–10 and 13–15 years) have been tape-recorded at this time. The 'Pediatric Pain Inventory' asks the children to describe the pain (CATdes), to specify probable causes (CATattr), to list coping strategies (CATcop) as well as attachment relationships (CATattach). A new categorisation system (CAT_SYS_PED_PAIN) has been developed allowing the exhaustive classification of the children's statements about different pain situations: headache (H), abdominal pain (AP), injection (INJ), bicycle accident (BIKE). Number of categories: CATdes = 17, CATattr = 16, CATcop = 22, CATattach = 16. Actually 76 interviews of second graders (53.7%♂, 46.3%♀) are rated. Interrater reliabilities will be provided at time of congress.

Results Children generate in total 3088 (mean 10.3) utterances to describe the four pain situations, H = 654/21.2%; AP = 998/32.3%; INJ = 603/19.5%; Bike = 833/27.0%. Relative distributions of categories:

CATdes > H = 27.2%; AB = 23.5%; INJ = 24.4%; Bike = 24.9%;
 CATattr > H = 25.4%; AB = 23.6%; INJ = 23.7%; Bike = 27.3%;
 CATcop > H = 22.5%; AB = 27.3%; INJ = 21.4%; Bike = 28.6%;
 CATattach > H = 26.3%; AB = 26.0%; INJ = 22.0%; Bike = 25.7%

Conclusions Children talk about their pain with interest but without exaggeration. More empathy for the children's view of daily pain experiences is not only theoretically demanded (inner body sensation can only be described by the experienter himself); it also contributes to acquire empirical knowledge that could provide the basis of a new way of looking at this issue.

C024

Verbal reports on pediatric headache descriptions of second graders

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Objectives Repeated studies reported that children use the concept 'general pain' when asked to define diseases. Investigations of self experienced infantile headaches on the basis of spontaneous verbal reports are seldom, although they should be given an increasing relevance for the medical diagnostic process. This study was enforced to empower the subjective view of children's headache experiences and to analyse the verbal reports exhaustively applying a newly developed categorical system.

Methods 180 German second graders were asked to describe their headache experiences. Actually the interviews of 82 children (43 with and 39 without recurrent pain experiences) were rated according to our new categorical system. The containing 17 categories will be presented. The frequency distributions and group comparisons were conducted by SPSS.12. Actually the interrater reliabilities are not yet available, they will be reported on the congress.

Results On average the children describe headaches with 2 categories, without gender differences. In total 227 units were used by the 82 children to describe headaches (RP 124, NRP 103). 65.9% of the children used general descriptions with intensifying additions; whereas girls use this category more often, RP prefer specific complex descriptors (RP 44.2% vs. NRP 25.6%). 30.2% of the children suffering from recurrent headache experiences apply metaphorical idioms while they are only used by healthy children in 7.7% of the cases.

Conclusion The systematic study and empirical appraisal of infantile headache descriptions is an appropriate basis in generating a pediatric categorical system for headaches.

C025

Children's view on headache causes – biased by medical or parental cognitions?

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Objectives Current studies postulate a strong relationship between stress and headache, naming stress as a cause of headache in 40% of all cases. This study analyses and reports the children's view on the causes of self-experienced headaches.

Methods 130 second graders (mean age 7.11 years) with recurrent pain experiences were examined. Preliminary results of 32 interviews (20 boys and 12 girls) about headache

causes as well as the recently developed categorical system for pain causes, including 19 categories, will be presented. The system allows an exhaustive classification of all causes named by children spontaneously. The previously suggested categories for recurrent pain experiences in the literature can be verified by aggregating single categories of our used categorical system. Frequency distributions and group comparisons were conducted by SPSS.12.

Results 21.9% of the children apply environmental conditions, 18.8% an accident or aching incidents and 12.6% behavioural reasons as causes for self-experienced headaches. 25.0% of the children are not able to name a specific cause. Only 3.1% of the children apply stress as a cause for their headache.

Conclusion For a better understanding of pediatric pain experiences, the children's view of pain must be integrated into the diagnostic process. The surprising gap between the experts' and the children's view on the impact of psychosocial stress as a headache-trigger, should intensify the effort of excluding the way of questioning (closed or open) as an objectionable interacting variable. The common opinion of experts or parents should not be imposed on children automatically.

C026

Coping strategies of children with recurrent pain experiences – analyses of headache and abdominal pain situations

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Objectives Our new categorical system allows the exhaustive classification of infantile coping strategies from colloquial stories about different pain situations (headache, abdominal pain, rheumatic pain, bicycle accident, injection). The coping-strategies of second graders in headache and abdominal pain situations shall be described.

Methods Out of 180 investigated second graders 32 interviews of participants with recurrent pain experiences (>1x/month headache and/or abdominal pain attacks) have been classified into 22 categories including 13 internal and 9 external coping strategies.

Results 4.7% of the analysed children have headaches, 25.6% have abdominal pain, 44.2% have both. All children were asked to generate coping strategies for both pain situations. In total 201 strategies were mentioned to manage headache and abdominal pain situations: 3.5 units per child for abdominal pain; 2.5 units for headache. Out of 22 categories 14 were chosen to cope with headaches (Hsit) and 11 for the coping with abdominal pain (APsit). The most frequently used category in both situations was 'withdrawal and relaxation' (Hsit 53.2%, APsit 56.2%) followed by 'physical auxiliaries' (Hsit 34.4%, APsit 40.7%), 'pharmacological means' (Hsit 18.7%, APsit 18.8%) and 'concrete actions' (Hsit 18.7%, APsit 31.3%). 'The wish to get emotional support' was mentioned only quite seldom (Hsit 9.4%, APsit 6.3%).

Conclusion More explanatory power will be expected when integrating the results of all participating children. Examining coping strategies with focus on the child's view will contribute to a better understanding and amelioration of the support through pediatric pain specialists.

C027

Coping behaviour of children with recurrent headache experiences (a comparison with healthy children)

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Objectives Pediatric headache is a relevant cause for discomfort in children and for the use of medical consultation. The diverse genesis of headache symptoms results in a need for multimodal therapeutic interventions. This study compares self-reported coping strategies between healthy and recurrent headache experienced children of second graders at primary school.

Methods Out of 180 participants 32 were classified as having recurrent headaches (RH: >2x/month) and 35 without recurrent headache (NRH <1x/month). All children were interviewed by using a 'Pediatric Pain Inventory' while tape-recording their spontaneous verbal reports. The answers were classified in a revised and extended categorical system on the basis of proposals noted in the literature. It consists of 22 categories subdividing internal and external coping strategies.

Results A wide range of coping strategies was reported. Internal coping strategies ('have a rest', 'relaxation', 'sleep' etc.) prevail with over 50% of the categorised units. Healthy children prefer 'physical' (NRH: 45.7%, RH: 34.3%) and 'pharmacological' measures (NRH: 11.5%, RH: 3.1%) and propose to 'consult the doctor' (NRH: 11.5%, RH: 3.1%). According to children with recurrent headaches 'help from other persons' do not relieve the pain (RH: 81%, NRH: 45.7%), the success rate in controlling the pain is very low in this group (RH: 3.1%, NRH: 17.1%).

Conclusions The extension of the categorical system allows an exhaustive differentiation of the numerous infantile coping informations. Preventive coping strategies from experts can tie in with this rich knowledge to develop prophylactic support and to avoid a chronicification process.

C028

Attachment network of children with and without recurrent headache experiences

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Objectives Attachment is influenced by many different factors during the developmental process. It is supposed that

second graders at primary school vary in their attachment networks depending on the extent to which they suffer from recurrent headache experiences. This study analyses the attachment relationships enumerated by the children during the 'Pediatric Pain Interview on headache situations'.

Methods 42 second graders with (RP) and 31 without recurrent headaches (NRP) (mean age 7.11 years) were analysed. During the interviews a picture showing a child suffering from headaches was used for motivation. The children were instructed to enumerate the attachment relationships during headache attacks for the child on the picture and for themselves. A categorical system including 18 units for the attachment network during headache attacks, has been used.

Results In total 73 children named 172 attachment relationships: NRP = 51 < min 1, max 4<; RP = 121 < min 1, max 7>. Healthy children find it difficult to imagine helpful people for pain prone children, whereas they name 10 helpful relationships for themselves. On the other hand headache children nominate the most dense attachment network; but for themselves less (26) than for others (31).

Conclusion Children with and without recurrent headaches differ in their perceived attachment network, that is described within a broader range by headache prone children than by healthy ones. There is an urgent need for a better understanding of these interesting results.

C029

Headache familial recurrence: a study on 200 children and adolescents

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Objectives Migraine is a complex disease, where genetic and biology interact with environmental factors, determining a polygenic multifactorial etiology. Main aim is analysing if migraine characteristics change according to familial recurrence of headache compared to other Headache sub-types (oHs).

Methods Two hundred children (92m; 108f; m.a. 10.99 yrs; range 4.6–17.9 yrs) and their parents have been enrolled in our Headache Center. To record headache history a semi-structured interview has been administrated (ICHD-II criteria). Data have been collected on the occurrence of headache in first and second-degree relatives. Loglinear and Pearson Chi-square analyses were computed to evaluate the influence of mother and father headache on headache severity and subtypes (migraine/oHs) in children, crossing data according to headache in grandparents too.

Results Considering headache recurrence in mothers, it was very frequent (74.64%) in migraine group and independent from severity; familial recurrence was less frequent in oHs children (66.67%) and prevalent only (83.33%) in less severe group. Considering fathers, familiarity was near to 50% both in migraine and oHs groups and prevalent only in less severe migraine group (72.55%). Significant associations were also found between the prevalence of headache in parents and grandparents.

Conclusion Considering only the prevalence of headache in parents, no direct familiarity effect was found on subtypes of headache in children. Extending headache assessment to second-degree relatives, combined effects of mother and father recurrence of headache have been found on severity of migraine or oHs.

C030

Headache clinical characteristics and familial loading: a study on 200 children and adolescents

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Objectives The interplay of genetic and environmental factors has been evidenced in migraine where nature and nurture may establish different phenotypic manifestations. Our aim is analysing if headache clinical characteristics change according to familial recurrence of headache.

Methods Two-hundred children (92m; 108f; m.a. 10.99 yrs; range 4.6–17.9 yrs) and their parents were enrolled in the Child and Adolescent Headache Center of our Department. To record headache history a semi-structured interview has been administrated, according to ICHD-II criteria (2004). Data were collected on the occurrence of headache in first and second-degree relatives. Two groups have been selected: a 'double familiarity headache group' (n = 97) (presence of headache in one parent and one of grandparents at least), and a 'no headache familiarity group' (n = 19). Loglinear analyses were performed in order to verify associations between familiarity, headache subtypes in children (migraine/oHs), intensity, drug efficacy, photophobia, Recurrent Abdominal Pain (RAP), vomiting and presence/absence of pre/perinatal complications.

Results Double familiarity was prevalent in 87.06% of migraineurs; prevalence of pre/perinatal complications was higher in double familiarity group (54.64%) than in no familiarity children (42.11%); the highest prevalence of photophobia (74.32%) has been found in migraineurs with double familiarity, while the lowest (12.50%) in oHs children with no familiarity. Vomiting was present only in 9.68% of the oHs group and in 26.32% of no familiarity children.

Conclusion Photophobia seems to be related to high familial loading. The presence of pre/perinatal complications in the whole sample needs attention, as the likely connection with familial loading. However, the few number of patients with headache-free relatives limits our findings.

C031

Topiramate in treatment of migraine headache in children

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The aim of this study is to present the efficacy of prophylactic treatment of Topiramate in 24 children with migraine

headache, who did not respond to other pharmacologic and nonpharmacologic treatment. The best toleration and the lowest side effects of Topiramate are with daily dose of 100 mg.

Methods This study includes 24 children with migraine headache: 15 girls/9 boys, with median age of 10.5 yrs. Five of them had migraine with aura and 19 migraine without aura. The average daily dose of Topiramate was 100 mg, and average treatment duration 14 mo.

Results Before the treatment, 75% of children had non-specific change in EEG, and 25% of them had normal EEG findings. After 4 months of treatment, EEG became normal in 67% of children, headache frequency and pain intensity diminished in 58% of children, and in 27% of them headache completely disappeared. 3% of children had no response to treatment. The most often side effects were parestesias, behavioral changes and fatigue, which were found in 27% of children.

Conclusion Topiramate is indicated for migraine treatment in children when conventional treatment is unsuccessful. The titration has to be gradually, and the best effect is with daily dose of 100 mg. It has better effect in migraine with aura compared to migraine without aura. Topiramate treatment has more advantage compared to other antiepileptic and anti-migraine drugs.

C032

Peri-ictal changes of cortical excitability in paediatric migraine

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Objective Migraine patients are characterized by an altered cortical excitability between attacks. Different studies have provided evidence for both increased and reduced cortical excitability. One possible explanation for these inconsistent conclusions is that excitability may vary between migraine attacks and different groups may have recorded excitability changes at different phases of the interval.

Methods To describe excitability changes between attacks, we performed transcranial magnetic stimulation (TMS, two 2.2-Tesla MagStim-200) over the motor cortex (EMG from the m.abductor digiti minimi) and occipital cortex (phosphene thresholds, suppression of perception with stimulus onset asynchronies between 40 and 180 msec) in 9 children suffering from migraine without aura just before, just after a migraine attack and during the interval between attacks. Moreover, motion and tilt visual after-effects (MAE/TAE) were also investigated. The psychophysical and TMS parameters of migraineurs were compared with those obtained in healthy children.

Results During the interval, migraine children demonstrated significantly reduced phosphene thresholds ($p = 0.002$) compared with healthy controls. Before an attack, a significant increase in phosphene thresholds ($p = 0.049$), suppression of visual perception ($p = 0.009$), an increase in MAE duration ($p = 0.026$) and a trend for an increased TAE ($p = 0.089$) was

observed. We found no significant changes in any of the parameters of motor cortex excitability.

Conclusion Although between attacks and after an attack children with migraine demonstrate increased cortical excitability, the excitability seems to normalize before a migraine attack. This normalization may represent either a protective mechanism or an abnormal decrease in excitability just before an attack.

C033

Do recurrent pain experiences exert influence on the habitual interference tendency of children?

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Objectives This study analyses the habitual interference tendency of children with and without recurrent pain experiences. The basic cognitive capacity to concentrate on concise stimuli qualities (colour) in view of other irrelevant, incongruent stimuli (typeface) should also be able to influence the cognitive coping with pain. Are such interrelations already existing in children at primary school age?

Methods 178 German second graders were examined (7.3 years, 50.6%♂, 49.4%♀). Experimental group: N = 77 children with recurrent pain experiences; Control group: N = 101 healthy children. The habitual interference tendency was detected by FWIT (subtests INT; test-tables 3, 6 and 9). The statistic analysis was conducted by SPSS (Vers. 12).

Results Recurrent pain experiences have an influence on the habitual interference tendency of the children (multivariate GLM: $F = 1.960$; $df = 442.13$; $p = 0.026$). Interaction effects show a tendency between pain group and sex (multivariate GLM $F = 1.741$; $df = 442.13$; $p = 0.056$). Gender differences in the concentrative resistance against other dominating reaction tendencies were not found. All children improved their performance over the 3 test cycles with decreasing standard deviations. For children with recurrent headaches most of the uncorrected mistakes in all test cycles were registered.

Conclusion The habitual interference tendency is influenced by recurrent pain experiences already in infancy. Standardized data for children at primary school age are still missing. The capacity of concentrative resistance against dominating reaction tendencies could be helpful for coping with recurrent pain experiences.

C035

Do functional or organic recurrent pain experiences change attention measures in children?

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Objectives This study aims to examine the impact of pain on attention processes of primary school children. In the current literature different views about the interrelationships between pain, attention and cognition are reported. Von Bueren Jarchow et al (2005) found that adult pain patients are significantly slower in attentional tasks than a non-affected control group. It is investigated here how pain impairs attentional functions in children.

Methods Children with recurrent headaches and abdominal pain are compared to those with organic pain (juvenile rheumatic arthritis) and without pain. Each of these groups consists of 19 subjects (11 boys, 8 girls), matched by gender and age (mean age 8.10 years). The attention processes are measured by the two subtests 'alertness' and 'selective attention' of the neuropsychological test battery TAP. The statistical analyses are conducted by SPSS.11.

Results Mean reaction times do not differ significantly over the three groups (multivariate GLM alertness: $F = 0.1.674$; $df = 2.50$; $p = 0.198$; selective attention: $F = 0.773$; $df = 2.50$; $p = 0.467$). All children ameliorate their normal alertness results from the first to the second test cycle and worsen it in the condition with audio warning (repeated measure GLM alertness $F = 17.660$; $df = 3.49$; $p = 0.000$).

Conclusions This study results imply that pain experiences do not influence children's attention processes at primary school age; at this point the results of our studies are still inconsistent and depend on the employed operationalisation. Repeated measure analysis shows increasing and decreasing performances in dependence of the test condition.

Reference

Jarchow et al. (2005).

C036

Interdependencies of selective attention capacity and recurrent pain experiences

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Objectives Recurrent pain experiences are a relevant topic in the health care of children at primary school. This project analyses how basal attention functions of children interfere with recurrent pain experiences. In school attention is normally defined as the capacity to recall learned topics. In our

project it is neuropsychologically operationalised as a basal cognitive construct consisting of different partial performances (Sturm et al. 2000), exemplified in this analysis by the selective attention capacity.

Methods 180 second-graders were examined. 54 of them with recurrent headache and abdominal pain experiences (RHAP) are compared to 50 healthy children (H). The selective attention capacity was collected by TAP, an attention test system, with the subtest 'incompatibility' (Fimm et al, 2002). Statistical analysis was performed with SPSS.12.

Results Mean reaction times in the TAP of children with recurrent pain experiences don't differ significantly from healthy children (anova meanRHAP = 574.96 ms, meanH = 599.55 ms; $F = 1.016$, $df = 1$; $p = 0.316$). Comparing false reactions in the different experimental conditions, pain experienced children differ significantly from those of healthy children in the experimental condition 'right compatible' (Mann-Whitney-U-test: errorsRHAP = 1.87; errorsH = 1.11, $Z = -2.083$, $p = 0.037$). Additionally children with recurrent headache show a lower interference disposition (detected with the parameter 'visual field \times responsive hand') (Mann-Whitney-U-test: MDRHAP = 0.825, MDH = 4.425, $Z = -2.306$, $p = 0.021$).

Conclusions Enlarging the attention construct normally used in school life via the introduction of the neuropsychological view is new and promising. The results suggest that recurrent pain experiences influence the secure and explicit selective attention capacity already in second-graders.

References

Sturm et al. (2000)
Fimm et al. (2002)

C037

Recurrent pain experiences and the general information processing speed at primary school age

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Objectives This study investigates the interrelations of recurrent functional pain experiences and the general sensumotoric information processing speed of second graders at primary school.

Methods 130 second graders of a small German town have been analysed. Children with recurrent headaches and abdominal pain experiences (RHAP N = 65) were compared to healthy children (HC N = 65). The self administered information processing speed was determined by the objective speed-power-test (FWIT Farbe-Wort-Interferenztest, subtest FWL). The statistical analyses were conducted by SPSS.12.

Results In all three test cycles girls read at a significantly faster speed than boys (tables: tbl1, tbl4 and tbl7) $<$ Friedman-Test: mean tbl1 $\varphi 61.8$ s vs. $\varphi 76.1$ s; tbl4 $\varphi 58.8$ s vs. $\varphi 75.7$ s; tbl7 $\varphi 56.4$ s vs. $\varphi 71.5$ s; Chi-Quadrat $\varphi 11.906$ vs. $\varphi 17.591$; $df = 2$; $\varphi p = 0.003$ vs. $\varphi p = 0.000$), with large standard deviations ($\varphi 20.2$ s bis $\varphi 29.3$ s vs. $\varphi 38.6$ s bis $\varphi 40.0$ s). As

expected, the reading time ameliorated for all participants from the first to the last cycle (Friedman-Test, mean $\text{tbl1} = 69.3$ s; $\text{tbl4} = 67.7$ s; $\text{tbl7} = 64.4$ s; Chi-Quadrat = 26.865; df = 2; p = 0.000). While there is no impact of recurrent pain experiences for children who achieve a high or middle reading speed, this impact can be found for children with a low reading capacity (T-Tests for the comparison of 'healthy' vs. 'recurrent pain experienced' children: tbl1 : T = 1.625, df 39, p = 0.112; tbl4 : T = 2.142, df 39, p = 0.039; tbl7 : T = 2.052, df 39, p = 0.047).

Conclusion Recurrent pain experiences of second graders with a low sensumotoric information processing speed seem to exert influence predominantly in repeated measurement designs. These results are a plea for a differentiated perspective on the impact of recurrent pain experiences in childhood.

C038

Divided attention in children with and without recurrent pain experiences

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Objectives Divided attention represents a daily challenge and is therefore of particular clinical importance. Reactions on two simultaneously given stimuli are compared between children with and without recurrent headache and/or abdominal pain experiences.

Methods Out of 179 pupils from primary schools of a German town (average age 7.7 years), 78 had experienced recurrent headache and/or abdominal pain and 101 do not experience this pain recurrently. The capacity for divided attention was measured by the corresponding subtest of the neuropsychological testbattery TAP. The reaction time, false answers, omissions and delayed reactions were monitored. Statistical analyses were conducted by SPSS.12.

Results Both pain groups do not differ in their capacity for divided attention. Since even for the error analysis the obtained results are similar between the groups, it can be pointed out that neither headache nor abdominal pain have any statistically firm impact on the analysed parameters. However, the mean reaction times differ significantly by gender: boys reacted faster than girls (one-way anova F = 3.856, df = 1.177; p = 0.05).

Conclusions Our investigation suggests that pain experiences do not influence the infantile cognitive capacity for divided attention. The long duration of the TAP-test (100 trials) had prematurely exhausted the ability (to keep up their attention) of the rather young children. Dividing the test into phases could presumably provide other results that differentiate between the pain groups.

C039

Cerebrovascular risk factors in children and adolescents with migraine with aura and other idiopathic headaches

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Aim To assess the prevalence of cerebrovascular risk factors, i.e. mitral valve prolapse (MVP) and coagulation abnormalities in children and adolescents with migraine with aura (MA) compared with other types of headache.

Patients and method We recruited 20 children and adolescents with MA (10 M and 10 F; age range: 8–17 yrs) and 20 control subjects (8 M and 12 F; age range: 8–17 yrs), i.e. patients suffering from other idiopathic headaches [migraine without aura (MwA; n = 13) and tension-type headache (TTH; n = 7)] diagnosed according to ICHD-2 criteria. All patients underwent M-mode echocardiographic examination to rule out MVP and the following laboratory investigations: Protein C (PC), Protein S (PS), Homocysteine (HCY), Lupus Anticoagulant (LA), Anticardiolipin antibodies (ACA IgG and IgM), Factor V Leiden (FVL) mutation and Factor II (FII) G20210A mutation. The results obtained in MA subjects were compared with those from controls.

Results The prevalence of MVP was significantly higher in MA subjects compared to controls (40% vs 10%; p < 0.05). Moreover MA patients showed a higher rate of positive ACA IgM titres (45% vs 10%; p < 0.05).

Conclusions MVP and ACA IgM are frequently associated with MA. The pathogenetic and clinical implications of these findings should be considered in clinical practice.

C040

Suicide risk and psychiatric comorbidity in adolescents with chronic daily headache: a community-based study

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Objectives To investigate the prevalence and correlates of comorbid psychiatric disorders and suicide risk in adolescents with chronic daily headache (CDH).

Methods We identified and recruited 122 adolescents with CDH from a non-referral student sample (N = 7,900). CDH subtypes were classified according to the most updated criteria in the International Classification of Headache Disorders, 2nd edition (ICHD-2). An in-person psychiatric interview was performed with each CDH subject to assess depressive and anxiety disorders and suicidal risk based on the Mini-International Neuropsychiatric Interview-Kid (MINI-Kid). Clinical correlates and impacts were investigated.

Results 121 subjects (31M/90F, mean age 13.8 years old) finished the psychiatric interview. Fifty-seven subjects (47%) had ≥1 assessed psychiatric comorbidities with major depression

(21%) and panic disorder (19%) as the most common. Current suicide risk was assessed as high (score ≥ 10) in 20% of subjects. Female gender and older age were associated with depressive disorders. Presence of migraine was associated with psychiatric comorbidities (odds ratio (OR) = 3.5, $p = 0.002$). The associations with psychiatric disorders were stronger for migraine with aura than for migraine without aura. Migraine with aura also independently predicted a high suicide risk (adjusted OR = 6.0, $p = 0.028$). In contrast, CDH subtypes, headache frequencies or medication overuse were not correlated. Comorbid psychiatric disorders were not related to physician consultations or more days of sick leave.

Conclusions The community-based study showed high comorbidity of psychiatric disorders and suicide risk in adolescents with CDH. The presence of migraine attacks, especially migraine with aura, was the major predictor for these associations.

D001

Sympathetic desensitization of muscle tenderness in the temporalis muscle in chronic tension type headache

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Objective To assess the relationship between sympathetic activity and muscle pressure pain sensitivity in tender points located in the temporalis muscle in patients with chronic tension type headache (CTTH).

Methods Fifteen women with CTTH and 10 age-matched women were included. Pressure pain threshold (PPT) was measured in both groups in a standardized tender point in the centre of the belly of the temporalis muscle during normal respiration and breathing hold (i.e. a manoeuvre of elevated intra-thoracic pressure [EITP] that causes increased sympathetic outflow to the muscle) for 10 seconds. Three PPT measurements were taken at each point with a 10-s interval in between. Parametric test were used for the statistical analysis.

Results Three way-ANOVA detected a significant difference in mean PPT values between left and right sides ($F = 8.725$; $P = 0.007$) and a significant difference in PPT values between normal breathing and EITP ($F = 11.414$; $P = 0.002$), but not significant differences between patients and controls ($F = 0.0123$; $P = 0.912$). No interaction ($F = 3.6$; $P = 0.07$) was observed between side (left or right) and breath status (normal respiration vs. EITP). Post hoc comparison revealed that PPT level was significantly lower in the left side as compared to the right side (SNK; $P = 0.006$). Further, EITP induced a significant increase in PPT than normal breathing (SNK; $P = 0.002$) in both patient and control groups, with no differences between them ($F = 2.325$; $P = 0.14$).

Conclusions Our results suggest a sympathetic desensitisation of muscle tenderness in both healthy subjects and in CTTH patients in tender points located on the temporalis muscle.

D002

Supposes an overload the headache in a consultation of primary care?

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Objectives The headache supposes an overload asitencial in any ambulatory consultation of neurology. Few studies exist that quantify the overload that supposes the headache in a consultation of Primary Care. The objective of the present study is to identify and quantify really the types of headache and the level of overload that this pathology supposes in two consultations of Primary Care.

Material and methods Prospective, observational and descriptive study, of six months of duration. They register: total of patients attended and number of patients attended by headache, and diagnostic classification.

Results They were evaluated to a total of 6014 patients. Only 46 patients consult by headache (0.76%). The tensional headache was the headache diagnosed with more frequency (43.48%), followed by the migraine (23.91%).

Conclusions Our study certifies it published by other authors and determines that the headache in our middle is a problem more of the innumerable medical problems which it must face the general practitioner. The little number of consultations by headache, along with the problems of diagnosis and handling that surround to this pathology, cause that the headache is not considered an overload from the healthcare point of view in many of the consultations of Primary Care.

D003

Unilateral atrophy of the rectus capitis posterior minor muscle in cervicogenic headache: a case report

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Objective MRI has demonstrated bilateral atrophy of some suboccipital muscles in chronic tension-type headache. Our aim was to analyse side-to-side differences in cross sectional areas (CSA) of the cervical extensor muscles in a patient diagnosed with unilateral cervicogenic headache (CeH).

Methods CSA of the rectus capitis posterior minor (RCPmin) and rectus capitis posterior major (RCPmaj) muscles were calculated from axial T1-weighted MR slides connecting the upper part of the odontoid process and the posterior arch of the atlas, while CSA of the semispinalis capitis and splenius capitis muscles were measured from axial MR slices aligned parallel to the C2/3 inter-vertebral disc. Measurements of the CSA were performed by depicting a region of interest (ROI) for each muscle on both sides.

Results CSA of the RCPmin was smaller on the symptomatic (62.5 mm^2) as compared to the non-symptomatic side (94 mm^2). CSA (symptomatic vs. non-symptomatic) of the

RCPmaj (111 vs. 116 mm²), semispinalis capitis (312 vs. 316 mm² at C3 level; 243 vs. 246 mm² at C4 level), and splenius capitis (213 vs. 205 mm² at C3 level; 176 vs. 168 mm² at C4 level) did not show asymmetries.

Conclusion MRI revealed unilateral atrophy of the RCPmin muscle, but not other cervical extensor muscles, in a patient with unilateral CeH. RCPmin might be more sensitive to trophic changes than other suboccipital muscles. RCPmin atrophy was ipsilateral to the clinical symptoms and signs. Muscle atrophy could possibly account for a reduction of proprioceptive output, and may contribute to the perpetuation of headache.

D005

Headache and hypertension in reversible posterior leukoencephalopathy syndrome (RPLS)

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Background Reversible posterior leukoencephalopathy syndrome (RPLS) is a recently proposed clinico-neuroradiologic category characterized by hypertension, seizures, headache and conscious disturbance. Headache and hypertension are commonly recognized in RPLS however, little is known about the characteristics and time course of headache and hypertension in RPLS.

Subject and methods For 12 cases of RPLS, we performed consecutive physical and neurological examination and neuroradiologic evaluation including head cerebral angiography, head CT, MRI and MRA.

Results Hypertension was recognized in 11 cases out of 12 however, extreme hypertension fulfilling the criteria as malignant hypertension was not recognized in any cases. Nine cases had elevated blood pressure less than 1 week before convulsion, but 2 cases showed hypertension for 2 months. 8 cases had headache: 4 cases presenting diffuse pulsating headache, 1 with pulsating occipital, 1 with pulsating frontal headache and 2 cases had non-pulsating occipital pressing headache. Hypertension synchronized with headache in 5 cases however, it independently occurred in 6 cases. One patient complained of headache with normal blood pressure and she did not remember headache at all when she recovered from RPLS. The portion of headache was not always consistent with abnormal lesions recognized in CT/MRI. The cerebral vasoconstriction was confirmed in 7 patients.

Conclusion Headache in RPLS is more various. Headache and hypertension are not always synchronous and headache could occur without hypertension, meaning the possibility that mechanism of headache in RPLS is different from that of hypertensive encephalopathy.

D006

History of ergotamine and dihydroergotamine from 1906 and forward

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In 1906 Sir Henry Dale discovered that a liquid extract of ergot inhibited the pressor effect of adrenaline. Conversely, when adrenaline led to relaxation ergot was not effective. In fact Dale had anticipated the alpha- and beta-adrenoceptor as proposed 40 years later by Ahlquist in 1948.

Ergotamine was isolated from ergot in 1918 and introduced in 1925 in the treatment of migraine as a sympatholytic agent. In 1936 Graham and Wolff in the U.S., however, showed that the temporal artery was dilated during migraine and that an ergotamine injection resulted in a decrease of the pulsations of the artery. Ergotamine was thus a vasoconstrictory drug as would be expected from the epidemics of ergotism in the Middle Ages.

Dihydroergotamine was introduced in 1943 in order to decrease the incidence of adverse events of ergotamine. It is still used by injection or by the intranasal route in the treatment of migraine attacks.

In 1958 methysergide, a prodrug of methylergometrine, was found to be a serotonin antagonist. Methysergide was introduced by Sicuteli in 1959 in migraine prophylaxis. In 1967 Graham reported retroperitoneal fibrosis after long-term use of methysergide.

From 1950 and further on several authors published on ergotamine-induced chronic headache, a major problem in patients with frequent attacks using ergotamine. Still rare cases of ergotism occurred and it was shown that nitroglycerin was an effective treatment. In a series of pharmacokinetic studies from Sweden it was shown that the half-life is 2 h and that the oral bioavailability of ergotamine was <1%.

A European consensus in 2000 concluded that ergotamine is not a drug of first choice in the treatment of migraine attack, but can be used by the rectal route in patients with multiple relapses over days.

D007

Neurovascular coupling in migraineurs with frequent migraine attacks

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Objective Neurovascular coupling may be altered in migraineurs. Therefore, visual evoked potentials (VEP) and visually evoked cerebral blood flow velocity responses (VEFR) were simultaneously recorded and their relationship was analysed.

Methods 33 healthy controls and 35 age matched migraineurs with frequent migraine attacks (2.8 ± 1.2 per month) during headache free interval participated in the study. The VEFR were measured in the posterior cerebral artery using transcranial Doppler and VEP were recorded

from occipital leads. Neuronal activity was changed by using a visual stimulus with increasing contrast of 1%, 10% and 100%.

Results We found an increase in VEFR and VEP in both the healthy and migraineurs groups ($p = 0.05$). Regression showed a significant association between VEP and VEFR in both healthy controls ($r = 0.64$).

D008

The extra-ocular muscles in chronic tension type headache: an irritative thorn for the trigeminal nucleus caudalis

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Objective To investigate the presence of referred pain from two extra-ocular muscles, i.e. superior oblique (SOM) and lateral rectus (LRM), in chronic tension-type headache (CTTH).

Methods In two separate studies, CTTH and healthy subjects without headache history were blindly examined for referred pain elicited by trigger points (TrPs) in both extra-ocular muscles. TrPs were diagnosed when: (a) referred pain was evoked by maintained pressure of the muscle (lateral corner of the orbit for the LRM, and trochlear region for the SOM) during 20 seconds, and (b) referred pain increased with eye movements which implied active stretching or contraction of the muscle for 15 seconds. TrPs were considered active if the evoked referred pain reproduced the usual headache pattern.

Results In the first study, 86% of CTTH patients ($n = 13$) experienced referred pain with manual exploration of the SOM. The pain was perceived at the retro-orbital or supra-orbital region, and the homo-lateral forehead. In the second study, 66% of CTTH patients ($n = 10$) showed referred pain with manual exploration of the LRM. The referred pain was perceived at the supra-orbital region or the homo-lateral forehead. All of them recognized the evoked pain as their usual frontal head pain (active TrPs). Referred pain from the extra-ocular muscles was scarce in controls (27%, $n = 4$, for the SOM; 0.07%, $n = 1$, for the LRM), and it never reproduced a familiar pain.

Conclusions Nociceptive inputs from the extra-ocular muscles may provoke a prolonged afferent bombardment to the trigeminal nucleus caudalis, thus contributing to central sensitisation and exacerbating headache.

D009

Clinical characteristics of migraine and tension-type headache in Korea

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Objectives To analyze the epidemiological and clinical characteristics of migraine and tension-type headache (TTH) in a secondary care hospital setting in Korea.

Methods 625 patients who presented with headache as chief complaints, were recruited prospectively. Information on

epidemiological and clinical characteristics was collected from the structured questionnaire and registry. A total of 95% of the patients had primary headache: migraine (26.9%), probable migraine (5.1%), episodic TTH (21.3%), probable episodic TTH (6.6%), primary chronic daily headache (19.4%) which includes chronic migraine, chronic TTH, hemicrania continua, and new daily-persistent headache, and other primary headache (15.7%).

Results Sixteen patients (9.5%) of those with migraine had migraine with aura. The mean age at onset was 24.6 ± 9.2 years in migraine and 37.9 ± 14.5 years in TTH ($p < 0.05$). Female sex was more prevalent in migraine ($p < 0.05$). Unilaterality of headache was not different in two groups ($p = 0.8$). Stress and fatigue were most common triggering factors for both headache types. Patients with migraine had a greater prevalence ($p < 0.05$) of medication overuse history. Beck depression inventory score was not different between migraine (22.0 ± 4.8) and TTH (23.4 ± 5.8). Beck anxiety inventory score was significantly higher in TTH group ($p < 0.05$). Only 21% of migraineurs and 29% of patients with TTH had received a diagnosis of their headache correctly. Sixty-five percent of misdiagnosed migraineurs reported a diagnosis of TTH. Thirty-one percent of misdiagnosed patients with TTH reported a diagnosis of migraine.

Conclusion Migraine and TTH consist of about 60% of all headache patients in secondary general hospital setting in Korea. Prevalence of depression and unilaterality of headache were not different between two groups. Migraine was most frequently misdiagnosed as TTH.

D010

The clinical presentation and affective disorders in burning mouth syndrome

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Objectives According to IHS classification, burning mouth syndrome (BMS) is intra oral burning sensation without obvious medical and dental cause. International headache society (IHS) diagnostic criteria of the disorder include the presence of burning oral sensation during the most period of day without obvious changes of oral mucosae. Local and systemic causes have to be excluded by appropriate diagnostic procedures. Subjective feeling of dry mouth, paraesthesia and taste changes could be associated symptoms. The BMS is of unknown path physiology.

Methods and aims The aim of the study was to analyze the clinical and affective characteristics in group of patients with primary BMS. We examined 100 patients fulfilled the diagnostic criteria for primary BMS. All patients underwent complete neurological examination, measurement of unstimulated salivary flow, the degree of burning sensation measured by visual analogue scale. Anxiety and depression symptoms were measured by Hamilton Rating Scales for depression and anxiety and by Beck Depression Inventory.

Results The average age was 65.5 ± 11.2 years, with female : male ratio 2 : 1. The disorder lasted more than 12 months in 62.7% of patients. The burning sensations were distributed on the whole oral cavity in 39.2%, on tongue or lips in 29.4%, while in the other patients the sensation involved the part of oral cavity. High scores were obtained on Hamilton Depression Rating Scale (16.5 ± 4.5), Beck Depression Inventory (17.4 ± 8.2) and Hamilton Anxiety Rating Scale (20.6 ± 5.6).

Conclusion As the other chronic pain conditions, BMS is strongly associated with anxiety and depression.

D011

Evidence of motor control impairment in the cervical spine muscles in chronic tension type headache

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Objective Motor control impairments of the cervical musculature have not been thoroughly investigated in headache disorders. Our aim was to investigate the presence of signs of motor dysfunction in the cervical muscles of patients with chronic tension-type headache (CTTH).

Methods The cervical muscles of CTTH patients and healthy controls were evaluated in three different studies. First, the holding capacity of the deep neck flexor muscles was assessed by means of the crano-cervical flexion test (CCFT). Second, the differences in the cross sectional area (CSA) for the rectus capitis posterior minor (RCPmin), rectus capitis posterior major (RCPmaj), semispinalis capitis, and splenius capitis muscles were calculated with magnetic resonance imaging (MRI). Third, surface EMG signals from sternomastoid (SM) and splenius capitis (SC) muscles were analysed during both cervical flexion and extension contractions of linearly increasing force from 0 to 60% of the maximum voluntary contraction.

Results CTTH patients showed: (a) reduced holding capacity of the deep neck flexor muscles ($P < 0.001$) as assessed with the CCFT; (b) reduced CSA for both RCPmin and RCPmaj muscles ($P < 0.01$), but not for semispinalis and splenius capitis muscles; (c) significantly greater co-activation of the antagonistic musculature -i.e. SM- during cervical ramped extension, but not during cervical flexion.

Conclusions Our studies demonstrate the existence of motor control impairments in the deep cervical flexor and extensor musculature in CTTH. These impairments could contribute to a reorganization of the central motor strategy which may be manifested as changes of muscle activation during functional tasks of the cervical spine.

D012

Chessington occupational therapy neurological assessment battery assessment in chronic tension type headache

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Objective To assess the differences in the performance of several ability subtests from the Chessington Occupational Therapy Neurological Assessment Battery (COTNAB) between patients with chronic tension-type headache (CTTH) and healthy controls.

Methods Six women with CTTH (age: 55; SD 3 years) and no other chronic disorder and 6 age-matched women (age: 53; SD 3 years) were included. Both patients and controls completed the following three subtests of the COTNAB: Manual Coordination, Visual Perception (Hidden Figures) and Constructional Ability (2D and 3D Construction). Each test was scored based on the subjects' ability, and was classified as: normal; borderline performance; impaired; or unable to attempt. A comparative analysis was done between both study groups.

Results CTTH patients showed a trend towards a greater disability as compared to healthy subjects in all the evaluated items. These differences were statistically significant for Manual Coordination (CTTH, $n = 2$ unable, $n = 2$ borderline, $n = 2$ normal vs. CONTROLS, $n = 6$ normal; $P = 0.045$); 3D Constructional Ability (CTTH, $n = 1$ unable; $n = 3$ impaired; $n = 1$ borderline; $n = 2$ normal vs. CONTROLS, $n = 6$ normal; $P = 0.04$) and Visual Perception (CTTH, $n = 1$ unable, $n = 4$ impaired; $n = 1$ normal, vs. CONTROLS, $n = 2$ borderline, $n = 4$ normal; $P = 0.03$) components.

Conclusions Our preliminary results suggest that CTTH patients may be more disabled in Manual Coordination, 3D Constructional Ability and Visual Perception in comparison with healthy subjects as assessed by the Chessington Occupational Therapy Neurological Assessment Battery (COTNAB). Further studies investigating the occupational abilities of patients with chronic headaches with a greater number of subtests and a greater number of subjects are required.

D013

Migraine in women-a qualitative study demonstrating impact on quality of life and identification of caring needs

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Objectives

- (1) To describe the quality of life experienced by migraineurs and to identify the caring needs (eg information, education, support) expressed by participants.
- (2) To identify the physical, social and psychological factors contributing to consequences experienced.
- (3) To recommend implications for health professional practice to facilitate improved quality of life.

Methods A qualitative design was employed using in-depth semi-structured interviews and participant observation. The

ethnographic approach was used studying the lived experience of participants. Twenty women aged 26–45 who met the criteria of the International Headache Society's Classification for migraine were selected. Identification of themes and patterns enabled a thematic analysis presenting common meanings.

Results The majority of participants sought treatment from orthodox and alternative practitioners but found treatment inadequate. Education, information, and coping strategies were virtually non-existent.

In regard to quality of life, the study found women with migraine have special and unique concerns which have largely been unrecognised. Isolation was defined as a central theme in understanding the consequences of living with migraine. Uncertainty, lack of information, education and knowledge, combined with a lack of support and understanding contributed to a loss of control over their lives. Frustration, anger, hopelessness and acceptance were constantly identified emotions in regard to these women's perceptions of migraine.

Conclusion Migraine has a unique, significant quality of life burden. These facts highlight the importance of education programs for health professionals and the community to increase understanding of the debilitating nature of migraine and the cost to sufferers- personally, socially and economically. Improved care, services and treatment are recommended.

D014

Transformed migraine – hypothesis of the cause and development of chronic migraine

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Objectives Thirty-eight patients who were diagnosed as transformed migraine (TM) were analyzed from the aspect how the episodic migraine turned into chronic.

Methods Thirty-five women and 3 men with mean age of 43-y-o were analysed by the systematic interview about the type and frequency of headache, sleep condition, presence of drug overuse, psychosocial episodes at their days of TM onset. Physical and mental conditions were tested by ordinary clinical techniques.

Results Depression and chronic anxiety were the characteristic comorbid states. Drug overuse were seen in 34 patients. Most patients revealed having myofascial pain in their paravertebral muscles, which could originate central sensitization through the continuous myofascial noxious stimuli to the nucleus caudalis of the trigeminal nerve. This myofascial pain was supposed the result of sleep disturbance which most patients mentioned. Their sleep disturbance might be due to REM sleep without atonia, resulting in the continuous muscle contraction at the paravertebral muscles. Almost all patients had fearful psychosocial episodes on their onset of chronic headache, that could elicit sleep disturbance, maybe REM sleep without atonia, continued with chronic myofascial pain in paravertebral muscles. This state might result in the central sensitization of the trigeminal nerve, along with the descent of pain threshold due to co-existence of serotonin depletion.

Conclusion Most important factor of developing TM may be the sleep disturbance, along with the depression and anxiety that exist concomitantly. Myofascial pain in paravertebral muscles can cause the central sensitization and may be improved by adequate treatment of the sleep disturbance, consequently decrease the headache episodes.

D015

Data sets to predict chronification: results of analogical neural networks (ANNs) and math model

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Objective Fundamental question are (i) why subjects with similar diagnosis will remain episodic sufferers whilst others become chronic sufferers, (ii) why it so easy to aid X and impossible to cure Y in spite of same diagnosis?

Methods Primary need was the introduction of different sets of logic input variables for chronification in an algorithm: (A) risk factors when child (score 0–5), (B) heredogenetic data (consanguineous till to fourth degree = degree/ severity score 0–5/subjects' number = x/grade: score 0–5), (C) somatic and vascular/visceral hyperalgesia/allodynia = score 0–5) psychometric evaluation score = 0–5 regarding psychosis depression and anxiety, alexithymia, emotional intelligence, stress, abuse (from sexual to mobbing) C) Q.I. Data base was composed of 1700 cases of chronic headache (1200 migraine sufferers and 500 tension-type headache) and 1350 (1100 migraine and 250 tension type headache) never tending to chronification in the entire life-span (testing). Validation was made by a second random sample (n = 780) never examined before. Error = Sigma (X/real – X/spread)². Reliability 98%.

Results Prediction were given by SDA mode – 88.3%, Discriminant Analysis 75.1% indicated dominant role of heredogenetic data. Results parallel with the previously suggested math law of 'notch effect'. In this case 'under-load/under-time forces' cycles' induce a logarithmic 'crack propagation'. ANNs indicate the 'forces' cycle for propagation' links sensibly (46.5%) to the logic bunch: alexithymia, poor emotional intelligence, psychosis, abuse.

Conclusion CNS is amidst the 'plastic' structures of our body. Heredity might be modulated, nonetheless comorbid conditions sharing some common transmitters might act for 'crack propagation'.

D016

Migraine and cardiovascular disease risk profile on Japanese physical check-up

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Objectives To study prevalence of migraine and cardiovascular disease (CVD) risk factors on physical check-up (PC).

Method A total of 37,651 adults underwent PC between July 2005 and December 2006. A headache specialist (K.I.)

interviewed headache history in consecutive 2,162 subjects (1,356 men and 806 women). Mean age (SD) of subjects was 52.6 (10.9) years. Migraine with aura (MA) or without aura (MO) was diagnosed according to the ICHD-II criteria. Prevalence of migraine and CVD risk were analyzed.

Results Prevalence of migraine was 12.7% (7.1 in men and 23.3 in women). Mean age (SD) was 42.8 (8.4) years [40.1 (7.2) in men and 44.1 (8.7) in women]. MA/MO ratio was 1.0/12.2 (0.4/6.6 in men and 1.9/21.5 in women). Mean duration of migraine (SD) was 16.7 (11.4) years [13.3 (9.1) in men and 18.7 (12.2) in women]. Frequency was ≥ 1 attack/month in 59.4% (45.9 in men and 66.2 in women). As for Headache Impact Test-6, women experienced severe attacks more than men.

Conclusions Migraineurs accounted for 12.7% of PC subjects. Migraineurs have unfavorable serum lipids levels. Male migraineurs are increased parental history of CVD/stroke. Our data are partly similar ways to CVD risk profile in previous Europe and USA migraine studies.

D017

Pregabalin effectiveness and tolerability in the prophylactic treatment of chronic migraine

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Objectives To evaluate the effectiveness and tolerability of pregabalin in the prophylaxis of chronic migraine.

Methods 17 patients (11 women, 6 men), 25 to 69 years, diagnosed of chronic migraine according to IHS criteria, and most of them (88%) refractory to previous prophylactic drug therapies, received pregabalin during 12 weeks in a starting dose of 75 mg/day subsequently adjusted according to patients' clinical response. The main outcome measure was the decrease in attacks' frequency. Secondary outcome measures included changes in attacks' severity and in the Headache Impact Test (HIT-6) score. Emergent adverse reactions to drug were recorded.

Results Pregabalin final dose ranged from 150 to 450 mg/day (303 ± 118). Monthly attacks' frequency decreased from 22.5 ± 5.8 to 18.5 ± 9.9 .

D018

Migrainous corpalgia: body pain and allodynia associated with migraine attacks

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Objective Migraine symptoms include more than head pain. For instance, cephalic and extra-cephalic allodynia is currently recognized as a common sign of sensitization during migraine episodes. However, the occurrence of non-headache spontaneous pain in association with migraine attacks has not been thoroughly explored.

Methods Here we describe the clinical features of three migraine patients presenting with recurrent attacks of extra-cephalic pain in connection with headache episodes.

Results A 41 year-old woman with migraine with aura since age 27, had been having attacks of face and body pain along with migraine episodes since age 30. Pain was felt in different anatomical regions on either side, more commonly on the right, and usually ipsilateral to head pain. Body pain started before, during or after migraine headache, and could last from minutes to days. A 39 year-old woman with right-sided migraine with aura since age 15, had been feeling pain in her right extremities for 30–60 min prior to most headache attacks since age 34. A 30 year-old woman with left-sided migraine without aura since age 23, had been perceiving pain in her left upper limb for 24–48 h prior to most headache attacks from migraine onset. All patients reported symptoms of allodynia, and showed evidence of mechanical allodynia over the painful areas.

Conclusions We have described spontaneous body pain associated with migraine attacks. Together with allodynia, this can be considered a consequence of sensitization. Migraine may be not only a headache disorder but also a more generalized pain disorder.

D019

Acute allodynia in different forms of headache

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Background Cutaneous allodynia during migraine attacks is complained by about 60% of migraineurs. It seems to be induced by sensitization of primary nociceptors and central trigeminovascular neurons.

Objective To determine prevalence of allodynia during headache attacks in different forms of primary headaches.

Methods Population: 114 migraineurs who had only attacks of migraine without-aura (MO), 63 migraineurs who had also attacks with-aura (MA), 28 patients who had episodic tension-type-headache (ETTH), and 52 patients with more than 15 days per month with headache, labeled as 'chronic-daily-headache' (CDH), including patients with chronic migraine or chronic tension-type-headache, with or without drug-overuse. Presence of allodynia was investigated by a semi-structured interview. Chi-square test corrected for multiple comparison was used.

Results Allodynia was complained by 47 out of 114 MO (41.2%), 41 out of 63 MA patients (65.0%), 10 out of 28 ETTH (35.7%), and by 34 out of 52 CDH patients (65.4%). A significant prevalence of acute allodynia in both MA and CDH patients with respect to MO and ETTH patients was found (MA vs MO $p = 0.002$, MA vs ETTH $p = 0.009$, CH vs MO $p = 0.004$, CH vs ETTH $p = 0.01$).

Conclusion Acute allodynia was common in all kinds of primary headache attacks being present in more than 35% of

patients in each studied group. A higher frequency of acute allodynia was observed in MA and CDH. These observations may suggest that both frequency of attacks and presence of aura episodes may contribute to induce modifications of neuronal activation threshold that are thought to sustain allodynia.

D020

Prevalence of migraine, probable migraine and tension type headache in Croatian population

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Objective The aims of this study were to assess the prevalence of migraine (M), probable migraine (PM) and tension type headache (TTH) in the Croatian population, medical attendance and to report the degree of disability.

Methods The design of the study was a cross-sectional survey using a self-completed questionnaire. The questionnaires were distributed to adults >18 years of age to contain a mix of urban, suburban and rural settings, and a spread of social class. Prevalence and demographic characteristics of headache types were analysed. Disability was measured using the Migraine Disability Assessment (MIDAS).

Results Of the total 1542 responders, 640 (41.5%) fulfilled the questionnaire indicating they suffer from headache. The proportion of females was 60.1% and males 38.1%. The prevalence of M was 7.5%, PM 11.5%, M + PM 18.9% and TTH 21.2%. Patients with high level of education are more likely to have M or PM than TTH ($p = 0.052$). Marital status does not influence the presence of migraine or TTH ($p = 0.3$), neither does the employment status ($p = 0.07$). The prevalence of M and PM is higher in subjects living in cities ($p < 0.0001$). Patients with M are more likely to visit a doctor regularly. More than a half of patients with TTH have never visited a doctor. Patients with PM have worse MIDAS assessment.

Conclusions The prevalence of primary headaches is relatively high in Croatian population. Low percentage of patients searching for professional help and poor MIDAS assessment indicates that the treatment of primary headaches should be improved in Croatia.

D021

Body mass index and episodic headaches – a population study

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Objectives To explore the influence of the body mass index (BMI) on the frequency, severity and patterns of treatment of migraine, probable migraine (PM) and severe episodic tension type headache (S-ETTH).

Methods A validated questionnaire was mailed to 120,000 households selected to be representative of the U.S. population. Headaches were classified according to the International Headache Society criteria. We divided participants, into five categories, based on BMI: 1 – Underweight <18.5), normal-weight (18.5–24.9), overweight (25–29.9), obese (30–34.9), and morbidly obese (>35). Analyses were adjusted by covariates.

Results Response rate was 65%. We identified 18,968 individuals with migraine, 7,564 with PM, and 2,051 with S-ETTH. The distribution of very frequent headache (10–14 days/month) was assessed by BMI and headache type. For migraine, contrasted to the normal weighted (6.5% had 10–14 days of headache) the proportion was non-significantly higher in the overweight (7.4%), and higher in the obese (8.2%, $p < 0.001$) and morbidly obese (10.4%, $p < 0.0001$). For PM, and S-ETTH, the differences were not significant in the adjusted analyses. The disability of migraineurs, but not PM or S-ETTH sufferers, also varied as a function of BMI. Among migraineurs, 32% of those with normal weight had some disability, vs. 37.2% of the overweight ($p < 0.01$), 38.4% of the obese ($p < 0.001$) and 40.9% of the morbidly obese ($p < 0.001$). **Conclusion** These findings support the concept that the obesity is an exacerbating factor for migraine, and not for headaches overall.

D022

The international classification of headache disorders revised criteria for chronic migraine

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Objectives To field test the revised criteria for chronic migraine (CM).

Methods We included individuals with transformed migraine with or without medication overuse (TM+ and TM-). We assessed the proportion of subjects that the revised ICHD-2 (ICHD-2R) criteria for CM (15 or more days of headache, 8 or more days of migraine or migraine specific acute medication use ergotamine or triptans). We also tested three proposals. In proposal 1, CM/CM+ would require at least 15 days of migraine or probable migraine per month. Proposal 2 required ≥ 15 days of headache per month, 50% of them being migraine or probable migraine. Proposal 3 required 15 days of headache and at least 8 days of migraine or probable migraine.

Results Of the 158 patients with TM-, just 5.6% met the former ICHD-2 criteria for CM. According to the ICHD-2R, a total of 92.4% met criteria for CM ($p < 0.001$ vs ICHD-2). The ICHD-2R criteria (92.4% of agreement with TM) performed better than proposal 1 (47.8% of agreement, $p < 0.01$) and was not statistically different than proposals 2 (87.9%) and 3 (94.9%). Of the 399 individuals with TM+, just 10.2% could be classified as CM+ in the ICHD-2. However, most (349, 86.9%) have 8 or more days of migraine per month and could be classified as MOH and probable CM in the ICHD-2R ($p < 0.001$ vs. ICHD-2).

Conclusions The ICHD-2R represents an important improvement in the definition of CM and should be adopted in clinical practice and research.

D023

Antidepressant effect of thymus species essential oils and extracts

Effects of essential oils and extracts from certain thymus species on swimming performance in mice

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Background and purpose The genus *Thymus* (Labiatae) comprises 14 species, which are found wild in many regions of Iran. In folk medicine, some *Thymus* species are used as an anthelmintic, antispasmodic, carminative, sedative, diaphoretic. Thyme (*Thymus vulgaris*) is attributed as having general stimulant properties and has antibacterial, antimutagenic, anticancer, anti-inflammatory, antioxidant, sedative, stimulant and CNS depressant activities.

Since some of the indications seem to be related to CNS, The effect of the methanol extracts and essential oils from the aerial parts of *Thymus fallax*, *Thymus kotschyanus* and *Thymus pubescens*, were studied using different doses.

Materials and methods Effects of different doses of methanolic extracts and essential oils of *Thymus* species on the swimming performance in mice were investigated in this study.

Result On the basis of our findings, the methanol extracts and oils shortened remarkably the immobility period during the forced swimming test in comparison with negative control and exhibited a dose-dependent antidepressant activity. The duration of immobility observed in the essential oils were less than extracts in these experiments.

Conclusion The results of tests showed that the extracts and oils of *T. fallax* had more antidepressant activity than *T. kotschyanus* and *T. pubescens*.

Keywords: swimming test, *Thymus fallax*, *Thymus kotschyanus*, *Thymus pubescens*, extract

D024

Prevalence of primary headaches in an adult-elderly rural population: the Zabut Aging Project

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Objectives To evaluate the 1-year prevalence of tension-type headaches (TTH), migraine headaches (MH), and chronic headaches (CH) in a rural adult-elderly population.

Methods A two-phase door-to-door survey was carried out on all adult-elderly (≥ 50 years) residents of a small town in southern Italy. Participants underwent a standardised headache questionnaire and a neurological examination. The International Classification of Headache Disorders 2nd edition criteria were used.

Results 1809 (72.5%) of the 2496 eligible persons completed the study protocol. One-year prevalence rates were

respectively 21.7% for TTH, 8.3% for MH and 3.1 for CH. The prevalence of headache in general was 29.0%. Prevalence rates of patients with headache were higher in women than men (35.7% vs 20.8%).

Conclusions A consistent proportion of adult-elderly people suffered from primary headaches. Age and sex differently affect prevalence figures in subjects with MH and TTH.

D025

Benign paroxysmal positional vertigo and headache

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Objective We sometimes experience that patients with benign paroxysmal positional vertigo (BPPV) complain about neck pains and or headaches. Several articles mentioned it, but ICHD-2 doesn't classify secondary headaches accompanied with BPPV. In this study we investigated the frequency and character of headaches accompanied with BPPV.

Methods We studied the records of outpatients and inpatients in our hospital for two years from September 2002 to October 2004. We revealed the accompanying frequency and detailed characteristics (location, duration and intensity) of the headaches associated with BPPV.

Results We experienced 387 cases of BPPV. Of these cases 67 (17% of whole BPPV cases, 22 males and 45 females, the average age is 55.4 years old) felt a headache a few days before or a few days after they felt vertigo. These all headaches stopped a few days before or after vertigo went away. Most of them complained of a dull neck pain, dull forehead headache or whole head headache. Frequently their chief complaint was vertigo, so we had to ask for the existence of a headache. The headache is very mild and without laterality like a tension type headache. Furthermore, 19 of 67 cases originally had a tension type headache, while 48 cases had not experienced it prior to a BPPV attack.

Conclusion A headache accompanied with BPPV is relatively common in clinical feature, but it hasn't been well established as a concept of a secondary headache. We recommend that investigators pay careful attention to the relationship between BPPV and headaches.

D026

Significance of the economy productivity losses assessment in cause of migraine in whole population of Russia

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Objective Migraine is very actual disease in cause of young age (25–55 years) working people disability. Migraine patients cannot work, have temporal disability, that can be reason of large social and economy losses. In social aspect migraine leads to disadaptation in patient's life and decrease its quality.

Methods We used materials of the Russian State Standard and Statistical Committee for January 2003 and own questionnaires studies of migraine patients.

Results The production of gross revenue in 2002 was 10 863.4 billions rubles. There are 14 543 migraine patients (17%) in general working population group. In calculation of general number of working population in Russia for 2002 (87.9 millions) and coefficient the value of production works 0.75, approximately evaluation of the part of internal gross revenue of each worker in calculation in US dollars is compose 2910 dollars per year. Taking account the numbers of working population in Russia and coefficient of taking part in the valuation of making production 0.75, the general quantity of migraine patients day lost is 6 working days per year increasing 0.7, that will be 395.55 millions patients-days or 1.58 millions in year. General gross revenue lost in US dollars will be 4604.2 millions. Mean cost of 1 day of disability is 90 rubles. Mean disability losses per year is constitute of 31 412 880 rubles.

Conclusion Migraine is high social-economical significance disease and its adequate therapy can decrease social and economical expenses of the population and increase the quality of life of migraine patients.

D027

Gastric emptying and absorption of a sumatriptan with RT™ Technology 85 mg and naproxen sodium 500 mg tablet

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Objectives To determine gastric emptying and absorption characteristics of sumatriptan and naproxen from a fixed single-tablet formulation of sumatriptan RT™ Technology 85 mg and naproxen sodium 500 mg (SumaRT/Nap) ictally (IN) and interictally (OUT).

Methods This study evaluated sumatriptan (SumaRT) and naproxen sodium (Nap) disintegration, gastric emptying and absorption in migraineurs (ICHD-II 1.2.1 or 1.1) following administration of SumaRT/Nap both IN and OUT. Two distinct radioisotopes were incorporated into the SumaRT and Nap portions of the SumaRT/Nap tablets to allow a separate evaluation of each component. Times to 10% gastric emptying (10%GE) and 50% gastric emptying (50%GE) of SumaRT and Nap were determined. Blood samples were collected and analyzed to correlate the gastrointestinal behavior with concentration-time data.

Results 5 female migraineurs received dual-labeled SumaRT/Nap both IN and OUT. Mean times to 10% GE were slightly slower IN vs OUT for SumaRT (14 ± 16 vs 6 ± 1 min) and Nap (91 ± 45 vs 71 ± 35 min). Mean times to 50% GE were slightly slower IN vs OUT for SumaRT (52 ± 35 vs 40 ± 21 min) and similar IN vs OUT for Nap (149 ± 68 vs 151 ± 49 min).

Conclusions The SumaRT portion of the SumaRT/Nap tablet disintegrated, emptied the stomach and was absorbed quickly both IN and OUT. The Nap portion disintegrated, emptied the stomach and was absorbed more slowly as compared to the SumaRT both IN and OUT. The disintegration and absorption of the SumaRT portion was similar to that previously observed for SumaRT administered alone both IN and OUT.

D028

Prevalence of chronic primary headache in the general population

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Objectives To provide prevalence data on chronic primary headache.

Methods In a cross-sectional epidemiological survey, a random sample of 30,000 persons from Akershus County, aged 30–44 years, received a mailed questionnaire. Those with self-reported chronic headache within the last month and/or year, were invited to a semistructured interview and a neurological and physical examination conducted by neurological residents with experience in headache diagnostics. The diagnoses were made according to the revised International Classification of Headache Disorders. The Regional Committees for Medical Research Ethics and the Norwegian Social Science Data Services approved the project.

Results Both the questionnaire response rate and the participation rate of the interview were 71%. Of those with chronic headache 42% had a primary form. Additional cases were given a probable primary diagnosis because of medication-overuse. The 1 year prevalence of chronic tension-type headache (CTTH) and probable chronic tension-type headache (pCTTH) was 1.6% and 1.2%, respectively. The prevalence of chronic primary headache in different subgroups were: CTTH with migraine 0.6%, CTTH without migraine 0.9%, pCTTH with migraine 0.7%, pCTTH without migraine 0.5%, chronic migraine 0.01%, probable chronic migraine 0.09% and others 0.04%.

Conclusion Chronic primary headache occurs in a large group of those with chronic headache. CTTH and pCTTH are the most common forms. Persons with CTTH and pCTTH often have co-occurrence of migraine. Chronic migraine and other chronic primary headaches were rare.

D029

Inpatient vs day hospital withdrawal for chronic migraine patients: results at 2 years follow-up

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Objectives Patients with chronic migraine and medication overuse are particularly difficult to treat, with no one approach being universally accepted. Some type of withdrawal program, however, is typically implemented before beginning a pharmacological prophylaxis treatment.

The purpose of this study was to determine (1) the clinical course of 2 samples of chronic migraine patients with medication overuse 24 months following two different treatment interventions (inpatient withdrawal or day hospital withdrawal); (2) whether functional impairment,

assessed by the MIDAS questionnaire, improved upon treatment.

Methods Two groups of patients were treated: group A, 80 patients, was treated by inpatient withdrawal, Group B, 104 patients, by outpatient withdrawal (day hospital schedule).

Results Patients of both groups improved significantly at the 12 and 24 months follow up: days of headache per month decreased (group A: 29.1 vs 11.2 vs 10.6; group B: 28.4 vs 12 vs 10), medications/month decreased (group A: 51.5 vs 11.1 vs 9.9; group B: 43 vs 11.4 vs 9.9), and a measure of functional impact from the MIDAS questionnaire improved (MIDAS total score: group A: 73.6 vs 31.7 vs 3.1; group B: 68.9 vs 16.2 vs 8.1).

Conclusions From these results the outpatient withdrawal by periodic clinical meeting seems to be as helpful for this category of patients as inpatient withdrawal. Day hospital treatment may be a more cost-effective alternative to inpatient treatment.

D030

Chronic migraine with medication overuse: treatment outcome and disability at 5 years follow-up

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Objectives Patients with chronic migraine and medication overuse are particularly difficult to treat. No clear consensus exists about treatment strategies to be used and few data exists about the functional impact of headache in these patients. Purpose of the study was to determine (1) the clinical course of a sample of chronic migraine patients with medication overuse 60 months following treatment intervention and (2) whether functional impairment, assessed by the Migraine Disability Assessment (MIDAS) questionnaire, improved upon treatment.

Methods Of 146 patients meeting criteria for chronic migraine with medication overuse, 58 went on to complete a structured inpatient treatment, consisting of medication withdrawal and then prophylactic treatment. The measures used to assess outcome were: days of headache/month; number of symptomatic medications consumed per month; MIDAS total score. The MIDAS and headache diary recordings were made prior to treatment and at 12, 24, 36, 60 months following treatment completion.

Results Patients were significantly improved at follow-up assessments, relative to pretreatment for all measures (days of headache/month 25.8 ± 4.1 vs 9.6 ± 8.9 vs 9.5 ± 8.1 vs 10.2 ± 9.4 vs 9.7 ± 8.3 ; Medications/month 46.3 ± 27.7 vs 10.3 ± 11.2 vs 8.9 ± 8.1 vs 12.3 ± 13.8 vs 9.1 ± 8.2 ; MIDAS total score 67.2 ± 52.6 vs 32 ± 43.1 vs 27.1 ± 35.7 vs 14.9 ± 31 vs 9.6 ± 27.4).

Conclusions Chronic migraine with medication overuse led to considerable disability prior to treatment. Significant improvement was noted for diary measures of headache activity, and for overall measure of disability obtained from the MIDAS questionnaire. These results suggest that successful treatment has more wide-ranging positive benefits beyond mere symptom reduction, even for this difficult-to-treat pop-

ulation. Although our results are highly encouraging, with a long follow-up period, they are by no means definitive.

D031

Impact of migraine in Spain. Results of the PALM program

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Objectives Qualitative and quantitative analysis of the personal, social and occupational impact of migraine in Spain.

Methods Subjects identified as strict migraine sufferers according to the 2004 IHS criteria. We used a structured questionnaire on the personal impact of migraine, disability (MIDAS), treatment needs (Migraine-ACT scale), quality of life and occupational impact. The study was approved by an ethics committee. Data are reported as percentages (95%CI), means or medians.

Results Three hundred and two subjects (85% women) aged 40.8 years (mean) agreed to participate; 75% reported some type of triggering factor. The patients referred 24 episodes of migraine (median) in the past year; 38.1% reported severe disability during the attacks. Consulting behavior: 22.5% had never consulted for migraine; 23.8% were current consulters, and 53.3% lapsed consulters of which 32.2% lapsed for lack of confidence in treatment or care. In turn, 34% suffered moderate-severe disability (MIDAS III or IV), and 35% had significant unmet treatment needs (Migraine-ACT score <3). Mean effectiveness at work during the attacks was 61% (remunerated) to 53.3% (non-remunerated). Productivity varied with Migraine-ACT score. A total of 61% subject claimed to be hardly informed or uninformed about migraine; over half of the subjects acquired drugs without prescription during the last 6 months.

Conclusion Migraine in Spain is highly disabling, under-diagnosed, has unmet treatment needs, and exerts a strong impact upon patient productivity and quality of life. Interventions are needed to reduce this impact and improve management of the disorder.

Study sponsored by MSD España.

D032

A new instrument for measuring the impact of migraine using questions about the most important factors of life

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Objectives Health-related quality of life (HRQoL) is a relevant measure because it estimates the influence of migraine from a perspective of the individual sufferer. There is need for a short, reliable and validated instrument in Swedish. The aim was to analyse if a questionnaire including the most impor-

tant factors of life, according to a large ($n = 423$) population based survey among Swedish self-considered migraineurs, could be used as a measure of migraine's impact on HRQoL.

Methods A consecutive sample of adult migraineurs ($n = 187$, 86% women) at a headache specialist clinic were given a written questionnaire in which they assessed (1–4) the impact of migraine on ten factors of life. A Cronbach's alpha analysis, pairwise correlations and factor analysis were performed to explore if this instrument measured a single one-dimensional construct. A validity analysis investigated if the construct constitutes migraine's impact on HRQoL. Hence, the relationship between the total score of the proposed instrument and different migraine characteristics were analysed.

Results A high Cronbach's alpha value of 0.93 and high values for pairwise correlations for the questions ($r > 0.40$) were received. Factor analyses showed that data was influenced by one component. The validity analysis resulted in correlation coefficients that agreed with the suggested hypotheses. However most of the correlation coefficients were low. The only statistically significant one was between the total score and recovery between attacks.

Conclusions The influence of migraine on the most important areas of life measures a single one-dimensional construct. Further investigation of the instrument's validity is needed.

D033

The attributable impact of menstrual related migraine on headache chronification and medication overuse

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Introduction Menstrual related migraine (MRM) is highly prevalent and has historically presented a therapeutic challenge. In the clinical setting, MRM may complicate chronic headache and medication overuse. This study seeks to measure the specific impact of MRM on headache chronicity and medication overuse.

Methods We identified 229 consecutive women seen in follow-up for hormonal prevention (HP) of MRM at an academic headache center. At each visit, consumption of all acute and preventive agents used in the preceding month was tallied. Patients kept standardized diaries from which separate menstrual-week (MW) and non-menstrual week (nonMW) headache indices were calculated and compared. Resolution of MRM was defined by reduction of the MW headache index to a score not exceeding the nonMW headache indices. We performed post-treatment comparisons of subjects in whom MRM was resolved with those in whom it was not resolved.

Results At baseline, transformed migraine was present in 92% of subjects; 72% were overusing acute medications. Resolution of MRM occurred in 81% of subjects who were compliant with HP. Resolution of MRM was associated with reversion to episodic migraine (59% vs. 18%, $p < 0.001$, Chi Square) and resolution of medication overuse (54% vs. 20%, $p < 0.001$, Chi Square). Resolution of MRM was associated with significant decreases in per capita use of triptans, opiates, all acute treatments, and traditional migraine preventives.

Conclusions This study suggests significant attributable impact of MRM on both the chronification process and medication overuse and offers preliminary data on the effectiveness of HP for treatment of MRM.

D034

Headache diary in evaluation of migraine patients: a comparison between headache questionnaire and diary data

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Objectives The diagnosis of migraine is based on the characteristic feature of the headache episode. But the patients are no always able to describe their headache episode and associated symptom accurately during the interview. Our study is aimed to evaluate the usefulness of headache diary and to know how much migraine patients can recall prior headache complaints accurately.

Methods Sixty patients were enrolled in the present study according to their headache status in a formed questionnaire and interview, at which time 43 patients had migraine, 17 patients had probable migraine. The patients kept the headache diary for prospectively 2 months after filling out the headache questionnaire. The headache frequency, duration, severity and other associated symptom during migraine attack on the questionnaire/diary were compared.

Results Forty-one (67%) of 60 migraine patients returned their headache diaries and total of 216 headache episode were reported in the diaries. The mean frequencies of headache episodes were not different between questionnaire and headache diary. The intervening nonmigrainous headache between migraine attacks occurred in 53% of 41 migraine patients in diary. Compared with the diary, duration of headache was overestimated on the questionnaire. Among the characteristic feature and associated symptom, the nausea/vomiting and phonophobia also showed the overestimated tendency from the headache questionnaire.

Conclusions As compared to headache questionnaire during interview, migraine characteristics can be evaluated differently and intervening nonmigrainous headache were occurred frequently from diary records. To minimize bias, the use of a diary when studying of migraine patients is recommended.

D035

The polysynaptic reflex excitability in tension-type headache

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Objectives The aim of present investigation is to study the changes of the polysynaptic reflex excitability (PRE) on the basis of blink reflex (BR) parameters in episodic (ETTH) and chronic (CTTH) tension-type headaches.

Methods The BR has been recorded for 187 patients (age 38.7 ± 0.8 years, 41 males and 146 females) with infrequent ETTH (n = 30), frequent ETTH (n = 105), CTTH (n = 52) and control group (n = 40).

Results In order to evaluate the changes of PRE on the basis of the R2 and R3 we have classified the different types of the BR: the <<normoexcitable>> type has the middle indexes; the <<hypoexcitable>> type has a high threshold, long-term latency, short duration and the low amplitude of R2, whereas R3 is absent; the <<hyperexcitable>> type is characterized by merging R2 and R3. Such <<(R2 + R3)>> component has a low threshold, the short-term latency, long duration and the high amplitude. In patients with infrequent ETTH we have registered only the <<normoexcitable>> type. The prevalence of the <<normoexcitable>> type (84.7%) has been observed in patients with frequent ETTH. On the contrary, in patients with CTTH we have revealed a complete dominance of the <<hyperexcitable>> type (98.1%). The findings have shown the significant tendency to the PRE increase alongside with the chronification of TTH.

Conclusions The results confirm the role of the insufficient inhibitory mechanisms and functional deficit of the antinociceptive system in the TTH progressing. The BR method can be used as an adequate neurophysiologic test for the evaluation of functioning of the brain suprasegmental structures.

D036

Prevalence of subtypes of chronic secondary headache in the general population

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Objectives To provide prevalence data on the different subtypes of chronic secondary headaches.

Methods In a cross-sectional epidemiological survey, a total of 30,000 persons from Akershus County, aged 30–44 years, received a mailed questionnaire. Those with self-reported chronic headache within the last month and/or year were invited to a semi-structured interview and a neurological and physical examination conducted by neurological residents with experience in headache diagnostics. The diagnoses were made according to the revised International Classification of Headache Disorders. The Regional Committees for Medical Research Ethics and the Norwegian Social Science Data Services approved the project.

Results Both the questionnaire response rate and the participation rate of the interview were 71%. Of those with chronic headache 58% had a secondary form. The overall last year prevalence of chronic secondary headache was 21.8%. The prevalence of chronic posttraumatic headache was 2.1%, chronic headache attributed to whiplash injury 1.8%, post-craniotomy headache 0.2%, medication-overuse headache 17.5%, cervicogenic headache 1.8%, chronic rhino-sinusitis 3.4% and other subtypes 0.4%. The last year prevalences of medication-overuse headache analyzed by the age groups 30–34, 35–39 and 40–44 years were 7.8%, 9.4% and 10.3% in men and 17.5% 25.9% and 29.7% in women.

Conclusion Secondary chronic headache occurs in more than half of those with chronic headache. The vast majority have medication-overuse headache, while about 1/3 have other secondary headaches often in combination with medication-overuse headache.

D037

New daily persistent headache as a manifestation of spontaneous CSF leak: report of 3 cases

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Objectives To describe 3 patients with new daily persistent headache (NDPH) as a manifestation of spontaneous CSF leak.

Background NDPH is a headache characterized by acute onset and persistency and it occurs in an individual without prior headache. The nature of the headache is similar to that of chronic tension-type headache. On the other hand, headaches in spontaneous CSF leak is not always orthostatic at the time of presentation.

Methods Case reports.

Results Three patients (2 women, 1 man), between the ages of 34 and 55, developed new-onset daily headache fulfilling IHS diagnostic criteria for NDPH. Duration of new-onset daily headache was from 21 months to 25 years. All patients had positional headaches at the onset, but at the time of presentation their headaches were not orthostatic. One suffered from sudden deafness of left ear twice after the onset of the headache. Enhanced head MRI revealed no abnormality in all of them. STIR T2-weighted spinal MRI revealed meningeal diverticulum at T11–12 and S1 in one and paravertebral liquid suggestive for CSF leak in 3 patients. Opening pressures on the spinal tap were normal in all of them. A radionuclide Indium cisternogram showed early appearance of the tracer in the bladder in all of them, and CSF leak in the thoracic region in one and the lumbar in one. After epidural blood patches, headache disappeared completely in 2 patients and moderately in one.

Conclusion On the evaluation of NDPH, spontaneous CSF leak should be ruled out.

D038

Comparison between migraine treatment by headache specialists and primary care physicians in the Czech Republic

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Objectives The aim of this multicentre study was to analyse acute (symptomatic) and prophylactic migraine medications

in headache centres and to compare it with the migraine pharmacotherapy prescribed by primary care physicians (PCP) in the Czech Republic.

Methods The study was conducted in 495 migraine patients (MP) with and without aura (according to IHS criteria) (437 females and 58 males, mean age of 40.9 years, range 15–69 years) treated in one of the 7 participating headache centres (HC). Data were obtained from medical charts and a short questionnaire about migraine history and management. Migraine treatment patterns used by headache specialists and by PCP were analysed and compared.

Results Triptans were used in 79.3% of HC patients and only in 23.0% of those treated by PCP. The most frequently prescribed acute migraine medications were sumatriptan (in 38.8%) and eletriptan (in 31.3%). Prophylactic medication was administered to 58.0% of MP in HC, while only to 27.4% of those treated outside of HC. Topiramate (in 17.8%) and valproate (in 13.9%) were the most frequently prescribed preventive agents. Only a low number of MP in HC used beta blockers and antidepressants (5.3 and 6.9, respectively). Administration of combination analgesics was significantly less frequent in HC (8.5% of MP) than in primary care (41.4%).

Conclusion This multicentre study revealed differences in acute and prophylactic migraine medications between headache specialists and primary care physicians. Data analysis demonstrated a significantly higher prescription rate of triptans and prophylactic agents and a significantly lower prescription rate of combination analgesics in headache centres.

D039

Central sensitization in chronic daily headache

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Objective Allodynia has been described in transformed migraine (TM) and more rarely in chronic tension-type headache (CTTH). The aim of this study was to compare dynamic (brush) and static (pressure and pinprick) mechanical allodynia across various forms of chronic daily headache (CDH) and identify their possible impact on headache chronicification.

Methods We recruited 15 patients with TM as defined by Silberstein and Lipton, 14 patients with IHS-defined CTTH and 15 control subjects. A questionnaire of headache features was administered. Brush allodynia (BA) was tested by cutaneous stimulation with a soft brush and static allodynia (PA) was tested by using a pinprick stimulator and pressure algometer in 5 bilateral skin areas on the head and neck. Wind-up was also measured.

Results Both types of headache presented with similar clinical features. In both headache groups pressure pain and pinprick thresholds were decreased and wind-up increased across all tested areas. Wind-up was also higher in migraine with aura compared with migraine without aura. DA was present in 14% and PA in 50% of patients with no significant differences between two headaches groups. There was a positive correlation between PA and pain intensity and frequency.

Conclusion Both PA and DA are prevalent in patients with various CDH forms during their mildest headaches. Allodynia intensity and prevalence is CDH type independent, suggesting similar pathological mechanisms of headache chronicification and chronicity maintaining. PA is more prevalent than DA. Because DA is found only in patients with PA, it may suggest an advanced stage of sensitization.

D040

Orgasmic headache manifestation after prophylactic treatment for migraine

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Objectives The International Headache Society classifies the primary headache associated with sexual activity into preorgasmic and orgasmic headache. The latter is diagnosed in those cases where subarachnoid haemorrhage, arterial dissection and low cerebrospinal fluid pressure are excluded. This primary headache is reported with migraine in approximately 50% of cases. We report a case of a 42 years old woman with a medical history of migraine who received prophylactic treatment with topiramate and she experienced orgasmic headache.

Methods The patient is suffering from migraine for the last 15 years. She received prophylactic treatment with topiramate for 6 months. The migraine frequency was three attacks per month, hardly sufficiently treated with triptans and topiramate. At the end of the 6 month period, she reported orgasmic headache for the first time, as an explosive headache occurred at orgasm lasted for 5–10 minutes, bitemporally without other features of migraine. She experienced that disorder for five times.

Results The patient visited our outpatient cephalalgetic clinic. Her medical and psychological examination was unremarkable. Brain computed tomography; magnetic tomography and ultrasound arterial vessel examinations were normal. Laboratory tests and gynaecological hormonal profile were normal. We performed a lumbar puncture to measure her CSF pressure, which was normal. She was treated with indomethacin successfully.

Conclusion The neurologist should always be aware about primary headaches. Common features or simultaneously reported cases with migraine are rather common in potentially reproductive women but uncommon after prophylactic treatment for migraine. Sufficient therapy is indomethacin and possibly the triptans.

D041**A CO₂ laser evoked potential study in patients with 'Probable Medication Overuse Headache'**

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Objectives The physiopathology of 'Medication Overuse Headache' (MOH) is complex and includes central sensitization from repetitive activation of nociceptive pathways. Our aim was to assess the habituation to experimental pain in patients with 'Probable MOH', before and after a detoxification scheme, by recording the scalp potentials evoked by CO₂ laser stimulation (laser evoked potentials – LEPs).

Methods We studied 5 patients affected by 'Probable MOH' + 'Chronic Daily Headache' before and after a detoxification scheme (a corticosteroid course as a transitional support during acute medication withdrawal followed by 3–6 months of prophylactic treatment). LEPs were recorded to stimulation of both the right hand and the right perioral region. The habituation of the negative-positive complex at the vertex (N2/P2) was assessed by measuring the LEP amplitude changes across three consecutive repetitions of 30 trials each.

Results In three patients with clinical improvement, LEP habituation, lacking before the treatment, was recovered after MOH had resolved. On the contrary, in the two patients who still had chronic daily headache and were still overusing acute medication at follow-up LEPs still showed reduced habituation.

Conclusion The lack of habituation to repetitive stimuli is thought to be due to an abnormal excitability of the cortical areas devoted to pain processing. The LEP habituation recovery after successful withdrawal of acute medication and reduction of headache frequency is a probable indicator of a normalization in the pain-processing mechanisms and of a 'desensitization' of central nociceptive pathways.

D042**Perimenopausal headache**

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Background and objectives During perimenopausal period, women frequently suffer from headaches. However, precise prevalence and characteristics of perimenopausal headaches have not been well studied. This study is an attempt, using a large clinical database in tertiary headache care, to better characterize headache during perimenopausal period.

Methods We recruited 326 consecutive women aged 40–54 years for 23 months. Perimenopause was defined as a change in cycle frequency, duration, quantity of menstruation, and vasomotor symptoms during the previous 3 to 11 months. Patients were excluded from the study if they were: incompletely interviewed, taking hormone-containing medications, undertaken hysterectomy. Sixty-one perimenopausal women were participated finally. Perimenopausal headache were

divided into three types-type 1 (aggravation of previous headache), type 2 (a new onset headache), and type 3 (no change of headache during perimenopausal period).

Results Migraine (40 women, 65.6%) and tension-type headache (17 women, 27.9%) were the most common headache types in perimenopausal women. Pre-existing headaches were diagnosed as migraine without aura in 37 (60.7%) and tension-type headache in 8 (13.1%) patients. Headache pattern was classified type 1 in 21 (34.4%), type 2 in 29 (47.5%), and type 3 in 11 patients (18%). Type 2 patients had migraine without aura in 12, tension-type headache in 13, and other primary headaches in 4 subjects.

Conclusions Perimenopausal women visited to tertiary hospital most commonly due to new-onset headache which were mostly migraine or tension-type headache. Aggravation of pre-existing headache was the second cause of women visited hospital during perimenopausal periods.

D043**Development of a cell phone-based headache diary**

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Background Headache diary has been effectively used for the clinical evaluation of headache, and the application of IT technology may offer convenient tool for the self-management of headache.

Objectives We developed a cell phone-based personal medical recorder for patients with chronic headache, to observe patients' condition continuously and to facilitate to self-control of chronic headache.

Methods The software is designed as a self-controllable tool for patients who are familiar with cell phone applications such as games. The software is based on a scheduler consisting of a calendar, data entry canvas, plot canvas, memory control module and an infrared module. A maximum of 2000 clinical data may be stored in text form in the memory (200 KB). The patient can send monthly or daily data to a PC by the infrared module.

Results The personal medical recorder was implemented as an 'i-Appi' (NTT DoCoMo, Inc., Japan) based on Java2 Micro Edition. All of the data, headache occurrence, severity, disability, aura, neck and shoulder symptoms, menstruation, medications, etc. on each day are listed on the data entry canvas. The phone owner selects answers from lists and types in numeric data and comments. Detailed graphic displays of data are shown on a plot canvas of year, month, week, or day. The application was adapted for 10 patients in one trial. The participated patients were favorably receptive this application and were willing to continue using it.

Conclusion We developed a cell phone-based medical recorder as a self-management tool for patients with chronic headache.

D044**Family medicine residents lack knowledge of the IHS diagnostic criteria for migraine**Jonathan Gladstone¹, A Grant²¹Gladstone Headache Clinic, ²Medical School, Dalhousie University, Canada

Objectives To investigate the knowledge level of family medicine residents with respect to migraine diagnostic criteria.

Methods Questionnaires were distributed as a pre-test to University of Toronto Family Medicine residents attending a headache education seminar in Toronto, Canada. As part of the questionnaire, residents were asked to list the diagnostic criteria for migraine.

Results Forty-three residents responded to this question (100% response rate). The criterion for five or more recurrent attacks (criterion A) was stated by 12% of the residents. The appropriate duration of attacks (4–72 hours, criterion B) was identified by 16% of residents whereas an additional 37% recognized that there was a time component but did not state the correct time interval. The quality of the pain (pulsating, criterion C1) was noted by 63% of the residents. Unilaterality (criterion C2) was mentioned by 65%. The requisite pain severity (moderate or severe, criterion C2) was stated by 9%. Aggravation by or causing avoidance of routine physical activity (criterion C4) was identified by only 9% of residents. No resident noted that only 2 of 4 pain criteria (criterion C) are necessary to satisfy criterion C. Nausea and/or vomiting (criterion D1) was reported by 65% of residents and photophobia and/or phonophobia (criterion D2) was reported by 79% of residents. Only one resident remember to state criterion E (not attributed to another disorder).

Conclusions Family medicine have limited and incomplete knowledge of the International Headache Society diagnostic criteria for migraine.

D045**Impaired trigeminal nociceptive processing in patients with classical and chronic trigeminal neuralgia**Mark Obermann¹, M-S Yoon¹, D Ese¹, M Maschke², H Kaube³, H-C Diener¹, Z Katsarava¹¹Neurology, University Duisburg-Essen, Germany, ²Division of Clinical Neurosciences, University of Southampton, UK, ³Neurology, Brüderkrankenhaus Trier, Germany

Objectives To determine trigeminal nociceptive fibre impairment in patients with trigeminal neuralgia (TN) comparing affected and non-affected sides using the nociceptive blink reflex (nBR) and pain-related evoked potentials (PREP) and to identify possible central mechanisms of pain chronicity in patients suffering from persistent dull background pain in between paroxysmal facial pain attacks (chronic trigeminal neuralgia, cTN).

Methods We investigated 24 patients with TN (mean age: 64.9 ± 10.1 years, range: 45–85 years), and 18 patients with cTN (mean age: 61.7 ± 11.9 years, range: 44–82 years). PREP and nBR were investigated following nociception specific

electrical stimulation of the forehead on both sides and in all three divisions of the trigeminal nerve (V1, V2, and V3).

Results We found prolonged PREP latencies and reduced PREP amplitudes as well as prolonged nBR latencies and decreased nBR area-under-the-curve (AUC) comparing pain and non-pain side in all patients with TN. In cTN patients PREP amplitudes were larger and PREP latencies shorter in all divisions of the trigeminal nerve on the affected facial pain side as well as the non-pain side compared to TN patients, while nBR results were similar across groups.

Conclusion Our findings suggest an impairment of the trigeminal nociceptive system on the affected side and may imply facilitation in central sensory transmission as one possible mechanism for the development of chronic pain.

D046**Medication overuse headache: is it part of the addictive spectrum?**Francoise Radat¹, C Creac'h², E Guegan-Massardier³, G Mick⁴, N Guy⁵, N Fabre⁶, P Giraud⁷, F Nachit-Ouinekh⁸, Michel Lanteri-Minet⁹¹Pain Clinic, CHU Bellevue, ²CHU Rangueil, ³CH, ⁴CHRU Charles Nicolle, ⁵Neurology, CHU Montpellier, ⁶Pain Clinic, CHU Pasteur, ⁷Pain Clinic, CH, ⁸GlaxoSmithKline company, ⁹Pain Clinic, Neurology, France

Psycho-behavioural disturbances are a major issue in patients with medication overuse headaches (MOH). The objectives of this study were (I) to estimate the proportion of patients with MOH presenting dependence on acute headache medication (AHM) and (II) to identify variables associated with this diagnosis. The study was performed within the framework of the Observatory of Migraine and Headaches, which included consecutive patients with probable MOH (1) in seven tertiary care centres in France. Two hundred and forty seven patients with MOH were identified, of whom 165 (66.8%) fulfilled DSM-IV (2) dependence criteria for AHM. Multivariate regression analysis identified six variables associated with this diagnosis: overuse of opioid analgesics, overuse involving several pharmacological classes of AHM, antecedents of medication withdrawal, current chronic headache with migraineous features, antecedents of migraine, and comorbid dependence on benzodiazepines, caffeine or tobacco. These results show that two-thirds of patients with MOH referred to tertiary care present dependence on AHM. Dependence could be proposed as a criteria for the diagnosis of complex MOH proposed by Saper (3). Treatment of such patients should always involve a psycho-behavioural intervention. Moreover, these results emphasise the deleterious effects of opioid analgesics in headache patients. Finally the association of dependence on AHM with dependence on other psychoactive substances suggests that MOH contributes to the addictive spectrum in some patients.

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D047**Predictive factors of long term outcome after drug withdrawal in patients with medication overuse headache**

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Objective Few data are available on the predictive factors of long-term outcome after drug withdrawal in medication overuse headache (MOH). Aim of the study was to investigate the prognostic factors contributing to long-term outcome in MOH patients after inpatient withdrawal treatment.

Methods Patients suffering from MOH were re-investigated 3–6 years after inpatient drug withdrawal. Demographic and clinical informations, profession, habits, co-morbidities, pre-existing headache, MOH characteristics, overused symptomatic medication were analysed as predictive factors.

Results Fifty patients (46 F, 4 M; mean age: 58 ± 10 years) participated in the study. Eleven patients (22%) developed recurrent drug abuse. Predictors of MOH relapse were: heavy cigarette smoking ($p = 0.003$); higher daily drug intake ($p = 0.003$); positive family history of headache ($p = 0.035$) and intensity of pre-existing headache ($p = 0.036$). A lower MOH relapse rate was found in patients with NSAIDs overuse ($p = 0.001$). Age, gender, educational level, profession, alcohol intake, living situation (alone or with other person), life event stressors, hobbies, age of onset, frequency, duration and type of pre-existing headache, duration, intensity and disability of MOH, co-morbidities like anxiety, depression, and hypertension, were not predictive of MOH relapse.

Conclusions Smoking, intensity of pre-existing headache, and high daily drug intake were significantly related to MOH relapse. Patients with NSAIDs overuse had significantly reduced relapse rate. These observations might be relevant for proper advice in treating headache patients.

D048**Third year medical students skills in headache history and physical examination**

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Objectives To evaluate headache history and neurological examination (NE) skills of third-year Neurology Clerks, and determine areas of strength and needs for future improvement.

Methods In an OSCE setting at Chicago Medical School (CMS) and midway through a 3-week clerkship, academic year 05–06 Clerks obtained blinded (to headache scenario) 15-min history, and performed 30-min NE on standardized patients (SP) who simulated three headache scenarios (meningitis, brain mass, migraine). Performance scores were: (a) History-taking = ratio of relevant history questions asked over total number of index questions established for each diagnosis (brain mass = 19 questions; meningitis = 18 questions; migraine = 23 questions; common to all diagnoses =

14 questions); (b) NE = sum of each individual test score (1 = performed correctly test item such as pupillary light test; 0 = incorrectly performed, or did not perform, test), based on 68-point checklist; (c) Communication skills = 5-point Likert scale score on 10-item questionnaire.

Results 61 students evaluated SP with brain mass, 61 assessed one with meningitis, and 65 tested one with migraine. History-taking scores were: Brain mass = $75 \pm 14\%$; Meningitis = $76 \pm 12\%$; Migraine = $73 \pm 10\%$. 51/187 (27%) did not ask about pain intensity and 107/187 (57%) did not query impact of headache on QoL. Students' neurological examination (90 ± 7) and communication skills scores (85 ± 11) were numerically superior to Hx-taking scores.

Conclusion CMS students perform very well when conducting Hx and NE on patients with HA. Gaps exist in quantifying pain intensity, assessing overall impact of pain, and determining precipitants of pain, which calls for emphasis through curriculum on these aspects.

D049**Hair-do headache – an independent entity or headache provoked by a specific precipitating factor?**

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Objectives There are many factors triggering headache attacks. Their analysis helps physicians to get more complete information about the clinical course of the disorder. Elimination of these factors is an important part of doctors' recommendations. Our attention has been attracted by the histories of several women who experience a headache attack after visiting a hairdresser's. We choose some most illustrative examples.

Methods Four clinical cases are presented.

Results In our case studies one patient experiences a headache attack only after fixing and styling her hair at home. Other patients with longstanding histories of migraine can have their typical migraine headache or tension-type headache after visiting a hairdresser's. In the cases mentioned above the patients at hairdressing salons had their hair curled, fixed and styled in a new direction, which caused migrainous headaches or tension-type headaches.

Conclusion The fact that in all the cases the headaches can be eased or stopped after the hair-do has been unraveled shows that the strain of hair caused by its fixation, curling and styling is the main and, evidently, the specific trigger factor for such a headache. The consequence of such strain may be irritation of susceptible receptors in the hair follicle and the strain of arrector pili muscles. In our observations all four patients continue to visit the hairdressing salons. It is difficult to say, what may have more negative effect on the quality of their lives: the headache caused by this provoking factor or its elimination.

D050**Outcome of medication-overuse headache after detoxification prophylactic treatment: analysis at 1-year**

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Introduction Management of medication-overuse headache (MOH) involves detoxification and a subsequent adequate preventive treatment. The reasons of the failure of this approach is that a discrete proportion of patients need to be clarified.

Patients and methods One hundred and twenty MOH outpatients (82 females and 38 males) were admitted to the study. Patients underwent discontinuation of overused drug/drugs, a 7-day outpatient detoxification regimen and subsequent prophylactic treatment. Clinical variables, at the basal time and after one-year, included: number of days with headache per month; type of drugs abused, daily drug intake (DDI) and Leeds Dependence Questionnaire (LDQ) scores.

Results Sixty-eight (56.7%) MOH patients were successfully detoxified (group A), 52 (43.3%) were not (group B). Fifty-one patients (42.5%) in group A returned to an episodic headache pattern, compared to 10 (8.3%) in group B ($p < 0.003$), independent of time and type of prophylactic treatment and type and DDI of abused drugs.

At the basal time, LDQ total scores were 9.27 ± 5.51 in group A and 11.10 ± 6.35 in group B. The LDQ scores were significantly reduced at one-year in group A (5.21 ± 2.78) but not in group B (10.20 ± 5.23) ($p < 0.001$).

Discussion MOH patients who did not discontinue abused drug/drugs maintaining a chronic pattern of headache showed a drug dependence pattern similar to that of drug addiction (higher items 9 and 3 in LDQ scores). In patients returning to an episodic pattern of migraine at one-year, drug dependence behaviour reflects the need of daily analgesic use to cope with everyday life.

D051**Clinical analysis of idiopathic thunderclap headache**

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Objective The aim of the study is to clarify the clinical features of idiopathic thunderclap headache.

Methods We analyzed backgrounds and clinical symptoms of 45 patients with idiopathic thunderclap headache (45.7 ± 18 years old; mean \pm SD) during past 4 years that did not show any abnormalities in CT scan and lumbar puncture. They were divided into 3 groups based on characteristic of headache; non-pulsating (N) group (11 cases), pulsating (P) group (15 cases) and exploding (E) group (19 cases). Their clinical features were compared among 3 groups.

Results (1) The gender ratio (female : male) was 7 : 4 in group N, 9 : 6 in group P and 16 : 3 in group E. (2) Duration was 2.3 ± 1.2 , 3.2 ± 2.0 , 4.3 ± 3.2 days, respectively. It was significantly

longer in group E as compared to group N ($p < 0.05$). (3) Attacks of headache during sleep were seen in 1 case (9%) of group N, 0 case (0%) of group P and 5 cases (27%) of group E. D-dimer was increased in 2 of 6 cases (33%) of group E.

Conclusion In exploding group, the ratio of female to male was higher, duration was longer, and frequency of headache attacks during sleep was higher than other 2 groups. Prognosis of ITH was good and no patient had recurrence of headache in our series.

D052**Chronic postural headache treated by lower thoracic or lumbar epidural blood patch**

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Objective Chronic headache following trauma is a difficult symptom to treat. Some patients with postural headache after trauma have been suggested to have spinal CSF leakage to which epidural blood patch (EBP) is one of the safe and effective treatment modalities. The purpose of this study is to investigate prospectively the effectiveness of EBP for the patients with chronic postural headache.

Methods We treated 100 patients with postural headache during September 2004 to January 2007. Previous treatments had failed to control their headache. They were evaluated neurologically and received brain MRIs. We performed 237 EBPs in these patients. All patients except 5 had clear history of trauma. There were 56 females and 44 males. The median age was 38 and the median period for the symptom was 19 months. The outcome was estimated in 4 grades, 'excellent (headache almost disappeared or the patients gained previous activities)', 'effective (headache was diminished but the patients did not gain previous activities)', 'not effective (headache was not diminished)', 'worsened (new symptoms were added)'. The follow-up period was one week to 2 years after EBPs.

Results The patients had no objective neurological deficits before and after EBPs. Brain MRIs did not show organic brain disorders but fronto-parietal high convexity subarachnoid spaces were enlarged in most cases. There were 33 'excellent', 60 'effective', 5 'not effective', and 2 'worsened' cases.

Conclusion This study showed that EBP is an effective method for the patients with chronic postural headache. The indications for EBP should further be searched.

D053**Disarray of affective regulation pattern in chronic headache patients**

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The study examined the role of alexithymia, anger management/expression and attachment style as psychological

variables connected to the affect regulation process, in patients with a diagnosis of chronic headache (tension-type plus medication overuse headache). The Toronto Alexithymia Scale (TAS-20), the Stait-Trait Anger Expression Inventory (STAXI-2) and the Relationship Questionnaire (RQ) were administered to a sample of 104 patients (day hospital and outpatients) comprising 70 subjects with CTTH plus 34 with MOH. Of the total sample, 16.3% of patients were classified as alexithymics, 20.2% as intermediates and 63.5% as non-alexithymics, according to the TAS-20 criteria; on the RQ, 33% showed a dismissing-avoidant attachment style, 15.9% preoccupied, 10.2% fearful and 40.9% secure. The self-report method of anger assessment employed in the chronic headache sufferers did not reveal any dysfunctional pattern of anger management compared to the normative sample. No significant differences were noted between CTTH plus MOH patients in affect regulation correlates; within the MOH group, patients with primary diagnosis of CTTH were shown to be more insecure and alexithymic than those with migraine. Findings supported a link between alexithymia, turning anger inward, and insecure attachment styles, suggesting the presence of a defective affect regulation pattern.

Reference

Pini M (2006). Psychopathological aspects of primary headaches. Master Degree Thesis in Headache Medicine, Sapienza University of Rome, Academic Year 2005–2006. FrancoAngeli Editor, Milan, pp. 1–128.

D054

Frequency of headache as a symptom related to neurocysticercosis

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Background Neurocysticercosis is a parasitic infection of central nervous system considered the first cause of symptomatic epilepsy in the developing world. It also has been persistently signaled as a frequent cause of headache.

Purpose To present a summary of published clinical studies in which the percentages of occurrence of headache in patients with neurocysticercosis have been shown.

Methods This review is based on a search of the literature citing neurocysticercosis and headache utilizing PUBMED for the years 1980 through the end of 2005. Case series and epidemiological studies were evaluated.

Results A total of thirteen published articles were included. When considered as a general symptom and not dissociated from intracranial hypertension, headache was referred to be present between a range from 22–61.5% of neurocysticercosis cases. If intracranial hypertension was excluded, but headache would occur in concomitance with another neurological symptoms, it was referred in a range from 19–60% of patients. Finally, headache as the patient's sole complaint was seen in less than 10% of cases, and in patients with solitary cysticercus granuloma just in 2.5%.

Conclusions Headache seems to be a frequent neurocysticercosis symptom, although it usually happens together with other neurological symptomatology. However, its presentation as a unique symptom might not be rare. This information could be relevant when considering the possibility of a secondary headache in an appropriate context, but further studies utilizing more specific criteria are required.

D055

Hemicrania continua responding to pregabalin

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Objectives Hemicrania continua (HC) is a persistent strictly unilateral headache completely responsive to indomethacin. We report a case fulfilling the ICHD-II criteria for HC, whose initial response to indomethacin was not sustained. The patient had a subsequent complete and prolonged response to pregabalin.

Methods We have prospectively followed up a 46-year-old man suffering from HC. At the onset of headache, the patient underwent extensive investigations, including cerebrospinal fluid examination, brain MRI and Angio-MRI, which were normal.

Results When the patient was 43, he presented with severe continuous strictly unilateral left-sided headaches, located in the ocular and frontal regions, associated with nasal congestion. Treatment with intravenous indomethacin 200 mg daily resulted in an immediate response, but when it was withdrawn, the headaches recurred with a continuous course and moderate intensity. The patient was thus commenced on oral indomethacin 150 mg daily and the pain promptly subsided. However, after 4 months, his response to indomethacin appeared to fade and gastric discomfort was reported. Indomethacin was replaced by pregabalin, that was titrated up to the dose of 600 mg daily. The headaches completely ceased, but when he reduced the dose, the pain returned. The tolerability was excellent, since the patient did not report any significant adverse events.

Conclusion Drugs other than indomethacin have proven to be effective in HC. They include anti-inflammatory agents, such as piroxicam β -cyclodextrin and rofecoxib, verapamil, melatonin and neuromodulators, such as topiramate and gabapentin. This is the first report of the effectiveness of pregabalin in the treatment of HC.

D056

Hypnic headache sine headache

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Objectives Hypnic headache (HH) is a primary headache, whose natural history is not well known. We report a new case fulfilling the ICHD-II criteria for HH, who initially for 2 years was awakened every night without complaining of headache.

Methods We have prospectively followed up a 60-year-old woman suffering from HH.

Results We first saw the patient when she was 58. Physical and neurological examinations were normal, as were routine blood tests and MRI of the brain. When she was 54, she started being awakened from sleep on a nightly basis, almost always at the same time, without any evident reason. Only very occasionally, up to once every two months, she complained of a mild bilateral frontal headache. She usually had to rise from bed, but was able to resume sleep 1 to 2 hours after waking up. At the age of 56, in strict association with the nocturnal awakening, a dull, moderate bilateral headache started to occur on a regular basis. When she came to our observation 2 years later, she commenced lithium and melatonin at bedtime and both the headaches and the associated awakenings almost completely ceased. Any attempt to discontinue the treatment resulted in the recurrence of the symptoms.

Conclusion We report the first case of a patient with HH sine headache. This pattern was temporary, lasting for 2 years, prior to the development of the complete clinical picture. Our case supports the hypothesis that HH might be a chronobiological disorder, possibly related to a hypothalamic dysfunction.

D057

Trigger point injection add-on pharmacological treatment in chronic migraine and medication overuse headache

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Objectives Treatment of chronic migraine and medication overuse headache is challenging. Pericranial muscle tenderness and referred pain had been described in chronic daily headache patients. This study was designed to evaluate the effects of trigger point injections (TPI) as an add on pharmacological treatment in chronic migraine and medication overuse headache patients having pericranial muscle tenderness.

Methods Twenty-eight chronic migraine, 27 medication overuse headache patients with pericranial trigger points were studied. 0.5% 14 ml of lidocaine was injected to 14 explored trigger points twice a week for 3 weeks, in addition to prophylactic drugs and/or withdrawal of overused medication. Before and after the treatment, the frequencies and verbal numeric scales (VNS) of pain were determined. VNS values were also recorded before and after the first trigger point injection.

Results VNS reduced from 5.55 ± 1.15 to 2.2 ± 1.77 following the first TPI ($p < 0.05$). The number of migraine attacks and VNS values were reduced after the treatment from 21.44 ± 6.12 to 6.65 ± 6.9 , 8.62 ± 1.15 to 5.33 ± 1.93 respectively ($p < 0.05$). Except mild dizziness in two patients no any other complication or side effect was seen related to injections.

Conclusion We found that TPI reduced VNS values significantly even after the first injections and probably influenced the reduced frequency and severity of migraine attacks in long-term treatment. TPI can be considered as an add on treatment in chronic daily headache patients to induce pain free

interval during the beginning of the pharmacological treatment and/or medication withdrawal.

D058

Chronic daily headache (CDH) and family history: a case-control study

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Background and aims Risk factors underling the evolution of episodic headache into CDH are still debating. The aim of our study was to assess how the family history of patients with CDH could underline the risk for CDH.

Methods CDH Patients were matched by age, sex and type of headache at onset with patients with episodic headache. Both groups underwent a structured interview assessing familiarity for episodic headache, for CDH with or without medication overuse, for substance abuse and for psychiatric disorders.

Results 105 patients with CDH (81 F, 24 M; mean age 48.6 ± 14 years) were compared to 102 controls (78 F, 24 M; mean age 48.1 ± 14 years). 65.7% of the cases and 67.6% of the controls reported familiarity for episodic headache respectively, while 41.2% and 44% reported familiarity for psychiatric disorder. 38.1% of the cases reported familiarity for CDH respect to 13.7% of the controls. Familiarity for CDH with medication overuse was reported by 25.7% of the cases and 9.8% of the controls. Relatives of CDH patients (20%) were more likely than controls relatives (5.9%) to have a substance abuse.

Conclusions CDH with and without medication overuse and substance abuse disorder are more frequent in the relatives of CDH patients. The vast majority of patients with familiarity for CDH with medication overuse and for substance abuse had medication overuse themselves. These results suggest a vulnerability to addiction, that increase the risk of analgesic overuse, in patients with familiar history of CDH with medication overuse or substance abuse.

D059

Post-traumatic headaches after mild head injury (ICHD-2 5.1.2/5.2.2): evidence from two controlled cohort studies

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Objectives To evaluate ICHD-2 diagnoses acute (5.1.2) and chronic (5.2.2) post-traumatic headache attributed to mild head injury, using data from two controlled cohort studies on headache after concussion from Lithuania, where there is little expectation of chronic symptoms or secondary gain.

Methods 348 individuals with concussion and 367 matched non-head injured controls answered questionnaires about headache frequency, severity, character and accompanying symptoms in (1) a prospective cohort study shortly after the

trauma, and after 3 months and 1 year; and (2) a historical cohort study after 2–3 years.

Results Acute posttraumatic headache was reported by 88% but had disappeared in 92% of cases after 3 months. In concussion patients migraine and phonophobia were more prevalent after 3 months, and photophobia both after 3 and 12 months. No significant differences in headache type, frequency, severity or accompanying symptoms was found after 1 year or more, even when the two studies were combined to increase the power. In the prospective cohort study, no positive dose-response relationship between severity of concussion and severity of headache was found.

Conclusion The prospective study clearly testifies to the existence of acute post-traumatic headache after mild head injuries. The headache may also last for more than 3 months in a few cases, which is required for making a diagnosis of the chronic type. However, there was no evidence that such headache persisted for a year or more, indicating that the long-term prognosis with regard to headache is good in virtually all cases.

D060

Neuroplasticity and modulation of pain is impaired in chronic tension-type headache. A brain map-ping study

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Objective To study localisation and magnitude of cortical response to painful stimuli at baseline and during tonic muscle pain in chronic tension-type headache.

Methods Nineteen patients with chronic tension-type headache and 19 healthy controls were included. Painful electrical stimulation was applied to the trapezius muscle and somatosensory evoked potentials (SEP) were recorded with 124-channel EEG during 3 experimental conditions (1) baseline (2) tonic pain induced by glutamate injection in the trapezius muscle and (3) post-baseline. Peak stages around 100, 200 and 300 ms were analysed with topography and equivalent current dipoles (x,y,z coordinates) were superimposed to magnetic resonance imaging slices of a standard brain to investigate source localization and changes in representational field in the cortex.

Results A significant difference between patients and controls was found in magnitude (17.3 nAm vs. 28.6 nAm; $p = 0.014$) and in the y-coordinate (42.9 mm vs. -10.3 mm; $p = 0.027$) of the 200 ms dipole at baseline. In controls, but interestingly not in patients, magnitude of the 200 ms dipole changed significantly from baseline to glutamate (-28.6 nAm vs. 9.9 nAm; $p = 0.001$) and from base-line to post-base-line (28.6 nAm vs. 12.6 nAm; $p = 0.002$), the y-coordinate changed from baseline to glutamate (-10.3 mm vs. -1.10 mm; $p = 0.097$) and the x-coordinate of the 300 ms dipole changed from baseline to post-baseline (5.8 mm vs. -13.2 mm; $p = 0.079$).

Conclusion A significant modulation of the cortical activity was achieved in response to tonic muscle pain in controls but

not in patients. These results indicate an impaired neuroplasticity and modulation of pain in chronic tension-type headache.

D061

Advice alone versus structured detoxification programmes for MOH: a 1-year prospective study

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Objectives The aim of the study was to compare the long-term effectiveness of strong advice to withdraw the overused medication with the effectiveness of two structured pharmaceutical detoxification strategies and to evaluate the predictors for relapse.

Methods Detail about population under study, study design, inclusion criteria and short-term effectiveness of the different withdrawal strategies have been already published (Rossi et al. 2006). Relapse was defined as frequent use of any acute medication on more than 10 days month for at least 3 months.

Results Complete datasets were available for 83 patients. At 1-year follow-up, the relapse rate was 21.3% (13.7% of those who received only intensive advice, 26.9% of those included in a standard outpatient withdrawal programme, and 25% of those included in a standard inpatient programme, $p > 0.05$). Univariate analysis showed that patients who relapsed had a longer duration of disease with more than 8 headache days/month, a longer duration of drug overuse, tried a higher number of preventive treatments, had a lower improvement in headache frequency after withdrawal and consulted a higher number of specialists. A binary logistic regression analysis was performed and two variables remained as significant predictors of relapse use: duration of disease with more than 8 headache days/month (OR = 1.85, $p = 0.04$), and number of previous preventive treatments (OR = 1.51, $p = 0.01$).

Conclusions In patients with migraine plus MOH and low medical needs, long-term effective drug withdrawal may be obtained through the imparting of advice alone and relapse seems to depend on a greater severity of pre-existing migraine.

Reference

Rossi et al., *Cephalalgia* 2006; 26:1097.

D062

Premonitory symptoms and response to rizatriptan treatment in women with ICHD-II menstrual migraine

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Objective To explore the association and impact on treatment outcomes of premonitory symptoms and menstrual migraine, as defined by the 2004 revision of the International Classification of Headache Disorders (ICHD-II).

Methods The two protocols (MM1 and MM2) were randomized, parallel, placebo-controlled, double-blind studies. Adult patients with menstrual migraine as defined by ICHD-II criteria were assigned to either rizatriptan 10-mg tablet or placebo (2 : 1). Patients treated a single menstrual migraine attack of moderate or severe pain intensity. Endpoints were 2-hour pain relief (primary) and 24-hour sustained pain relief (secondary). Patients recorded the presence and type of premonitory symptoms at baseline in a headache diary.

Results A total of 707 patients (MM1: 357, MM2: 350) patients treated a menstrual migraine attack. The percentage of patients reporting 2-hour pain relief was significantly greater for rizatriptan than for placebo (MM1: 70% vs. 53%, MM2: 73% vs. 50%, $p \leq 0.001$ for both studies), as was the percentage of patients reporting 24-hour sustained pain relief (MM1: 46% vs. 33%, $p = 0.016$; MM2: 46% vs. 33%, $p = 0.024$). Approximately 88% of women in both studies reported at least one premonitory symptom. The most common symptoms were 'tiredness/weariness/fatigue' (49%) and 'irritability' (43% to 50%). There was no substantial difference in efficacy of rizatriptan between those with or without premonitory symptoms.

Conclusion Rizatriptan 10 mg was effective for the treatment of menstrual migraine, as measured by 2-hour pain relief and 24-hour sustained pain relief. Most patients reported at least one premonitory symptom. The presence of premonitory symptoms did not predict treatment efficacy.

D063

The demand for ambulatory neurological care of headache patients in the region of Madrid

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Objective Headache is the most common symptom seen by neurologists in ambulatory neurological clinics (ANC). The objective of this study was to describe the demand for care of headache patients in ANC of the Public Health System in the Region of Madrid (population 6 millions)

Method and patients Prospective sampling study realized over a 2 months period among 3815 patients attended by fifteen neurologists in eight ANC of different Health Areas within the region. A specially structured interview was conducted with headache patients to collect epidemiological data, type of headache, appointment waiting time and the care level they were referred from. Demand rate index was calculated as the number of first-time visits of headache patients/1000 inhabitants-year.

Results Headache patients attended were 924 (24% of total), almost half of them (49%) on a first-time visit and with a considerable immigrant proportion (10.6%) mainly from Latin America. Women represented 71.7% and the mean age was 38.8 years. The demand rate was 7.4 (2.2–14.7) meaning a total of 44,140 (13,100–87,700) new headache patients per year. They were referred by family doctors (81%) for diagnosis and

treatment and average appointment waiting time was 45.7 days. Migraine (54%), tension-type headache (21%) and medication-overuse headache (3.4%) were most frequently encountered.

Conclusion Demand for headache care in ANC of Madrid is high. Average delay to receive attention is excessive, reinforcing the need to increase the number of neurologists in ambulatory care. Focused training in this pathology among Primary Care physicians would also help improve the selection of referred patients.

D064

Severity of migraine in Japanese patients

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In Japan, frequency of migraine patients is about 8.6% that is lower than western countries. International Headache Classification says one of criteria of migraine is moderate or severe headache. We feel severity of headache in migraine patients in Japan is lower than western countries, so we investigate severity of headache in migraine patients at our hospital.

30 patients was evaluated about severity of headache and divided into severe, moderate, mild and frequency of migraine attack according to International Headache Classification. Only 13/30 patients can't work and send ordinary life due to attack but most of the migraine patients can work or send ordinary life. Triptan drugs was effective in most of the patients but some patients was effective at OTC.

International Headache Classification is gold standard in diagnosis of migraine but we feel severity of headache is different from country or district and consider that migraine in Japanese patients can not be always moderate or severe headache in western countries.

D065

High altitude headache in Lhasa inhabitants: Chinese–Japanese Women's Mt. Qomolangma Medical Expedition 2005

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Headache is a frequent complication of ascent to high-altitude, occurring in more than 80% of cases. The Japanese and Chinese women climbers combined forces to form a joint expedition on Mt Qomolangma (Everest 8844 m) in 2005. During the expedition, we investigated whether there existed a difference in clinical manifestations of high-altitude headache between the native inhabitants of highland (Lhasa) and those of lower heights. The expedition team consisted of 39 individuals (26 males and 13 females), in which 26 persons were Lhasa inhabitants and 13 persons lived at lower altitude. Development of headache was associated with younger age, gender (female) and a history of headache at high altitude. At Lhasa (3780 m), 15.3% of lower inhabitants experienced headache, and the incidence increased to 46.2% at Base Camp

(BC, 5200 m) and 61.5% at Attack Base Camp (ABC, 6500 m). In contrast, none of the Lhasa inhabitants complained of headache at Lhasa, and only 7.7% presented with headache at BC. However, the incidence of headache rose up to 65.4% at ABC, which was as high as that observed in inhabitants of lower heights. Exposure to more pronounced hypoxic/hypobaric conditions was thus associated with the development of headache even in individuals of Lhasa inhabitants. Therefore, high-altitude headache is also common in highland dwellers.

D066

Analysis of a clinical sample of headache patients in a busy ER in the United States: evaluation of treatment practices

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Objectives To analyze the epidemiology, diagnostic accuracy and treatment patterns of headache in a US ER.

Methods Retrospective analysis of 100 charts with discharge diagnosis (ICD-9 codes used) of headache seen by the ER at the Los Angeles County Hospital (the second busiest ER in the US).

Results The majority of patients were female (74%), and Hispanic (76%). Ages ranged from 11 to 69 years. 18% of patients were admitted for concerns regarding secondary headache. Only 17% of headache patients were seen by neurology consult. The commonest diagnosis made by ER was non-specific 'headache' (42%), followed by migraine (39%). The final ER diagnosis matched the neurologist's diagnosis in 68%. Only 69% of patients presenting with migraine symptoms were correctly diagnosed with migraine. 10% of patients diagnosed with migraine were misdiagnosed. 51% of patients received a head CT, 9% a lumbar puncture. The commonest category of medications used for acute treatment of headaches was narcotics (30%), followed by antiemetics (27%), NSAIDs (20%), and acetaminophen (18%). 28% of patients diagnosed with migraine received narcotics. Only 5% of patients diagnosed with migraines received triptans in the ER (2% overall). **Conclusion** The advent of better medications like triptans for migraine headaches has not changed clinical practices in the ER. There is lack of standards of care for diagnosis and treatment of headache, especially migraines, and neurology consult is under utilized even in an academic ER setting.

D067

Pericranial muscle tenderness in migraine by physical examination

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Objective To identify physical signs confirming the diagnosis of migraine headaches.

Background Although it lists pericranial tenderness in the requirements for categorizing various types of tension-type headaches, the International Classification of Headache Disorders – II (ICHD-II) does not mention muscular or ligamentous

tenderness in its definitions of the headaches of migraine. Muscular tenderness is known to accompany migraine. This study reports the likelihood of firm pressure on head and neck muscles reproducing the headache of migraine.

Methods 49 patients with migraine defined as having migraine without aura (ICHD-II 1.1), migraine with aura (1.2), and chronic migraine (1.5.1) were examined by firmly pressing the trapezius, sternocleidomastoid, splenius and semispinalis cervicis and capitis, and temporalis muscles bilaterally to see if this pressure would cause the patients' typical migraine headache pain.

Results In 23 of 23 patients with 1.1, 5 of 11 with 1.2, and 15 of 15 with 1.5.1 firm pressure on head and neck muscle reproduced the headaches of patients with migraine.

Conclusions In this study, firm pressure on head and neck muscles reproduces the headache of migraine in all patients having migraine without aura and chronic migraine. The presence of this tenderness confirms the diagnosis of migraine headache in these two entities and the absence of tenderness brings these diagnoses into doubt. This information and the presence of tenderness in many having migraine with aura should be used to identify the source of these headaches and to design treatment.

D068

Coping strategies and the relationship between preceding mood states and tension-type headache

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Objectives Psychological stress and mood states were reported as aggravating factors of tension-type headache (TTH). However, a few prospective studies have been conducted. Ecological momentary assessment (EMA) using electronic diaries, i.e. computerized EMA, is now proposed as a method to record symptoms in daily settings avoiding recall bias and faked compliance. Therefore, this study was aimed to investigate the relationships between preceding psychological factors and TTH intensity and the effects of coping strategies on the relationships in a prospective way using computerized EMA.

Methods Thirty-one TTH patients (22 women and 9 men, age 38.4 ± 10.4 yrs) wore watch-type computers as electronic diaries for one week and recorded momentary headache intensity, psychological stress, anxiety, and depression using visual analog scale (0–100) approximately every 6 hours, at awakening, at bedtime, and at headache exacerbations. Problem- and emotion-focused coping strategies were rated using the Stress Coping Inventory. The effects of preceding psychological stress, anxiety, and depression within 6 hours on headache intensity, and the interaction of preceding psychological factors and either type of coping strategies were tested using multilevel modeling.

Results The effects of preceding psychological stress, anxiety and depression were significant ($\beta = 0.152$, $p = 0.0071$; $\beta = 0.157$, $p = 0.0188$; $\beta = 0.332$, $p = 0.0004$, respectively), and the

preceding anxiety x problem-focused coping interaction and the preceding depression x problem-focused coping interaction were also significant ($\beta = -0.0126$, $p = 0.0002$; $\beta = -0.0138$, $p = 0.0059$, respectively).

Conclusion These results suggested that psychological stress, anxiety, and depression might be aggravating factors of TTH and utilizing more problem-focused coping might mitigate the effect of anxiety and depression.

D069

Epicrania fugax: a paroxysmal and ultrabrief epicranial pain

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Objective To report a distinctive headache disorder, apparently originated in the scalp, but with particular traits that clearly deviate from all known epicranial headaches and neuralgias.

Methods Four patients (1 male, 3 females) without remarkable past medical history presented with the same clinical features. Neurological examination was always normal. An X-ray of the skull and CT or MRI of the head, were invariably performed with normal results. Blood work-up and ESR were also normal.

Results Mean age at onset was 41.2 (range 31–63). All the patients complained of strictly unilateral, shooting pain paroxysms starting in a focal area of the posterior parietal region and rapidly spreading forward to the ipsi-lateral eye along a linear or zigzag trajectory, the complete sequence lasting one to a few seconds. In two cases, once the pain reached the ipsi-lateral eye lacrimation without conjunctival injection ensued. The attacks could be either spontaneous or triggered by pressing on the stemming area, which could otherwise remain tender or slightly painful in between the paroxysms. The frequency was 2–8 attacks/day. The temporal pattern was either remitting ($n = 3$) or episodic ($n = 1$). Anaesthesia of the supra-orbital nerve in one of the patients inhibited the radiation, while blockade of either the greater occipital nerve or the trigger zone abolished all the symptoms. **Conclusions** Epicrania fugax is a clear-cut clinical picture that might be a dynamic variant of primary stabbing headache or nummular headache, but might also represent a novel syndrome. Clinical features point to a peripheral origin/trigger in this disorder.

D070

The sensitivity and specificity of ID Migraine test in neurology outpatient clinics in Turkey

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Background The aim of the study was to investigate the validation of ID migraine test in neurology outpatient clinics (NOC) from different geographical regions of Turkey.

Methods Patients presenting for their routine appointments in 41 NOCs were screened during the course of a week. Eligible subjects ($n = 3682$; 61.9% female, mean age 45.2 ± 16.5 years) were screened with the 3-item of ID migraine test and evaluated by a neurologist for the headache diagnosis according to IHS criteria.

Results 66.4% of all patients reported headache, furthermore in 35.1% headache was the primary cause for admission without prominent regional differences. The 2 pre-screening questions of the ID migraine test were answered positively by 1816 patients (49.3%). Of these 1816 patients, 917 (24.9% of all patients) were diagnosed as migraine by the neurologists according to the IHS criteria whereas 1171 (31.8%) were found to be ID migraine test positive. Sensitivity of ID migraine test for neurologist's diagnosis of migraine was 91.8%, specificity was 63.4%, positive predictive value was 71.9% and negative predictive value was 88.4% for the main group. The highest category answered positively by the patients was related to disability with 68.7% of all screened subjects and 33.9% of all patients admitted.

Conclusion The ID migraine test is a valid test that could be used as a screening test in NOCs. It is also an easy to use test and could alarm the neurologist to diagnose patients having other complaints. Disability is the highest positive item that predicts migraine diagnosis.

D071

Chronic headache in nurses: a study for risk management

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Objectives Because nurses have stressful jobs, they may have frequent headaches, and their headaches may make their jobs riskier. We conducted a survey on chronic headache in nurses from a risk-management viewpoint. More specifically, we tried to identify factors causing headaches, and examined whether headaches influenced their job.

Methods We gave a questionnaire to 2357 nurses. The questions included: (1) diagnostic questions such as frequency and location of headache, (2) epidemic questions such as age, sex, department, experience and job title, and (3) job-related questions such as frequency of absence, leave, and errors and/or near-misses. We classified their headaches based on ICHD-II.

Results (1) Out of 2357 nurses, 224 nurses had migraine, 727 had tension-type headaches, 3 had cluster headaches, 63 had migraine and tension-type ('combined headache'), and 1340 had no chronic headaches. (2) Job title had a significant effect on the frequency of headaches ($p < 0.05$), and the effect of department was almost significant, too ($p = 0.058$). (3) Regarding treatment, more than half of the nurses with a chronic headache took over-the-counter drugs. Only less than 20% took absence or leave. Nurses with chronic headaches were more prone to errors and/or near-misses than nurses without headaches ($p < 0.001$).

Conclusion Our survey showed that (1) more than 40% of nurses had a chronic headache, (2) there may be

headache-causing factors in their job, and (3) a chronic headache can be a risk factor in their job. Treatment and prevention of chronic headaches is a form of risk-management.

D072

Persistent 'corona phenomenon' following catheter ablation in a patient with WPW syndrome

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Objectives Corona phenomenon refers to the visual illusions of an extra edge around an object. We reported a patient who has perceived persistent corona phenomenon since she underwent catheter ablation to treat her Wolff-Parkinson-White (WPW) syndrome.

Methods The patient was a 46 year-old woman who had severe headache and visual symptoms from age 42. Her visual symptoms included phosphenes, double vision, and visual perseverations. She had normal intelligence and normal memory. MRI, SPECT, EEG, and visual-evoked potentials (VEP) in the patient were normal. No abnormalities in her fundus, visual field, or electroretinogram were found, either. We evaluated her sensitivity to the edges of the objects using psychophysics. The patient viewed stripes or grids and evaluated their subjective brightness on a 10-point scale. Transesophageal echocardiography with bubble study was also performed in order to examine her heart.

Results The results indicated that she was hypersensitive to the edges of the objects: as the grids became smaller, the patient perceived increasing brightness. She also perceived extra edges of the visual stimuli in the complementary color. Transesophageal echocardiography with bubble study indicated that she had a preexisting right-to-left shunt.

Discussion The above results indicated the patient's hypersensitivity to the visual stimuli. Kosmorsky et al. (1988) reported that ten patients experienced temporary visual symptoms and headache during the catheterization. In addition, previous studies showed a possible link between patent foramen ovale and visual auras in migraine. Catheter ablation in patients with preexisting shunts may lead to exacerbations in migraine symptoms.

Reference

Kosmorsky et al. (1988)

D073

Glaucomatous findings in migraineurs

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Objectives To investigate whether an association exists between migraine and normal tension glaucoma.

Background Inconsistent results have been reported about the association between migraine and glaucoma.

Methods Patients with migraine were consecutively registered in our headache clinic. Migraine was diagnosed by a

standardized questionnaire based on International Headache Society (IHS) criteria. The diagnosis of glaucoma was based on visual field, intraocular pressure, cup/disc ratio, and history.

Results Sixty-seven patients with migraine were enrolled. The mean age (\pm standard deviation) was 39 ± 12 . The duration of headache history was 13 ± 10 years. The prevalence of glaucoma-like change increased with age, with rates of 33%, 28%, 60%, and 64% among persons aged less than 31 years, 31 to 40 years, 41 to 50 years, and 51 years or older, respectively. Similar trend was also noted on duration of headache history, with rates of 39%, 26%, 60%, 62%, and 75% among patients with headache history less than 6 years, 6 to 10 years, 11 to 15 years, 16 to 20, and longer than 20 years, respectively. In comparison with migraineurs with less headaches, those with frequent attacks ($>3/m$) had more glaucoma-like change (45% vs 15%), however, without statistical significance.

Conclusion These data revealed higher proportion of glaucoma-like change in migraineurs. Their association with age and duration of headache history were suggested. However, the frequency and laterality of headache had no significant contribution to such change. Further large scale controlled study is needed to discover the real role of migraine in the normal tension glaucoma.

D074

Two cases presented both elements of migraine and cluster headache

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Objectives The migraine and the cluster headache were classified as vascular headache in the classification of Ad hoc committee. In IHS classification presented in 1988, the migraine and the cluster headache were classified as different category. However, we experienced the headache patients with both elements of migraine and cluster headache.

Methods and results The first case was 20 years old woman. She had throbbing headache for 2 hours on the left side only with sound irritation, photophobia from spring of 2001. Duration of headache was short and headache occurred in the early morning every day. She also showed dacryorrhea and nasal obstruction every time. Oxygen inhalation therapy was effective. Afterwards, she had same headache attack during one month every spring. She showed both elements of migraine and cluster headache in her every attack.

The second case was 41 years old man. He showed typical migraine with fortification spectrum since 1998. Since 2002, the characteristic of his headache was drastically changed. He had severe ocular pain on right side only for one hour every day. He also showed dacryorrhea, nasal obstruction and a sense of restlessness. He presented typical symptoms of cluster headache after his migraine attack was disappeared.

Conclusion These two patients showed both characteristics of migraine and cluster headache in different way. Recently, research in cluster headache patients showed the generator in hypothalamus. These cases suggested that migraine and

cluster headache might be closely related in basic mechanism, such as the generator of both headaches.

D075

Sensitivity and specificity of migraine symptoms – a population-based study

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Migraine is exclusively diagnosed according to the criteria of the IHS based on the description of the patient and after exclusion of secondary causes. It is, however, unknown which symptoms are the most specific and sensitive ones to diagnose migraine. It might be helpful in some situations (uncertain diagnosis, need of fast diagnosis) to classify the different migraine symptoms accordingly. We performed a population-based study which was part of a large epidemiological study on headache prevalence in Germany (the DMKG epidemiological study). Out of a representative sample of 1312 inhabitants of the city of Dortmund, all headache sufferers were asked for their headache symptoms in a direct interview. Then, the specificity and sensitivity of the different symptoms were calculated based on the diagnosis of migraine which was made according to the IHS criteria by an experienced headache specialist. The most specific symptoms for migraine were aura symptoms (0.96), vomiting (0.92) and osmophobia (0.89). The most sensitive symptoms were photophobia (0.82), impairment of daily activity (0.82), and phonophobia (0.78). The three most important factors loading on the diagnosis of migraine were nausea, phonophobia, and unilateral headache. There were also relevant sex differences. In conclusion, the diagnosis of migraine can be made with a probability of more than 95% if nausea and phonophobia occur together with one of the three most sensitive or specific symptoms. As compared to similar studies, there are also cultural differences in the importance of the different migraine symptoms for establishing the diagnosis.

D076

Prevalence of migraine in headache specialists and neurologists

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Studies in the USA and Italy have suggested that the prevalence of migraine is higher among headache experts and among neurologists as compared to the general population. However, the consequences of this phenomenon for treatment decisions and attitudes towards migraine have not been analysed. We performed a survey among German headache experts (n = 82) in order to evaluate the prevalence of migraine and other headaches. Neurologists (n = 133), general pain specialists (n = 152) and general practitioners (n = 130) formed different control groups. The lifetime prevalence of migraine was 48.8% in headache specialists, 33.1% in neurologists, 24.6% in general practitioners, and 21.7% in general pain

specialists. The difference between headache specialists and neurologists was significant as were the differences between these two groups and the other two groups. Headache experts with migraine and without migraine differed in several aspects of attitudes towards migraine and of treatment recommendations. In general, headache experts and neurologists with migraine agreed to a more somatic concept of migraine whereas those without migraine agreed more to a biopsychosocial concept of migraine. We conclude that suffering from migraine has a considerable impact on attitude and on treatment decisions in headache experts and neurologists.

D077

Prevalence of headaches in the population of patients with TMD according to IHS classification of headache – 2004

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Objective Investigate the prevalence of headache in patients with TMD from Orofacial Pain Clinic of Dental Schools and compare it with the headaches in the patients who visited the Pain Clinic of the medicine school, according to IHS Classification of Headache-2004.

Methods We studied forty-one consecutive patients of the Orofacial Pain Clinic of the Dental School UNIGRANRIO (Universidade do Grande Rio) e UERJ (Universidade do Estado do Rio de Janeiro) with complaint of headache in the RDC (Research Diagnostic criteria for TMD). We compared them with forty-two consecutive patients who visited the Pain Clinic of the medical school (UERJ) with headache. The statistical analyze was made using χ^2 de Friedman test and the study was approved by the ethics committee of UERJ medical school.

Results In both groups the age was closer and the female gender was predominant. In the TMD group, the gender proportion was 5 ♀ : 1 ♂ and in the control group it was 3 ♀ : 1 ♂. In the general comparison of the headaches, both groups differed significantly ($\chi^2 = 3023,996$, $p < 0.05$). In the TMD group there were more migraine without aura and chronic migraine and less chronic tension-type headache than the controls; they didn't differ in the probable medication – overuse headache.

Conclusion Our study showed the headaches migraine without aura and chronic migraine is the most prevalent headaches in TMD patients according to the HIS Classification of Headaches – 2004. This result was contrary to the oldest studies where chronic tension-type headache was the most prevalent headache in TMD group according to the HIS Classification of Headaches – 1988.

D078**Prevalence of headaches in patients with articular TMD, myofascial TMD and articular/myofascial TMD**

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Objective To investigate the prevalence of headaches in each type of TMD: articular (TMD art), miofascial (TMD myo) and articular/miofascial (TMD art/myo) according to IHS Classification of Headache Disorders – 2nd edition.

Methods We investigated forty one consecutive patients with TMD and headache who visited the Orofacial Pain Clinic of the dental school UNIGRANRIO (Universidade do Grande Rio) and UERJ (Universidade do Estado do Rio de Janeiro), with complaint of headache in the RDC (Research Diagnostic Criteria of TMD) and compared them with forty two consecutive patients who visited the Pain Clinic of the UERJ Medical School. The headaches founded were grouped in: migraine (IHS.1), tension-type headache (TTH) (HIS 2) and probable medication-overuse headache (PMOH) (HIS. 8.2.7). We also did a group of chronic headaches, which are the headaches that occur 15 days per month for more than 3 months: chronic migraine (CM) (HIS. 1.5.1), chronic tension-type headache (CTTH) (HIS.2.3) and PMOH. The statistical analyze was made using T-student for proportions and the study was approved by the ethics committee of UERJ – School of Medicine.

Results Forty-six percent of the patients had TMD art/myo and migraine was the headache significantly more prevalent in this group ($t = 3.65$, $p < 0.05$) and there were significantly more female than male ($t = 3.65$, $p < 0.05$). Thirty-six percent of the patients had TMD myo and the chronic headaches were significantly more prevalent in this group ($t = 2.10$, $p < 0.05$), PMOH less frequent than the others types and female and male didn't differ. The TMD art was the less frequent, twenty-two percent, and PMOH was the most prevalent headache in this group, which had only female.

Conclusion TMD art was the less frequent but had the most excessive use of analgesics, suggesting, may be, that the pain was more intense than the others. In the TMD myo group, chronic headaches were the most prevalent headaches and it could be in place of the CTTH which was the most prevalent headache associated with TMD in the oldest studies. It's essential in any kind of study about TMD and headache to use both IHS Classification of Headache – 2nd edition and the RDC TMD to improve the knowledge in this area.

D079**Use of emergency medical services by headache patients in a Greek metropolitan population**

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Objectives In the absence of effective pre-hospital health care facilities in Greece, patients with acute or chronic pain are

forced to present immediately to the Emergency Outpatient Departments (EOD) of the on-call public hospitals. Thus, the treatment of headache patients may result in a relevant increase in the burden of work of the EOD.

Methods In an open prospective study design, epidemiological and clinical data were collected from all patients presenting with headache as their main symptom at the Emergency Outpatient Department (EOD) of Papageorgiou Hospital, a tertiary health care facility in metropolitan Thessaloniki, from August 2006 to January 2007.

Results During the study period, a total of 2813 patients presented at the EOD. 420 (14.9%) of those patients complained about headache as their main symptom. They were 133 (31.6% of headaches) men, 291 (68.4%) women, with a mean age of 36.6 years in male and 39.7 years in female headache patients. A primary headache was diagnosed in 214 (50.9%) patients, secondary headache in 101 (24.0%) patients and 105 (25.1%) patients did not fulfil the diagnostic criteria for a distinct headache. 65 (15.4%) patients were admitted to hospital, about half of them ($n = 30$, 7.1%) to a one day care unit, and 35 [8.30%] to a ward. 24 (5.7%) patients arrived with EMS, but only 11 of them were admitted to hospital.

Conclusion Subjective and objective severity of headache considerably increases the burden of the local EOD to a degree that turns use of EOD into misuse.

D080**Long-lasting migraine alters amplitudes and habituation of contingent negative variation**

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Introduction There is some experimental evidence that duration of migraine disease and hypervigilance possibly enable the transformation from episodic into chronic migraine. Aim of the present study is to determine the influence of the patient's duration of migraine disease on attentional parameters recorded by contingent negative variation (CNV).

Methods 28 patients (episodic migraine, four subjects with aura) were compared with 16 healthy controls. CNV analysis included amplitudes and habituation parameters (slope and intercept of total and initial CNV). Data were correlated with duration of migraine disease. Patients with long lasting migraine history (more than 10 years suffering from migraine) were compared with subjects suffering from short lasting migraine (<10 years).

Results Migraine patients produce more negative amplitudes than controls and showed dishabituation. Pearson correlation coefficient between duration of disease and the iCNV was $r = -0.767$. Patients with long lasting migraine showed a lower dishabituation and higher intercept compared with patients suffering from short lasting disease ($p < 0.05$).

Conclusion Both pronounced correlation between duration of disease and attentional parameters and the changing dishabituation can be interpreted as an enhancement in cortical preactivation level in patients with long lasting migraine. We assume that this change could be a critical factor for transformation from episodic into chronic migraine.

D081

Influence of allodynia and the autonomic system activation on the response to triptans in migraineGiorgio Dalla Volta¹, S Griffini², P Zavarise², A Pezzini²¹U.O Neurologia, Istituto Clinico Città di Brescia, ²Stroke Unit, Neurologia Vascolare, Spedali Civili Brescia, Italy**Background and object** Allodynia and the activation of the autonomic nervous system influence the response to triptans during acute attacks of migraine without aura (MA-).**Methods** The presence of autonomic symptoms was evaluated in 76 MA- subjects (M/F 27/49) by structured interview and telemographic investigation. The entire group was dichotomized into a subgroup with autonomic symptoms (A+; n = 42) and a subgroup without (A-; n = 34). Clinical response to eletriptan 40-mg during 3 consecutive migraine attacks was recorded in each subject. End points were pain-relief and pain-free response at 1 and 2 hours on the entire group of patients and on the number of crises.**Results** Pain-relief was reported in 58.2% and 75.0% of migraine attacks at 1 hour and in 75.8% and 83.0% at 2 hours, while pain-free was observed in 27.3% and 38.0% at 1 hour and 28.0% and 42.0% at 2 hours in the A+ and A- subgroup, respectively.Response to treatment was related to the co-existence and the complexity of autonomic symptoms. In particular, the more complex the autonomic activation, the less evident the benefit of treatment. A significant difference between the two subgroups was observed in pain relief at 1 hour ($P = 0.009$) and pain free at 2 hours ($P = 0.023$).**Conclusions** Our findings support the assumption that the activation of the autonomic nervous system plays a pathogenic role in clinical response to triptans. The degree of activation of the autonomic system might be used as a marker to predict clinical outcome to triptan therapy.

D082

Impaired cerebrovascular reactivity, stroke risk factors and clinical features of migraine

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Objective To evaluate the impact of stroke risk factors and clinical features of disease on cerebral hemodynamic changes and presence of white matter lesions (WMLs) in migraine.**Methods** Basal mean flow velocity (MFV) and breath-holding index (BHI) were measured in both middle cerebral arteries (MCAs) of 60 migraine outpatients (38 without aura and 22 with aura) and 60 matched healthy controls. WMLs were evaluated with FLAIR sequences at MRI.**Results** In basal conditions, univariate analysis of variance didn't show any statistically significant difference between groups. BHI was significantly higher in the MCAs of all migraine patients (1.68 ± 0.88) than in controls (1.14 ± 0.18), ($F = 4.97$, $p < 0.001$) without side effects. At multiple regression analysis, age resulted an independent factor for lower BHI in both patients and controls but not for WMLs. In migraine

group, duration of disease and number of attacks were directly associated with probability of having a lower BHI and WMLs. MWA, PFO and cigarette smoking were independently associated with lower BHI and WMLs in both sexes.

Discussion Since MFVs were normal in basal conditions, higher cerebrovascular CO_2 reactivity in both MWO and MWA may be due to an unbalanced adaptation ability of the intracranial vessels. These changes seem not related to the presence of WMLs, a possible marker of risk of stroke. Severity and chronicity of migraine, the presence of aura and the association with some vascular risk factors should reduce the exaggerated vasodilatory response to hypercapnia, increasing risk of stroke in migraineurs.

D083

Are the clinical characteristics of medication overuse headache influenced by the overused drug?

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Objectives ICHD-II introduced clinical criteria for medication overuse headache (MOH) differentiating headache induced by different overused symptomatic medications (SM). Thereafter such criteria were abolished. Aim of this study was to systematically analyse clinical characteristics of MOH.**Methods** Patients with chronic daily headache taking SM once or more per day for ≥ 3 months and treated within our inpatient withdrawal detoxification protocol were enrolled.**Results** We studied 73 patients (64 F, 9 M; mean age: 54 ± 13 years). Overused SM were: combination analgesics (41.1%), simple analgesics (31.5%), triptans (16.4%), ergotamine (8.2%), opioids (2.7%). Migraine without aura was the commonest pre-existing headache (75.3%). Pain was more frequently pulsating (52.1%), bilateral (54.8%), and severe (65.8%). The commonest accompanying phenomenon was nausea and phono-photophobia (42.5%). The clinical characteristics did not significantly differ among overusers of different SM. Patients with pre-existing tension type headache had more frequently pressing/tightening headache ($p = 0.003$), but there were no differences in the site, severity and accompanying phenomena compared to patients with pre-existing migraine. Time to SM resolution of pain was super imposable for the different SM classes and it didn't influence clinical characteristics of MOH.**Conclusions** Clinical characteristics of MOH are more frequently like migraine headache, regardless of overused SM. Our findings, therefore, indicate that different forms of MOH cannot be separated with regard to different types of overused SM.

D084**Headache characteristics in substance abusers**Musa Ozturk¹, M Ozturk², B Sahinoglu², Y Altunkaynak²,B Mutluay², R Balkan³, A Ozge³, D Cakmak³, S Baybas²¹Neurology, ²Psychiatry, Bakirkoy State Hospital, ³Neurology, University of Mersin, Turkey

Headache is widely seen in every phase of substance abuse. In this study, we investigated the coexistence and characteristics of headache in the use of various types of substances and abuse processes.

We included 460 random patients who were diagnosed as substance abusers and treated as inpatient and/or outpatients in AMATEM between July 2006 and January 2007. All subjects were evaluated with headache data form.

The patient group consisted of 445 male, 15 female subjects with a age range of 16–68 (mean age 30.8 ± 9.827). The patients using only psychodrepressants were 256 (55.7%), and psychostimulants were 13 (2.8%). 191 patients (41.5%) were using multiple substances. The substance abuse period range was 1–50 years (mean 10.56 ± 9.251).

The percentage of headache during substance use was 21.7. Of these patients, 86% had bilateral 14% had unilateral, 50% had pulsatile and 24% tightening pain. The most frequent substance used was cannabis, followed by multiple substances in this patient group.

The percentage of headache during abstinence was 26.1 and onset of pain was 26 hours. Of these patients, 85% had bilateral 15% had unilateral, 41.7% had pulsatile and 35% had tightening pain. The multiple substance use (38.3%) was most frequent, followed by cannabis (29.2%).

The percentage of headache during stopping substance use for a long period or totally was 16.6. 73.7% of these patients had tension type, 14.5% had migraine and 11.8% had other types of headache.

The information on the percentage of headache triggered by substance abuse and characteristics of headache prevents unnecessary investigations and helps to make correct diagnosis.

D085**Prognosis of migraine – a diary study in unselected patients**Christian Wöber¹, S Bartl¹, D Samal¹, S Salhofer¹, A Prajsnar¹, R Massl¹, E Freydl¹, P Fathinia¹, Ç Wöber-Bingöl²¹Dept. of Neurology, ²Neuropsychiatry of Childh. & Adolesc., Medical University of Vienna, Austria

Objectives To examine headache frequency, use of medication and psychiatric comorbidity in unselected patients with migraine.

Methods In 2002, we recruited 393 patients with migraine via articles in newspapers and thirty months later we performed a follow-up examination. At baseline and follow-up, the patients underwent a semistructured interview, they filled in the Self-rating Depression Scale (SDS) and the Self-rating Anxiety Scale (SAS) and they kept a headache diary for 30 days.

Results Of the 393 patients (mean age 42.2 years, 86% female) 151 (38.6%) were seen at follow-up. None of the patients was treated at our clinic. The baseline data of patients with and without follow-up were similar for almost all variables. At follow-up the number of headache days per month had decreased from 9.9 ± 6.2 to 8.2 ± 5.9 .

Conclusion This longitudinal study of unselected patients with migraine does not support findings suggesting that migraine is a progressive disorder and it confirms the importance of psychiatric comorbidity. Even though the dropout rate was high, the similar baseline data of patients with and without follow-up are an important argument against a selection bias.

D086**Serbian migraine epidemiology**Srdjan Sretenovic¹, A Stanic², S Kostic³, V Dedic⁴, A Mitrovic⁵¹Institute for Mathematics and Statistics, ²Clinic for Neurology, ³MD,⁴Clinic for Neurology KBC Zvezdara, ⁵Migraine Centre, Serbia

Introduction and objective Migraine is a special type of periodical headache occurring within 5–10% of the population. Newer research shows that 17.5% of Women and 5.7% of Men are suffering from one or more migraine headaches during the one year period. Objective of this study is to present its epidemiological characteristics.

Methodology Epidemiological facts are delivered in accordance to the survey performed on 2000 respondents of age between 16 and 82 years, of different sex (M : F = 772 : 1226), in accordance to standard predefined questionnaire. Field study has been performed in Belgrade during May 2006.

Results Migraine prevalence on average Belgrade population in accordance to the total sample was 11%, for Female 12.8% and for Male 8%. Distribution of migraine, age dependent, showed various percent values for different age groups: <20:6%; 20–29:42%; 30–39:16%; 40–49:16%; 50–59:13.7; >59:7. The symptoms of Aura is involved with 3.2% of respondents. Usual Migraine attack triggers are: Stress 14.5%, Weather changes 10%, tiredness 6.3%, Menstrual period 5.9% (Fig. 2). Most often side effects of Migraine Attack were photophobia 14.9%, nausea 11.8%, both photophobia and phonophobia 9.5% (Fig. 3).

Conclusion In accordance to the produced results, there are not significant value differences of evaluated parameters in comparison to similar studies performed in Europe and USA.

D087**Towards a definition for 'intractable chronic migraine'**Ninan T. Mathew, L Meadors
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Background An acceptable definition for 'intractable chronic migraine' is important for planning newer treatments (e.g. Botulinum Toxin occipital nerve stimulation, PFO closure etc) and further research.

Purpose To define 'intractable chronic migraine.'

Methods 1134 patients with chronic migraine treated for 6 years were analyzed to determine the effectiveness of prophylaxis based on reduction of MIDAS and number of migraine/probable migraine days by at least 40%. Long-term tolerability and ability to continue medications were assessed. Appropriate tolerable doses and adequate length of treatment (at least 3 months for each medication) were given using one or more agents from each class of evidence-based drugs used in migraine prophylaxis (beta-blockers, antidepressants, anticonvulsants, 5-HT2 antagonist and calcium channel blockers). If single agents failed, combinations depending on comorbidities were tried. All patients had behavioral interventions and biofeedback training after correcting medication overuse.

Results After a minimum treatment period of 24 months, 320 out of 1134 patients were considered intractable because (1) MIDAS and migraine/probable migraine days showed no, or less than 40% improvement with at least one agent from each class of drugs or combinations or (2) because of inability to continue medications due to intolerance.

Conclusion 'Intractable chronic migraine' may be defined as (1) chronic migraine with no or inadequate improvement or inability to continue medications due to intolerance after using at least one of the agents from each class of evidence-based migraine prophylactic drugs and (2) combination of two or more different classes based on comorbidities if single medications failed.

D088

Possible precipitation of migraine attacks with prophylactic treatment

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The initiation of a prophylactic treatment in migraine depends upon the stratification of the patient's frequency and disability of attacks as well as acute consumption and comorbid diseases.

We report 14 patients who developed an increase in frequency of migraine attacks when a prophylactic treatment was introduced. By clinical description, migraine attacks were the same but the frequency of the attacks of migraine without aura, were dramatically increased. This is, to our knowledge, the first description of possible precipitation of migraine without aura attacks with a prophylactic treatment. There is no link with a specific class of prophylactic treatment. We hypothesize that migrainous patients with paradoxical aggravation after introduction of a new prophylactic drug had a paradoxical increase of cortical spreading depression (CSD). Mechanisms of such an increase are unknown and probably multifactorial but experimentally it has been demonstrated that changes in serotonin neurotransmission modify cortical excitability and favor CSD.

The aggravation was described strictly in patients with migraine without aura but with only 14 patients it is not possible to predict that the type of migraine is a factor of predisposition. While additional cases are necessary, physicians

should be aware of the possibility that prophylactic treatment may exacerbate migraine attacks.

D089

Study of correlation between skin potential level and menstrual cycle phases

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There are changes in the regulation of the autonomic nervous system during the menstrual cycle. Knowledge of these changes may help improve diagnosis and treatment of periodic migraines, pre-menstrual syndrome, and menopausal disorders. The menstrual cycle modifies thresholds for body temperature, for vasodilation, and for sweat onset, possibly due to hormonal concentration (Charkoudian, 2001, Inoue et al. 2005; Freedman & Subramanian, 2005). Autonomic indices of arousal and relaxation (van den Akker, 1989) and cardiovascular reactivity (Girdler et al. 1993; Saeki et al. 1997) also depend on menstrual phase. However, the effect of the menstrual cycle on autonomic function has been argued in other studies (Ozisik et al. 2005). Skin potential level (SPL) depends on the electrolyte balance on the skin surface, presumably related to sweat gland afferentation (Uchida, 1999; Denda et al. 2001; Vetrugno et al. 2003). We investigated SPL in women in various phases of menstrual, and in men, (age 18–20 y.). A voltmeter (50 megohm input resistance) was applied by attaching Ag/AgCl electrodes to two different zones of facial skin. The SPL values of women in the four phases of the menstrual cycle were arranged in groups (postovulatory (PO) (n = 15), premenstrual (PrM) (n = 29), postmenstrual (PO) (n = 32) and preovulatory (PrO) (n = 27) phases) and compared. There was significantly higher SPL. Differences in left forehead (LF) and nasal (LN) skin potential levels (SPL) between women in either the postovulatory (PO) (n = 15), premenstrual (PrM) (n = 29), postmenstrual (PO) (n = 32) and preovulatory (PrO) (n = 27) phases, and also those of men (n = 79).

References

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D090

Abnormalities of head-neck motion in migraine patients

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Objectives Migraine attacks may be accompanied by tension headache-like symptoms, such as neck and shoulder pain with muscle contraction.

Headache due to cervical dystonia has been recognised by the new IHS classification of headache disorders.

The aim of this study was to assess head-neck posture and motion in migraine patients (who did not suffer from tension-type headache) without any disorders of cervical spine or soft tissues of the neck.

Methods We studied head-neck static posture and motion in 35 headache-free migraine patients (IHS classification criteria) and 35 controls.

Static posture was assessed with a photographic method.

Head-neck motion was assessed with a specific computerized device that evaluated the following movements: right/left rotation, flexion/extension and right/left sidebending.

The results were expressed as angles (in degrees).

Results Head-neck static posture was normal in migraine patients and controls.

In motion testing, head rotation was decreased on one side and extension was less marked than flexion in migraine patients when compared with controls.

Right/left sidebending was similar in patients and controls.

In particular, statistically significant differences between right versus left side head rotation ($p \leq 0.001$) and head flexion versus extension ($p \leq 0.01$) were found in migraine patients, but not in controls.

Conclusions Head-neck motion may be abnormal in migraine patients. Muscle tenderness and contraction, possibly associated with pain, may be responsible for these abnormalities. Alternatively, more complex central sensitisation mechanisms may be evoked in the interpretation of our results.

D091

Clinical characteristics of triptan overuse headache

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Objectives To study the semiology of headaches in patients suffering from pure triptan overuse headache (pure TOH) and in patients suffering from triptan overuse combined with other forms of medication overuse headache (combined TOH).

Methods The French Migraine and Headache Observatory conducted a clinical study of patients consulting for probable medication overuse headache (1) in seven specialised headache centres. Patients with TOH underwent a structured interview to describe retrospectively the typology of their headaches. Multivariate regression analysis was used to assess determinants of the type of TOH.

Results 163 patients (41.6% of patients with medication overuse) fulfilled criteria for TOH, 82 with pure TOH and 81 with combined TOH. 68% of patients with pure TOH described only discrete episodic headache attacks without continuous headache, whereas this was the case for only 24% of patients with combined TOH ($p < 0.001$).

A headache frequency of less than 30 days of headache per month, the presence of discrete episodic headache attacks

without continuous headache, recent chronic headache onset (<30 months) and male gender were associated with pure TOH.

Conclusion These results showing an increased frequency of TOH in France are consistent with studies from other countries (2). They confirm previous clinical data on pure TOH (3), but highlight the heterogeneity of TOH when triptans are combined with other medications. Among patients with TOH, continuous headache may develop from interactions between pre-existing tension-type headache and pharmacological effects of analgesic overuse leading to central trigeminal sensitisation.

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D093

Iron deficiency, with or without anemia, as a systemic pathogenetic co-factor in chronic migraine

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Clinical practice indicates that migraineurs with anemic disorders have a high frequency of attacks. Iron deficiency is the most common cause of anemia. This study was carried out on 71 patients affected by both iron deficiency and chronic migraine (daily headache and frequent acute attacks). Forty-eight patients (45 ♀ 31.02 ± 4.11 and 3 ♂ mean age 49.33 ± 4.33) had low iron and hemoglobin. Twenty-three (all ♀, mean age 24.56 ± 4.32) showed only low iron. The only causes of the alterations found were abundant menstrual cycles in women. No history of analgesic misuse. All patients were treated with iron sulfate (120 mg/day) for 3 months. No headache therapy was prescribed, except acute medications. The headache and accompanying symptoms were evaluated before, during and after treatment with a daily questionnaire. Iron treatment (20 mg/day for 3 months) produced a normalization of the hematologic parameters. A concomitant improvement of headache was found in 40 patients with low iron and low hemoglobin and in 19 with only low iron. The daily occurrences of the headaches were discontinued (amelioration from 40 to 70%) and the number of exacerbations were reduced (average of 40%). The present results indicate that an iron deficiency could be a pathogenetic co-factor in chronic migraine. The mechanism could be related either to anemia (decreasing oxygenation?), which is not always present, or to a consequence of the insufficient non-hemoglobin iron on various substrates, including the nervous tissue. Systemic disruptions should be taken into consideration as possible factors affecting migraine clinical course.

D094

Duloxetine as a therapeutic alternative for chronic tension headache: an open label study

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The most common chronic daily headache is the chronic tension form. The pathogenesis is related to vicious circle mechanisms at both peripheral and central levels. The therapy of chronic tension headache is intricate. Antidepressant drugs are used because the psychological implications, however, they are not completely satisfying. Duloxetine is a recent antidepressant drug also having an analgesic action, particularly in neuropathic pain. In addition to acting on the central analgesic pathways, the drug could also act on central sensitization circuits. This open label study evaluates the effect of daily administrations of duloxetine (60 mg oral dose for 2 months) on 18 subjects (10 women and 8 men, mean age 37.43 ± 6.4) suffering from chronic tension headache. The headaches were monitored for 4 months (before, during and after treatment) by a daily questionnaire which was given to each patient and which included the occurrence, duration and intensity of headache (numeric scale (0–100) and pain satisfaction scale. Beck Depression Inventory was also administered. Statistical evaluation was carried out with the χ^2 square test. Eleven patients showed a statistically significant reduction of the occurrence of the headache. In 15 patients the intensity of the headache was significantly reduced. The pain satisfaction scale was positive in 14 patients. An amelioration of the mood was found. Side effects were not significant except in 3 cases (which dropped out). The study indicates that duloxetine could be a therapeutic alternative for chronic tension headache. The open label design of the study limits a definitive conclusion.

D095

Endocannabinoids in chronic migraine and medication overuse headache

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Background Chronic migraine (CM) is frequently associated with medication overuse headache (MOH). Endocannabinoid system plays a role in modulating pain and is involved in the common neurobiological mechanism underlying drug addiction and reward system. Anandamide (AEA) and 2-arachidonoylglycerol are the most biologically active endocannabinoids, which bind to both central and peripheral cannabinoid receptors. The level of AEA in the extracellular space is controlled by cellular uptake via a specific AEA membrane transporter (AMT), followed by intracellular degradation by the enzyme AEA hydrolase (fatty acid amide hydrolase, FAAH). AMT and FAAH have also been characterized in human platelets.

Subjects and methods We assayed the activity of AMT and of FAAH in platelets isolated from four groups of subjects: MOH (n 30), CM without MOH (n 21), episodic migraine (n 28) and controls (n 23). Diagnosis of headache type was made according to the revised IHS criteria.

Results AMT and FAAH levels in platelets were found selectively increased in women with episodic migraine. Conversely, these markers were significantly reduced in CM and MOH in respect of either controls or episodic migraine group. This latter finding was observed in both males and females with CM and MOH.

Discussion Changes observed in the biochemical mechanisms degrading endogenous cannabinoids may reflect an adaptative behaviour induced by chronic headache and/or drug overuse. We cannot exclude that abnormalities in endocannabinoid system are occurring at peripheral level rather than at central level. Thus, it is possible that peripheral inflammation may also play a role in the observed effects.

D096

A nationwide population-based study of headache in Brazil

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Objectives To estimate the 1-year prevalence of headache, migraine and tension-type headache (TTH), according to the 2004 IHS criteria, in a representative sample of the adult population of Brazil, and migraine prevalence in its different geographical regions.

Methods This is a cross-sectional, population-based study. We interviewed, by telephone, 3,848 people (2,307 females; 1,541 males), aged 18–79 years, randomly selected, in the 5 geographical regions, in the 27 States of Brazil, proportionally to the population of each State. Trained lay interviewers conducted the structured questionnaire. To avoid recall bias, the whole interview was completed only with subjects with headache within the last year.

Results The 1-year prevalence of headache was 72.5%, migraine 16.3%, and TTH 11.9%. Prevalence of migraine was 20.9% in women and 9.3% in men, with a female : male ratio of 2.2 : 1. Migraine's prevalence was higher at 30–39 years of age. Prevalence of TTH was 9.5% in women and 15.4% in men. TTH's prevalence was higher at 18–29 years of age. The prevalence of migraine was 20.5% in the Southeast region of Brazil, 16.4% in the South, 13.6% in the Northeast, 9.5% in the Midwest, and 8.5% in the North.

Conclusions This is the first nationwide epidemiological study of headache done in Brazil. The 1-year prevalence of headache, migraine and TTH, in Brazil, was similar to the reported in other countries. Brazil is a very large country, with different cultures and socioeconomic status in the 5 geographical regions. The prevalence of migraine was different in the various regions of Brazil.

D097**Research in low and middle income countries on the primary headache disorders over the past decade**Farrah Mateen¹, T Dua², T Steiner³, S Saxena²¹*Mental Health and Substance Abuse, World Health Organization, Switzerland, and ²Neurology, Mayo Clinic, USA, and ³Neuroscience & Physiological Medicine, Imperial College School of Medicine, UK*

Objective Primary headache disorders are a common cause of underrecognized, undertreated, and lifelong morbidity worldwide, and the majority of people affected by headache live in the developing world. The contribution of low and middle income (LAMI) countries to headache research is unknown, but is germane to the mission of the Global Campaign to Reduce the Burden of Headache 'acquiring knowledge for action' phase.

Methods A search was performed for clinical research publications between the years 1997 and 2006, for all countries, using the search terms headache, headache disorders, primary and migraine in 57 databases, including PubMed, Embase, the World Health Organization regional medical indexes, and country-specific search engines. Articles in English or with abstracts in English translation were included. Income status for each country was determined according to the 2006 World Bank classification.

Results 197 publications from 32 countries were found. Only 23 publications (12%) of these came from low income countries. More than half (52%) of the publications came from three LAMI countries: Brazil, Turkey, and China. Forty-four percent focused on migraine research and 13% concentrated on pediatric headache exclusively. Fewer than a third (27%) of articles focused on the treatment of headache.

Conclusions The contribution of LAMI countries to headache research is small and derived from a limited number of countries. The available data, however, are instructive for targeting policy and implementing health priorities for headache research worldwide.

D098**Headache attributed to neurosarcoidosis**

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Objectives Neurological complications in sarcoidosis are rare (5%). Headache may occur in neurosarcoidosis and diagnostic criteria are given in the IHS classification. Aim of the study was to describe headache characteristics in patients diagnosed as suffering from neurosarcoidosis. The IHS criteria for headache attributed to neurosarcoidosis have been applied.

Methods Patients admitted to our Institute from 1999 to 2006 and diagnosed as suffering from neurosarcoidosis were retrospectively reviewed. Neurosarcoidosis was diagnosed according to brain or spinal MRI, thoracic CT scan, and/or gallium scintigraphy, bronchoscopy, cerebrospinal fluid, angiotensinogen converting enzyme and response to treatment. History of the patients was reviewed and headache characteristics were obtained from charts. Thirteen patients were included: 8

males, 5 females mean age at onset 48 years (29–72), illness duration 4 years (1–12).

Results Headache was reported by six (46%) patients and was the onset symptom in five of them (38%). In two (15%) cases the headache was the only neurological phenomena. In three patients (23%), the headache was associated with oculomotor palsy. In four patients headache had acute onset; in the remaining two patients headache was reported as mild at the beginning, but subsequently worsened. The IHS criteria were fulfilled in 5 (83%) patients. An intracranial lesion was observed at MRI in all the headache patients: a lesion into the ipsilateral cavernous sinus was founded; in the other two there was increased meningeal enhancement around the brainstem.

Conclusions Patients included in this study fulfil the IHS criteria for headache attributed to neurosarcoidosis.

D099**The migraine interictal burden scale (MIBS): a new instrument to measure global burden of migraine between attacks**Dawn C. Buse¹, ME Bigal², MFT Rupnow³, ML Reed⁴, D Serrano⁴, DM Biondi³, JF Hulihan³, RB Lipton²¹*Albert Einstein College of Medicine, ²Ortho-McNeil Janssen Scientific Affairs, ³Neurology, Albert Einstein College of Medicine, ⁴Vedanta Research, USA*

Objectives Develop and validate a tool measuring migraine burden between attacks; examine the relationship between ictal and interictal burden.

Methods Researchers held focus groups with migraineurs and thoroughly reviewed existing instruments to develop candidate items. Thirty candidate items were mailed to a population sample of 2500 migraineurs with a validated diagnostic screener and measures of quality of life (QoL) (MSQ), ictal burden (MIDAS), and psychopathology (PHQ). Data from subjects meeting ICHD-2 criteria for migraine were included in analyses. Categorical confirmatory factor analyses (CCFA) and Markov Chain Monte Carlo graded-item response theory models (IRT) were used to determine factor structure and item quality.

Results 1691 surveys were returned; 1353 met ICHD-2 criteria for migraine (80%). CCFA revealed five factors that were used in a 5-factor IRT model. Discarding the weakest items yielded a 4-factor, 16-item scale with 4 domains: work and school, family and social life, difficulty planning, and emotional consequences. All domains were significantly correlated with ictal burden, QoL, and psychological factors ($P < 0.0001$). Total MIBS scores significantly predicted MIDAS disability ($P < 0.0001$) with a moderate R-squared value of 0.15 in a linear regression model controlling for demographic variables and prescription medication use.

Conclusion MIBS was developed to assess global burden of migraine in clinical practice and research. It shows good internal consistency within and across domains. Because 15% of the variance in ictal burden (MIDAS score) is accounted for by our measure of interictal burden, we conclude that these impairment constructs are correlated but distinct.

D101**The prevalence of headache disorders in the Republic of Moldova: a population-based study**Ion Moldovanu¹, G Pavlic², S Odobescu³, L Rotaru³, C Craciun²,L Ciobanu³, G Corcea³, T Steiner⁴, Z Katsarava⁵, I Moldovanu²¹Institute of Neurology and Neurosurgery, ²State Medical and Pharm University, Republic of Moldavia, ³University of Essen, Germany, ⁴State Medical University, Republic of Moldavia, ⁵Neurology, Imperial College London, UK

No population-based epidemiological study of headache disorders has been conducted previously in the Republic of Moldova. The aim of the present study was to estimate the one-year prevalence of migraine, tension-type headache (TTH) and chronic daily headache (CDH) in the general population of Moldova. Eight neurology residents, who were trained by the principal investigator (IM), contacted adjacent households in the Capital of Moldova, Chisinau, and in a rural area of Hancesti and collected data from approximately 3,000 subjects by using a structured questionnaire. As a check, 10% of all subjects who reported headache were later interviewed and examined by IM personally. Overall, 3,165 subjects were contacted, of whom 2,511 (79%) responded. Of these, 1,341 (53.4%) reported headache in the last year. Migraine was diagnosed in 440 subjects (17.5%; 95% CI: 16.1–19.1%), of whom 382 (15.2%) had migraine without aura and 58 (2.3%) migraine with aura. TTH was diagnosed in 450 subjects (17.9%; 95% CI: 16.5–19.5%), of whom 26 (1.0%) had infrequent TTH, 346 (13.8%) had frequent TTH and 78 (3.1%) had chronic TTH. Chronic daily headache was diagnosed in 119 subjects (4.7%; 95% CI: 4.0–4.6%). The estimated prevalences of migraine and CDH are comparable with findings from other countries in Europe. TTH prevalence, however, appears lower. A possible explanation for this is that headache is not considered as a medical problem by the general population in Moldova, and many individuals, most likely those with infrequent TTH, may not have reported occasional headache.

D102**Diagnostic distribution of headache patients in primary care in Spain**Julio Pascual¹, E Quintela², J Castillo², P Muñoz³¹Health Center, ²Primary Care, ³Service of Neurology, University Hospital, Spain

Background Even though tension-type headache is more prevalent than migraine, the number of consultation for migraine is clearly higher than that of tension-type headache in our specialised setting.

Objectives To analyse the diagnostic distribution of patients consulting their GP due to headache.

Patients and methods Those patients spontaneously consulting their GPs during two consecutive years their GPs in a Health Center in Cantabria, Spain were carefully interviewed and examined. Their headache was classified according to the current IHS operational criteria.

Results A total of 221 patients consulted their GP specifically about headache. Migraine was the most frequent diagnosis

(144 patients, 65.2% of the total series). The majority (119, 83%) were women, their mean (range) age being 39 (15–65) years. Migraine with aura criteria were met by 22 (15%) migraineurs. Tension type headache was the second diagnosis in frequency (74 patients, 33.5%). Thirteen of these 74 patients (18%) met criteria for chronic tension type headache. The remaining 3 patients were diagnosed as cluster headache (2 patients) and temporal arteritis (1 patient).

Conclusions Migraine is the most frequent headache in terms of consultation in primary care setting in Spain, accounting for two-thirds of diagnoses. Therefore, migraine should be the first diagnosis to bear in mind when confronting a headache patient, also in a GP setting.

D103**What headaches do neurologists suffer? How do they treat themselves?**Samuel Diaz-Insa¹, P Traver², L Colomina², V Mateos³, D Ezpeleta⁴, M Huerta⁵, P Pozo⁶¹Headache Unit, Hospital de Gandia, ²Headache-Neurology Unit, Hospital Francesc de Borja, ³Neurology Service, Hospital Gregorio Marañon,⁴Neurology Section, Hospital de Viladecans, ⁵Hospital Central de Asturias, ⁶Headache Unit, Hospital Vall d'Hebron, Spain

Objectives The aim of present paper is to know what types of headache are neurologists suffering and which drugs are they using to treat them.

Methods We sent a brief questionnaire to the web mailing list of the Neurological Spanish Society. Age, gender, IHS headache type, symptomatic and preventive treatment use of the respondents are described. The answers were by web mail, anonymous and centralized in Spanish Headache Study Group secretary. Here we describe and analyse the epidemiological aspects of the obtained answers.

Results There were 257 answers, 224 valid for analysis: 90 women (36.4 years), 134 men (42.02). Headache in 60.27%; 67.78% of women, 55.22% of men. 91 neurologists were migraineurs (40.62%), with aura 30.77%; 76 had Tension-Type Headache (TTH) (33.93%), 1.34% other primary headaches and 0.89% secondary. No one had Medication Overuse Headache (MOH). 64.47% from neurologists in TTH group uses NSAIDs, overall ibuprofen, 44.74% uses paracetamol, and aspirin 10.53%. For Migraine attacks, neurologists use: 68.13% NSAIDs, triptans 32.97%, paracetamol 28.57%. Just 2.63% of neurologists with TTH are using preventives and 6.59% of migraineurs.

Conclusion Neurologists suffering headache are more prone to answer the questionnaire, overall migraineurs. Between Spanish neurologists, men are older than women. MOH is not present in neurologists with headache, good medical education and management may prevent it? NSAIDs are the preferred drugs for TTH and Migraine symptomatic treatment; but the rate of triptan use (33%) is quite greater than in migraine general population. The use of preventive drugs is quite low.

D104**Tolosa-Hunt syndrome treated as cluster headache**

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Cluster headache is a primary headache disorder characterized by episodes of severe unilateral headache that are accompanied by prominent ipsilateral autonomic features (such as lacrimation, nasal congestion, rhinorrhea, forehead/facial sweating, miosis, ptosis) and often demonstrate a remarkable periodicity.

The diagnosis of cluster headache is primarily clinical, but, according to the criteria if the HIS, a structural lesion must be excluded. Clues that may indicate a symptomatic cluster headache include absence of periodicity, the presence of neurological signs other than miosis and ptosis, a low-grade background headache that does not subside between attacks and incomplete response to therapy.

We present a case of a 47-year-old man suffering from headache for the last 3 months. The headache was characterized by cluster periods lasting for 7–8 days, separated by almost pain-free periods lasting for 15 days and was associated with mild ptosis, eyelid oedema and conjunctival injection. The results of neuroimaging studies (brain CT and MRI no contrast-enhanced) performed soon after the beginning of the symptoms were normal. The patient reported also mild relief with oxygen inhalation but worsening of the symptoms with sumatriptan.

The neurological examination revealed diplopia, due to paralysis of the left oculomotor and the left abducent nerves. The new, contrast enhanced, brain MRI revealed an abnormal tissue in the left cavernous sinus, which markedly increased in signal intensity after contrast injection. The painful ophthalmoplegia responded dramatically to steroid therapy and the biopsy confirmed a granulomatous inflammation, which corresponded to Tolosa-Hunt syndrome.

D105**The effect of age on headache frequency in post-traumatic headache (PTH)**

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Objective To evaluate the effect of age on headache frequency in PTH.

Background Reports have suggested that older patients with PTH have greater headache frequency (HF). This study evaluates HF across the age spectrum in PTH subjects.

Methods The Oklahoma University Headache Registry consists of consecutive patients seen by the same neurologist (JRC). From 12/1992 to 4/2003, 105 patients with PTH (headache precipitated or markedly exacerbated by head injury) were enrolled. Subjects were divided into three groups based on age at which head injury occurred: <20 years (n = 25), 20–39 years (n = 52), and 40+ years (n = 28). These age groups were further subdivided into three independent

groups based on attack frequency: <15/month (episodic), 15–29/month (frequent), and 30+/month (daily) headaches.

Results As age at which head injury occurred increased, the proportion of patients presenting with daily headaches increased, rising from 48% in the <20 age group to 56% in the 20–39 year olds and to 78% in the age 40+ group. The trend test for the increasing proportion of subjects with daily headache by age group was statistically significant (p = 0.013). Stratifying by age, individuals 40+ were more than twice as likely to have daily headaches as those under 40 (OR = 3.2, 95% CI: 1.75–8.81).

Conclusions This study suggests that, among persons with the PTH syndrome, headache attack frequency increases with increasing age, and that after age 40 subjects may be more susceptible to the pathophysiological changes underlying PTH.

D106**Migrainous stroke after the short use of drospirenone**

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Migraine is a chronic, multifactorial and common neurovascular disorder which is characterized by recurrent attacks of disabling headache and autonomic nervous system dysfunction (migraine without aura). Up to one third of the patients also present neurological aura symptoms before the headache.

Some observational studies have shown an increase in the risk of stroke among people with a history of migraine, but others have failed to find an association—which finally seems to be restricted to certain subpopulations (women with migraine and aura who smoke or use oral contraceptives).

We report a case of a 32-year-old woman who presented suffering from intense headache focused in the left frontotemporal area and right hemiparesis. The headache appeared immediately after the morning awakening and accompanied by phonophobia and photophobia. Two hours after the appearance of the headache, weakness of the right upper and lower extremities was added. The brain MRI revealed an ischemic lesion in the posterior limb of the left internal capsule.

From the medical history, migraine attacks without aura were present for at least 10 years, treated with mild analgesics. Furthermore, 4 months ago the patient terminated a pregnancy due to severe anemia caused by menorrhagia and the gynecologist suggested a new 'safe' oral contraceptive, consisted of ethinyl estradiol (20 mcg)/drospirenone (3 mg) – a new progestogen with antimineralocorticoid activity.

We discuss the incidence of stroke in a young woman, with migraine without aura 20 days after the use of the drospirenone.

D107

Prevalence and profile of headache in medical students: a preliminary investigation in a Nigerian UniversityFrank Ojini¹, M Danesi¹, N Okubadejo²¹Department of Medicine, ²Department of Medicine, College of Medicine, University of Lagos, Nigeria**Objectives** To determine the prevalence and symptom profile of headache in medical students at the College of Medicine, University of Lagos, Nigeria.**Methods** A structured headache questionnaire was used to obtain information about last-year prevalence of headache from medical students in the college of medicine of the University of Lagos. Besides demographic data, headache characteristics and treatment pattern were evaluated. Migraine and tension-type headache were diagnosed according to the criteria in the International Classification of Headache Disorders, 2nd edition.**Results** Prevalence of headache was 50.9% (16.7% in males, 66.7% in females). The prevalence rate of migraine was 8.8% (5.6% in males, 12.8% in females) while that of tension-type headache was 24.6% (11.1% in males, 30.8% in females). A family history of headache was present in 31%. Among patients with migraine, headache was aggravated by routine physical activity in 100%, associated with nausea and/or vomiting in 55.6%, and photophobia in 55.6%. About a third sought medical attention for their migraine. Among patients with tension-type headache, headache was throbbing in 33.3%, worsened by physical activity in 20% and associated with photophobia in 6.7%. About 26.7% sought medical attention. Self-medication was commonly with paracetamol (55.6%) or aspirin (19.4%).**Conclusion** Headache is common in medical students, with a prevalence of 50.9%. Tension-type headache occurs more often than migraine in both sexes. However, females have a higher prevalence of both types of headache than males.

D108

Interdisciplinary pain clinic: headache and other diagnoses in chronic pain patientsSonja Eugster¹, S. Eugster¹, R. Agosti², H. Sprott³, U. Hepp⁴, H. Isler¹, I. Marbé-Sans¹, P. Sandor¹¹Hirslanden Clinic, Zurich, Headache Centre, ²Neurology, University Hospital Zurich, Headache And Pain Unit, ³Psychiatry, University Hospital Zurich, Department of Psychiatry, ⁴Rheumatology, University Hospital Zurich, Department of Rheumatology, Switzerland**Background** The interdisciplinary pain clinic (IPC) of Zurich University consists of outpatient consultations by a neurologist, a rheumatologist, an anaesthetist and a psychiatrist on an outpatient basis within a week, which are integrated and discussed with the patients at a final pain conference. Headache diagnoses are made by the neurologist.**Objectives** To describe the IPC patient population concerning their diagnoses, including headache.**Methods** Retrospective analysis of the patient-charts.**Results** 233 chronic IPC patient-charts from 1996 to 1999 were evaluated. 55.8% were men, 73.8% were married. The

mean pain duration was 7 + 7.16 (s.d) years. Identifiable causes for pain were accidents (n = 96; 41.2%), illness (n = 64; 27.5%), operations (n = 18; 7.7%) or others (n = 55; 23.6%). The number of diagnoses attributable to certain specialities was: rheumatology n = 173; 74%, neurology n = 166; n = 71%, psychiatry n = 152; 65% and others n = 59; 25% (more than one possible diagnosis). Twenty-eight (12%) patients were diagnosed within one subspeciality, 104 (45%) in two, 83 (36%) in three 17 (7%) in four. The most common diagnostic combination was from rheumatology + neurology + psychiatry (n = 60), then the combinations of neurology + rheumatology and psychiatry + rheumatology (n = 34, each), followed by neurology + rheumatology (n = 18). The most commonly diagnosed conditions were back pain (n = 140, 60%), headaches (n = 92; 39.5%), neuropathic pain (n = 101; 43.3%), affective disorders (n = 65; 27.9%). Other neurologic disorders were diagnosed in 47 patients.

Conclusions This study documents that headache is diagnosed in about 40% of IPC patients, and is most often one of multiple diagnoses. The question of its etiology needs to be addressed in further studies.

D109

Effect of pregabalin in a model of stress and nitroglycerin-induced hyperalgesia in the ratAlfredo Costa¹, A Smeraldi², C Tassorelli¹, R Greco¹, F Casoni¹, P Bini¹, F Antonaci¹, G Nappi³¹Institute of Neurology C. Mondino, UCADH, University of Pavia,²Neurology, Universities of Pavia/Rome La Sapienza, ³Institute of Neurology C. Mondino, UCADH, University of Pavia, Italy**Objectives** Nitroglycerin activates spinal and brain nociceptive structures via nitric oxide (NO), and plays an important role in initiation and maintenance of pain. Chronic stress affects both pain threshold and behaviour, and unavoidable stress paradigms such as immobilization are used to study nociception. We have recently reported that chronic stress enhances the hyperalgesia induced by nitroglycerin in the rat. This may be particularly relevant to migraine, since nitroglycerin triggers spontaneous-like attacks in humans, and an unfavourable migraine outcome (transformation into a chronic daily headache) is associated with chronic stress and comorbid depression.

Pregabalin is an anticonvulsant and analgesic drug provided with significant effects on thermal allodynia and mechanical hyperalgesia; we therefore investigated the effect of pregabalin in this experimental model of chronic migraine.

Methods Pain perception was measured using the latency of response to a tail flick test (hot stimulus). Measures were made 1, 2 and 4 hours following nitroglycerin (10 mg/Kg i.p.) in rats immobilized for 7 days using dedicated plexiglass restraining cages, and treated with pregabalin at the dose of 60 mg/Kg p.o. or vehicle.**Results** Chronic stress caused hyperalgesia, which was further enhanced by nitroglycerin after 2 and 4 hours ($p < 0.05$). By contrast, chronic stress-induced pain perception decreased in pregabalin treated animals ($p < 0.05$); in the same group, the hyperalgesic effect of nitroglycerin was also found to be significantly dampened ($p < 0.05$).

Conclusion These preliminary data suggest that pregabalin acts as antinociceptive drug by affecting the mechanisms leading to hyperalgesia in the rat. Pregabalin may thus represent a novel therapeutical option in the management of chronic migraine in humans.

D110

Re-consultation of patients with chronic headache

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Background The purpose of this study is to evaluate factors to be related with re-consultation of chronic headache sufferers.

Objectives Two hundred and forty-one consecutive patients who visited our Headache Department were retrospectively evaluated.

Methods Diagnosis of headache was made according to International Classification of Headache Disorders 2nd edition. Information about medical history, neurological examinations, prescriptions and re-consultation were obtained from medical records. Correlation between types of headache and re-consultation was closely evaluated.

Results In 241 patients, 71.0% had the primary headache, 11.2% had the secondary headache, and remaining 17.8% had cranial neuralgias, central and primary facial pain and other headaches. Among patients with the primary headache, numbers of consultation were only once in 76 (44.4%), twice in 41 (24.0%), and three times or more in 54 (31.6%) patients. Forty-one of 171 patients (24.0%) with the primary headache were followed-up regularly. A rate of regular follow-up in patients with migraine without aura was 44.9% and significantly higher than other types of headache. Patients who were not diagnosed at the first consultation did not visit again. There were no relationship between neuroradiological examination or prescription and re-consultation. One hundred and thirty of 171 (76.0%) patients were not regularly followed-up. Follow-up visit was terminated by doctors in 77 patients and by themselves in 53 patients.

Conclusions Re-consultation rate of patients with chronic headache is not high. A rate of regular follow-up in patients with migraine was higher than other types of headache. Accurate diagnosis and appropriate treatment can satisfy patients who had better to take regular follow-up.

D111

Allodynia prevalence in Spanish neurologists suffering headache

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Objectives Allodynia prevalence between migraine patients varies depending on the studied population. Patient education and training in its recognition influences in its prevalence.

Trying to solve this problem, we have studied a highly educated and sensitized population: neurologists with headache.

Methods We sent a brief questionnaire to the web mailing list of the Neurological Spanish Society. We describe in respondents: age, gender, IHS headache type, symptomatic and preventive treatment use, knowledge about allodynia, its presence or not, intensity and extent of allodynia. The answers were by web mail, anonymous and centralized in Spanish Headache Study Group secretary. A statistical analysis about items than could be related with allodynia is made.

Results 91.71% of the respondents know what allodynia is. Allodynia prevalence between migraineur neurologists is 28.57% (35.71% in Migraine with Aura (MA) and 20% in Migraine without Aura (MO)). Curiously, 3.95% of TTH neurologists have allodynia symptoms. The greater prevalence of allodynia is found in the group having TTH + MA + MO (71.43%). Allodynia prevalence trends to be higher in men. Its intensity in MA is 2.33/3 in front of 1.33/3 in MO. The use rate of preventive treatment in migraineurs without allodynia is 1.54%, and 19.23% between allodynic migraineurs.

Conclusion The actual allodynia prevalence in migraine patients seems to be near 30%. Its prevalence is greater in MA. In MA is even more intense and extensive. The presence of allodynia seems related with a higher use of preventive treatment.

D112

Relation between different attributes of medication overuse headache and drug groups

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Objective Categorize the different drug groups concerning their capacity to favour the appearance of a Medication Overuse Headache (MOH).

Methods Between September and November 2005, 97 neurologists were inquired in order to categorize different drug groups and their eventual connection to the onset of MOH. The discussion was led by a facilitator, using the Metaplan® method. This study was supported by Menarini-Spain.

Results Ergotics and analgesics were the drug groups identified by participants as main implicate in the appearance of a MOH. In opinion of the participating neurologists, ergotics are drugs highly capable of producing abuse (99%), headache of rebound (99%), and abstinence syndrome after their withdrawal (95%). The consulted neurologists also considered that with these drugs the period of latency to develop a MOH is short (80%). Equally that their consumption is associated, often, to that of other drug group (71%). As far as it is concerned, analgesics also were identified as capable of producing abuse (92% of the participants) as a rule associated with other pharmacological groups (96%). For the participating neurologists, triptans were identified as the drugs with smaller capacity to produce a MOH.

Conclusions In opinion of the participating neurologists, of the different drug groups used in the treatment of the headache, the triptans are the drugs with a minor potential to develop a MOH while, in the opposite side, ergotics are the drugs that more they can favour this situation.

D113

Neurologist's prioritisation about what to do to prevent and treat chronic daily headache

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Objectives Managing patients with frequent headache is difficult. The Headache Study Group from Spanish Neurological Society sought to determine how practicing neurologists manage these patients, as well as the best way to prevent and treat this condition.

Methods In a first structured interview addressing chronic daily headache (97 neurologist from 9 cities in Spain) the 12 more voted clinical characteristics were selected. In a second phase, these 12 issues were randomly given to an independent group of 79 neurologists to prioritise the 5 more clinically relevant issues, scoring them from 5 to 1. In this paper we describe and analyse this prioritisation. This study was supported by Menarini-Spain.

Results The 5 most voted clinical aspects in chronic daily headache patients were: (1) To provide patients with adequate clinical information regarding the illness, the medication and the risk of medication overuse, to establish an appropriate doctor-patient relationship and to stress the need of frequent visits. (2) To use a preventive treatment and programmed discontinuation of analgesics. (3) An accurate diagnosis of primary headaches. (4) To identify and treat psychiatric comorbidities and precipitating factors. (5) An accurate drug prescription. Information and preventive treatment were voted by 76% and 71% of participants, respectively, and accounted for 41% of all the votes.

Conclusion Of all the possible aspects addressed, neurologists considered that providing the patients with adequate and continuous information is the most valued treatment approach. As expected, preventive medication was also regarded as a keystone to manage these patients.

D114

Neurologist's prioritisation regarding patients at risk of suffering from chronic daily headache

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Objectives Chronic Daily Headache (CDH) is a very common illness. Managing patients with this disorder is quite

difficult. The Headache Study Group from the Spanish Neurological Society sought to determine how practicing neurologists manage these patients, as well as their opinion on the best way to prevent and treat this condition.

Methods In 2005, a total of 97 neurologists were held throughout Spain using the Metaplan® method about the question: Which clinical data do you think are important in noticing whether our patients suffer or are at risk of suffering from CDH? We selected the 12 most repeated categories. In 2006, they were randomly presented to an independent group of 79 neurologists, in order to prioritise the 5 most clinically relevant issues, scoring them from 5 to 1. This study was supported by Menarini-Spain.

Results The five most voted issues were: (1) Inadequate treatment (preventive and symptomatic); (2) Psychiatric comorbidity (anxiety, depression); (3) Transformed migraine with tension-type features; (4) Increase in frequency of attacks and (5) Increase burden of migraine in daily life. The first option obtained a total of 260 points, which means that it was given an average of 3.6 points by all 79 neurologists.

Conclusion All the listed clinical data are relatively easy to recognise and should be taken in account for CDH detection and prevention. According to Spanish neurologists, misuse or lack of preventive and symptomatic pharmacological treatment and psychiatric comorbidity, are the main characteristic leading to CDH in patients with headache.

D115

Putative role of life-events on cluster headache pathophysiology

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Objectives To report on the putative relevance of life-events on cluster headache (CH) occurrence.

Patients Sixteen CH patients (12 ECH; 7M-9F; median age 39) with a history of major life-events are reported. Neurological examination and neuroradiological investigation were unremarkable. In all patients the tight relationship between headache worsening and their life-events became evident only after both several interviews and deep empathetic enquiry was established.

Results In all patients life-events occurrence were closely related to the illness onset and or worsening. The life-events were divorce, mourning, undesired abortion, failure in professional working; in three patients there was a long-lasting violent parental dispute; conflictual mother relationship was observed in 6. All patients astonishingly neglected their unsolved psychological problems.

Conclusions CH may occur as both primary or symptomatic headache suggesting it is a complex disorder. The role that anxiety and behavioural/mood disorders have on CH pathophysiology is not recognised. Functional neuroimaging studies showed hypothalamic activation in CH. A recent PET study showed a complex activation/deactivation pattern when stimulating the posterior hypothalamus in CH patients.

Brain areas involved in this activation/deactivation pattern are involved both in pain matrix and in some behavioural conditions such as anxious states, mood and anger. Our hypothesis is that, due to emotionally traumatic experiences, a dysfunction in these brain areas could lead to a failure in the top-down regulation on pain regulating structures. At least in some patients, this failure could be the primum movens in lowering the activation threshold of the ipsilateral hypothalamus and the trigeminofacial reflex.

D116

Cost effectiveness of treatment of medication overuse headache in a multidisciplinary tertiary headache center

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Background There is an increasing interest in treatment strategies for medication overuse headache (MOH) but the cost-effectiveness has not been substantiated.

Objective To describe the cost-effectiveness of multidisciplinary treatment in patients with MOH from the Danish Headache Center (DHC).

Methods DHC is the only national multidisciplinary center for severely affected headache patients in Denmark (5.5 mill. inhabitants). Patients characteristics are based on standardized diaries, registration forms, and ICHD-2 diagnosis. MOH is treated with abrupt discontinuation of analgesics and migraine specific drugs for a 2 months period on an outpatient basis with intense staff support. After detoxification restricted acute therapy, preventive pharmacological and behavioral treatments are applied.

Results 175 MOH patients were analyzed after an average treatment period at 327 days. The mean age was 49 years (range 17–86) and the male/female distribution was 1/3. The mean headache frequency was reduced from 27 to 15 days per month (–46%) ($p < 0.0001$). At dismissal, the total mean consumption of triptans and analgesics were reduced with 87.5% and 93% resp. and 47% were on pharmacological prophylaxis. Likewise, the average absence rate was reduced from 6 to 3 days per month ($p < 0.0001$). When the estimated costs in DHC and the prophylactic treatment were subtracted the annual net result was 4055 Eur per treated patient.

Conclusion A multidisciplinary treatment programme for MOH seem to be highly cost-effective. Despite neither other direct costs and impaired work performance were included, a marked net economic result was achieved in addition to a significant improvement in headache. Such results are very important in the future planning of prophylaxis and treatment of MOH.

D117

Outcome of treatment in a tertiary headache center

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Background There is an increasing societal interest in multidisciplinary headache clinics due to the substantial global

burden of headache disorders. In Denmark, 32% of the adult population has had a headache related consultation with a primary care physicians during their life, 16% had visited a neurological specialist and 3% had been hospitalized because of headache. Such prevalent disorders demands a national health care plan and European guidelines for organization of headache clinics are now created.

Objective To describe the characteristics of patients from the Danish Headache Center (DHC) and their treatment outcome.

Methods DHC is the only national referral and multidisciplinary center for severely affected headache patients in Denmark (5.5 mill. inhabitants). Patients characteristics are based on standardized diaries, registration forms, and ICHD-2 diagnosis.

Results A complete dataset of 1326 treated patients over a 2 year period were analyzed. The mean age was 43.7 years (13–92 years) and the male/female distribution was 3/7. In total, 57% had chronic headaches and 25.5% had a diagnosis of medication overuse headache. The mean frequency of headache was reduced from 20 to 11 days pr month after treatment ($p < 0.0001$). The total absence rate was reduced from 5 to 2 days pr month after treatment ($p < 0.0001$).

Conclusion Patients referred to a tertiary headache clinic are severely affected and high absence rates indicating a major personal and socioeconomic impact. A major improvement can be achieved in a multidisciplinary specialized setting. Such characteristics are important in the planning and organization of future headache clinics.

D118

Burden of cluster headache

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Objective To analyse the socioeconomic burden of cluster headache in patients from a tertiary headache centre.

Methods 100 consecutive patients from the Danish Headache Centre were invited to an interview about socioeconomic impact of cluster headache. Work absences and use of medical services were compared with a population-based survey.

Results 78% of the patients reported restrictions in daily living, and 13% reported inhibition also outside of cluster periods. 25% reported major decrease in their ability to participate in social activities, family life and housework. The disease caused lifestyle changes for 96%, most frequently on sleeping habits and avoidance of alcohol.

The absence rate among patients was 30%, which was significantly higher than 12% among the general population ($p < 0.001$). Use of health services due to headache were also higher among the patients ($p < 0.001$).

Conclusion Cluster headache, although periodic in most cases, has considerable impact on social functions, quality of life and use of health care.

D119**Prevalence of fibromyalgia in patients with chronic daily headache**

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Objective To determine the prevalence of Fibromyalgia in a CDH population, particularly transformed migraine (TM), and clinically characterize this subgroup of patients.

Methodology We studied 41 consecutive patients with CDH, and TM, according to IHS 2004 criteria. We analysed age, sex, previous history of migraine, daily headaches, pain intensity, analgesic overuse, insomnia and disability. Patients with Fibromyalgia (F) were compared to patients without Fibromyalgia (WF).

Results The prevalence of F was 31.3%. Patients were older in the F compared with WF group. There was a female preponderance in both groups. In F group headaches were more incapacitating and patients had more insomnia when compared to the WF group. Analgesic overuse, pain intensity and previous history of migraine and daily headaches had no statistically significant difference.

Conclusion F is a co-morbid disease in CDH patients. This subgroup of patients are older, have more insomnia and more incapacitating headaches than patients WF.

D120**Medication overuse headache: clinical features and application of diagnostic criteria**

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We have developed a course of CARE for the management of medication overuse headache (MOH). We have enrolled patients with probable MOH and evaluated the applicability of MOH criteria 2 months after discharge.

Of the 140 patients recruited (mean age: 44.5 ± 11.4 years), 10 were lost to follow up and 130 observed two months after discharge. In 92 patients (71%), the MOH diagnosis was confirmed (group 1), and in 38 patients (29%) it was not: of these latter patients, 29 (22%) still presented a chronic headache despite stopping symptomatic overuse (group 2) and 9 (7%) still showed both chronic headache and symptomatic overuse (group 3). A coexistence of migraine and tension-type headache was statistically more frequent in group 2 ($p < 0.001$) than in group 1. The relative reduction of days of drug intake varied considerably, showing a median reduction of 80% in group 1, 67% in group 2, and 30% in group 3 ($p < 0.001$). The reduction in number of doses also differed between the three groups, showing a median reduction of 85% in group 1, 80% in group 2 and 53% in group 3 ($p = 0.008$).

The MOH diagnostic criteria were applicable in 2/3 of the patients in this series. However, two subgroups (group 2 and 3) emerged that could not be classified as MOH despite

showing a partial response to detoxification (reduction of drug intake). We suggest that a future revision of the classification should take into account other aspects, such as the previous primary headache diagnosis and percentage reductions of drug overused.

D121**Sensitization of spinal cord pain processing in medication overuse headache involves supraspinal pain control**

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Objective The present study investigates the temporal summation threshold (TST) of the nociceptive withdrawal reflex (NWR) and the activity of the diffuse noxious inhibitory controls (DNICs) in medication overuse headache (MOH) patients before (bWT) and after withdrawal treatment (aWT).

Methods Thirty-one MOH patients bWT and aWT, 28 patients with episodic migraine (EM) and 25 healthy subjects were evaluated. TST of the NWR and the subjective painful sensation were measured before, during and after activation of the DNICs by the cold pressor test (CPT), which involved immersing the hand in cold water (2–4°C). After 7–10 days of withdrawal treatment all MOH patients were re-evaluated.

Results Significantly ($p < 0.01$) lower NWR TST were found in patients (MOH and EM) versus controls. In patients the CPT induced a significantly ($p < 0.01$) lower TST increase with respect to both EM and healthy subjects. In MOH aWT we found an improvement of the evaluated parameters, and a highly significant increase ($p < 0.01$) in the TST during CPT with respect to MOH bWT.

Conclusions We hypothesized an abnormal spinal cord pain processing probably as consequence of a lack of function of the DNICs in MOH. The improvement in MOH aWT suggests that medication overexposure could interfere with inhibitory central pain mechanisms. Moreover the reduced TST detected in EM could reflect a general sub-clinical hypersensitivity in the pain pathways that may increase susceptibility to the triggering of a migraine attack.

D122**Natural history of elderly chronic daily headache: a 12-year longitudinal community-based study**

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Objectives To investigate the long-term natural history of chronic daily headache (CDH) in the elderly.

Methods We established a community-based sample of 60 (48F/12M, mean age 74.0 ± 7.4 years, range 65–98 years) elderly subjects (≥ 65 y/o) with CDH out of 1,533 in 1993. Neurologists followed up these subjects by a structured

questionnaire and clinical interview in 1995, 1997 and 2005. CDH was defined as ≥ 15 days/month, average ≥ 4 hours/day, for ≥ 3 months; its subtypes were classified based on the International Classification of Headache Disorders, 2nd edition.

Results Twenty-nine subjects (48%, 25F/4M, mean age 82.7 ± 5.1 years) survived in 2005 and all finished follow-up. Eight patients (all females) (36%) still had CDH and 5 of them had daily headache. Their 2005 headache diagnoses were 3 chronic migraine, 3 chronic tension-type headache, one medication overuse headache and one unclassified. The persistence rate of CDH was 28% in 2005. Medication overuse declined from

15% (baseline) to 3% at 12 years. Persistence of CDH in 1995 ($p = 0.029$) and having a baseline geriatric depression score ≥ 5 ($p = 0.03$) predicted persistence of CDH in 2005 (Fisher's exact test).

Conclusions This is the first long-term longitudinal study for elderly CDH in the community. It showed, without specific treatment, a significant portion of elderly patients with CDH could continue to suffer from this headache syndrome up to 12 years. Early intervention is warranted in those with short term persistence of CDH in this age group.

LUNCH SEMINARS

LS4

Trigeminal autonomic cephalgias (TACs)

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Trigeminal autonomic cephalgias (TACs) are grouped in section III of the second edition of the International Classification of Headache Disorders (1). They consist of cluster headache, paroxysmal hemicrania and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing/cranial autonomic symptoms (SUNCT/SUNA). One could argue that hemicrania continua should be in this group. The division is based on the shared marked activation of the trigeminal-autonomic reflex (2).

There have been a number of important developments in the diagnosis and management of these syndromes in recent times. New treatments and ways of managing cluster headache and a better understanding of SUNCT/SUNA in terms of diagnosis and management all assist headache interested physicians in helping these patients.

This seminar will discuss some of the more interesting and clinically useful developments of the last few years.

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LS5

Hormones and headache/pregnancy

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Effect of migraine on pregnancy Migraine improves during pregnancy in 60–70% of migraineurs; in around 20% of these, attacks completely disappear. Women with pre-existing migraine without aura generally improve, particularly if they had menstrual or menstrually-related migraine. In contrast, women with pre-existing migraine with aura are more likely to continue to have attacks during pregnancy, or aura may develop for the first time. Although headache is common in

the week following delivery, affecting around 30% to 40% of women, breastfeeding protects against migraine.

Effect of pregnancy on migraine Migraine, either with or without aura, does not have any adverse effects on the outcome of pregnancy in otherwise healthy women. However, there is an increasing body of evidence to support an association between migraine, pre-eclampsia and eclampsia. Further, the risk of post-partum cerebral infarction may be greater for women a history of migraine and for women with pre-eclampsia and gestational hypertension.

Management of migraine during pregnancy and lactation

For treatment of migraine attacks, paracetamol is safe throughout pregnancy and lactation. Aspirin and NSAIDs are also safe but best avoided after 30 weeks. NSAIDs (but not aspirin) can be taken during lactation. Prochlorperazine and domperidone can be used through pregnancy and lactation. Triptans are not recommended during pregnancy although there is evidence to support minimal, if any, risk from inadvertent exposure to sumatriptan during pregnancy. Sumatriptan can be taken during lactation. For prophylaxis, propranolol has best evidence of safety during pregnancy and lactation.

LS6

Periodic syndromes of childhood that represent precursors of migraine

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Migraine may manifest in young children in unusual clinical forms. The key feature will be episodes of vertigo, vomiting, abdominal pain, or movement disorders, separated by symptom free intervals. The 2004 International Classification of Headache disorders include these entities under the category of 'periodic syndromes of childhood that represent precursors of migraine'.

The purpose of this luncheon seminar to provide a case-based, audience participation, discussion using video demonstrations of several of these syndromes with specific focus on benign paroxysmal vertigo, cyclic (or cyclical) vomiting syndrome, and abdominal migraine. Also discussed will related episodic disorders of infants and children such as benign paroxysmal torticollis, 'Alice in Wonderland', basilar-type migraine, and hemiplegic migraine.

SCIENTIFIC SESSION

Scientific session 4: Chronification

ScS4-Introductory Lecture

Chronic headache: where are we now?

Zaza Katsarava

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Chronic headache has been defined by the International Headache Society as headache (migraine or tension-type headache) occurring on more than 15 days per month. Population based studies revealed that approximately 5% of the general population suffer from chronic headache. This is true for West European Countries, US and Canada as well as for developing countries in South America or East Asia. Up to 30–50% of these patients overuse acute headache drugs. Recent population based longitudinal studies clearly showed that the overuse of headache medication is the main risk factor for development of chronic headache. The International Headache Society introduced therefore the term medication overuse headache (MOH) which has been defined as a chronic headache which occurs following overuse of headache drugs and improves after withdrawal. The improvement of headache after withdrawal was mandatory for the diagnosis of MOH. Last year the International Headache Society revised the classification criteria and established a broader concept of MOH no longer requesting improvement after discontinuation of medication overuse.

Very few is known about the risk factors and predictors of headache chronicity. Early recognition of patients at high risk for chronicity, however would enable intervene early and avoid development of chronic headache.

Current treatment strategy is based on a clinical experience that withdrawal of overused medications leads to improvement of daily headache. Long term follow up studies demonstrate that up to 40% of patients relapse, overusing headache drugs and developing chronic headache again despite an initially successful withdrawal. Preventive strategies are however, lacking.

ScS4-1

The epidemiology of chronic daily headaches in adolescents

Richard Lipton¹, J Ricci², E Chee², A Lorandau², Z Li³, C Turkel³, M Bigal³

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Objectives To assess the prevalence and disability burden of the chronic daily headaches (CDH) and its subtypes in a large sample of adolescents representative of the U.S. population.

Methods This is a 2-stage population-based panel study. In Stage 1, questionnaires were mailed to 88,408 adolescents, with ages ranging from 12 to 19 years, representative of the adolescent US population. In Stage 2, we conducted computer assisted telephone interviews (CATI) in a random sample of CDH sufferers and episodic headache sufferers using validated tools for diagnosis, disability assessment and allodynia. We diagnosed the CDH subtypes according to the ICHD-2R in chronic migraine (CM), medication overuse headache (MOH), chronic tension type headache (CTTH) and other CDH (o-CDH).

Results Questionnaires were returned by 24,712 adolescents: 892 (3.6%) had CDH and 15,686 had episodic headaches. The adjusted one-month period prevalence of CDH was 2.9% overall; CDH was more common in females than in males (4.6 vs.1.2; $p < 0.001$) and increased with age. Of adolescents with CDH, 61% had severe disability (MIDAS grade IV). CDH subtypes included CM (prevalence 0.76%), CTTH (0.04%), MOH (0.87%) and o-CDH (1.19%). The prevalence of allodynia varied with headache type ranging from 59% for CM to 33% in CTTH.

Conclusions CDH is common and disabling in adolescents, afflicting an estimated 950,000 teens. Prevalence is lower than in adults. Risk factors for CDH include female gender and increasing age. The two most common subtypes are CM and MOH. Allodynia is particularly linked to CM among teens with CDH.

ScS4-2

1 year population-based prevalence of migraine in Spain. Results of the PALM program

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Objectives Validation of a computer-assisted telephone interview (CATI) questionnaire based on the criteria of the IHS (2004). To determine the 1-year prevalence of migraine in the adult Spanish population.

Methods CATI-based epidemiological population-based, cross-sectional survey throughout mainland Spain, involving individuals aged 18–65 years, randomly selected using quotas for age, sex and habitat, between April and July 2006. The study was approved by an ethics committee. The subjects answered a questionnaire based on the 2004 IHS criteria. Questionnaire's validity was evaluated on a random sample of 36 subjects with positive and negative diagnostic criterion subsequently interviewed by neurologists. Data are presented as percentages (95% CIs).

Results Validity for strict migraine criterion: sensitivity 82.8% (69, 96.5); specificity 100%. Validity for probable migraine: sensitivity 90% (69, 95.5) specificity 100%. A total of 5668 quotas accepting to participate were contacted. One year headache prevalence: 32.7%. Prevalence of probable migraine: 12.6% (11.6, 13.6). Prevalence of migraine in females is 2.15 times that of males (17.2% vs 8%). Prevalence of strict migraine: 8.4% (7.7, 9.1): migraine without aura 4.5%; migraine with aura 2.1%; mixed type 1.9%. The criterion for duration of attack accounted for 2.3% of the probable migraine prevalence. Differences were observed among Spanish Autonomous Communities, from 18% (Canary Islands) to 7.6% (Navarra). One third of the subjects claimed never to have been diagnosed of migraine.

Conclusion The one-year prevalence of migraine in Spain based on the 2004 IHS criteria was 12.6%. Differences in prevalence were observed among Spanish Autonomous Communities.

Study sponsored by MSD España.

ScS4-3

Does the pattern of migraine change over time? A 12-year perspective

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Objective To evaluate the changing pattern of migraine during 12 years' follow-up of migraineurs managed at the Gothenburg Migraine Clinic, Sweden.

Methods 374 patients (200 women, mean age 55.5 years) were randomly selected from a total population of 2812 patients with episodic migraine (IHS 1.1 and 1.2) and an attack frequency of 1–6 attacks/month. Telephone interviews were conducted to evaluate the pattern of migraine between 1996 and 2006, in terms of the proportion of patients who became symptom-free and frequency/duration/severity of migraine attacks among persistent migraineurs. Satisfaction with current treatment was also determined.

Results Over the 12-year period, migraine had resolved in 110/374 (29%) patients (57 women). Among the remaining 264 patients who continued to experience migraine at 12 years' follow-up, 80% reported a change in frequency of migraine (of these, 80% reported a decrease in frequency of attacks/month) and 55% reported a change in duration of attacks (of these, 66% experienced shorter attacks). Of the 66% of migraineurs reporting a change in pain intensity over time, 84% reported milder pain at follow-up). Only 6 subjects (1.6%) had developed chronic migraine. Satisfaction with current medication was high (78%), perhaps due to the high proportion using triptans (62.5%).

Conclusion Migraine does not appear to be a progressive disorder in most patients. Many persistent migraineurs reported less frequent, shorter and/or milder attacks over time, which probably reflects the improvements in available treatment options (most notably triptans in different formulations) and/or migraine management over the last 12 years.

ScS4-4

Triptan use and overuse in the Netherlands, a national pharmaco-database analysis

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Objective To study the prevalence and costs of triptan overuse in the Netherlands.

Methods Analysis of the Drug Information Project (GIP database) of the Health Care Insurance Board (CVZ), which registers prescribed drugs dispensed at pharmacies for all patients insured by sickness funds (N = 6.7 million) year 2005. We defined triptan overuse as intake of at least 120 defined daily doses (DDDs) per year (International Headache Society (IHS) criteria) and as 216 DDDs per year (stringent criteria).

Results Amongst 85,172 triptan users, 8,844 persons overused according to the IHS criteria (10.4%, 95% CI 10.2 to 10.6), and 2,787 persons according to the stringent criteria (3.3%, 95%CI 3.2 to 3.4). Overusers were 5 years older than non-overusers. Compared to sumatriptan, the overuse according to the IHS criteria was smaller for rizatriptan tablets (OR 0.27; 0.25–0.28) and for frovatriptan (OR 0.11; 0.08–0.17). By the stringent criteria the OR was 0.13 (0.12–0.15) for rizatriptan. Total costs of triptans were 29.7 million Euros in 2005. Patients overusing triptans according to IHS criteria account for 46% of total costs and according to the stringent criteria for 23%. Of the patients overusing triptans according to IHS criteria 30% used medication which can be prescribed as prophylaxis for migraine and according to the stringent criteria 32%.

Conclusion 10% of triptan users are overusers, which accounts for half of total triptan costs.

ScS4-5

Management of probable medication-overuse headache: 1-year randomized multicenter open-label trial

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Objectives The aim of this randomized multicenter study was to evaluate the effect of early introduction of prophylactic treatment in patients with probable medication overuse headache (pMOH) compared to the effect of abrupt withdrawal or no treatment.

Methods The prophylaxis group received preventive treatment from the start without a detoxification while the withdrawal group underwent a standard out-patient detoxification program. The control group did not receive preventive medication or direct advice to withdraw the overused medication. Preliminary data from the first 3 months of follow-up is presented.

Results Out of the 64 randomized patients with pMOH, 56 were included in the efficacy analyses. The preliminary data from 53 of these patients showed that all three groups had a significant reduction in days/month with analgesic use versus baseline during the first 3 months of follow-up ($p < 0.01$), whereas only the prophylaxis group had a significant reduction in headache days (18.9 days versus 25.2 days, $p = 0.001$) and total headache index (HI) (headache days/month \times headache intensity, \times headache hours) (345 versus 492, $p = 0.001$). Compared to baseline, HI/month was reduced in the prophylaxis group with an average of 147 and among controls with 30, whereas the withdrawal group increased with 68 ($p = 0.002$).

Conclusion These preliminary analyses strongly indicate that introduction of preventive treatment without a previous detoxification program was the most effective way to reduce headache days and suffering during the first 3 months. These preliminary results indicate that early introduction of preventive medication can be an appropriate first step in managing pMOH.

ScS4-6

Botulinum toxin type A for the prophylaxis of chronic migraine with medication overuse

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Background There is a paucity of placebo-controlled studies investigating prophylactic therapy in chronic migraine patients with acute medication overuse.

Objective To evaluate the efficacy of botulinum toxin type A (BoNTA) in chronic migraine with acute medication overuse.

Methods A randomized, placebo-controlled, double-blind study involving patients with chronic migraine headache with acute medication overuse. 67 patients were randomized (38 to BoNTA and 29 to placebo). Patients received either saline or 25 to 100 units of BoNTA using a fixed-dose and follow-the-pain paradigm. A daily diary was utilized to record headache frequency, associated symptoms and disability during a one-month run-up and the three month post-treatment period.

Results In both groups, approximately 90% were female, mean age was 50, mean duration of migraine was 30 years, mean duration of chronic migraine was 15 years and mean headache frequency was 23 days per 4 weeks. No significant difference was demonstrated between the BoNTA and placebo-treated groups in the primary endpoint of change from baseline headache frequency at weeks 4–8 post-treatment (-5.28 vs -5.07 , $p = 0.89$). There was also no difference at 8–12 weeks (-5.11 vs -6.08 , $p = 0.60$). There was not significant difference in the responder rate ($\geq 50\%$ reduction in headache frequency) between BoNTA and placebo (37% vs 28%, $p = 0.46$) or in the rate of adverse events.

Conclusion BoNTA was not superior to placebo in reducing headache frequency in patients with chronic migraine with acute medication overuse.

Scientific session 5: Secondary headaches

ScS5-1

Migraine aura or TIA? A 5-year follow-up case-control study of women with transient CNS disorders in pregnancy

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Objectives To differentiate migraine aura from other transient neurological disorders in pregnant women, and to study the prognosis with regard to cerebrovascular events.

Method 41 patients with transient neurological symptoms during pregnancy and 41 pregnant controls were studied in detail with thorough clinical and laboratory investigations, shortly after the episode and with questionnaires every year for 5 years.

Results Among the 41 patients, migraine with aura proved to be the most common cause of symptoms during pregnancy, occurring in 34, while two were diagnosed with stroke, two carpal tunnel syndrome, one partial epilepsy, one multiple sclerosis and one presyncope. Patients and controls were not significantly different with regard to risk factors for atherosclerotic disease, and none of the patients or the controls reported cerebrovascular episodes during the 5-year follow-up.

Conclusion The diagnosis of migraine aura in pregnancy was difficult because many experienced their first attack and headache tended to be absent or of non-migrainous type. The aura features were more complex with several aura symptoms and higher prevalence of sensory and dysphasic aura than usual. The 5-year follow-up clearly indicated that migraine with aura in pregnancy usually has a good prognosis with regard to cerebrovascular events. A meticulous history and clinical neurological examination is usually sufficient to distinguish migraine aura from other conditions in pregnancy.

ScS5-2

Temporal evolution of vasospasm in patients with benign CNS angiopathy: a transcranial color-coded Doppler study

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Objectives To investigate the temporal evolution of vasospasm in patients with benign (reversible) CNS angiopathy.

Methods We prospectively recruited patients presenting with recurrent thunderclap headaches who also had magnetic resonance angiography findings demonstrating multi-focal segmental vasoconstrictions, fulfilling the ICHD-2 diagnostic criteria of benign CNS angiopathy (code 6.7.3). Serial transcranial color-coded Doppler (TCCD) studies were employed to evaluate the vasospasm of the middle cerebral arteries

(MCA). Mean flow velocities and the Lindegaard index (LI) of the MCA were recorded.

Results Fifteen patients (all women, 51.4 ± 8.7 years) were enrolled, with 72 total TCCD studies conducted. All patients were treated with nimodipine. Two of them (13%) were complicated with ischemic changes. The mean follow-up duration was 70 (range 16–142) days. Ten patients had MCA flow velocity greater than 120 cm/s, but none exceeding 200 cm/s. The mean LI was 2.6 ± 0.6 (range 1.4–3.6) with higher values (3.2 and 3.6) in the two patients with ischemic complications. Headache attacks remitted at a median of 16 (range 8–93) days; whereas, flow velocities and LI of MCA reached maximum at an approximate timing median of 16 (range 2–88) days. The flow velocities returned to normal at a median of 43 (range 8–127) days.

Conclusion Compared with subarachnoid hemorrhage-induced vasospasm, the degree of vasospasm was much less severe in patients with CNS angiopathy, which explains partly the low incidence of ischemic complications. TCCD should be considered to monitor the altered cerebral hemodynamics even after headache remission.

ScS5-3

Headache in 48 patients with benign intracranial cysts in relation to anatomical location

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Objective Benign intracranial cysts (BIC) present in patients of all ages and vary in location and symptomatology.

Headache is the most common symptom. The aim was to investigate the character of headache in patients with BIC in relation to cyst localisation.

Methods Forty-eight consecutive patients with BIC, referred to the Department of Neurosurgery in Göteborg from Western Sweden, were included in this study. The characteristics of the headache were recorded; including duration, type, intensity, laterality, location, variation, daily rhythm and if headache required pharmacological treatment and related to cyst location; lobar, infratentorial or central.

Results Thirty-seven (77.1%) patients had headache. Both patients with lobar and patients with central cysts described their headache more often as pressing than patients with infratentorial cysts ($p = 0.03$ and $p = 0.019$). Patients with infratentorial cysts had more often occipital headache compared to patients with lobar ($p = 0.024$) and central cysts ($p = 0.057$). Patients with central cysts had constant headache with exacerbations more often than patients with both lobar and infratentorial cysts ($p = 0.004$ and $p = 0.072$), while patients with lobar cysts more often than patients with central cysts had an episodic headache ($p = 0.023$). Patients with central cysts tended to have a more intense headache compared to patients with lobar cysts ($p = 0.071$) and they tended to more often have evening headache than patients with infratentorial cysts ($p = 0.051$).

Conclusions Headache was the most common symptom in patients with BIC. We found differences in headache characteristics between different cyst locations.

DEBATE

First parallel session

D1-1.CON

Does tension-type headache exist?

Rigmor H Jensen

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Tension-type headache is far the most prevalent type of headache but in most cases it is regarded as a 'normal' headache, and not as a disease. In the general population 87% of young adults have experienced TTH but only very few seek medical advice due to their TTH. In contrast, 67% of migraineurs seek their primary care doctor and 31% a specialist for their migraine. Although 94% of migraineurs also suffer from coexisting TTH the patients and their doctors only rarely separate the different headache types and focus only on the treatment of migraine. Epidemiological and clinical evidence for the existence of TTH will be presented.

D1-1.PRO

Tension-type headache doesn't exist (PRO)

Jean Schoenen

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Tension-type headache (TTH) is considered the most frequent headache type in the general population. It does not have stringent diagnostic criteria and is chiefly a 'featureless' headache. It can be mimicked by a number of secondary headaches, but the major controversy in recent years is to know whether it is an autonomous entity or simply one end of the migraine spectrum.

There is evidence that tension-type like headaches occurring in migraineurs between typical migraine attacks are most probably mild migraine attacks and respond to anti-migraine treatment. In at least two studies otherwise typical TTH patients responded acutely to injectable sumatriptan and prophylactically to topiramate, both drugs known to be effective in migraine. Moreover, other drugs used in migraine prophylaxis, such as the tricyclics, may also be effective in TTH.

From a pathophysiological perspective, there are several examples of overlap between migraine and TTH. For instance, subgroups of chronic TTH patients may have increased blood levels of CGRP, akin to migraine patients during an attack.

Clinically, TTHs are heterogeneous in frequency, but also in disability, co-morbidity and response to therapy. In infrequent tension-type headache ('everybody's headache') muscular factors appear to play a dominant role, while in frequent/chronic TTH ('medicalised TTH') central dysnociception seems to be the culprit, probably facilitated by depression.

To summarize, my message for researchers is that we need urgently better clinical and pathophysiological studies comparing migraine and TTH, for clinicians it could be: 'don't label a patient TTH before you have excluded other diagnoses including migraine'.

Second parallel session

D2-1.CON

Can patent foramen ovale (PFO) cause a migraine? (CON)

Marie-Germaine Bousser

Hôpital Lariboisière Université, France

PFO, the persistent opening between the right and left atrium is present in 25% of the general population, equally in both sexes. Migraine, a primary headache disorder, affects 12% of the population with a 3/1 female preponderance. Recent studies have shown a statistical reciprocal association between PFO and migraine with a relative risk of 2 to have a PFO in the presence of migraine and to have migraine in the presence of PFO. However, the presence of this statistical association does not mean that PFO can cause migraine for 2 main reasons:

A – No association have been found with migraine without aura which is by far the most frequent variety of migraine
B – In the only double blind randomised trial so far reported (MIST), there is no evidence that PFO closure cures migraine, which should be the case if PFO was the cause of migraine. If PFO does not cause migraine in general, could it cause migraine with aura? The answer is also 'no' for the following reasons:

- 1 – Statistical association does not imply causality
- 2 – Most patients with migraine with aura do not have PFO and most patients with PFO do not have migraine with aura.
- 3 – Comorbidity has not yet been ruled out
- 4 – In MIST, migraine with aura has not disappeared after PFO closure

What could then be the meaning of the statistical association found between PFO and migraine with aura? It should be remembered firstly, that migraine with aura may also be secondary to a variety of chronic disorders such as arteriovenous malformations, MELAS, small artery diseases of the brain such as CADASIL and, secondly that an attack of migraine with aura may be a symptom that can be triggered by numerous factors including cerebral ischemia. It is therefore possible that in some genetically predisposed patients with PFO, there is a link between PFO and attacks of migraine with aura. The available studies suggest that some large PFO, as well as other right to left shunts may favor symptomatic attacks of migraine with aura. The mechanism is probably

multiphasic involving hypoxia, platelet emboli, paradoxical emboli or vasoactive substances bypassing the lung filter and triggering the cortical spreading depression. PFO closure might be effective in those PFO related symptomatic migraine attacks with aura, but this remains to be demonstrated. Even if this is the case, it would be erroneous and dangerous to extrapolate from the improvement or even the cessation of symptomatic migraine attacks after PFO closure in some patients to the treatment of migraine as a primary headache disorder.

In summary, there is at present no scientific evidence that PFO causes migraine, even with aura. There is a suggestion that in some subjects, PFO, in bypassing the pulmonary filter, favors the occurrence of symptomatic attacks of migraine with aura. At present, there is no indication for PFO investigations or closure just for migraine.

D2-2.CON

Migraine should not be considered a progressive disorder (CON)

Julio Pascual
Neurology, Spain

Migraine is considered as an episodic disease. In fact, epidemiological studies have confirmed a dramatic decrease in its prevalence after adulthood. Chronic migraine (CM) has only recently been accepted by the IHS and even CM is not really chronic, as many patients come back to an episodic condition even without proper treatment. Contrary to this, recent data open the issue of whether migraine is a progressive condition. Kruit et al, in the work responsible for the development of this concept, compared the prevalence of brain infarcts and white-matter lesions between people with migraine and controls. They found an increase in posterior circulation lesions in patients with migraine with aura and more deep white matter lesions in women with migraine. These results come at a time when a link between migraine and right-to-left cardiac shunts has been suggested.

A progressive disorder (Oxford English Dictionary) is one when there is a continuous increase in severity or extent.

Progression can refer to symptoms but also to other objective measures, such as brain imaging. The study by Kruit et al, as it is cross-sectioned, provides a possibility but not a proof, and does not demonstrate that lesions in the brain produce CM.

In conclusion, there is no definite evidence that migraine is a progressive disorder. This does not negate the fact that some migraine sufferers go through disabling periods of frequent attacks, but progression should not be ascribed to the vast majority of sufferers. Migraine should not be blamed until proven so.

D2-1.PRO

Migraine is progressive (PRO)

Richard B. Lipton
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Objective To review the evidence that migraine is a sometimes progressive disease.

Method The published literature and unpublished longitudinal data from the American Migraine Prevalence and Prevention Study will be reviewed, focusing on the transition from episodic (migraine with less than 15 days of headache per month) to chronic daily headache (attacks 15 or more days per month). Evidence from neuroimaging studies assessing the relationship between brain changes and attack frequency will be presented.

Results In the general population, persons with episodic headache develop chronic daily headache at the rate of about 3% per year. In clinic-based studies of migraine sufferers the transition rate is about 14% per year. Risk factors for incident CDH include baseline attack frequency, medication overuse, caffeine consumption, obesity, snoring, traumatic brain injury and stressful life events among others. Imaging studies show that posterior circulation stroke, deep white matter lesions and iron deposition in the red nucleus are associated with attack frequency in migraine sufferers.

Conclusion Migraine tends to worsen over time in a subgroup at risk. Though many migraine sufferers do not progress the group at risk requires additional study to identify strategies to prevent progression.

POSTER

Poster session 3

E001

Nummular headache: eight new cases and therapeutic results in China

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Background Nummular headache was first described by Pareja (2002). Herein, Eight cases fulfilling the ICHD-II proposed criteria (code A13.7.1) for nummular headache are reported. Objective to evaluate the clinical feature of nummular headache and the efficiency of treatment in China.

Method From February 2006 to October 2006, we collected 8 patients with nummular headache.

Results They are 2 men, 6 women, 22 to 63 years old (mean age: 44.25 ± 14.24 years). Headache history ranged from 7 days to 30 years. Four patients reported head pain confined to a circular area of 1 to 2.5 centimeter, and the other 4 patients had pain in an elliptical area of 1.5–2 centimeter \times 2–3 centimeter. The symptomatic area was located in the parietal ($n = 3$), occipital ($n = 2$), temporal ($n = 3$) regions. The right side was affected in 4 patients and the left side in the remaining 4. Three patients had mild pain, 2 patients had moderate pain and 3 patients had severe pain. The characteristics of headache was presented stabbing pain ($n = 3$), sharp pain ($n = 3$), pulsating quality ($n = 1$), grinding pain ($n = 1$). Three patients were treated by local nerve block with lidocaine plus dexamethasone phosphate/acetate and one of them got some 30 hours of prominent pain relief, no relief was obtained for other two patients. One patient obtained pain remission by acupuncture after amitriptyline, paroxetine had been tried ineffectively. One patient, woman, 38 years old, was treated by carbamazepine (tegretol) and amitriptyline for 3 months and the pain relief was obtained gradually and the head pain disappeared finally.

Reference

Dareja (2002)

E002

Most cases labeled as 'Retinal Migraine' are not migraine

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⁴Ophthalmology, Emory University School of Medicine, USA

Objectives Transient and persistent monocular visual loss has often been labelled 'retinal migraine.' Yet there is reason to believe that many such cases do not meet the criteria set

out by the International Headache Society (IHS), which defines 'retinal migraine' as attacks of fully reversible monocular visual disturbance associated with migraine headache and a normal neuro-ophthalmic examination between attacks.

Methods We performed a literature search of articles mentioning 'retinal migraine', 'anterior visual pathway migraine', 'monocular migraine', 'ocular migraine', 'retinal vasospasm', 'transient monocular visual loss' and 'retinal spreading depression' using Medline and older textbooks. We applied the IHS criteria for retinal migraine to all cases so labelled. To be included as 'definite retinal migraine', patients were required to have had at least two episodes of transient monocular visual loss, associated with, or followed by, a headache with migrainous features.

Results Only 16 patients with transient monocular visual loss had clinical manifestations consistent with retinal migraine. Only 5 patients met IHS criteria for definite retinal migraine. No patient with permanent visual loss met IHS criteria for retinal migraine.

Conclusion Definite retinal migraine, as defined by the IHS criteria, is an exceedingly rare cause of transient monocular visual loss. There are no convincing reports of permanent monocular visual loss associated with migraine. Most cases of transient monocular visual loss diagnosed as retinal migraine would more properly be diagnosed as 'presumed retinal vasospasm.'

E003

Qualitative RI cisternography in patients with chronic headache or neck pain – analysis of 250 consecutive cases

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Objectives The aim of this study was to evaluate cerebrospinal fluid (CSF) dynamics in patients who have chronic headache or neck pain.

Methods Qualitative RI cisternography was performed in patients who have chronic headache or neck pain for more than 3 months. Two hundred and fifty consecutive patients (110 men and 140 women) with mean age of 39.3 ± 11.8 (meanSD) were examined. RI cisternographic images were obtained before and 2 h, 4 h, 6 h after the injection of $37\text{MBq}^{111}\text{In-DTPA}$.

Results The CSF leakage at the nerve root sleeve was found in 154 patients (61.6%). Of those 154 patients, 120 had history of mild trauma whereas 34 did not. In the 33 patients (13.2%), the CSF leakage at the nerve sleeve was not found but early RI accumulation in the bladder was observed, suggesting existence of leakage of the CSF at somewhere in the spinal column. Among these 33 patients, 30 had history of mild trauma but 3 patients did not have such history. These data suggest that certain number of the patients who have

intractable chronic headache or neck pain have CSF leakage at somewhere in the spinal column irrespective of history of trauma.

Conclusion It is concluded that qualitative RI cisternography is useful in diagnosing CSF leakage in patients with chronic headache and neck pain.

E004

Do not forget Cerebral Venous Thrombosis in stroke patients who present with headaches

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Purpose Cerebral venous thrombosis is an uncommon disorder and commonly presents as headaches. We aim to study the clinical features, neuroimaging, treatment and outcome of this disorder in Singapore.

Method We retrospectively reviewed the Department Registry of records over the last 15 years.

Results There were 41 patients (23 female, 18 males) and ages ranged from 21–81 years. Presentation: headaches (68%), seizures (73%), unconsciousness (51%), focal deficits (49%), vomiting (46%). Predisposing factors: none (44%), pregnancy (12%), prothrombotic (12%), contraceptive pills (10%), thyrotoxicosis (10%), malignancy (10%), mastoiditis (2%). CT scan: hematoma (44%), cerebral edema (39%), empty delta (32%), dense triangle (29%), SAH (24%), venous infarct (15%), cord sign (7%). Location of thrombosis on MRV / CT venogram / angiography: sagittal sinus (95%), either right or left transverse sinus (80%), both transverse sinuses (40%), straight sinus (22%). Treatment: anticoagulation (85%), 3 patients received thrombolytics and of these 2 died. Outcome at discharge: Modified Rankin Scale: 0–2 (54%), 3 (10%), 4–5 (29%), died from illness or complications (7%).

We had 2 unusual cases: the first was a 45 year-old man with seizures, dehydration, thyrotoxicosis, and had both arterial and venous infarcts on MRI. The second was a 47 year-old female with headaches for 2 weeks which worsened acutely over one day. She had both cerebral venous thrombosis and spontaneous intracranial hypotension on MRI/MRV.

Conclusion A high index of suspicion is required in view of its myriad presentation. Do remember this diagnosis in stroke patients who present with headaches.

E005

Dolichobasilaris presenting as migraine with basilar aura dolichocarotis mimicking cluster headache symptomatic or idiopathic headache. Clinical and neuroradiological picture

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While discussing about when and if necessary to order special neuroradiological investigations in patients presenting with a typical history and typical symptoms of 'idiopathic' headache, it is necessary to present more case studies, to be

aware of possible underlying pathology. Shall we over diagnose or do we underdiagnose?

If we find a pathology, it may also be a coincidence.

Four patients, 3 males and 1 female aged from 16 to 52, with a history of typical migraines with nausea, vomiting and photophobia, in only two cases preceded with complex aura, lasting from 20 minutes to 90 minutes, occasionally lasting during headache phase. Medical and neurological examination did not reveal abnormalities between migraine attacks. Good response to triptans, non-steroid antiinflammatory agents, NSAIDs, and occasionally to metoclopramide, chlorpromazine and steroids.

Brain CT was normal, although enlargement of basilar artery was mentioned in 2 cases. CT Angiography showed enlarged, tortuous basilar artery impressing the brain stem, no signs of Arnold-Chiari deformation/abnormality/.

One man, now aged 45, observed for 22 years, with typical periods of cluster headaches, predominantly right sided, with typical accompanying signs such as eye injection, slight ptosis, myosis, tearing and running nose on symptomatic side. Attacks repeating every year, especially in spring and fall, increasing in frequency and severity, becoming more resistant to treatment. Angio CT and traditional angiography showed enlarged 'swollen' like right internal carotid artery. It is not clear why the symptoms occur with certain regularity, just like in typical cluster patients.

E006

Smell and taste abnormalities in Korean migraine patients

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Objectives Sensory system might be activated during migraine attack. Recently activation of olfactory and gustatory systems during migraine attack has been occasionally commented. This study is intended to assess smell and taste abnormalities in Korean migraine patients.

Methods Fifty nine consecutive headache patients who visited outpatient clinic from March 2006 to June 2006, were evaluated for characteristics and associated features such as frequency, duration, location, quality of pain, nausea, vomiting, photophobia, phonophobia, smell abnormalities and taste abnormalities. Smell abnormalities were classified as hyperosmia, hyposmia and dysosmia. Taste abnormalities were classified as hypergeusia, hypogeusia and dysgeusia.

Results Of the 59 patients, 46 were classified as having migraine. 39 were migraine without aura and 7 were migraine with aura according to ICHD-II. 20 (43.5%) of 46 migraine patients complained of smell abnormalities (95.0% very frequently, 5.0% frequently) about migraine attacks. 10 (50.0%) of them reported hyperosmia, 9 (45.0%) reported dysosmia and 1 (5.0%) reported hyposmia. 15 (32.6%) of 46 migraineurs complained of taste abnormalities (93.3% very frequently, 6.7% frequently) about migraine attacks. 10 (66.6%) of them reported dysgeusia and 5 (33.3%) reported hypogeusia. Taste abnormalities were significantly more common among

migraineurs with smell abnormalities than migraineurs without smell abnormalities.

Conclusions Smell abnormalities were observed in about 40% of migraine patients, and taste abnormalities were observed in about 30% of the migraine patients. Dysosmia was the most common form of smell abnormalities and dysgeusia was the most common form of taste abnormalities.

E007

Acute pathological laughter induced by sumatriptan

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Subcutaneous sumatriptan, a selective 5HT1B/1D receptor agonist, is the reference standard for the acute treatment of cluster headache. It penetrates poorly into the CNS and is believed to act peripherally by inducing vasoconstriction in large cerebral blood vessels and by blocking neurogenic inflammation within the trigemino-vascular system. Nevertheless, sumatriptan may act centrally, at least in some circumstances, as suggested by reports of extrapyramidal effects, and ³H-sumatriptan-binding sites are widely diffused throughout the human brain, especially in the basal ganglia. We report a unique case of transient acute pathological laughter as a sumatriptan-induced phenomenon in a patient with cluster headache. The patient reported episodes of involuntary mirthless laughter not elicited by other external or internal stimuli occurring about 5 minutes after sumatriptan injection and lasting 4–5 minutes. These episodes occurred after every sumatriptan injection and were witnessed by his wife. No such episodes appeared after he inhaled O₂ or during untreated attacks.

We hypothesize that pathological laughter was a consequence of acute sumatriptan stimulation of 5-HT1B/1D receptors within the basal ganglia which might have subcortically suppressed the cortical frontal inhibitory afferents to the dorsal area of the upper pontine mesencephalon, thereby exerting a releasing effect on brainstem areas generating laughter.

Our report underlines that, as well as arising from CNS lesions or stimulation, pathological laughter can appear as an acute, transient drug-induced phenomenon and also confirms that subcutaneous sumatriptan can act on the extrapyramidal circuitry.

E008

Risk factors, quality and characteristics of headache in patients with brain tumor

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Objectives To describe characteristics and risk factors of brain tumor-associated headache.

Methods 85 consecutive brain tumor patients were interviewed and examined. The chart and neuroradiologic as well

as pathological record were used in addition to work out characteristics of brain tumor-associated headache.

Results The overall prevalence of headache in this population was 60%, but headache was the sole symptom in only 2%. Pain was generally dull, of moderate intensity, and not specifically localized. Grading after ICHD-II revealed a similarity to tension type headache in 39.2%. Classic characteristics such as worsening in the morning or during coughing were not found; this might be explained by the patients not having elevated intracranial pressure.

Univariate analysis revealed that a positive family history of headache and meningiomas are risk factors for tumor-associated headache, and the use of beta-blockers is prophylactic. Preexisting headache was the only risk factor according to logistic regression, suggesting that patients with preexisting (primary) headache have a greater predisposition to develop secondary headache.

Dull headache occurs significantly more often in patients with glioblastoma multiforme, and pulsating headache in meningioma. Besides infratentorial tumors which are associated more with occipital pain than with frontal pain, no localizing value of the headache could be found.

Conclusion Headache is found in about two third of patients with brain tumors and resembles tension type headache. Preexisting headache is the most important determinant. Headache has no localizing value but its quality depends loosely on tumor pathology.

E009

Study of severe headache patients without SAH on CT scan

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Objectives Evaluation of cerebral arterial dissection is sometimes difficult when the patient complains just a headache without obvious findings of subarachnoid hemorrhage (SAH) on the CT scan. It is said that some cerebral arterial dissection cases without serious neurological deficit do not ask for any medical consultation. Even such cases may do well.

Method Authors analyzed the evaluation and treatment of 6 cases (3 men and 3 women) of cerebral artery dissection that presented for a severe headache without findings of SAH on the initial CT scan.

Results Patient age was from 32 to 65. All of them complained a severe headache that happened for the first time. Cerebral angiogram or MR image performed after the initial CT scan showed intradural vertebral artery dissection in all 6 cases. In 2 cases, SAH occurred within 1 week from the first headache. Five cases underwent the occlusion of dissection with coils by endovascular technique or the angioplasty with fenestrated clips by craniotomy. These 5 cases have not complained headache after the surgery.

Conclusion Initially happened severe headache over 30 year-old person should be carefully diagnosed. Careful analysis of the patient history is helpful. Magnetic resonance image is useful for the evaluation of arterial dissections. Subarachnoid

hemorrhage makes the outcome poor. As the vertebral artery dissection with SAH is more common than the carotid artery dissection in over 30 year-old patients, authors think that the surgical treatment is recommended for intradural vertebral artery dissections.

E010

Many headaches attributed to craniocervical dystonia masked in tension-type headache

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Patients with headache attributed to craniocervical dystonia with slight postural abnormality, were diagnosed as tension-type headache according to ICHD-II criteria. We investigated such cases among tension-type headache.

Among ninety-four cases of tension-type headache with neck and shoulder muscle tenderness in my clinic in 2006, 42 cases revealed a difference between right and left in terms of muscle tenderness. Thirty-nine cases showed slight abnormality of neck posture, and of rotatocollis in 23 cases, laterocollis in 14, lateral shift in 7 and shoulder elevation in 6, including overlap findings. Affected muscles of the abnormality showed tenderness. Neck pain was more dominant than headache in each case. In Japan, there are many cases of headache with shoulder, stiffness. Not a few among them should be diagnosed as headache attributed to craniocervical dystonia.

E011

The relation of aura in the prognosis of migraine

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Objective To evaluate the relation of aura in the prognosis of migraine.

Methods 160 patients (25–64 years), 80 presenting migraine with aura (MA) and 80 migraine without aura (MO), obtained from the Neurology Clinic at the University of the Andes Hospital during the period from 1999 to 2006. Were studied according to the IHS criteria. The frequency, the intensity, and duration of the crisis, remission of the painful episodes, and the degree of incapacity were determined. Later, the results of the two groups were compared and their correlation was analyzed with a prognosis of migraine. The visual aura were evaluated according to the VARS scale and the degree of incapacity according to the MIDAS questionnaire.

Results The frequency of crisis of more than 36 episodes per year was observed in 67.74% of the MO and 32.26% of the MA, 75.64% showed the time of remission less than 1 month, the percentage of remission in intervals of 1 to 24 months was always greater in the MA. The female gender with MA present an average time of remission of 38.22 weeks, the male 19.6. Intensity and duration of the headache showed no difference. Severe incapacity was observed in 60.26% of the MA. Of the MA, 59.76% presented moderate incapacity. Pregnancy,

menstruation, and oral contraceptives, the time of remission showed a tendency towards being greater in MA.

Conclusion The finding of this study permit concluding that the prognosis of the MA is more favorable than that of the MO.

E012

A Scandinavian case series of Chiari I malformation. Clinical and neuroimaging findings in 24 operated patients

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Objectives The aim was to undertake the first systematic Scandinavian analysis of treatment of Chiari I malformation (CMI).

Methods Twenty-four consecutive patients (62% female, mean age 28 years, range 4–54 years) who underwent occipitocervical decompression and dura graft insertion due to CMI at the Sahlgrenska University hospital throughout 1998–2006 were included.

Results The most consistent morphometric MRI-finding was herniation of the cerebellar tonsils (median 15.5 mm, range 4–35). Syringomyelia was found in one half of cases (12/24). Median preoperative duration of symptoms was 3 years and 4 months (range 3 months to 25 years).

Headache was the most common (22/24, 92%) symptom, usually triggered by coughing and/or Valsalva manoeuvre. The duration was hours to days, and the location often occipital or suboccipital. Transient visual symptoms were sometimes reported (n = 7, 29%). Clinical findings signaling disturbance of the spinal cord, brain stem, lower cranial nerves and/or ataxia or dysmetria was regularly found (n = 17, 71%).

There was no mortality or permanent morbidity. Two patients obtained intracranial infections. Four patients were reoperated within 3 months after decompressive surgery due to progress of the syringomyelia, CSF fistula, infection of the dura graft or concomitant hydrocephalus, respectively. One patient was reoperated after one year due to ossification and scarring of the dura. In 22 patients, the symptoms were significantly improved (n = 8) or abolished (n = 14) within 3 months postoperatively. The long term improvement in the five re-operated patients was similar to the others.

Conclusion Postoperative improvement was a regular feature in this retrospective and uncontrolled setting.

E013

New suggestion: arteriosclerotic headache

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Objectives The aim of this study was to determine the possible underlying etiologies of nonspecific dizziness and headache in an attempt to understand the pathophysiological

mechanisms underlying nonspecific dizziness and headache.

Methods The suspected underlying etiologies of non-specific dizziness and headache were investigated between March 2004 and December 2006. A total of 235 patients who complained of nonspecific dizziness and headache were enrolled in this study. The medical history of each patient was reviewed and the brain MRI, brain SPECT and simple cervical spine X-ray findings were analyzed along with the hematology data. Twenty-eight of the 235 enrolled patients underwent vestibular function tests (VFT).

Results Cerebrovascular insufficiency was the most common cause of the nonspecific dizziness and headache. Other frequent causes were spinal degenerations, psychic problems, anemia, vestibular dysfunctions, and so on. The brain MRI (partly including MRA) findings were analyzed. MRI abnormalities, including infarctions, lacunes, periventricular ischemia, small vessel diseases, and cerebral atherosclerosis were identified in 135 patients. An abnormally decreased blood flow was identified in the brain SPECT of 20 patients who showed normal MRI findings. Cerebral ischemia was responsible for about 66% of the cases of nonspecific dizziness and headache.

Conclusion This study found that cerebral ischemia is one of the most common causes of nonspecific dizziness and headache. Therefore, such headaches caused by cerebral ischemia could be classified as 'arteriosclerotic headaches.'

E014

Numb-cheek syndrome: investigation on the clinical characteristics

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Objectives Hypesthesia isolated to the infraorbital nerve distribution has been referred to as the 'numb cheek syndrome (NCS).' It has been considered an ominous symptom, usually heralding the neoplastic involvement of the infraorbital foramen. We have experienced 34 cases of numb-cheek syndrome over the past 5 years. Several of our patients reported cheek numbness that was not restricted to the innervation area of the IN. Notably, cases of central origin showed somewhat different clinical characteristics. The correct localization of the pathologic process is mandatory for radical treatment in varied cases of NCS. This study was conducted to evaluate the clinical characteristics of NCS.

Methods Thirty-two patients with NCS were enrolled the present study. The clinical features, etiologies, and clues for the localization of NCS were analyzed.

Results There were many causes of NCS identified in the present study. A definite etiology was found in 94% of the cases, and cerebrovascular disease was found to be the cause of 85% of the cases of numbness. Only one out of the 34 cases was caused by a neoplasm. 'Dental sensation' and 'associated signs' were the most valuable clues for localizing the pathologic processes.

Conclusion Numbness restricted to the cheek may herald an underlying neoplastic etiology. However, as the present study

indicated, many other disorders or conditions can cause NCS. NCS is often, but not always, an ominous sign. Furthermore, the present study indicated that 'dental sensation' and 'associated signs' are the most valuable clues for localizing the pathologic processes.

E015

Posttraumatic headache treated with botulinum toxin

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Objective It is difficult to treat PTH (Post-traumatic headache) with satisfaction despite the numerous treatment options available. This study was conducted to evaluate the effectiveness of botulinum toxin A (BTX-A) in the treatment of patients with chronic daily PTH.

Methods Sixteen patients with chronic daily PTH were enrolled in the present study. Dosing was individualized to obtain the optimum therapeutic effect. The patients were asked to give a percentage of improvement for the frequency and intensity of the headaches in the follow-up examination.

Results The average age of the patients was 34.9 years, and the mean duration of PTH was 1.2 ± 0.4 years (range 1 month–3 years). A mean dose of 60 ± 15 units of BOTOX/session/person (range 45–120 units) was injected into the cervical muscles and scalp depending on the location of tender points. The mean number of sessions was 3 (range 2–5 sessions). Twelve out of 16 patients showed mild to moderate improvement in chronic daily PTH. Some patients reported a disappearance of the other symptoms (dizziness, nausea, etc) of post-traumatic syndrome. Five patients complained of local pain at the injection sites, lasting as long as 15 days, and three patients complained of transient neck weakness.

Conclusion BTX-A has been found to be safe and effective for the treatment of PTH. Furthermore, BTX-A has also been found to be effective in treating the other symptoms of post-traumatic syndrome.

E016

Pillow compression headache: a new external compression headache

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Objectives The IHC described an external compression headache (ECH) as a headache resulting from the continued stimulation of cutaneous nerves by the application of pressure, for example by a band around the head, a tight hat or goggles worn to protect the eyes during swimming. Until now, there have been a few case reports on ECH. We recently experienced a new type of ECH and found that a pillow can cause a compression headache to occur during sleep. This study was conducted to evaluate the clinical characteristics of a new type of ECH, Pillow Compression Headache (PCH).

Methods Sixteen patients with PCH were enrolled the present study. The characteristics of the clinical features were analyzed.

Results The average age of the patients was 62.8 years, and the mean duration of PCH was 2.4 ± 0.8 years (range 10 months–5 years). All of the patients experienced disturbed sleep by pain originating from sites of compression with a pillow. Most patients complained of dull pain with moderate severity. The mean duration of the pain after arising from bed was 5.8 ± 1.4 minutes.

Conclusion A relatively older age than those typically associated with other types of headaches and a causal relationship between a headache and compression by a pillow suggested that the arteriosclerosis of the vasa nervosum of the upper cervical branches ascending to the occipital areas might be responsible for the development of PCH.

E017

Heavily T2-MR myelography in patients with spontaneous intracranial hypotension: a case-control study

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Objectives To characterize the findings of heavily T2-weighted magnetic resonance (MR) myelography and its clinical correlation in patients with spontaneous intracranial hypotension (SIH).

Methods We consecutively recruited patients with SIH based on the ICHD-2 and age- and sex-matched control subjects. All subjects received whole-spine heavily T2-weighted MR myelography using a single-shot fast spin-echo pulse sequence. In addition, patients with SIH received at least one follow-up MR myelography 3 weeks after treatment. We also compared the changes in clinical presentations and MR myelography findings at follow-up.

Results Seventeen patients with SIH (8M/9F) and 17 control subjects participated in this study. Our MR myelography showed three kinds of abnormal CSF collections in 15 patients with SIH (88%): epidural fluid collection ($n = 15$, 88%), C1-2 extra-spinal collections ($n = 6$, 35%) and CSF collections along nerve roots in the lower cervical or upper thoracic spines ($n = 6$, 35%). One patient (6%) showed a meningeal diverticulum. None of the controls showed these findings. In contrast, perineural cysts were found in both patients and controls ($p = 0.169$). Our MR myelography findings facilitated early diagnosis of SIH in four (24%) patients because their initial brain MRIs were negative. Follow-up MR myelography results were compatible with the clinical changes with kappa statistics of 0.52 and an agreement rate of 76%.

Conclusions Heavily T2-weighted MR myelography provided a rapid, non-invasive and high yield method to diagnose and follow-up patients with SIH. Whether the CSF collections along the nerve roots represent the ongoing leakage sites warrants further study.

E018

Pituitary adenoma. Post-surgical replacement of type of headache. A case report

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Introduction The presence of headache is a common issue in patients suffering from pituitary adenoma before and after surgery.

Objective The present study tries to explain the change of the type of headache post-surgically in a patient suffering from pituitary adenoma and to clarify the role of surgical techniques and the role of post-surgical radiation in the appearance of a new type of headache.

Methods It is described the case of a female patient suffering from episodes of cluster headache the last 10 years in a base of pituitary adenoma. After the nasal transphenoidal hypophysectomy and after the post-surgical radiation the patient appeared a new type of headache: migraine without aura, localized strictly on the opposite part of the head, compared to the localization of pain she experienced pre-surgically.

Conclusion There are several references in the international bibliography which deal with the post-surgical and post-radiation headaches. The surgical techniques and the radiation are often proposed as the risk factors for the appearance of these headaches. During the study of the current bibliography we conclude that these risk factors are not well clarified and the treatment is often very difficult. In our case, the patient was treated with amitriptyline and anti-migraine agents and she is free of symptoms the last 1 1/2 years.

E019

Large scale screening and subsequent effects of optimal migraine treatment at work

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Objectives To reduce the migraine-specific burden and productivity losses in a working population by screening and implementing treatment.

Methods A crossover multicenter effect study was implemented in a large retail business group (Maxeda) with 30,978 employees. Company doctors sent the ID Migraine Screening Test to employees with 3 or more periods of work absence in the last year. Responders with positive test results were invited for clinical consultation with a neurologist specialized in headache. If migraine specific treatment was indicated, patients were randomly assigned to a condition in which the first attack was 'treated as usual' and the second attack with eletriptan, or to a condition with the reversed order. Outcomes were pain intensity, quality of life and productivity. Measurements were made at baseline, after a first attack and after a

second attack. Pfizer supported the research with an unrestricted grant and ethical approval was obtained.

Results Company doctors sent out 2,356 screening tests (7.6%) and 683 employees responded (29.0%). Of the 205 employees screened positive, 97 agreed to consult the neurologists and 59 could be included in the trial. In the patients with a 'non-triptan usual treatment', eletriptan reduced pain intensity and improved quality of life significantly more than the 'usual treatment' but we could not detect a difference in productivity. In employees who already used a different triptan, there was no statistical significant effect of using eletriptan above usual treatment.

Conclusions In-company screening can enhance optimal migraine treatment.

E020

How does 'sinister' Tolosa-Hunt syndrome related to Dural Arteriovenous Fistula. A case report

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Objective Numerous publications showed that causative lesions of the region of the cavernous sinus such as dural Arteriovenous Fistula (dAVFs) have a close relation to Tolosa-Hunt syndrome (THS).

Methods We report a 62 years old patient with (THS). She was treated with steroids in high doses and after 3 days there was an improvement. Because of dAVFs in cavernous sinus, embolism was taken place and it was successful. She is free of symptoms 3 years after.

Discussion Although it is believed that the response to the steroid therapy and the exclusion of other causative lesion by neuroimaging are the diagnostic criteria for THS, steroid-responsive painful ophthalmoplegia (PO) has been observed also in numerous pathological cases such as aneurysms, pachymeningitis and dAVFs. As dAVFs is concerned, the etiology is still controversial. While sinus thrombosis, trauma and congenital origin have been proposed like probable causes, the inflammatory process is considered to be the most plausible. Therefore THS that is attributed to nonspecific granulomatous inflammation in the cavernous sinus, is considered to be a candidate for the development of dAVFs. Furthermore the complete efficacy of steroid therapy suggests that inflammation was a key factor in dAVFs. On the other hand it is not sure that there wouldn't have been a remission without embolism.

Conclusion It is clear that further study is necessary to clarify dAVFs treatment and its etiology. It is also necessary the revision of the criteria of THS because firstly it can no longer be considered as being exclusive of neuroimaging abnormality and secondary its 'steroid responsiveness' must be reconsidered.

E021

Idiopathic intracranial hypertension and venous thrombophilia. A case-control study of risk factors

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Objectives Idiopathic intracranial hypertension (IIH) is a condition of increased intracranial pressure of unknown pathology predominantly seen in obese young women. A more frequent predisposition to venous thrombosis in IIH has recently been reported. Coagulation abnormalities linked to the obese phenotype itself was not considered. Existing but inconsistent imaging methods may also have failed to demonstrate underlying venous pathology and it is unclear whether subjects with intracranial hypertension secondary to venous thrombosis have been excluded in previous studies.

Our aim was to examine thrombophilic parameters in a well-defined IIH population and a control population of identical demography.

Methods Prothrombotic abnormalities among 19 IIH patients with normal MRV and MRI were compared with 15 healthy sex-, age- and BMI-matched controls.

Biochemical markers tested were: homocysteine, protein C activity, total protein S antigen, antithrombin III activity, coagulation factor VIII activity, activated partial thromboplastin time, lupus anticoagulant (DRV), anticardiolipin antibodies, G1691A Leiden genotype, antinuclear antibody screening and androgene hormones.

Results Median BMI was 29.8 kg/m² (range 20.4–48.8 kg/m²) in cases and 26.4 kg/m² (range 20.2–42.6 kg/m²) in controls, $p = 0.2$. No single parameter differed significantly between cases and controls (Fisher's exact tests). 13 of 19 cases (68%) and 12 of 15 controls (80%) had one or more abnormal test result.

Conclusion The present controlled study does not support hypercoagulability in IIH. Although based on a small population a significant difference between cases and controls should be expected if coagulation abnormalities were of importance in IIH. Other neurobiological mechanisms should be identified.

E022

Cerebrospinal fluid hypovolemia as a cause of post-traumatic syndrome

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Objectives Pathogenesis of post-traumatic syndrome (PTS) is not well known. Effective treatment for PTS is not established. The aim of this study was to evaluate neuroradiological findings and efficacy of epidural blood patch (EBP) in patients with PTS.

Methods 176 cases of PTS after whiplash injury and minor head injury were evaluated. Cerebrospinal fluid (CSF) leak was studied by radioisotope (RI) cisternography and magnetic resonance (MR) myelography. Decreased CSF was evaluated by gadolinium enhanced MRI. All patients were treated

by EBP. Outcome was evaluated by performance status and improvement of symptoms.

Results Of 176 cases of PTS, 89 cases revealed definite CSF leakage in RI cisternography. 27 cases were male and 62 cases were female. Mean age was 39 y/o (13–78 y/o). Causes of trauma were motor vehicle accident (1), fall (8), sport injury (4), assault (4). MRI showed dilatation of vein (50), inferior displacement of cerebellar tonsil (41), subdural effusion (35), dural enhancement (16), slit ventricle (12). MR myelography revealed definite cervical leak in 12 cases, definite lumbar leak in five cases. Clinical outcome was good recovery in 18 cases, moderate recovery in 34 cases, partial recovery in 18 cases and no change or follow-up in 19 cases.

Conclusion RI cisternography revealed lots of CSF leakage in cases of PTS. Cases with CSF leakage showed decreased CSF in cranial MRI. The effect of EBP for CSF leakage was remarkable. CSF hypobolemia caused by continuous traumatic CSF leakage plays an important rule in pathogenesis of PTS.

E023

Acanthamoebic keratitis presenting like paroxysmal hemicrania

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Background Paroxysmal hemicrania (PH) sometimes is linked to secondary causes such as brain tumors, cerebrovascular disease, trauma, and ophthalmic zoster.

Objective To detail the clinical presentation of a rare ocular infection mimicking PH.

Case presentation: 24 year old woman sought neurological opinion for a 10-day history of recurring and severe left-sided headaches. Against a background of nagging left medio-nasal ache and continuous photophobia, she described 4–6 attacks/day (duration = 10–20 minutes/attack) of piercing, left infraorbital, severe pain with worsening eye-redness, clear tearing, nasal stuffiness, and without nausea or neurological accompaniments. The first experience of these pains was 2 years prior to presentation, and she reported one 2-week bout every 2–3 months. She identified no precipitants to her headaches. Non-revealing were her medical, surgical, medication, and family histories, as well as her review of systems. The physical and neurological examinations were normal except for left conjunctival injection and ptosis that twice worsened when two attacks were witnessed during the interview. She was discharged on rapidly escalating doses of indomethacin (target = 150 mg on day 3). She experienced incomplete relief for a few days after which she noted progressive visual loss. Then, corneal edema was noted on ophthalmological examination, and corneal scraping with cultures revealed acanthamoebic keratitis. Few days after antiamebic therapy, her pain and vision improved.

Conclusion An underlying infectious, structural, traumatic, or neoplastic etiology always should be considered in patients presenting with signs and symptoms of PH.

E024

Posture-dependent headache in a case of hyperphosphatemic tumoral calcinosis

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Objectives Tumoral calcinosis is manifested as hyperphosphatemia and juxta-articular tumorous calcifications. It could be transmitted in a dominant autosomal manner with variable clinical expressivity. Neurological manifestations are scarce. We report a case of a position-headache due to a intracranial calcified mass as initial manifestation of familial tumoral calcinosis.

Results A 47-year-old man presented with 6-months history of position-dependent headache. His sister and nephew had a mineral metabolism disorder. Characteristically, the headache appeared in a short time after lying down and was completely relieved by standing up. It was associated with nausea. Neurological examination revealed no abnormal signs. Magnetic resonance demonstrated a well-defined solid mass attached widely to the medial side of the tentorium. The fourth ventricle was slightly distorted by the solid mass. No perifocal edema was noted and a peripheric enhancement was observed after an intravenous infusion of contrast. A computed tomography showed a complete calcification of the mass. A meningioma was suspected. A complete blood count and serum calcium level was normal although there was moderate hyperphosphatemia. The headache was relieved by indometacin at night. The mass was not removed because the patient refused it.

Conclusion In contrast to headache associated with the intracranial hypotension syndrome this postural headache is aggravated by lying down. It is described in tumours of the posterior fosse and was secondary to intermittent hydrocephalus produced by disrupting the CSF dynamics after resuming a recumbent position.

E025

Primary headaches in an outpatient neurology clinic in Japan

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Objectives To assess the prevalence and characteristics of primary headache among patients who visited a single neurological outpatient clinic in Japan.

Methods All consecutive new patients who visited our neurological outpatient clinic between August 2005 and June 2006 were asked to fill in a questionnaire on headache characteristics.

Results Total number of the new patients were 711 during this period. The number of effective respondents was 562. Among these, 361 patients (64%) were experienced headache at least once in the life time, and 246 patients (35%) were visited to neurological outpatient service with headache as a chief complaint. A total of 246 patients had some form of

primary headache: 21% migraine without aura, 8% migraine with aura, 26% tension-type headache. Among many jobs, service job is much more prevalent in migraine (24%) than in tension-type headache (9%) and non-headache patients (11%). The well-educated patients of migraine headache was 48% in men and 31% in female. On the other hand, such differences could not be observed in patients with tension type headache. **Conclusion** The authors performed a survey of the prevalence and characteristics of primary headache among new patients who attended a single neurological outpatient clinic in Japan.

E026

Validation of a German questionnaire for migraine, tension-type headache and trigeminal autonomic cephalgias

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Objective We aimed to develop a German language self-administered headache questionnaire for screening for migraine (MIG), tension-type headache (TTH) and trigeminal-autonomic cephalgias (TAC).

Methods Validation was performed in two steps: First, we studied 278 headache patients from the headache outpatient clinic (MIG = 97, TTH = 60, TAC = 98, MIG plus TTH = 23), 42 patients with low back pain without headache and 47 healthy subjects comparing in a blinded fashion questionnaire based diagnoses to those of headache experts. Second validation phase was performed in a population based setting. One hundred and ninety three headache patients diagnosed by the questionnaire as MIG = 49, TTH = 46, MIG + TTH = 53 and Cluster = 45 were blindly investigated by headache experts as well.

Results First step: Sensitivity and specificity for migraine were 0.73 and 0.96, for TTH 0.85 and 0.98, for TAC 0.63 and 0.99 and for MIG + TTH 0.62 and 0.97 respectively. Cohen's kappa = 0.93 [95% CI 0.83–1.0]. The re-test-reliability (4 weeks later) was 0.95. Second step: Sensitivity and specificity for migraine were 0.85 and 0.85, for TTH 0.6 and 0.88 and for MIG + TTH 0.82 and 0.87 respectively. Cohen's kappa = 0.6 [95% CI 0.50–0.71]. Of 45 patients with a questionnaire's diagnosis of TAC physicians diagnosed cluster headache in two patients only.

Conclusion This study demonstrates that validation of a headache questionnaire in patients of tertiary headache centres could be misleading overestimating its quality even though this step might be necessary for other reasons. The final validation should however, be done in a population based sample of headache patients.

E027

Influence of migraine intensity and timing of treatment on the efficacy of zolmitriptan oral tablet

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Objective To explore the efficacy of zolmitriptan oral tablet (2.5 and 5 mg) according to baseline intensity of migraine and timing of treatment after headache onset.

Methods This pooled analysis concerned 5 clinical trials of zolmitriptan oral tablet in the treatment of adults with migraine. Efficacy according to baseline intensity of migraine and timing of drug administration was evaluated: pain-free response at 2 h; relief of associated symptoms (nausea, photophobia, phonophobia) at 2 h; sustained pain-free response at 24 h (pain-free at 2 h and no recurrence or use of further medication within 24 h); and need for a second dose or escape medication.

Results Evaluable data were available for 38,766 attacks treated with zolmitriptan oral tablet (5 mg, n = 34,489; 2.5 mg, n = 4,277). High efficacy rates were apparent irrespective of baseline intensity of headache, with sustained efficacy rates and second-dose use being similar for both doses of zolmitriptan. The 5 mg dose was generally superior to the 2.5 mg dose for relief of pain and associated migraine symptoms at 2 h, reaching 79% pain-free in those with mild headaches. When stratified by time to treatment after headache onset, there was no difference in response rates for attacks treated early or late in any of the subgroups for either dose.

Conclusion This analysis confirms the high efficacy of zolmitriptan oral tablet (2.5 and 5 mg) for acute migraine treatment. For both doses, efficacy is influenced by intensity of headache at the time of treatment (with the 5 mg dose being superior to the 2.5 mg dose), but not time to treatment after headache onset.

E028

Difference of the Headache Impact Test (HIT-6) score according to type of primary headache

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Objective The Headache Impact Test (HIT-6) is a brief questionnaire designed to assess headache-related disability. To evaluate difference of the headache-related disability according to type of primary headache, we used HIT-6 for patients who suffered presented for treatment at our headache clinic.

Methods Participants were 174 new patients who presented for treatment at a headache-specialty clinic in our hospital: 56 men (32%) and 118 women (68%), mean age 38 years (9–75), including 105 migraine (60%), 38 tension-type headache (TTH) (22%), 15 coexisting migraine and TTH (Mixed) (9%), 14 cluster headache and other trigeminal autonomic cephalgias (TAC) (8%), 2 Other primary headaches (OPH) (1%). Patients suffering from medication-overuse headache were excluded.

Results HIT-6 scores ranged from 42 to 78, with an average of 62.3 (SD = 7.1) and the majority (68%) had 'severe impact' (60 or higher) in all patients. Mean HIT-6 score of migraine (63.4), Mixed (62.8), and TAC (65.6) were significantly higher than that of TTH (58.3) and OPH (52.5) ($P < 0.001$). Severe impact patients were 79 of migraine (75%), 18 of TTH (47%), 10 of Mixed (67%), 11 of TAC (79%), and 1 of OPH (50%).

Conclusion These findings suggest that the majority of the patient who suffered presented for treatment at our headache clinic had severe headache-related disabilities, and migraine, Mixed and TAC had great impacts on the daily life of patients.

E029

Fast and lasting efficacy drives patient satisfaction with zolmitriptan nasal spray for migraine

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Objective To evaluate the relationship between the speed of onset and duration of efficacy of zolmitriptan nasal spray (NS) and patients' satisfaction with treatment.

Methods As part of a randomised, placebo-controlled, dose-ranging study, patients treated a maximum of 3 migraine attacks (moderate/severe intensity) with zolmitriptan NS 5 mg. Efficacy was assessed by: headache response (mild/none) at 30 min, 1 and 2 h; complete response at 24 h (headache response at 2 h and no recurrence or use of further medication within 24 h); and absence of associated migraine symptoms at 2 h. For each patient, the percentage of attacks with a positive outcome for each of the response variables was calculated and compared against subjective data for global impression ('excellent', 'good', 'fair' and 'poor') and satisfaction ('yes' or 'no').

Results Data were evaluable for 203 patients. For patients who rated zolmitriptan NS as 'excellent' (n = 31), 32% had a headache response within 30 min, increasing to 59% at 1 h and 84% at anytime up to 2 h in all attacks treated (vs. 60% [55/90] of those rating it as 'good', 36% [18/50] as 'fair' and 16% [5/31] as 'poor'). Of patients 'satisfied' with zolmitriptan NS (n = 100), 69% achieved a headache response at anytime up to 2 h in all attacks treated (vs. 34% [34/101] of 'dissatisfied' patients). Result for complete response and relief of associated migraine symptoms also showed an association between favourable opinion/satisfaction with treatment and efficacy.

Conclusion Zolmitriptan NS provides fast and lasting efficacy for the majority of patients with acute migraine, contributing to high levels of patient satisfaction.

E030

Migrainous otalgia

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Objectives Migraine headache is typically unilateral in the anterior half of the head but cases with headache in extra trigeminal territory could occur.

We present three patients with recurrent unilateral otalgia who fulfilled diagnostic criteria of primary headache collected among two thousand migraine patients visited in 6 years.

Cases (1) 20 year-old woman, with weekly dull episodic headache deeply in left ear with nausea, vomiting, photo and phonophobia since age of ten. Neurological and otological examination including audiometry, CT and MRI were normal. Nadolol reduced the frequency to less than monthly and acute zolmitriptan was effective.

(2) 70 year-old woman with migraine without aura since age of 20 increased the frequency around menopausal age presenting weekly severe episodes of throbbing left earache accompanied with photo-phonophobia without vertigo or deafness. Neurological, ear examination and temporal bone CT were normal. Nadolol and flunarizine prevent the episodes and zolmitriptan resolve the headache in 20 minutes.

(3) 28 year-old woman presented in the last 6 years left earache episodes lasting 30–180 minutes in a daily profile during a month every year. Headache was severe, dull and throbbing deeply in left ear irradiated to occipital area, with photo-phonophobia and left nasal obstruction. Audiometric study, neurological and ear exams and cranial CT were normal.

Conclusion Our cases fulfil migraine or cluster headache criteria. Neither had temporomandibular joint nor red ear signs. Ear exam and neuroimaging discard primary otalgia. Migraine headache has to be considered in cases of recurrent earache.

E031

Increasing patient information to reduce burden of migraine: a new project: 'The Headache days'

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Objective In 2005, through 'The Headache week' (a free informative-point for a week in a headache-centre) we found that 78% of participating patients, affected by severe headache, don't know where to refer for their headache. Our aim was now to extend and give continuity to the initiatives for patients information increasing the sites (more headache-centres) and their overall period of activity.

Methods To favour the participation of more headache-centres, we reduced the activity of each information site to 1–2 days calling the initiative 'The Headache days'. 9 headache-centres in the city and province of Palermo participated, covering a period of two months. The initiative was advertised in local newspapers and network and at the headache national websites. Participating patients were examined by a headache-specialist, received informative materials and compiled a

questionnaire about physician visited, knowledge and usage of symptomatic (triptans) and preventive treatments.

Results 210 patients participated (migraine: 75%; tensive: 18%; cluster: 4%; other: 3%); about 70% of migraineurs never used triptans while these drugs were erroneously taken by 15% of patients with tensive headache; about 70% of migraine and tensive headache patients never received prophylaxis; about 50% of patients receiving preventive treatment, chose non-conventional approaches (acupuncture, homeopathic medicines etc).

Conclusions lack of information represents a major cause of poor recognition and treatment of migraine in population. Giving continuity to initiatives like 'headache days' can increase patients' knowledge about headache with the final goal (through more appropriate diagnosis and treatment) to reduce disability and burden of migraine.

E032

Orbital myositis mimicking SUNCT syndrome

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Introduction Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome is a rare primary trigeminal autonomic headache although secondary causes, namely posterior fossa lesions and prolactinomas, have been described. Two cases of orbital lesions (a cyst and a bronchial carcinoid metastasis) were previously reported presenting as an otherwise typical case of SUNCT. We report another case of secondary SUNCT due to an orbital inflammatory disease.

Case report A 27 year-old female presented to our emergency department due to left frontal and orbital pain. The pain was excruciating, lasted seconds to 2 minutes, repeated every 7–10 minutes (day and night) and during the attacks there was marked photophobia, conjunctival injection and tearing. Between attacks there was no ocular pain and neurological and ophthalmologic observation were entirely normal. After taking 100 mg of indomethacin twice a day she was pain free. Cranial MRI revealed left lateral rectus myositis. One week later, a right ptosis and eyelid oedema was noted. With steroid therapy (prednisolone 60 mg/day) there was complete resolution of symptoms and MRI findings. Laboratory investigation of inflammatory conditions was negative.

Discussion Orbital myositis may cause frontal unilateral headache, usually with associated ocular signs: (pain on eye movement, eyelid oedema, proptosis, visual disturbances or ophthalmoparesis). It can however present as a trigeminal autonomic cephalgialgia (cluster-like as previously reported or SUNCT-like as in our patient), with no other ocular signs, at least in the initial stages of the disease, therefore stressing the need for orbital imaging.

E033

Pain in cervical artery dissection: a comparison between internal carotid and vertebral artery

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Background Headache is frequently the initial symptom in spontaneous cervical artery dissection and it often precedes other manifestations. Besides location, there are no distinctive features of this dissection associated headache.

Methods We present a hospital series of consecutive patients with cervical artery dissection admitted in the last 10 years and compare the headache and clinical features in carotid and vertebral artery dissection.

Results From a total of 61 patients, 6 aphasic were excluded as it was impossible to get headache data. There were 55 patients, 35 males and 20 females with a mean age of 47.7 ± 10.7 years. 35 had internal carotid artery dissection (ICAD) and 20 vertebral artery dissection (VAD). Headache was present in 31 patients (56%) and it was significantly more frequent in VAD than in ICAD (70% vs 41%, $p = 0.044$). Most patients had headache onset in the same day as other signs, and it lasted less than 8 days. Most ($n = 20$) had a cephalic location of pain (including 11 VAD patients) and only 9 had neck pain. Patients with past history of migraine had more headache at presentation ($p = 0.031$). In ICAD, visual symptoms were more frequent in cases with headache compared to those without headache ($p = 0.003$).

Discussion In our series VAD presented itself with headache more frequently than ICAD, contrary to what was previously reported. Also our ICAD patients suffered cervical pain as often as VAD patients in contrast to what would be expected. Migraine seems to predispose to the occurrence of headache in artery dissection.

E034

Headache as the presenting symptom of herpes simplex meningoencephalitis

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Objectives To analyze the frequency of headache as the presenting symptom of herpes simplex meningoencephalitis and its value as a predictor for patients' outcome.

Methods We studied 10 patients with PCR proven and 20 with probable herpes simplex meningoencephalitis (characteristic neurological symptoms and results in CSF, cranial MRI and EEG but negative PCR) with regard to headache as the presenting symptom. Headache was the first symptom in 13 (43.3%) patients (3 male, 10 female, aged 19 to 70, mean 41.8), all had a good outcome after therapy. The other 17 patients (8 male, 9 female, aged 31 to 82, mean 62.5) did not report headache at admission. Two patients in this group died, six had a bad outcome, and eleven had a good outcome. From these 17 patients, eleven were already unconscious or analgesicated at admission, therefore anamnesis regarding initial headache was not possible.

Results Patients with initial headache had a significantly better outcome ($p = 0.009$), were younger ($p = 0.001$) and had a higher cell count in the CSF ($p = 0.049$). Furthermore, patients with a good outcome have reported initial headache significantly more often ($p < 0.001$), had higher protein levels ($p = 0.016$) and a higher CSF cell count ($p = 0.02$).

Conclusion About half of the patients with herpes simplex meningoencephalitis present with headache as the primary symptom which is accompanied by a better outcome. This prognostic factor is maybe due to earlier search for medical help by these patients.

E035

Language disturbances as a side effect of prophylactic treatment of migraine

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Background Language disturbances have been reported as a side effect of topiramate treatment in epileptic patients. The present study was aimed at verifying the occurrence of language disturbances in migraineurs under topiramate treatment.

Patients and methods Thirty migraine patients treated with topiramate for at least 3 months, 20 migraine patients treated with other prophylactic drugs (excluding antiepileptic drugs) and 20 migraine patients without prophylactic treatment were enrolled.

Language functions was explored with the following neuropsychological tests: Trail Making Test (TMT-A and B), a test of Phonemic and Semantic Verbal Fluency and a Denomination test.

Results Language disturbances were referred by 26.7% ($n = 8$) of patients under topiramate treatment but by none of the patients of the two control groups. The majority of patients it were accompanied by other side effects. Significantly worse scores for TMT-B subtest and two of the three categories of semantic verbal fluency (flowers and cities) were found in topiramate patient group, especially in patients with referred language disturbances. Patients without referred language disturbances in the topiramate group showed in any case a worse performance of all tests compared to patients in other prophylactic treatments or untreated migraine patients.

Discussion Language disturbances occur in a discrete proportion of migraine patients. They can be the expression of a more generalized impairment of cognitive processing. Their occurrence and characteristics should be investigated in prospective studies involving larger migraineurs samples treated not only with topiramate but also with other antiepileptic drugs used as preventive drugs for migraine.

E036

Prevalence of headache disorders in the Republic of Georgia: a population based study

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We report the prevalence of migraine, tension-type headache and chronic headache in Georgia. No data currently exist on prevalence and impact of headache disorders in the Post-soviet Countries. This study was performed as collaboration between the Global Campaign to Reduce the Burden of Headache Worldwide and the Russian Linguistic Subcommittee of the International Headache Society. We studied a population-based sample of 1,500 biologically non-related individuals in the Capital of Georgia, Tbilisi, and in a rural area of Kakheti in the east part of the country. Medical residents performed a door-to-door survey using a structured questionnaire which had been validated previously¹. In order to control the quality of questionnaire-diagnoses, 30% percent of subjects reporting headache were examined by one of two headache-experienced neurologists. Currently 75% of the study has been completed. The response rate is 82%. Of respondents, 48% reported headache during the last year. The preliminarily estimated prevalence of migraine in these populations of Georgia is 10.3%, of probable migraine (meeting all but the criterion for duration) an additional 7.3%, of tension-type headache 20% and of chronic daily headache (otherwise undiagnosed) 4.5%. Final estimates of the prevalences of these headache disorders, which have public-health importance, of headache-related disability and of willingness to pay for effective treatment will be reported.

Reference

1 Katsarava Z et al. A pilot methodological validation study for a population-based survey of the prevalences of migraine, tension-type headache and chronic daily headache in the Country of Georgia. *J of Headache and Pain*, 2007 accepted.

E037

Internal carotid arterial dissection manifested as recurrence of thunderclap headache: a case report

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Objective To report a case of internal carotid artery (ICA) dissection presented as recurrence of thunderclap headache.

Methods and results A 43-year-old woman experienced several episodes of intense headache, all occurring in the showers or related to straining. They were hyper-acute onset (reaching the maximum in 30 seconds), throbbing, located at right parietal or bi-temporal areas, aggravated by physical activity, and had no associated symptoms. These headaches lasted 1–2 hours and, unlike her prior migraine attacks, responded poorly to painkillers. Her physical and

neurological examinations were normal. Blood tests including thyroid function and 24-hour urine vanillylmandelic acid were normal. The brain MRI and MRA did not show evidence of cerebral ischemia or vasoconstriction. Primary thunderclap headache was impressed. Her headache responded dramatically to oral nimodipine (30–60 mg q4-6h).

There was no similar headache until 8 months later, when another thunderclap headache seized her in the showers. The headache did not respond to oral nimodipine. There were no trauma history and no focal signs noted, but carotid Doppler study revealed low flow in right ICA, and the MRA and conventional angiography confirmed long-segment narrowing of right ICA suggestive of arterial dissection. She received a carotid stenting procedure and was treated with anti-platelet agents thereafter. There was no recurrence of thunderclap headache in the one-year follow-up period.

Conclusion Primary thunderclap headache may recur within the first weeks of onset, but its resurrection several months later and poor response to nimodipine are atypical and justify a new investigation to exclude other possibilities.

E038

Migraine and associated disability in Nigerian University students

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Objectives The objectives of this study were to determine the prevalence of migraine among students in a Nigerian university and determine the disability associated with it using the Migraine Disability Assessment (MIDAS) questionnaire.

Method A cross sectional study in which students of Ambrose Alli University, Ekpoma, Nigeria were requested to fill self-administered, close-ended questionnaires in a two-stage random sampling. The first stage involved the identification of those with migraine using the International Classification of Headache Disorders (ICHD-II) criteria of 2004 while in the second stage, MIDAS questionnaire was applied to those with migraine

Results A total of 1,000 questionnaires were distributed out of which 846 were returned with complete information. There were 426 males and 420 females giving a male: female ratio of 1:1. Overall, the prevalence of migraine was 9.1% with a lower prevalence rate of 8.7% in males compared to 9.5% in females. Level of disability on MIDAS scale was little or none in 52.9%, mild in 11.4%, moderate in 18.6% and severe in 17.1%.

In spite of the fact that 35.7% of the migraineurs had moderate-severe disability, none of them was on any effective preventive therapy and majority (73.3%) was on simple analgesics for prevention. Only 5.5% use ergotamine preparations during acute attack while none of them use triptans.

Conclusion Prevalence of migraine in Nigerian university students is 9.1% which is comparable to studies elsewhere. Although about 36% of the sufferers have moderate-severe disability, none is on any effective preventive therapy.

E039

Diagnostic delays and mismanagement of Hemicrania Continua

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Objectives To investigate a clinical population of patients suffering for Hemicrania Continua (HC) with regard to diagnostic problems encountered, pattern of health care resources use, and problems pertaining effectiveness of treatments.

Materials and methods We directly interviewed 19 patients fulfilling ICHD-2 diagnostic criteria for HC selected among 2105 subjects attending the Headache Clinic INI Grottaferrata over a 2 years period.

Results No patient had received the correct diagnosis before the visit to the Headache Clinic. 85% of the patients consulted a physician within 5 months by the onset of symptoms but mean time to diagnosis was 5 ± 4.7 years. The average number of physicians seen before the proper diagnosis was made was 4.4 ± 2.2 . GPs (100%), neurologists (81.2%), ENT surgeons (47.3%), ophthalmologists (42%) and dentists (31.5%) were the physicians most commonly consulted. All patients had received a wrong diagnosis. Migraine (57.8%), CH (26.3%), sinus headache (21%) and atypical facial pain (15.7%) were the most common wrong diagnosis reported. 31.5% of patients received ineffective invasive treatments. Patients tried on average 3.84 ± 2.19 class of drugs. NSAIDs (94.1%), triptans (26.3%), antidepressants (31.5%) and antiepileptics (21%) were the most commonly used. Patients rated 66.5% of medications as ineffective, 28% as partially effective (all NSAIDs) and 4.5% as effective (rofecoxib and nimesulide).

Conclusions HC is largely misdiagnosed and mistreated even by neurologists. There is need for increased awareness and education about CH.

E040

Care pathway of headache admissions to a district general hospital

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Headache accounts for 1.7%–4.5% of all visits to emergency departments. Clinical differentiation between primary and secondary headaches can be challenging. Features predictive of secondary headache such as age ≥ 55 , sudden onset of headache, 'worse' headache and abnormal neurological findings indicate a need for admission and investigation. Despite this, 50% of all headache admissions have a primary headache syndrome.

A retrospective case note study was performed in a district general hospital. The aim was to audit the pathway of patients admitted with primary presenting diagnosis of 'headache' over a 5 month period with regard to diagnosis, treatment, length of stay and follow-up.

Of 180 cases identified, a sample of 62 records were studied. 47% had a secondary headache (including 5 subarachnoid hemorrhages). Of the 53% of patients with a final diagnosis of

a primary headache, 40% spent ≥ 2 days in hospital, only 1 patient received a triptan, 50% received codeine based analgesia in hospital, 13% were discharged on codeine, only 59% received a definite diagnosis at discharge and 93% were discharged without follow up arrangements.

A number of inadequacies in patient management were identified. Hospital-based guidelines outlining standards for the treatment of acute headache may improve the current under-use of triptans, and reduce overuse of codeine based analgesia for primary headaches. Emergency care physicians should be trained as much in the management of primary headaches as in secondary headaches as they are at least as common on medical take and often spend several days in hospital.

E041

Patients seeking teleadvice for headache

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Objectives The aim of the study was to analyze the identity, clinical problems and expectations of patients seeking teleadvice to an ask the doctor service for headache and to evaluate the appropriateness of their requests and the potential for teleadvice to improve medical support for headache.

Methods Exploratory survey and quantitative content analysis of the e-mails sent to an ask the doctor service on a website dedicated to headache from September 2005 to August 2006.

Results 332 e-mail were received in the study period. 69% were sent directly by the patients. 50% of the writers were aged between 15 and 35 years. 54% of the writers reported a headache diagnosis (migraine 27.2%, cluster headache 24%, MOH 13%). Almost 50% of those not reporting a diagnosis declare to use symptomatic medication on an almost daily basis. 74% of the writers declared to have seen a physician before. On content analysis the most frequent reasons to write were informations about visit/physicians, general advice, information about therapy. 40% of the writers expressed frustration or disappointment about previous physicians. 68% of the e-mails were judged as suitable to be answered via e-mail.

Conclusions Seeking teleadvice is not a frequent activity. It is used by young patients suffering for chronic or highly demanding headaches, frustrated by previous medical experience, in different stages of their decision-making process regarding their need for medical help. E-mail supplement rather than replace the traditional visit and has the potential to improve several aspects of the medical support for headache

E042

A case of iatrogenic intracranial hypotension

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Objectives We report this case and discuss the possibility of complication of shunt for a long time.

Method (Case report) A 15-year-old man with severe headache, nausea, vomiting, diplopia and drowsiness of 1 week duration was admitted to our hospital. He had previously undergone ventriculoperitoneal shunt because of hydrocephalus after traumatic accident when he was 5 years old. He had a mild trauma on his head with a soccer ball one week ago. On neurological examination, he had the limitations of lateral gazes of both eyeballs, left eyeball predominantly. The MRI of head revealed no specific intracranial lesion. On admitted day, opening pressure was 85 mm H₂O in lumbar puncture. Headache was aggravated and not responded to pain killers. After several weeks without remission of symptoms, we performed radionuclide scintigraphy via the reservoir of shunt. That revealed rapid drainage relatively. We clamped the shunt and observed the complications and alleviating the symptoms. Then we removed the shunt and the patient fully recovered.

Conclusion We report an atypical case of iatrogenic intracranial hypotension caused by shunt overdrainage.

E043

Blink reflex habituation in migraine and tension-type headache

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In this study we determine the role of Blink Reflex (BR) as a neurophysiological method in the differentiation of headache types.

Sixty patients with migraine, sixty with Tension-Type of Headaches (outside and during attacks) and thirty control subjects were examined with the method of BR.

A habituation program was used to deliver paired pulses with an interstimulus interval that ranged from 100 to 600 msec.

We recorded the early R1 and R2 responses after the first stimulus and the late

R2' only after the second stimulus. A comparison between the early R2 and the late R2' was made in various aspects.

Results The R1, R2 and R2' latencies, amplitudes, areas and interstimulus intervals were similar in normal controls and patients with TTH in both symptomatic and asymptomatic phases.

In migraineurs, although R1, R2 and R2' latencies were normal, R2' late response was elicited with shorter interstimulus interval (100–200 msec), in comparison to normal subjects. In contrast, longer (>500 msec) interstimulus intervals were required during the headache phase of migraine.

Furthermore, R2 and R2' amplitudes and surface areas were reduced in patients with migraine attacks, in contrast to free periods.

In conclusion, BR habituation studies show significant differences between migraineurs and TTH plus healthy controls.

BR may play an important role in distinguishing the two aforementioned types of headache.

E044**Comparison of the prevalence of chronic headache in patients with TMD and headache**Norma Fleming¹, JA Sousa², FJ Pereira Jr³, O Nascimento²¹*Pain Clinic, Universidade do Estado do Rio de Janeiro, ²Neurology, Universidade Federal Fluminense, ³TMD-Dentalschool, Universidade do Grande Rio, Brazil*

Objectives Our objective was to investigate the prevalence of chronic headaches and possible differences between TMD group with chronic headache, from the Orofacial pain clinic of the dental school, and a control group of headache patients from the Pain Clinic of the medical school.

Methods We investigated forty one consecutive patients with TMD and headache who visited the Orofacial Pain Clinic of the dental school UNIGRANRIO (Universidade do Grande Rio) e UERJ (Universidade do Estado do Rio de Janeiro), with complaint of headache in the RDC (Research Diagnostic Criteria of TMD) and compared them with forty two consecutive patients who visited the Pain Clinic of the UERJ medical school. The chronic headaches, which occur more than 15 days per month, for more than three months, had occurred in both group, TMD and controls, and were grouped as chronic headache (chronic migraine – HIS 1.5.1, chronic tension-type – IHS 2.3, headache probable medication-overuse headache – IHS 8.2.7). The statistical analyses was made using T-student for proportion. We excluded two cases of HC from the control group because this type of chronic headache didn't occurred in the TMD group.

Results Twenty-one TMD patients had chronic headaches and it had happened in seventeen control patients. Using the T-student for proportions the value was $t = 0.987733$, $p = 0.05$, so there weren't differences between TMD and controls. Then, we investigated the prevalence of chronic migraine with the T-student and the result was that this type of headache was significantly more prevalent in TMD ($t = 2.083$, $p < 0.05$) than in controls.

Conclusion The proportion of chronic headache didn't differ between TMD group and headache control group. Nevertheless, chronic migraine was significantly more prevalent in TMD group than controls. This is especially relevant for the evaluation of possible shared mechanisms on the same time of both pathologies, because it seems that TMD may be a trigger for migraine, and the Trigeminal caudal nucleus may be involved in the convergence.

E045**Impact of early versus late intervention on productivity and clinical disability in migraineurs**Michael 'Chris' Runkin¹, S Landy², S Silberstein³, S Burch⁴¹*HMI, GlaxoSmithKline, ²Wesley Headache Clinic, ³Global Health Outcomes, GlaxoSmithKline, ⁴Jefferson Headache Clinic, USA*

Objective Determine the effect of Early (EI) and Late (LI) Intervention on work productivity and clinical disability in subjects treated with a single-tablet formulation of Sumatriptan with RT TechnologyTM and Naproxen sodium (SumaRT/Nap) during a single migraine attack.

Methods Two sets of identical studies were conducted in randomized, multi-center, double-blind, placebo-controlled, early and late intervention cohorts. EI studies randomized subjects (1 : 1) to Placebo (PBO) or SumaRT/Nap. LI studies randomized subjects (1 : 1 : 1 : 1) to PBO, SumaRT, Naproxen or SumaRT/Nap. Post hoc analyses of productivity and clinical disability were conducted. Lost productivity, activity, and total productivity were assessed 24 hours post dosing. Clinical disability was assessed at 2 and 4 hours in the EI studies and hourly for 24 hours in the LI studies using a 5-point scale from 'normal functioning' to 'required bedrest'. Only SumaRT/Nap treatment groups were compared for these analyses.

Results Study populations [$n = 556$ (EI) and $n = 726$ (LI)] were demographically similar. Subjects in the LI group missed 75% more work hours due to migraines than EI subjects (1.75 vs. 1.0) ($p < 0.003$). When working through a migraine, the EI cohort was significantly more productive (74% vs. 56%) ($p < 0.001$) than the LI cohort. Average total productivity loss was also significantly different: 2.7 hours (EI) versus 4.6 hours (LI) ($p < 0.001$). Clinical disability was significantly different too: more subjects in EI than LI cohorts reported 'normal' functioning at 2 (38 vs. 48%) ($p < 0.004$) and 4 (60 vs 72%) ($p < 0.001$) hours.

Conclusions Early intervention with SumaRT/Nap during a migraine significantly improves productivity and clinical disability when compared to late intervention.

E046**Consistent medication satisfaction with Sumatriptan RT TechnologyTM and Naproxen for acute migraine treatment**Roger Cady¹, J Goldstein², F O'Donnell³, SP Burch⁴, MC Runkin⁴¹*GlaxoSmithKline, ²Headache Clinic, Headache Care Center,*³*San Francisco Headache Clinic, ⁴Ohio University Ortho Neuro, USA*

Objective To determine if a single-tablet formulation of Sumatriptan with RT TechnologyTM and Naproxen sodium (SumaRT/NAP) consistently results in superior patient medication satisfaction versus placebo in migraineurs treating four consecutive migraine attacks.

Methods Two identical randomized, double-blind, placebo-controlled, 4-period cross-over, multi-attack, multi-center, outpatient studies of moderate to severe adult migraineurs were conducted to compare SumaRT/NAP to Placebo. Subjects were asked to complete the 32-item Patient Perception of Migraine Questionnaire-Revised (PPMQ-R) at 24 hours post dosing after four consecutive migraine attacks. The PPMQ-R consists of 3 satisfaction subscales, a total satisfaction score, 3 global satisfaction items, and a 'Tolerability' subscale assessing side effects. Subscale and total scores range from 0 to 100 with higher scores reflecting more satisfaction or higher tolerability. Global items are measured using a seven-point scale ranging from very satisfied to very dissatisfied.

Results PPMQ-R subscale and total scores for patients receiving SumaRT/NAP were consistently high (≥ 67.4) across all attack periods in both studies. The mean percentage of subjects across both trials who reported being satisfied/very

satisfied with SumaRT/NAP overall in each attack period (62.0%, 65.5%, 63.0%, 68.0%) was consistently higher than placebo (30.5%, 39.5%, 39.5%, 36.0%) ($p < 0.001$). Likewise, significantly more subjects across both trials reported being 'consistently satisfied/very satisfied' with the effectiveness of SumaRT/NAP in each attack period (63.5%, 66.0%, 64.5%, and 67.0%) versus placebo (28.0%, 39.0%, 38.5%, and 34.0%) ($p < 0.001$).

Conclusions SumaRT/NAP consistently demonstrated superior patient medication satisfaction in four consecutive migraine attacks when compared to placebo.

E047

Reappearance of absence seizures in a woman treated for persistent idiopathic facial pain by pregabalin

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Objectives Antiepileptic drugs are routinely prescribed in the treatment of pain regardless of any history of epilepsy. We discuss a case of recurrence of epilepsy with pregabalin introduced for an idiopathic facial pain.

Methods A 43 years old female was hospitalised for persistent idiopathic facial pain (13.18.4 in IHS classification) resisting to initial treatment by carbamazepine (400 mg per day). Later this treatment was replaced by a monotherapy with Pregabalin (300 mg per day) during 3 weeks. The first day of hospitalisation we observed frequent episodes of confusion associated with anterograde amnesia and behaviour troubles. The patient had absence seizures diagnosed in childhood and treated with valproate sodium until the age of 25 when the treatment was stopped without any epilepsy recurrence. The EEG revealed a generalised petit mal status with 3-per-second spike-and-wave discharge pattern. Cerebral MRI examination, CSF and standard biology results were normal. The treatment by pregabalin was immediately stopped and replaced by the valproate sodium and we observed a spectacular clinical and EEG improvement.

Discussion Pregabalin and gabapentine have the similar mechanism of action, consisting in the inhibition of voltage dependent $\alpha 2-\delta$ calcium channels. Absence seizures deterioration after gabapentine introduction was previously reported. However, to our knowledge, this is the first case report of petit mal reappearance with pregabalin treatment. **Conclusion** We propose to exclude the existence of any absence seizure before introduction of treatment by the pregabalin, indicated in both epilepsy and neurogenic pain.

E048

Treatment of headaches in the Graeco-Roman world

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Although descriptions of migraine as a separate entity can be found in the texts of Galen and Aretaeus of Cappadocia in the second century CE, treatment of headaches was already recorded and classified a century earlier by Discurides.

His book 'de Materia Medica' is the first pharmacology book in classical antiquity and remained the main reference for centuries.

We reviewed the book to identify if in addition to the analgesics, specific drugs for the treatment of headaches.

A total of twenty-three substances were noted; all were of botanical origin with the exception of one mixture of the ash of the wool of various animals with rose oil that was applied as a plaster on the head.

The plants were used in various forms: plasters, poultices, ointments were applied on the forehead; burning of incense or vapors were used for inhalation; decoctions, ptisans, wine or mixtures with honey were given orally.

Among the various plants recommended by *Dioscurides*, four are still mentioned in alternative medicine recipes: *Papaver rhoes* (corn puppy), *Peucedanum officinale* (hog's fennel), *Mentha sylvestris* (horsemint) and *Ruta graveolens* (rue). This may indicate a distrust of traditional medicine by some patients and their need to search for alternative 'natural' treatments, some of which have survived over the centuries.

E049

Headache as a symptom of acute cerebrovascular disease in emergency department

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Objective To analyse the prevalence and management of patients presenting to the Emergency Department (ED) with headache attributed to cerebrovascular disease (HACD).

Methods A six-month retrospective analysis of all HACD patients presenting at the ED of the University Hospital of Trieste was performed. Demographic data, diagnostic tests, therapies were obtained.

Results Four hundred and fifty-nine patients had a diagnosis of acute cerebrovascular disease in ED setting: ischaemic stroke (54.2%), transient ischaemic attack (28.3%), intracerebral haemorrhage (9.2%), subarachnoid haemorrhage (1.7%), other intracranial vascular disorder (6.6%). Nineteen patients (4.1%) (9 F, 10 M; mean age 45 ± 19 years) had HACD. The frequency of headache was 1.6% among all patients with ischaemic stroke, 3.8% in transient ischaemic attack, 14.3% in intracerebral haemorrhage, and 50% in subarachnoid haemorrhage. Fourteen HACD patients (73.7%) underwent a CT of the skull. Three out of 6 treated HACD patients received specific therapy for headache (NSAIDs plus antiemetics).

Conclusions Headache was an underestimated symptom of cerebrovascular disease in ED setting, probably because rarely investigated. Almost one-fourth of HACD patients didn't undergo a CT of the skull, due to immediate hospitalisation. Only a few HACD patients received a specific therapy for headache. Adequate strategies are needed.

E050**Balint syndrome and chronic daily headache**

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Two patients were reported with Balint neurobehavior disorder in patients with chronic daily headaches.

Evolution showed changes in the pattern of the crisis, these being in crescendo in intensity and frequency.

Physical findings evidenced phenomenology of optic ataxia and optic apraxia with fragmented ocular pursuit and normal ocular saccade.

EEG, CT scan, MRI, and lab studies were performed. Structural injuries were observed in the left parietal occipital region of the brain. Furthermore the two patients showed anosognosia and fabulation without hallucination, seen more in Anton type syndrome disorder.

E051**A self-help program (PROAA) improves quality of life in patients with migraine and/or tension-type headache**Manuel Seijo-Martinez¹, MJ Lozano², M Castro del Río³, J Paz-Esqueite⁴¹*Neurology Service, ²Department of Social Services, ³Preventive Medicine Service, Complexo Hospitalario de Pontevedra, ⁴Neurology, Hospital do Salnés, Spain*

Objective To evaluate the effectiveness of a non-pharmacologic self-help program (PROAA) in the quality of life (QoL) of patients with migraine and/or tension-type headache.

Methods Prospective study in a hospital setting. Patients meeting IHS criteria for migraine and/or tension-type headache were included (period: 2/January/2003 to 31/December/2006). The PROAA program consists of a seven-week personal-training program improving stress-control and anxiety. Inclusion criteria and program application were based on unacceptable control of headache-symptoms. Patients were remitted sequentially and consent was obtained. QoL was measured using the SF-12 questionnaire (Spanish version) before and one month after the program.

Results 167 patients were included: 150 (89.8%) women and 17 men (10.2%). Median age was 37 years. 93 patients (55.7%) had tension-type headache, 47 migraine (28.1%) and 27 (16.2%) both types. For all headache-types, the perceived physical health score (PPHS) before the program was 38.5 ± 9.77 ; after 48.8 ± 7.86 ($p < 0.001$). The perceived mental health score (PMHS) before the program was 31.6 ± 11.23 ; after 47.8 ± 8.53 ($p < 0.001$). For migraine, the PPHS before 37.4 ± 9.96 ; after 48.3 ± 8.50 ($p < 0.001$); PMHS before 33.4 ± 12.97 ; after 48.4 ± 9.02 ($p < 0.001$). For tension-type headache, the PPHS before 39.1 ± 10.30 ; after 48.9 ± 7.60 ($p < 0.001$); PMHS before 31.2 ± 10.61 ; after 48.2 ± 8.14 ($p < 0.001$).

Conclusions Application of the self-help program PROAA significantly improves the quality of life of patients with migraine and/or tension-type headache. It may be of value as a non-pharmacologic adjunct therapy in these patients.

E052**Confirmation of the association between SNPs and haplotypes of the HCRTR2 Gene and Cluster Headache**Innocenzo Rainero¹, S Gallone², E Rubino¹, W Valfrè¹, L Savi¹, L Pinessi¹¹*Department of Neuroscience, Neurology II – Headache Center, Italy*²*Department of Neuroscience, Neurology II – Headache Center, Italy*

Objectives We recently showed a significant association between the G1246A polymorphism of the hypocretin receptor-2 (HCRTR2) gene and cluster headache (CH). This association was confirmed in a study from Germany but was not replicated in a dataset of CH patients of Danish, Swedish, and British origin. To further evaluate this association we performed a meta-analysis of previously published studies, we genotyped our patients for additional intronic SNPs of the HCRTR2 gene, inferring gene haplotypes, and we searched for gene mutations.

Methods Meta-analysis of published case-control studies was performed using Review Manager 4.2. Pooled odds ratios (ORs) were estimated using both random (RE) and fixed effects (FE) models. Then, we genotyped our populations (109 CH patients and 211 controls) for five different polymorphisms, selected from the SNPs database of NCBI. Haplotypes of the gene were inferred using the PHASE program. Complete HCRTR2 gene sequencing was undertaken for 15 CH patients.

Results Allele G of the G1246A HCRTR2 polymorphism resulted significantly associated with CH (FE OR 1.58; C.I. 95% 1.27–1.95 – RE OR 1.58; C.I. 95% 1.27–1.95). Four additional intronic polymorphisms of the HCRTR2 gene resulted significantly associated with CH. The GTAAGG haplotype resulted more frequent in cases than in controls (OR: 3.68; 95% C.I. 1.85–7.67). In the genotyped patients, no deleterious sequence variants of the HCRTR2 gene were detected.

Conclusions The present study confirms that the HCRTR2 gene significantly modulates the risk for cluster headache and strengthen the hypothesis that the hypocretinergic transmission may be involved in the pathogenesis of the disease.

E053**Optic neuritis and status migrainosus**

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Dull headache or orbital pain may precede optic neuritis, however, status migrainosus is a rarely reported manifestation. A 29-year-old woman visited emergency room due to severe, pulsating headache localized to right temporal area. The headache was persistent for more than 72 hours and recurrent nausea/vomiting was associated. She also complained of visual blurring. Since 2 weeks before admission, she also had suffered from bilateral orbital pain aggravated by eye movement, however, visual symptoms were absent at that time. She was previously healthy, and had no history of migraine or recurrent headache or visual symptoms. On neurological examination, left apparent pupillary defect was detected and visual acuity was decreased to 0.5 on both eyes.

Brain and orbit MRI was normal except for suspicious increased contrast enhancement on left orbital area. Visual evoked potential study was abnormal, suggestive of left optic nerve lesion. CSF study showed lymphocytic pleocytosis with normal protein and glucose level. Initially, she was treated with NSAIDs or triptans, which were not responsive at all. After intravenous dexamethasone injection followed by oral prednisolone (30 mg/day), headache was dramatically improved. After 1 month schedule of prednisolone therapy, follow-up tests of visual function are awaited. Whether it is a by-chance association or an unusual manifestation of optic neuritis will be clarified by further reports or case series. Careful history taking of visual symptoms and detailed neurological examination of visual function is recommended in patients with probable status migrainosus.

E054

Sporadic hemiplegic migraine = postraumatic migraine?

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Background Sporadic Hemiplegic Migraine (SHM) is rare and most frightening form of migraine. The relation of SHM with postraumatic migraine is not confirmed.

Objective To describe a difficult case of SHM as a possible case of postraumatic migraine.

Methods A 21 year (y) old man was hospitalized with attack, when he suddenly begun to feel diplopia, lost consciousness for a few minutes and after developed left hemiparesis and severe headache.

The migraine with (MA) and without vision aura (MWA) started from 14 y of his age. At the age of 19 he experienced light head trauma (HT). Just after he lost consciousness, developed nausea and left hand paresis. The symptoms lasted for 2 days. During period of 1 y after HT he experienced 3 attacks of headache, loss of consciousness and left hemiparesis with several days duration. There were no attacks during next 1 y period.

During the hospitalisation the attack was treated with analgetics, NSAIDs, diuretics, steroids. The headache/hemiparesis was gone after 2/12 days, but just 1 day after, the same attack was repeated and lasted 2/7 days. For prophylactic treatment the patient begun to use verapamil. During 6 months after the hospitalisation the patient is attack free.

Results The headache trauma provoked the transformation of MA and MWA to SHM attacks. There were no changes revealed in investigations (MRA, angiography, EEG etc.) The suggested in literature attack treatment was successful. Prophylactic treatment with verapamil was preventive.

Conclusion A head trauma could provoke the transformation of MA and MWA to SHM.

E055

Attacks of loss of consciousness and atonia after hypothalamic stimulation in cluster headache

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Objective Deep brain stimulation of the inferior posterior hypothalamus has been shown to be an effective therapy in therapy resistant cluster headache (CH). We report a patient with attacks of loss of consciousness and atonia after implantation of deep brain electrodes.

Case presentation A 42-year-old female with chronic therapy refractory CH underwent electrode implantation for right hypothalamic stimulation, with diminishing benefit over 2 years.

Four months after implantation the patient first suffered from attacks with sudden loss of consciousness and fall to the ground, lasting several seconds, with prompt reorientation afterwards; no triggering factors could be identified. On valproate or topiramate, the attacks ceased. After discontinuation of the stimulation, topiramate was stopped. After 6 months, attacks reoccurred. As a new feature, they were followed by CH. Further investigations including CCT, tilt-table-test, orexin levels, and video-surface-EEG with ECG of an attack did not add valuable information. On valproate attacks stopped.

Discussion The attacks of loss of consciousness and atonia might be explained by epileptic seizures due to an intracerebral lesion caused by the electrodes. The regularly associated CH points towards hypothalamic involvement.

Conclusion Attacks of loss of consciousness and atonia of possibly epileptic origin might be a side effect of deep brain stimulation in CH.

E056

A study of cranial autonomic symptoms in primary headaches

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Background Cranial Autonomic Symptoms e.g., lacrimation, conjunctival injection, periorbital swelling and rhinorrhea are commonly associated with certain primary headaches and may be related to central sensitization. Moreover, central sensitization of trigeminal nucleus has been reported both in migraine and TTH. Hence, it is not illogical to expect CAS in primary headaches other than TAC.

Methodology A survey of primary headaches was conducted in school students of ninth to twelfth grades with the help of a questionnaire. The questionnaire was based on the ICHD-2 criteria and its validity has been established in clinic's population.

Information regarding physical health was gathered from the students and corroborated from the school's medical record. The students were explained the rationale for the study by trained psychiatrists and their oral consent was

taken prior to administration of the self-reported survey questionnaire. Individual items of questionnaire were explained sequentially and students were asked to respond on each question immediately after it was explained to them. Moreover, if any of the students raised any query, it was resolved immediately.

Afterwards, the diagnosis was made on the basis of information gathered in the performa and if required, the students were contacted individually to confirm the history. Statistical analysis was carried out with the help of SPSS v. 11.0. Chi-square test was applied on the categorical variables.

Results Prevalence of headache in this sample was 53.2% and prevalence of CAS was 27.3% in general.

Red eye was more prevalent in males (18.5% males versus 10.4% females; $p < 0.001$). It was also associated with history of disabling headache ($p = 0.004$), particularly increased frequency since onset ($p = 0.001$); longer duration of each episode (more than 24 hours; $p = 0.01$). It was most commonly seen in TAC (54.5%) followed by migraine (17.2%), unspecified headaches (13.2%) and TTH (7.7%); $p < 0.001$.

Lacrimation was prevalent in subjects, in whom the duration of each headache episode has increased since onset ($p = 0.015$), who had yawning as a premonitory symptom ($p = 0.006$), and in TAC (63.6%) followed by migraine (31.3%), unspecified headache (22.1%) and TTH (18.5%); $p < 0.001$.

Periorbital swelling was most common in subjects whose headache became disabling since onset ($p = 0.04$) and in subjects with TAC (24.2%) followed by migraine (8.6%), unspecified headache (5.9%) and TTH (24%); $p < 0.001$.

Conclusion Cranial autonomic symptoms are most prevalent in TAC but they are also common in migraine and TTH sufferers. Different autonomic symptoms are associated with different headache characteristics and it appears that they develop independent of each other.

E057

MRI and MR-venography in patients with pseudotumor cerebri: reversibility of intracranial venous sinus stenoses

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Objectives To distinguish between idiopathic and secondary intracranial hypertension by the means of cranial MRI and MR-venography.

Methods 14 Patients with typical signs and symptoms of pseudotumor cerebri were examined. Cranial MRI with special emphasis on the optic nerve sheaths and the hypophysis and phase contrast venous MR-angiography was performed when CSF pressure was documented to be increased on lumbar puncture. A second MR examination was done after elevated CSF pressure was reduced to normal levels. Treatment included oral acetazolamide (8/14) or surgical shunting procedures (n = 6/14). In the follow up of patients (1–22, mean 6 months) clinical data and follow up MRIs were correlated.

Results MRI / MR venography of all patients showed intracranial venous stenoses in the initial examination.

Radiological signs of increased intracranial pressure such as widening of the optic sheaths and 'empty sella' were in all patients in accordance with elevated pressure on lumbar puncture. In 10/14 patients, CSF diversion lead to partial or total abolishment of intracranial sinus stenoses, indicating that intracranial pressure induced the stenosis and not vice versa. In these patients, signs of elevated intracranial pressure were reversed. Follow up MRI was in accordance with clinical signs. In 4/ 14 patients, venous sinus stenoses and signs of increased intracranial pressure prevailed.

Conclusions MRI and MR-venography prior to and after CFS diversion can help diagnosing pseudotumor cerebri and distinguishing between idiopathic and secondary intracranial hypertension. It can be used as a valuable non-invasive tool in the follow up of patients.

E058

Orofacial manifestation of migraine

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Objective Pain in migraine is usually localized in the 1st trigeminal division and typically associated with hypersensitivity and autonomic symptoms, respectively. We observed patients fulfilling the diagnostic ICHD-II criteria for migraine, but – rather than headache – their presenting complaint is pain in the distribution of the 2nd/3rd trigeminal division.

Patient 1 A 44 year-old female has experienced throbbing episodic pain localized always in the left mandible starting off as a diffuse toothache. She reports accompanying phonophobia and photophobia, but denied nausea. Attack therapy with zolmitriptan 2.5 mg resulted in significant pain relief within 30 minutes, and complete relief within an hour.

Patient 2 A 48 year-old female reported pain episodes since early childhood beginning with unilateral throbbing pain around the temple. They are occasionally preceded by lateral visual field restriction. Within an hour the pain usually spreads to the right side of the face with the most intense ache persisting in the maxillary front teeth until the end of the attack. These attacks are accompanied by phono- and photophobia. Severity is increased by physical activity. A combination drug containing ergotamine and diclofenac, had been taken with satisfactory pain relief.

Conclusion Our patients as well as similar cases in the literature suggest that migraine pain may not be restricted to the first trigeminal division but extend to the maxillary and mandibular divisions, with an underlying pathophysiology distinct from persistent idiopathic facial pain. Establishing the correct diagnosis is critical for successful treatment in these patients and prevents inadequate dental treatment.

E059

Cluster-like headache in patient with central pontine myelinolysis

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Backgrounds It has been suggested that trigemino-cervical complex mechanisms have a role in the Trigeminal Autonomic Cephalgias (TAC) including cluster headache. To our best knowledge, there is no report that cluster-like stabbing headache can develop in Central Pontine Myelinolysis (CPM). We report our experience with a case of CPM presenting as cluster-like headache.

Case A 60-year-old male patient was admitted with 1 month history of frequent episodic stabbing headache lasting about an hour. The headache developed repeatedly on left hemicranium with subjective complaint of eyelid swelling. He had undergone the bladder cancer operation 2 years ago. On neurologic examination, he had no focal neurologic deficits, and no trigger point, tenderness or allodynia on the pain area. His blood pressure was elevated (170/90 mmHg) and the serum sodium level was decreased (124 mEq/L). There were confluent hyperintensity pontine lesions extending to left cerebellum, medulla and midbrain on brain MRI, which was thought to CPM. Although hyponatremia categorized in SIADH through evaluation was corrected within 2 days and the blood pressure was controlled, the headache had sustained until 2 months later, when the follow-up MRI showed much improvement of the lesions.

Conclusion Our case of cluster-like headache was attributed to nothing but the pontine lesions thought to be CPM, which has temporal correlation with headache. It may be supposed that aberrant neural discharge or disequilibrium of vasodilator peptides come out from the trigeminal root entry zone involved in the rostral dorsal pons may have a role in the pathogenesis of the headache.

E060

Osmophobia in TACs and other primary headaches

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We investigated the presence of osmophobia in TACs and other primary headaches (OPHs), to evaluate the importance of this symptom on their differential diagnosis of primary headaches. We recruited 104 consecutive patients from our Headache Centre (73 M, 31 F; median age 41.7 years; range 16–75 years), of whom 52 had episodic cluster headache (ECH), 9 chronic cluster headache (CCH), 7 probable cluster headache (PCH), 2 chronic paroxysmal hemicrania, and 35 OPHs (13 patients had primary stabbing headache, 2 primary cough headache, 8 primary exertional headache, 3 primary headache associated with sexual activity, 5 hypnic headache, 3 primary thunderclap headache, 1 hemicrania continua). Among them, 7% with cluster headache (CH) reported osmophobia during the attacks; none of OPHs patients suffered this

symptom. Interestingly, among the 5 osmophobic patients with CH, 4 (80%) also reported nausea or phono- and photophobia during the attacks; whereas, among the 63 non osmophobic patients with CH, only 5 (8%) reported these neurovegetative symptoms. Therefore, osmophobia seems to be present in the form of CH sharing neurovegetative symptoms with migraine. Considering that in a previous study we found the presence of osmophobia in over than 40% of migraineurs vs none of the patients with episodic tension-type headache, we confirm that this symptom is a good candidate as a new criterion for the diagnosis of migraine, as proposed in the appendix of the ICHD-II, since it helps to clinically differentiate migraine also from OPHs and, apart a small, peculiar subgroup, from CH.

E061

Validation of a very brief self-administered questionnaire for cluster headache (CH) cases screening

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Objective Cluster headache remains substantially under-diagnosed and undertreated. Early neurologic referral is indicated in patients with a suspected diagnosis of CH so that management can be optimized and unnecessary procedures avoided. The aim of this study was to validate a brief self-administered questionnaire designed to screen CH cases.

Methods The review of clinical studies led us to identify the 3 more prevalent criteria of the second edition of the IHS classification (ICHD II) for all forms of CH (episodic and chronic forms). These 3 criteria were: strictly unilaterality of pain, attacks duration <180 min if untreated, ipsilateral conjunctival injection and/or lacrimation. These criteria were transformed in questions formulated in such a way that they could be self-administered and easily understood. Answer to each question was yes or no. Patients were unaided. The self questionnaire was compared to the gold standard, the ICHD II criteria used by specialists at the university of Bordeaux headache center. The self-questionnaire was consecutively and prospectively submitted to 37 cluster headache and 59 patients with migraine. We calculated the sensitivity and specificity for the 3 questions and for each pair of questions.

Results The three-item questionnaire had a 78.4% sensitivity and a 100% specificity. The two-item questionnaire only using the attacks duration associated with conjunctival injection and/or lacrimation was more sensitive (81.1%) with the same specificity (100%).

Conclusion This two-item questionnaire could be a useful tool for screening cluster headache cases in general population.

E062**Cutaneous allodynia in episodic cluster headache does not affect the outcome of parenterally administered triptan**Carl GH Dahlöf¹, Jan-Erik Hardebo²¹Inst. of Neuroscience and Physiology, SU, Gothenburg Migraine Clinic,²Neurological Department, University of Lund, Sweden

Introduction Allodynia is an abnormal sensory state where normally innocuous stimuli are felt as painful. Signs and symptoms of cutaneous allodynia are surprisingly common in migraineurs and the reported prevalence varies between 30 to almost 90%. Furthermore, it has been verified that migraineurs who claimed that they typically develop cutaneous allodynia during their attacks could be confirmed to be allodynic by Quantitative Sensory Testing (QST) in about 85% of the cases.

Patients with cluster headache may also describe cutaneous allodynia during their attacks. This increased skin sensitivity is by and large reported to be located in the periorbital area involving the cutaneous distribution of the first divisions of the trigeminal nerve and ipsilaterally to where the pain is perceived.

Objective The primary aims of the present study were to find out the prevalence of subjective cutaneous allodynia among patients with episodic cluster headache (N = 91) and if presence has any impact on their acute symptomatic treatment with parenteral administration of a triptan.

Results We found subjective cutaneous allodynia (tenderness over the eyebrow/temple, 1st to be present division of the trigeminal nerve) ipsilaterally in 54% of the patients with episodic cluster headache and that its existence did not affect the treatment outcome.

Conclusion It appears that cutaneous allodynia can be seen in different forms of primary headache and that its presence does not alter therapeutic outcomes.

E063**Bath headache – a Brazilian case**João José Carvalho¹, FJA Mont'Alverne², GLS Malveira²¹Prontoneuro Neurologistas 24 Horas, ²Neurology, Prontoneuro 24h, Brazil

Background Bath headache has been described as a form of thunderclap headache, triggered or worsened by direct contact of the scalp and face with water. In cases with completely normal complementary investigation, it is considered a primary headache, but it can be a phenotype of cerebral angiopathy with vasospasm.

Case report A 52 years-old female Caucasian patient presented with a 48 hours history of sudden, excruciating, continuous, diffuse, non-pulsatile and refractory headache, which had started right after a warm water shower. This factor had been considered casual, but became clear after the second contact with water over the head and face, a couple hours later. A glomus timpanicus had been resected from left ear 15 years earlier, and she also had migraine without aura (IHS 2003). No family history was reported, and she had completely Caucasian ancestry. Neurological examination was

normal, as well as non-contrast head computerized tomography (CT). Lumbar puncture revealed completely normal cerebrospinal fluid (CSF), with normal CSF opening pressure. Magnetic resonance (MR) imaging was also unremarkable. Digital cerebral angiography (DCA) showed multi-segmental arterial constrictions, without other structural abnormalities. Symptomatic relief was initially unsuccessful. Treatment regimen was nimodipine, aspirin and prednisone. Pain took four weeks to subside. Patient is now painless.

Discussion CVA has a broad spectrum of presentation, from moderate unexplained headache to multiple strokes. However, specific triggering factors are not necessarily present. Indeed, this case depicts consistently the trigemino-vascular system, from the very peripheral extremity to its vascular component.

E064**Headache attributed to spontaneous intracranial hypotension in a large population**Eliana Mea¹, L Chiapparini², M Savoardo², G Bussone¹, M Leone¹¹Neurology and Headache Centre, ²Neuroradiology, C Besta Neurological Institution, Italy

Objective Early recognition of spontaneous intracranial hypotension (SIH) may avoid dangerous worsening due to delayed diagnosis. Orthostatic headache is the main symptom in SIH and may be of great help in the early diagnoses of the syndrome. Our aim was to report on headache characteristics in 90 consecutive patients referred at our centre and diagnosed as SIH.

Methods Patients were referred to our Institution between 1993 and 2006: 55 (61%) women, mean age 45 years (range 15–71). The International Headache Society (IHS) criteria for headache attributed to SIH were applied. Brain enhanced MRI confirmed the SIH diagnosis in all patients. Headache characteristics were obtained by direct semistructured interview; in a minority of cases detailed information on headache characteristics was retrospectively obtained through phone call.

Results All SIH patients suffered from headache. In 57 (63%) patients the headache worsened within 15 minutes and in 12 (13%) worsened 15 minutes after standing position. In 20 (22%) patients, the headache was not related to position. Nine (32%) out of the twenty-eight patients who underwent blood patch (BP) improved. Only 3 patients (3%) fulfilled the IHS criteria for headache attributed to SIH.

Conclusions This study shows that the IHS criteria did not allow to properly diagnose many of our SIH patients. This seems mainly due to the fact that many patients did not receive nor improve after BP. A revision of these criteria may be necessary.

E065

Neuroimaging preferences of Spanish neurologists in the presence of red flags in headache patients

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Objective To establish the neurologists' preferences in clinical practice for a particular neuroimaging technique in the presence of red flags in headache patients.

Methods 79 neurologists from the Spanish Society of Neurology were interviewed about their preferences for brain CT scan or MRI when dealing with headache patients with red flags. They were also questioned about the probability of finding abnormalities on neuroimaging in these patients. This study was supported by Menarini, Spain.

Results Most neurologists choose CT scan in the presence of sudden-onset headache (79% of participants), primary headache refractory to therapy (66%), recent worsening (63%), and increasing pain intensity or frequency (58%). They prefer MRI with headaches precipitated by cough, posture or exercise (91%), atypical or unclassifiable (66%), or strictly unilateral (62%). In the presence of fever, papilledema, meningismus or vomiting, no preference was established (50%). The highest probability of abnormal findings was expected in patients with sudden-onset headache (70% of participants), as well as with fever, papilledema, vomiting or abnormal neurological exam (63%). The likelihood was much lower in headache precipitated by cough, posture or exercise (19%), primary headache of increasing severity (5%), atypical or unclassifiable headache (1%), and recent worsening (1%).

Conclusions A differential choice of neuroimaging is observed depending on the type of headache-associated red flag in clinical practice. Although many red flags are suggested in headache patients, practicing neurologists expect neuroimaging abnormalities in only a minority of them.

E066

Main criteria used to request neuroimaging for patients with not acute headache

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Objectives To analyze the clinical practice of 79 neurologists in the use of neuroimaging for patients with not acute headache.

Methods During 2006, a total of 79 neurologists participated in 9 workshops. All workshops followed the same methodology. Participants were inquired about the main criteria considered in order to request a neuroimaging test, and which one, in patients with not acute headache. The debate was led

by a facilitator using the Metaplan® method. The study was supported by Menarini (Spain).

Results According to the participants, the main criteria to request neuroimaging tests were (62% of contributions): Detection of an abnormal physical exam or the presence of focal neurological symptoms (31%); patient's request (16%) and changes in the clinical characteristics of the pain profile (15%). Less frequent criteria were the presence of other health problems, absence of clinical response to treatment (6%), presence of atypical headache (5%), of recent appearance (4%) or the aggravation of pain with Valsalva or positional changes (4%) and the headache that does not fulfill IHS criteria for primary disorders (2%).

Conclusion In general the true clinical practice for ordering neuroimaging tests in patients with headaches follow the guidelines. The demand of neuroimaging from the patient may become a source of pressure to the neurologist, who may well order more tests than what is absolutely necessary.

E067

Emergency headache calls and the new moon

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Objectives The objective was to exam the relationship between emergency calls related to headaches and the lunar cycle.

Background The moon's effects on health have been recognized since the days of the Pax Romana. There are frequent references to emergency room utilization, birth of babies and psychiatric illness and the full moon. Only seizures, schizophrenia and sleep disorders research studies have corroborated this view.

During 25 years of headache practice, it seemed that there was an overabundance of emergency calls related to the New Moon.

Methods The computer recorded call records of the Clinic, which lists the reason for calls, were reviewed for 2006. Correlations to the four lunar phases were made. Additional correlations were made to days of the week and month of the year. Calls were specifically related to a headache complaint.

Results There was a significant increase in headache emergency calls related to the New Moon with 4.9 calls per night ($p > 0.001$ CI 4.24, 5.56). Significant differences were also found between the other lunar phases. The highest frequency of calls occurred during the New Moon in November with an excess of nine calls per night.

Conclusions This is the first study to suggest that the New Moon may have health implication, at least regarding headache.

E068**Factors associated with moderate to severe depressive symptoms in migraineurs**

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Migraine has a significant psychological burden on the sufferers, suggested by the high comorbidity with anxiety as well as symptoms of depression. In this study 102 patients with International headache Society (IHS)-defined migraine were investigated to identify factors associated with moderate to severe depressive symptoms. At the time of the examination, all the patients were pain-free or experienced only little pain. Patients diagnosed with depression, taking antidepressant medication, or having non-migraine disabling diseases were excluded. The Self-Rating Depression Scale (SDS) was used to assess the presence and severity of depressive symptoms. A multivariate logistic regression analysis was carried out with sociodemographic (age, gender, education, socioeconomic status, marital status) and clinical (hypertension-comorbidity, migraine-related disability, headache frequency, pain intensity, presence of aura, headache duration) independent variables, and moderate to severe depressive symptoms acting as the dependent variable. Moderate to severe depressive symptoms were present in 18.6% of the patients. The mean SDS score was 42.1 ± 15.4 . Our findings indicated that an increased headache frequency (OR: 1.5, 95%CI: 1.1–2.0), low socioeconomic status (OR: 4.5, 95%CI: 1.3–15.5), comorbid hypertension (OR: 3.4, 95%CI: 1.1–10.4), and older age (OR: 1.2, 95%CI: 1.0–1.4) were associated with severity of depressive symptoms. These findings may have potential therapeutic implications for improving psychopathology in migraine.

E069**A review of inpatient intravenous dihydroergotamine (DHE) for the treatment of headache**

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Objectives To evaluate the efficacy of inpatient intravenous DHE on headache frequency and duration.

Methods From 2001 to 2006 at the Institute of Neurology, 446 course of DHE were given. Charts from 162 treatments were retrospectively reviewed and those patients were interviewed.

Results Of patients interviewed, 114 had chronic migraine (CM), 34 had chronic cluster headache (CCH), three had another trigeminal autonomic cephalgia, eleven had new daily persistent headache (NDPH), one had hemicrania continua (HC). Nine patients received incomplete courses due to adverse effects. 113 inpatient records provided information regarding headache freedom upon completion of the DHE course. At discharge, 37% of migraine patients, 64% of CH patients, and one HC patient were headache free. Mean time to follow up of all 162 patients was 11 months. Following dis-

charge from hospital 86% of migraine patients reported attack freedom. Of those, 29% remained attack free for one or more months. When attacks returned, 62% reported >50% reduction in frequency. Of CH patients, 69% reported attack freedom following discharge from the hospital. Of those, 23% were attack free for one or more months. When attacks returned, 45% reported >50% reduction in frequency. The HC patient reported attack freedom following discharge from the hospital.

Conclusions In our review, intravenous DHE is an effective at providing headache relief for a proportion of patients with CM and CH.

E070**Two cases of cluster-like headache secondary to carotid cavernous fistula**

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Background Cluster headache is the most frequent trigeminal autonomic cephalgia. Cluster-like headache has been described related to intracranial pathologies, usually with atypical features.

Cases The first patient, a 51-year-old woman presented with a 1-month history of left retroorbital pain. The attacks were accompanied by ipsilateral tearing, nasal congestion, and conjunctival injection lasting for 2 hours. Between those severe attacks background headache persisted. After 2 weeks left third and sixth nerve palsy developed. Brain MRI showed prominent vascular flow voids at the left cavernous sinus (CS) and enlarged superior ophthalmic vein. Conventional angiography showed dural carotid cavernous fistula (CCF). After intravascular embolization, her headache subsided. The second patient, a 71-year-old woman with hypertension noted diplopia without pain. Neurologic examinations were normal except for left third nerve palsy. Brain MRI, MRA and cerebrospinal fluid study were unremarkable. Three weeks later, she visited a neurologic clinic for intermittent severe left orbital pain with autonomic symptoms that lasted for an hour. The follow-up MRI showed abnormal vascular flow voids at the left CS. Angiographic findings showed bilateral dural CCF, leaking predominantly from left side. After selective embolization, she complained no headache.

Comments Headache in these patients could be attributed to irritation of the CS portion of trigeminal nerve by local high venous pressure and following abnormal activation of the trigemino-autonomic pathway. Unilateral deep orbital pain with autonomic features, cluster-like headache, could be a part of signs of CS lesion. Careful clinical diagnosis and imaging evaluation are mandatory before treatment of cluster headache.

E071**Family medicine residents feel less comfortable managing migraine than other common medical conditions**Jonathan Gladstone¹, A Grant²¹Neurology, University of Toronto, ²Medicine, Dalhousie University, Canada

Objectives To compare family medicine residents self-reported comfort with the diagnosis and management of migraine compared to other common chronic medical conditions.

Methods Questionnaires were distributed as a pre-test to University of Toronto Family Medicine residents attending a headache education seminar in Toronto, Canada at the end of the first or second (final) year of training. Residents were asked to rate whether they were 'very comfortable', 'comfortable', or 'uncomfortable' with the diagnosis and management of 6 chronic conditions: asthma, diabetes, depression, hypertension, migraine and osteoarthritis.

Results Fifty-four residents completed this section of the survey (100% response rate). 31% were 'very comfortable' with diagnosing and managing hypertension, 22% with osteoarthritis, 15% with diabetes, 11% with asthma, and 6% with migraine. 82% of residents were 'comfortable' with diagnosing and managing asthma, 78% with diabetes, 67% with hypertension and osteoarthritis, and 44% with migraine. 50% of residents reported that they were 'uncomfortable' with the diagnosis and management of migraine, 11% with osteoarthritis, 7% with asthma and diabetes, and 2% with hypertension. Correspondingly, family medicine residents were significantly less likely to report that they are very comfortable diagnosing and managing migraine compared to each of the five other chronic conditions investigated ($p < 0.05$).

Conclusions This sample of family medicine residents reported that they felt significantly more uncomfortable diagnosing and managing migraine compared to five other common chronic medical conditions seen in primary care.

E072**Family medicine residents and triptans: is there a knowledge gap?**Jonathan Gladstone¹, A Grant²¹Neurology, University of Toronto, ²Medical School, Dalhousie University, Canada

Objectives Triptans have revolutionized migraine treatment, but they are often underutilized or inappropriately used in primary care. This study investigates the knowledge level of family medicine residents about triptans in Canada, and contraindications to their use.

Methods Questionnaires were distributed as a pre-test to University of Toronto Family Medicine residents attending a headache seminar in Toronto, Canada. As part of the survey, they were asked to list the available triptans in Canada, their formulations and the contraindications to triptan use.

Results Sixty-three residents responded (100% response rate). Most residents (90%) correctly named ≥ 1 triptan (of a total of six available in Canada); however, 41% of respondents

could name only one. None of the residents named more than four triptans. Sumatriptan was the most frequently identified (named by 81%) followed by zolmitriptan (40%), rizatriptan (32%), naratriptan (8%), almotriptan (6%) and eletriptan (2%). With regard to formulations, nasal sprays were identified as a formulation by 11% (sumatriptan) and 6% (zolmitriptan) and dissolving wafers by 8% (for both rizatriptan and zolmitriptan). Respondents most commonly named angina/history of myocardial infarction/coronary artery disease (31%), uncontrolled hypertension (21%) and triptan hypersensitivity/allergy (16%) as contraindications to triptan use; less than 10% listed any of the other contraindications.

Conclusions Despite their proven benefit in acute migraine management, more than 50% of family medicine residents surveyed were unable to name more than one triptan, only a small minority was aware of the variety of available formulations, and the residents generally lacked full knowledge of the contraindications to triptan use.

E073**To investigate family medicine residents' awareness of therapeutic options for migraine prophylaxis**Jonathan Gladstone¹, A Grant²¹Neurology, University of Toronto, ²Medical School, Dalhousie University, Canada

Objectives To investigate family medicine residents' awareness of therapeutic options for migraine prophylaxis.

Methods Questionnaires were distributed as a pre-test to University of Toronto Family Medicine (Primary Care) residents attending a headache education seminar in Toronto, Canada. Residents were at the end of either their first or second (final) year of residency training. As part of the questionnaire, residents were asked to list the available therapeutic options for migraine prophylaxis.

Results Sixty-two residents responded to this question (100% response rate). The most frequently cited class of medication were beta-blockers named by 48/62 (77%); 22/62 listed 'beta-blocker', 16/62 propranolol, 5/62 metoprolol, 4/62 atenolol, 1/62 nadolol. Next was the tricyclic antidepressants identified by 25/62 (40%); 14/62 listed amitriptyline, 8/62 'TCAs', 2/62 nortriptyline, and 1/62 imipramine. Calcium-channel blockers were cited by 20/62 (32%); 'calcium-channel blockers' were noted by 18/62, verapamil by 1/62 and amlodipine by 1/62. Anti-convulsants were noted by 15/62 (24%); 4/62 listed 'anti-epileptics', 4/62 valproic acid, 4/62 gabapentin, and 3/62 topiramate. NSAIDs were mentioned by 14/62 (23%), SSRI's by (5%) and feverfew by 1/62 (2%).

Conclusions This study demonstrates that family medicine residents have a knowledge gap in their awareness of the available therapeutic options for migraine prophylaxis. The American Migraine Prevalence and Prevention Study highlight that only a minority of patients who are candidates for 'offering or considering prophylactic therapy' are currently utilizing a preventative therapy. Lack of familiarity with the available therapeutic options for migraine prophylaxis may be one of the barriers for appropriate utilization of preventative therapy.

E074**Self-diagnosis and self-treatment of headache in Canadian medical students**Allison Grant¹, Allan Purdy², J Gladstone¹¹Neurology, University of Toronto, ²Neurology, Dalhousie University, Canada

Objectives To investigate the prevalence of headache among 1st and 2nd year medical students and to gain an appreciation for their headache self-treatment strategies.

Methods Questionnaires were distributed to 185 medical students at Dalhousie University in Halifax, Canada.

Results 163 students responded (88% response rate); 44% male and 56% female, mean age 25.7 years (SD 3.2). 1-year prevalence of headache was 92%. 1-year prevalence of self-reported tension-type headache (TTH) was 73%, sinus headache 27%, migraine 26%, cluster 5% and cervicogenic 3%. For self-treatment of TTH, over-the-counter (OTC) agents were utilized by 88%; 70% used Acetaminophen and 70% NSAIDs. Acetylsalicylic acid (19%), acetaminophen + codeine (6%) and acetaminophen + caffeine (4%) were also utilized. Massage was the alternative therapy most often utilized for TTH (9%). None of naturopathic, homeopathic, chiropractic manipulation or acupuncture was utilized by $\geq 1\%$ of students. For migraine, OTC analgesics were utilized by 90% of respondents and prescription medications by 21%. Migraine treatment utilized in the previous year included NSAIDs (63%), acetaminophen (53%), triptans (13%), acetylsalicylic acid (13%), acetaminophen + codeine (13%) and acetaminophen + caffeine (8%). Massage therapy (5%), acupuncture (5%), chiropractic manipulation (2%) and naturopathic/homeopathic/herbal therapy (2%) were infrequently utilized.

Conclusions Pre-clerkship medical students have a one-year headache prevalence of $>90\%$. Inflated rates of self-diagnosed sinus headache (27%), cluster (5%) and cervicogenic headache (3%) suggest their lack of familiarity with the relevant diagnostic criteria. Medical students' pharmacologic self-treatment of TTH and migraine is similar to the general population; in contrast, aside from massage, use of allied health professionals (chiropractors, naturopaths/homeopaths, and acupuncturists) is uncommon.

E075**Headache in professional soccer players of Italian 'Serie A'**Federico Mainardi¹, E Alicocco², F Maggioni³, F Devetag⁴, C Lisotto³, G Zanchin³¹Tor Vergata University, Sports Medicine, ²Neurological Unit,³Department of Neurosciences, Headache Centre, ⁴SS Giovanni e Paolo Hospital, Venice, Headache Centre, Neurological Unit, Italy

Objectives To assess the occurrence of primary headaches in soccer players of the first Italian Soccer League division ('Serie A').

Methods An anonymous questionnaire was used: in the retrospective part, the presence of headache was investigated; in the second, the occurrence of headache was evaluated prospectively. It was filled at regular intervals during the summer athletic preparation (time 0, baseline), and then at the

championship days 1, 8, 16, 24, 32; informations were completed with a direct interview and general and neurological exams.

Results Eighty-three players, belonging to four teams were involved; four of them changed football team during the season and so did not complete the study: all of the remaining denied the presence of headache in their personal history and during the study championship until day 16. Three cases (3.6%) of headache were found thereafter, with features fulfilling ICHD-II criteria for episodic tension-type headache (ETTH). Among them, an important and sustained physical effort was reported as aggravating factor in one case.

Conclusions Among a sample of professional soccer players of Italian first division championship, the occurrence of headaches is very unusual with respect to the general population, and represented by ETTH. The probable reason is that migraineurs or persons suffering of other forms of recurrent headaches are not able to follow this professional career.

E076**Episodic hypnic headache**Federico Mainardi¹, A Palmieri², C Lisotto³, G Zanchin⁴¹San Vito al Tagliamento Hospital, Headache Centre, ²SS Giovanni e Paolo Hospital, Venice, Headache Centre, Neurological Unit, ³San Donà di Piave Hospital, Headache Centre, ⁴Department of Neurosciences, Headache Centre, Italy

Case 1 A 63 years-old woman reported 2 years of sporadic episodes of a dull, severe headache in the vertex, only during sleep, that awakened the patient, with a complete remission within 30 minutes and without any accompanying signs or symptoms. Headache recurred with a frequency of one episode every six months. No therapy was used because of the short duration of the attacks. She also complained of migraine without aura and infrequent episodic tension-type headache attacks since her 20's. General and neurological exams, laboratory tests and MRI with contrast medium resulted normal.

Case 2 A 40-year-old female patient reported a 6-month history of episodic headaches. The spells started exclusively during the night, waking the patient between 2.00 and 3.00 AM, with a frequency of 2 to 3 episodes every month. The pain was dull, bilateral, localised over the frontal and temporal aspect of the skull, severe in intensity but not accompanied by migrainous symptoms such as nausea, vomiting, phonophobia, photophobia, osmophobia. The headache lasted for about 3 hours. NSAIDs taken during the spells did not help. The patient denied any personal or family history of headache and was otherwise well. Her physical and neurological examinations were unremarkable.

Conclusions These two cases add to our recent observation (1) concerning a possible sporadic pattern of hypnic headache, that consequently could be classified into an episodic and a chronic form.

Reference

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E077

Headache prevalences in medical doctors

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Objectives In an American study (Silverstone et al. 2003) it was ascertained, that neurologists do have a higher life-time prevalence of migraine, than individuals in the general population. This study aims to replicate these data in Germany. Additionally the following questions should be answered: Do Doctors active in surgical fields suffer from more headaches than non-surgical practitioners? Do neurologists sustain more headaches than other doctors from other non-surgical specialties?

Methods Data sets: normal population N = 6000, medical doctors N = 1667 (with 215 neurologists and 1086 other non-surgical specialties). 1466 participants at the age of 35 to 45 years (855 normal population <48.0%♂ vs 52.0%♀>, 611 medical doctors <66.8%♂ vs 33.2♀ females>) were compared concerning their headache experiences. The analyses were conducted by SPSS.12.

Results In the general population more headaches are observed than among doctors (crosstabs, $\chi^2 = 51,188$, df = 1, p = 0.000). There is no difference between surgical and non-surgical practitioners. Neurologists report more headaches than other non-surgical practitioners ($\chi^2 = 10,514$, df = 1, p = 0.001), but the general population in Germany reveals more migraine than neurologists ($\chi^2 = 28,932$, df = 1, p = 0.000).

Conclusions The data reported by Silverstone could not be replicated for Germany. The prevalence rate for migraine as well as for other headaches are lower in the medical than in the general non-medical. Although in both surgical and non-surgical groups the headache prevalences are comparable, Neurologists in this study sample exhibit a higher headache rate as compared to other non-surgical specialists.

Reference

Silverstone et al. (2003)

E078

Episodic SUNCT syndrome attributed to cerebral meningiomas and responsive to lamotrigine

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A 85 year-old woman was admitted because of the progressive worsening of her general conditions; she had two known cerebral meningiomas, located respectively in the falx cerebri (frontal lobe) and in the right ponto-cerebellar angle; she also presented a severe dementia; consequently, she was not able to give any medical informations. Her relatives reported a progressive impairment of walking. Physical examination did not show apparent neurological focal deficit; she was confused and only partially collaborative.

MRI, apart the findings of cerebral atrophy and chronic vascular lesions, confirmed the presence of a 4 cm meningioma in the falx cerebri with an extensive oedema and mass effect on the frontal horns of lateral ventricles; another smaller meningioma was present in the right ponto-cerebellar angle.

During her stay in the hospital she had attacks of very severe pain in the right peri-orbital and maxillary region lasting 15–20 seconds, associated with ipsilateral conjunctival injection and profuse tearing, recurring every 15–30 minutes. The pain could appear spontaneously but more frequently was triggered by touching the maxillary ipsilateral region. Additional anamnestic data collected with the relatives revealed that the onset of pain was at the age of 81. The frequency was irregular, with active periods lasting 2–3 months and remissions of 2–3 months. With lamotrigine 50 mg symptoms disappeared within 4 days from the beginning of the therapy. The treatment was withdrawn after 2 months; its efficacy persisted for one month more until the death of the patient due to severe cardiac impairment.

E079

The significance of clinical and laboratory characteristics in etiology and pathogenesis of migraine

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Introduction The aim of the study was to determine in patients with migraine characteristics and frequency of EEG changes, changes in platelet function (PF), echoangiographic characteristics (EC) of the cervical artery circulation and frequency of some radiological variants on the skull base and cervical spine. The study was based on the hypothesis that in patients with migraine, except for the classic symptoms and signs, there were also definite permanent functional disorders and anatomical variations as a trait of patients constitution.

Methods and patients The study comprised 60 patients with different types of migraine and 30 patients of the control group.

Results The results of the study have shown increased platelet aggregation in 36 patients (60%), relatively common finding of EEG nonspecific disarraythmia in 21 patients (35%), frequently presence of stimulative postprandial hypoglycemia in 23 patients (38.3%), circulatory disregulations at echoangiographic examination in 22 patients (36.6%), over-bridged sella turcica (24 patients or 40%) and foramen arcuale of the atlas 19 (31.1%).

Conclusion It has been concluded that the results of the study have pointed out that in patients with migraine there are broader disorders of the hypothalamus function as a permanent characteristic of the constitution of these patients. The results are both of theoretical and practical importance, they can be used as diagnostical criteria and in selection of drugs and procedures in prophylaxis and treatment of migraine attacks.

E080**Interictal cognition in migraineurs: a study correlating psychometric and neurophysiological tests**

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Background A deficit in habituation of evoked potentials (EP) characterises migraineurs interictally. Habituation is thought to facilitate learning. Whether migraineurs have persistent interictal cognitive disturbances remains controversial.

Objective To investigate if selective cognitive deficits can be found interictally in migraineurs and if cognition is correlated with visual/auditory EP patterns.

Methods An extensive neuropsychological evaluation (digit span, Block-tapping, CVLT, d2 cancellation, Stroop tests; computerized subtests from the attention test battery (TAP-1.7); alertness [simple, cued reaction time with a warning signal], divided attention, flexibility, working memory; MIDAS, BDI, STAI) was performed in 28 headache-free migraineurs (MIG; 22 without-, 6 with aura) and in 17 matched controls (CTRL). Visual (VEP) and intensity-dependent auditory EP (IDAP) were recorded as described before.

Results Cognitive performances did not differ significantly between MIG and CTRL. In MIG, a positive correlation was found between IDAP slope and D2 test (omitted responses) exploring selective attention ($p = 0.03$). A similar correlation was found for divided attention test ($p = 0.02$), while it was inversed for the number of omitted responses in that test ($p = 0.02$). Higher attack frequency and longer disease duration were associated with increased (corrected) errors in Stroop reading test ($p = 0.02, 0.01$) and with decreased correct responses in phasic alertness test ($p = 0.02, 0.01$).

Conclusions In our small cohort, cognitive performance was normal in headache-free migraineurs. However, in individual patients selective attention and reaction time were correlated to IDAP slope, probably reflecting impaired central serotonergic transmission. Phasic alertness test suggests that coping with interfering stimuli worsens with disease duration and severity.

E081**Idiopathic intracranial hypertension in chronic migraine patients**

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Objectives Chronic migraine (CM) is a common and debilitating disorder, affecting 2 to 3% of the general population. It is a difficult to treat disorder even in tertiary clinics. Idiopathic intracranial hypertension (IIH) is found in 5 to 14% of refractory chronic migraine patients without papilledema, but its prevalence in consecutive or non-refractory CM patients is unknown. We studied the prevalence of IIH in a consecutive, non-refractory CM population.

Methods We enrolled 61 consecutive, newly diagnosed patients diagnosed with CM according to the ICHD-II. They all had MRI / MRA, and underwent lumbar puncture with initial pressure measured in order to diagnose IIH. The protocol was approved by the ethics committee.

Results From 61 patients studied, 7 patients (11.5%), presented CSF hypertension (initial pressure above 200 mmH₂O). They all had normal neurological examination (no papilledema) except for one patient with papilledema.

Conclusion Our study shows a high IIH prevalence in consecutive, non-refractory CM patients, similar to previous studies in the literature (5–14%) in refractory patients. CSF examination is an important diagnostic tool in the evaluation of CM patients, its role in refractory patients is already established. Routine and systematic CSF investigation in newly diagnosed CM patients should be considered in future management guidelines. Further studies are necessary to clarify this issue.

E082**Impact of dizziness and visual symptoms associated with headaches**

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Objectives Headache is an underestimated cause for the health, emotional and financial burden in society. Accompanying symptoms of headache episodes might influence this impact.

Methods In a survey in the Luxembourg population on the social and emotional impact of headaches, participants were asked about accompanying symptoms of their headache episodes including, amongst others, visual symptoms (aura and blurred vision) as well as dizziness.

Results In a total of 1909 participants with episodic (<15 days per month) headaches (77.1% women) visual symptoms (52.4%) and dizziness (51.1%) were the most frequent accompanying symptoms of headache episodes. The association for each was independently stronger with migraine than with other headaches for both genders. These accompanying symptoms were correlated with headache-related disability (MIDAS), depression and in the WHO Disability Assessment Schedule and negative aspects within professional careers and family life.

Discussion Visual symptoms and dizziness are frequent accompanying symptoms of migraine and other headaches. They both might have a negative impact on disability and depression associated with headaches. Dizziness may need more attention in the International Classification of Headache Disorders.

E083

Balint syndrome and chronic daily headaches

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Objectives Two cases were reported of neurobehavior disorders Balint type in patients with chronic daily headaches.

Methods Physical findings evidenced phenomenology of optic ataxia and optic apraxia with fragmented ocular pursuit and normal ocular saccades.

In addition EEG, CT scan, MRI and laboratory studies were performed.

Results Structural injuries were observed in the left parietal-occipital region of the brain. Furthermore the two patients showed anosognosia and fabulation without hallucination, seen more in Anton type syndrome disorder.

Conclusion Evolution showed changed in the patterns of the crisis, these being in crescendo in intensity and frequency. Balint Syndrome was late complication in these patients with chronic daily headache.

E084

'Alarm bell headache': a sinister secondary headache

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Objective To describe a form of stabbing headache associated with intracranial potentially dangerous abnormalities, such as unruptured aneurysms, vascular malformations and tumours.

Methods From 2003 to 2006 we have observed 34 patients with intracranial abnormalities (16 pituitary adenomas, 6 meningiomas, 5 acoustic schwannomas, 2 glomus jugularis, 4 unruptured saccular aneurysms, 1 frontal oligodendrogloma, and 1 occipital arterio-venous malformation) associated with stabbing headache.

Results The characteristics of the secondary stabbing headache attacks observed in those patients were: (a) gradual enhancement in pain severity with an increase in frequency over the last months or years (crescent pattern); (b) dura mater contact with the lesion; (c) focal in just one or a few points over the head; (d) unilateral at the same side of the lesion; (e) precipitated by head movements; (f) association with abnormal signs (i.e., visual loss, proptosis, amenorrhea, galactorrhea, hearing loss, epileptic seizure, etc.); (g) Associated with larger intracranial lesions (later appearance); (h) woman predominance; and (i) resolution after surgery or dexamethasone treatment.

Conclusions Stabbing headache is characterized by a sharp, rapid pain over the head that may happen once in a lifetime or several episodes on a day. It is a relatively common cephalgia referred by 2–8% of the population, but when stabbing headache presents one or more of those characteristics described above we should consider it as an alarm sign.

showing that something is going wrong inside the head. In that case an evaluation with neuroimaging must be performed.

E085

Orgasmic headache associated with reversible segmental vasospasm. A report of two cases

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Background Orgasmic headache has been rarely associated to cerebral vasospasm. We present two patients who had orgasmic headache with reversible segmental vasospasm in absence of subarachnoid hemorrhage and cerebral vasculitis. **Cases report** Patient 01: a 57-year-old man referred for evaluation of orgasmic headache type 2 (ICHD-II) 3 days before. The pain that reached the peak in seconds, persisted in the next days, in smaller intensity, even with the use of simple analgesics. A cerebral digital angiography showed segmental vasospasm involving the right inferior and superior cerebellar arteries and both the posterior cerebral arteries. CSF examination revealed discreet pleocytosis and proteins slightly increased. Patient 02: a 51-year-old man referred for evaluation of orgasmic headache type 2 (ICHD-II) 24 hours before. The pain that also reached the peak in seconds, still persisted, in smaller intensity, even with the use of simple analgesics. The CSF examination was normal but a cerebral digital angiography revealed segmental vasospasm involving the right inferior cerebellar artery. In both patients, the neurological examination was normal and cerebral vasculitis were excluded by appropriated exams. They evolved with resolution of the pain in 7 and 5 days, respectively, and remain pain free on nimodipine 60 mg 4 times a day. Three months later an angiotomography showed normal cerebral arteries in both patients and nimodipine was discontinued.

Conclusion The association of reversible segmental vasospasm with orgasmic headache can be commoner than suspected and apparently do not modify the usual benign outcome.

E086

Conditioning by high frequency visual stimuli of the visual evoked potential in healthy volunteers and migraineurs

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Background The mechanisms underlying the interictal habituation deficit in visual evoked potentials (VEP) found in migraineurs are unknown. Neuronal changes induced by repetitive stimuli, such as long term depression (LTD) or potentiation (LTP), could be involved. They are, like habituation, thought to be modulated by serotonin.

Objectives To evaluate LTP/LTD of the VEP after high frequency visual stimulation (HFS) in healthy subjects (HV) and in migraine without aura (MO) patients.

Methods Ten HV and 6 MO patients underwent VEP recordings before and after 2 minutes of HFS at 9 Hz. We measured N1-P1 and P1-N2 amplitude and habituation.

Results After HFS in HV, VEP N1-P1 amplitude was significantly decreased ($-26.62 \pm 20.1\%$, $p = 0.006$) and VEP P1-N2 tended to decrease ($-10.68 \pm 18.2\%$, $p = 0.12$). In MO patients these changes were not significant ($-9 \pm 40.3\%$, $p = 0.55$; $-6.2 \pm 36\%$, $p = 0.34$). Moreover, HFS significantly reduced habituation in HV ($p = 0.027$) and aggravated slightly the potentiation found in MO patients ($p = 0.71$). There were no between or within groups differences during the control session.

Conclusions The decrease of N1-P1 amplitude suggests that HFS is able to induce LTD in the visual cortex. The accompanying loss of habituation is in line with our findings showing a direct relation between VEP 1st block amplitude and habituation. This effect could be ascribed to a deficient serotoninergic input to thalamus and cortex. The lack of significant effects in migraine could be due to the fact that thalamocortical activity is already reduced at baseline.

E087

Socio-economic impact of migraine in Belgrade

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Objectives Migraine is an important chronic illness that has the major impact on the working sector of population. Goal of this paper is to assess basic socioeconomic features of patients with migraine in Belgrade.

Method We have conducted a survey by utilizing a questionnaire conveyed through the field study. The interviewing process was face-to-face. We have used 14 items, both Likert-scaled and numerical. Interviewers were selected from the final-year students of medicine at Belgrade University School of Medicine.

Results Prevalence of migraine in general population was 11%. In female population we have found prevalence of 12.8%, while in males we have found prevalence rate of 8.0%. The highest incidence rate was found in middle-age and young active population (40–49 years 16.7% and 30–39 years 11.6% respectively). Distribution by education shows that majority of migraineurs is found in educated population (54.3% were with high school diploma, 43.4% were college/university graduates, while only 2.3% were with only elementary school). Household income distribution was also discussed and it is assessed that people who are earning very low income are less influenced (4.5% of poorest are influenced, 15.4% of richest, 44.3% of good earners and 35.3% of very good earners).

Conclusion The highest incidence rate was found in middle-age and young active population. We found that better educated and richer population suffers more of migraine. We did not find any significant connection between onset of migraine and household size. We have found that stress is reported as

the most important migraine-provoking factor, regardless to income or education.

E088

Bath headache with cerebral segmental vasospasm: a Brazilian case

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Background Bath headache has been described as a thunderclap headache, triggered or worsened by direct contact of the scalp and face with water. In cases with completely normal complementary investigation, it could be considered a primary headache, but in other cases it can be a phenotype of cerebral angiopathy with vasospasm.

Case report A 52-year-old Caucasian female patient was referred for evaluation of two sudden, excruciating, continuous, diffuse, non-pulsatile and refractory headache episodes in the last 48 hours started right after taking hot baths. She has a history of sparse migraines headaches without aura (ICHD-II) from the adolescence and a resection of a glomus tympanicus from the left ear 15 years earlier. Neurological examination was normal, as well as non-contrast cerebral computed tomography (CT). Lumbar puncture revealed normal cerebrospinal fluid (CSF), with normal opening pressure. Magnetic resonance (MR) imaging was unremarkable. Digital cerebral angiography (DCA) showed multi-segmental arterial constrictions without other structural abnormalities. Symptomatic relief was initially unsuccessful. Pain subsided after nimodipine 60 mg, 4 times a day, and prednisone.

Discussion This case emphasizes that bath headache can be related to abnormal neurovascular mechanisms and is not exclusive to Oriental ethnic groups.

E089

Risk factors for postdural puncture headache: experience with spinal anesthesia

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Objective To evaluate the risk factors of postdural puncture headache (PDPH, ICHD-II) in patients submitted to spinal anesthesia.

Methods In the period between 2005 and 2006, 640 (332 female) consecutive patients (8–65 years of age) were prospectively studied. All patients were submitted to a lumbar spinal anesthesia, with needles type Quincke, caliber 25G or 27G. Patients with obstetrical surgery and gestation in course were excluded. The chi square test was used to statistic analysis.

Results 48 (7.5%) of the patients developed PDPH. The binary regression analysis identified as a risk factor for PDPH: female sex [3.6% vs 11.1%, odds ratio (OR) 3.39 (1.70–6.77); $p < 0.01$], previous history of PDPH [5.8% vs 26.4%, OR 5.84 (2.89–11.78), $p < 0.01$], 25G needle caliber [5.5% vs 10.9%, OR 2.10 (1.16–3.80), $p < 0.01$], perpendicular orientation insertion of the needle bevel [OR 3.18 (1.70–5.94), $p < 0.01$], and

gynaecological surgery [OR 3.19 (1.26–8.06), $p < 0.03$]. Did not represent risk factor for PDPH: age [OR 1.00 (0.99–1.03), $p < 0.37$] BMI [OR 1.01 (0.94–1.08), $p = 0.97$], previous history of headache [6.8% vs 10.7%, OR 1.64 (0.82–3.26), $p = 0.16$] and position of the needle insertion [OR paramedian 0.64 (0.33–1.22), $p = 0.16$]. The odds ratio adjusted by logistic regression was 2.61 (1.28–5.34) to female gender, 4.02 (1.92–8.41) to previous history of PDPH, 0.42 (0.24–0.76) to 27G caliber of the needle, and 2.25 (1.13–4.51) to perpendicular insertion of the needle.

Conclusion The risk factors of PDPH in this study were: female gender, previous history of PDPH, the bigger 25G caliber, and perpendicular insertion of the bezel.

E090

Heart septal defect closure and migraine with aura: case reports

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Aims Previous studies have suggested a possible cause-and-effect relationship between heart septal defects and migraine with aura (MA). Recently some authors detected increased frequency or new onset of MA after atrial septal defect (ASD) closure. We report the effects of ASD closure on the occurrence of MA in three patients.

Sample and methods Three patients (2 females, 1 males) underwent percutaneous ASD closure. After the procedure transesophageal echocardiography was normal; all patients received aspirin 100 mg/die for 6 months.

Results A 43-year-old woman, suffering from migraine without aura (MO), underwent ASD closure because of dyspnoea on effort: since the following day she developed MA, with a frequency of 1/week. Migraine disappeared with Lamotrigine. (Follow-up 16 months).

A 22-year-old woman, suffering from infrequent attacks of MO, underwent ASD closure because of tachycardia and asthenia: after three months she started MA, with a frequency of 1/45 days. She didn't take any prophylactic therapy. (Follow-up 6 months).

A 24-year-old man, suffering from MA since he was 12 years old, with a low frequency of attacks (1–2/year), although asymptomatic was subjected to ASD closure: after the procedure the frequency of attacks increased from 1 to 4/month. (Follow-up 3 years).

Comments To date it is still unknown whether PFO is causally related to MA or if it's comorbidity. The increased frequency or the new onset of MA after ASD closure may be related to intra-atrial pressure imbalance after closure, as previously suggested, and consequent altered levels of atrial natriuretic peptide (ANP) that could start cortical spreading depression.

E091

Are there cases of secondary cluster headache? Origin, side of the pain and latent period

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Objectives To describe the clinical characteristics of 17 patients with cluster headache (CH) associated with intracranial or orofacial abnormalities.

Methods 17 patients (12 men) with CH (ICHD-II) were evaluated in the period between 2000 and 2006. All were submitted to neuroimaging evaluation and when an abnormality was encountered we tried to correlate the finding with that particular unilateral type of headache.

Results We found possible events that could precipitated the CH, such as: carotid artery aneurysms ($n = 3$, 18%), head/face trauma ($n = 11$, 65%), cavernous angioma ($n = 1$), chronic subdural hematoma ($n = 1$), electric discharge ($n = 2$), ocular surgery ($n = 1$), ethmoidal sinusitis ($n = 1$), temporal cyst (mesial, $n = 1$), and dental inflammatory process ($n = 1$). The age of the patient at the first cluster episode was 39 ± 16 (10–68) years. A close relationship was observed between the location of the trauma and the side of the pain. A latent interval of 60 ± 14 (0–360) months was observed between the moment of the precipitating event and the onset of the headache. The left side of the head was involved in 81% of the cases; if compared with 190 patients with probable idiopathic CH (Farias da Silva series) in which pain was felt on the left side in 45% of the cases, there was a significant difference ($p = 0.01$, Fisher test).

Conclusions This preliminary study, including a small series of cases, suggests that secondary CH predominate in men, on the left side of the head, a latent period of months or years may occur, and trauma is the lead precipitating cause.

E092

Is cervical kinaesthetic sensibility impaired in cervicogenic headache patients?

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Objectives We compared the cervical kinaesthetic sensibility of cervicogenic headache (CEH) patients with that of asymptomatic controls. Our purpose was both diagnostic and therapeutic. In case an impaired kinaesthetic sensibility can be demonstrated, its assessment can have diagnostic value in the evaluation of patients with suspected CEH. Additionally, specific exercises to improve cervical kinaesthesia can be prescribed.

Methods Subjects with a combination of headache and neck pain were recruited in outpatient physiotherapy offices and at a university hospital using leaflets. A standardised questionnaire, developed to screen for CEH (Sjaastad criteria, 1998)

was used for patient selection. No diagnostic blocks were performed. Only CEH patients without a history of neck trauma were selected for further analysis. Asymptomatic subjects were recruited as controls.

Cervical kinesthetic sensibility was assessed using a Head Repositioning Task: subjects were asked to relocate their head as accurately as possible to a previously memorised neutral head position following an active movement (flexion, extension and both rotations). The repositioning error was registered using a validated electromagnetic tracking device (Flock of Birds). A greater repositioning error is indicative of an impaired kinaesthetic sensibility.

Results After screening for eligibility, the repositioning error of 19 patients and 23 asymptomatic controls was measured. No significant differences were found between the asymptomatic controls and the CEH patients (Independent-Samples T-Test).

Conclusions We addressed some methodological shortcomings of two earlier studies and were able to draw similar conclusions cervical kinesthetic sensibility is not impaired in non traumatic CEH.

E093

Portuguese version of id-migraine® – Validation study

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Objectives Translate and validate a reliable screening instrument for migraine headaches in the primary care setting, the ID-Migraine®, for the Portuguese population.

Methods The original version of ID-Migraine® was translated and adapted to Portuguese, after written consent from the original authors. The Portuguese version was applied to consecutive patients in Hospital de Santa Marias' headache outpatient clinic, before each appointment. Clinical data of participants was collected, including headache diagnosis according to the ICHD-II and data was subjected to appropriate statistical analysis.

Preliminary results Up to today, 106 patients were included in the study. Seventeen patients were excluded for not fulfilling all criteria of any ICHD-II diagnosis, or having more than one headache diagnosis, including medication overuse headache. Our current sample has 77 (86.5%) female subjects with an age average of 37.5 years old (range 16 to 73 years old). Migraine was diagnosed in 62 patients (14 had migraine with aura). ID-Migraine® sensibility was 0.952 (IC 95%: 0.867–0.983), specificity was 0.519 (IC 95%: 0.340–0.693) and the positive predictive value was 0.819 (IC 95%: 0.715–0.891).

Conclusion The Portuguese version of ID-Migraine was easy to apply, was well accepted and had higher sensibility than the original (0.81) and the Italian (0.94) versions of the same test. Specificity and positive predictive value however, were inferior to the previous versions of this test. These preliminary results indicate that the Portuguese version of the ID-Migraine® can be a useful screening instrument for the Portuguese speaking community but the sample needs to be enlarged for definite results.

E094

How often does the typical migraine aura occur during the headaches?

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Objectives The timely relation of migraine aura is quoted in the vast majority of the literature as 'neurological symptoms preceding headaches'. However, our clinical experiences are often contradictory to this. We tried to substantiate our clinical observation, namely migraine aura also occurring simultaneously with headaches, and assessed the qualities of aura symptoms in temporal relation to headaches.

Methods All patients diagnosed with migraine with aura at the Headache Centre Hirslanden Zurich from December 2002 until August 2003 were sent a newly developed questionnaire.

Results 75 questionnaires were analyzed, using descriptive statistics. Aura either exclusively simultaneous or before headache was found in 52% and 42% of patients respectively, only 6% reported both. Qualitatively aura symptoms preceding the headache phase were more often classical visual symptoms (scintillating scotomas, etc), whereas aura symptoms synchronous with headaches were of more heterogeneous character.

Conclusions We emphasize that migraine auras occur not only before but also frequently with headaches. Since there were only a few patients reporting auras before AND during headaches two clinical or genetic variants of migraine with aura may be distinguished. Larger groups of migraine with aura patients need to be studied to substantiate our findings. Prospective data need to be added.

E095

Funding of headache research in Europe

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Migraine costs European Society 27 billion Euros, per year. Other headaches may account for a similar amount. Given this enormous impact, the question arises as to whether the funding of research efforts in this field are sufficient. A recent European study called the Resource Allocation to Brain Research in Europe (RABRE) examined funding of brain research identified charities and Government agencies in Europe filled out a questionnaire regarding their funding of brain diseases. Industry spending was evaluated by three different previously validated methods. We present detailed results for migraine and other headaches.

In 2004, migraine research was funded by nearly 315 billion Euros. Thereof, 308 million was invested by the pharmaceutical industry while public funding was estimated at 7 million Euros. No funding was identified for non-migraine headache disorders. Out of the public spending, 714 thousand Euros came from private foundations. There was a very large difference between European countries in the funding of headache research. When funding was compared to cost of

different brain disorders, migraine funding was in the middle range. This was due to relatively large industry funding. Compared to societal costs migraine received the least funds amongst all brain disorders, this is 0.025%. We conclude that migraine attracts reasonable interest from the pharmaceutical industry but Governmental and charity funding is extremely low and no funding was identified for non-migraine headache disorders. Considering the huge economical impact of these disorders, public funding of research into migraine and other headaches should be greatly increased in the future.

E096

SUNCT syndrome with paroxysmal midriasis: a case report

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Objective Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is a rare primary headache disorder. Miosis has usually been described during pain; however, there are reports on different clinical features. We here report a case with juvenile onset and unusual occurrence of midriasis during attacks as part of autonomic phenomena.

Method A 22-year-old female with a one-year history of headache with characteristics suggesting SUNCT was first seen at our Centre 2 months ago.

Result The patient from the beginning complained of short-lasting (3–5 min duration) unilateral retro-orbital attacks on the left side, with a frequency of 3–15/day and a mild to moderate background pain, fulfilling the IHS criteria for SUNCT. The autonomic component of the attack consisted of pronounced tearing and conjunctival injection. However, since the first 2 months of headache, the patient had also noticed a concomitant, brief pupillary dilatation on the symptomatic side. Over the last two months the temporal pattern had been characterized by 2–3 severe pain attacks/day with autonomic symptoms and signs, several attacks (10–20/day) of mild-moderate pain with pronounced paroxysmal midriasis, conjunctival injection and tearing on the symptomatic side, and mild to moderate background pain around the eye. Brain MRI and angio-MRI were normal. Patient was put on topiramate 100 mg/day, with a significant reduction in frequency occurring in both pain attacks and attacks with paroxysmal midriasis.

Conclusion This case emphasizes the possibility of unusual localization of autonomic symptoms and pain in SUNCT syndrome, which may reflect a different involvement of ocular sympathetic supply.

E097

Bathing headache: a study of 19 consecutive patients

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Objectives We first proposed bathing headache as one variant of primary thunderclap headache or benign CNS angiopathy. Till now, no large series has been reported so far. This study aimed to characterize bathing headache.

Methods We consecutively recruited patients with thunderclap headaches, which at least once, were triggered by bathing. Headache profile, neuroimaging findings, treatment response and follow-up data were analyzed.

Results Out of 76 recruited patients, a total of 19 (all women, mean 54 ± 8 (32–76) years) with bathing headache were identified, accounting for 25% of the thunderclap headache group. Bathing was the initial trigger in 7 patients (37%) and the only trigger in 6 (32%). Sixteen patients had multiple bath-related attacks. Most patients ($n = 15$, 79%) reported that headache occurred immediately when warm (84%), hot (26%) or cold (11%) water was poured over their body. The headache profiles were mostly explosive (100%), bilateral (68%) and over the vertex (42%). Median duration of each attack was 2 hours. Brain MRA showed segmental arterial constrictions in 9 patients (47%). Fourteen patients (74%) changed bathing habits for a mean duration of 13 (3 to 30) days. Nimodipine was effective in 83% (15/18) patients. One patient (5%) developed ischemic posterior leukoencephalopathy. No relapse was reported at a mean follow-up of 29 (3 to 61) months.

Conclusions Bathing headache occurred exclusively in women and predominantly in middle age. Half of our patients fulfilled the criteria of benign CNS angiopathy. Its close relationship with bathing should alert physicians to recognize this treatable and potentially stroke-prone headache disorder.

F001

Mollaret's meningitis may be caused by cerebral toxoplasmosis

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Rationale Mollaret's meningitis (MM) is a condition occurring mainly in females and characterized by recurrent episodes of headache, transient neurologic abnormalities, and cerebrospinal fluid containing mononuclear cells. Recently, we found that the recurrent headaches in non-HIV-infected subjects were due to reactivation of latent cerebral toxoplasmosis (CT). The aim of this study was therefore to focus on the pathomechanisms that may lead to simultaneous reactivation of both latent herpes simplex virus (HV) and acquired/inborn CT.

Methods Literature data cited in this work were selected to illustrate that various factors may affect latent CNS *T. gondii* and HV infection intensity and/or host defense mechanisms, such as the production of NO, cytokines, tryptophan degradation by indoleamine 2,3-dioxygenase, mechanisms

mediated by an IFN- γ responsive gene family, etc., and finally manifest as choroid plexitis.

Results Examples of various triggers revealing MM with accompanying disturbances of IFN- γ -mediated immune responses that control *T. gondii* and possibly HV in both phagocytic and non-phagocytic cells, are the following: female predominance: female mice are more susceptible to *T. gondii* infection than males by showing clear differences in the kinetics and magnitude of T-cell responses and the production of TNF- α , IFN- γ , and IL-10; HV infection: increased IL-12, INF- γ , TNF- α , IL-4, IL-6 (types 1 and 2); Ibuprofen: increased TNF- α , INF- γ , IL-1, IL-2 and IL-6 levels; systemic lupus erythematosus: increased NO, TNF- α , INF- γ , IL-1, IL-2, IL-6, IL-8 levels; decreased IL-10.

Conclusion Subjects with MM should have test(s) for *T. gondii* infection obligatorily performed.

F002

Subcutaneous histamine versus botulinum toxin type a in migraine prophylaxis: a double blind study

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Objectives To compare the efficacy and tolerability of subcutaneous administration of histamine and Botulinum Toxin Type A (BoNTA) in the treatment of severe migraine attacks in migraine prophylaxis.

Methods One hundred migrainous patients were selected and enrolled in a 12 weeks double-blind controlled clinical trial to evaluate the efficacy of subcutaneous administration of histamine (1–10 ng twice a week for 12 weeks) n = 50, compared to administration of 50U of BoNTA (1 injection cycle) n = 50. Variables studied were: headache intensity, duration and frequency of migraine attacks, MIDAS and analgesic intake.

Results Eighty-five patients completed the study. During the 4th week of treatment, histamine and BoNTA caused a significant reduction ($p < 0.01$) of all variables in relation to baseline. But in the 8th and 12th weeks, intensity and frequency of attacks returned to basal values in the BoNTA group, proving that 1 injection cycle has a 40 days efficacy.

Conclusion This randomized study demonstrated that both histamine and BoNTA are similarly effective and well tolerated in reducing or eliminating headaches in migraine prophylaxis. While BoNTA required less applications, histamine proved painless and less expensive. Histamine has a selective affinity for H3 receptors and may specifically inhibit the neurogenic inflammation involved in migraine. Low doses of histamine applied subcutaneously may represent a novel and effective therapeutic alternative in resistant migraine patients and lay the clinical and pharmacological groundwork for the use of H3 agonist in migraine prophylaxis.

F003

Low-dose gabapentin in treatment of high-altitude headache

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Objective Headache is the most prevalent symptom of acute mountain sickness. We conducted a randomized, placebo-controlled double-blind, pilot trial in Tochal mountain hotel (Tehran, Iran) clinic (3500 meters above sea level) to evaluate the efficacy of low-dose gabapentin in treatment of altitude headache (AH).

Methods Twelve adult AH patients (4 females/8 males; average age: 25.9 ± 2.3 yr; range = 18–50 yr) came to Tochal hotel clinic from January 1 to January 7, 2007. Patients were randomly assigned (1:1 ratio) to receive either 300 mg of gabapentin capsule or identical placebo. Assessor visited all patients after 1 hour of treatment and asked them of AH presence and their need to receive supplementary analgesic (400 mg ibuprofen tablet) that was considered as protocol deviation. Duration of AH-free phase was considered as time to event whether an individual received supplementary ibuprofen. Mann-Whitney and Kaplan-Meier tests were used to analyze data.

Results Three participants in gabapentin group had protocol deviation after 1st hour of treatment while all 6 placebo recipients did not find medication satisfactory after 1 hour and asked for supplementary ibuprofen ($p = 0.046$). Mean AH-free period was 13.50 (95% CI: 12.52–14.48) hours in gabapentin group that was significantly higher than placebo group with a mean AH-free period of 5.20 (95% CI: 3.63–6.77) hours ($p = 0.03$).

Conclusion This preliminary observation which needs to be confirmed in further controlled trials indicates that gabapentin is effective in treatment and alleviation of high altitude headache.

F004

Crossover comparative study of two drugs of the triptans

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Objectives It is known that the effectiveness and adverse events of triptan therapy for migraine vary among different drugs of the triptans. Although existing guidelines for the treatment of migraine recommend triptan as the first choice drug to be used during acute stages of the disease, there are few published data comparing the tolerability of different drugs of the triptans in Japanese patients. Furthermore, few data are available concerning the tolerability of these drugs when used at early stages of the disease.

Methods Rizatriptan benzoate (rizatriptan) and eletriptan hydrobromide (eletriptan) were administered within 15 minutes after an attack of migraine, and the remission rate of migraine, incidence of adverse reactions 2 hours after the treatment and the recurrence rate 24 hours after the treatment

were compared between the two triptan groups. A total of 34 patients participated in this cross-over design. Clinically, Group treated with rizatriptan appeared to be significantly effective against migraine.

Results In contrast, Group treated with eletriptan showed a tendency toward a low incidence of adverse reactions as compared to Group treated with rizatriptan. The clinical efficacy tended to be more differential between the two drugs in patients complicated by tenderness symptoms such as shoulder or neck stiffness, suggesting that rizatriptan appeared to be more effective than eletriptan.

Conclusion It is preferable to pile up the data in more patients so that the drug can be selected for more suitable patients, leading to improve QOL of the patients suffering from migraine.

F005

Efficacy of sublingual rivastigmine versus sumatriptan in acute treatment of multiple migraine attacks

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Objectives To compare the efficacy of rivastigmine with sumatriptan in the treatment of 2 consecutive migraine attacks of severe migraine following a randomized crossover plan. Iris reaction to homatropine 1% was a semi-objective parameter to assess differences between controls and migraine regarding cholinergic system.

Background Central cholinergic system has been shown to be a powerful analgesia system in mammals. Second generation anticholinesterases are the first possibility to impact this system in man, *in vivo*. We previously demonstrated that sumatriptan can induce a release of acetylcholine in mice brain. That suggested a possible cholinergic mechanism of sumatriptan.

Methods Fifty-six patients suffering from migraine with or without aura according to IHS criteria were randomized to treat 2 migraine attacks with rivastigmine (3 mg/sublingually) and 2 attacks with sumatriptan (100 mg/orally). Twenty-five patients were compared to a demographically matched group of exempts in a pupillopharmacological observation where mydriasis was monitored.

Results Mydriasis peak value was at 45.5 min + 2.1 SD in migraine (6.0 mm + 0.98 SD) versus 44.4 min + 2.3 SD (5.08 mm + 0.74 SD) in controls. It lasted longer ($p > 0.001$) in migraine: 1.2 days + 1.4 SD 2.4 + 1.1 SD. In this experience rivastigmine was superior to sumatriptan at the following end-points: pain-free at 2 hrs postdose (83% versus 50%, $p > 0.0001$), sustained pain-free response (83% versus 46%, $p > 0.0001$), a significant response was achieved for rivastigmine in the 4 treated attacks. Drugs were both well tolerated.

Conclusions Rivastigmine, analyzed according to the recent guidelines for controlled study showed significant efficacy. Migraine sufferers seem characterized by a cholinergic supersensitivity which can explain the results.

F006

A workplace cognitive and physical program decreases headache and neck pain. A longitudinal, controlled study

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Objectives This study was aimed at examining the effects of a cognitive and exercise instruction program on frequency of headache, neck and shoulder pain in a working community.

Methods 344 employees of the city of Turin were distributed in two groups – group 1 ($n = 169$) and group 2 ($n = 175$) – and were given a diary to record daily from March 2005 (month 1) to April 2006 (month 14) frequency, severity and duration of the headache, neck and shoulder pain episodes. At month 3, a program of shoulder and neck and relaxation exercises and instructions of how to reduce muscle hyperfunction was administered to group 1. At month 9 the instruction program was administered to group 2 as well. For each subject, the difference of symptom frequency between each month and months 1–2 was calculated, and the mean differences between the two groups compared with parametric and nonparametric tests.

Results Between month 3 and 8 the monthly frequency of headache significantly decreased over time in group 1 compared to group 2 ($p < 0.001$ at month 8); the same pattern was observed for the frequency of neck and shoulder pain. Data at month 14 compared with data at month 8 were not statistically different in group 1 while in group 2 a significant ($p < 0.001$) reduction of frequency of head, neck and shoulder pain was observed.

Conclusion The administration of a simple instruction program can significantly decrease the prevalence of headache and cervical pain in large population samples.

F007

iNOS inhibition in acute migraine: pharmacokinetic characteristics, safety and tolerability of GW273629

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Objectives To investigate the pharmacokinetics, safety and tolerability of a 1500 mg single oral dose of GW273629, a selective inhibitor of inducible nitric oxide synthase (iNOS), when given during and outside of a migraine attack.

Methods In a 2-period open label study, 1500 mg of GW273629 was administered, once during a moderate or severe migraine headache and once during a headache free period. Adverse events, vital signs, ECG monitoring and laboratory data were filed. Using a non-compartmental approach, AUC from 0 to 2 hours (AUC₀₋₂), 0 to 4 hours (AUC₀₋₄) and 0 to infinity (AUC_{0-∞}) were calculated. The

time before drug detection (t_{lag}), C_{max} and t_{max} were also assessed.

Results Fifteen patients (4 male, 11 female; mean (SD) age 31 (11) year) completed the study. No clinically significant changes in vital signs, lab values and ECGs were reported. No AE's were considered to be related to GW273629 by the investigator. The ratios during/outside a migraine attack (90% Confidence Interval) were 0.59 (0.45, 0.78) for AUC0-2, 0.65 (0.48, 0.88) for AUC0-4, 1.05 (0.92, 1.20) for AUC0-∞ and 0.79 (0.70, 0.88) for C_{max}. The median (range) for t_{lag} and t_{max} were 0.25 (0.00-0.25) and 4.0 (2.0-8.0) h during versus 0.08 (0.00-0.25) and 2.5 (1.5-6.0) h outside a migraine attack, respectively.

Conclusions Early absorption was reduced when GW273629 was administered during a migraine attack as reflected by a significantly lower AUC0-2, AUC0-4 and C_{max}.

- The overall extent of absorption (AUC(0-∞)) of GW273629 was not affected.
- GW273629 was well tolerated.

F008

Headache patients' EEG changed by breath counting exercise

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Objectives Headache patients show increased spectral power in slow EEG frequency bands compared to controls in resting EEG (e.g., Thomaides et al. 1996). Migraine patients also showed decreased Omega Dimensional Complexity (ODC) during attacks compared to attack-free times (Strenge et al. 2001). Breath counting exercise (BC) was reported to reduce chronic pain (Mehling et al. 2005). We studied the effects of a single 4 minute BC exercise on the EEG of chronic headache patients.

Methods 19 channel EEG of 10 headache patients (mean age 19.5 years, SD = 0.85; one man) were recorded with closed eyes on attack-free days during pre-BC-resting, BC, and post-BC-resting (4 min each). During BC, headache patients were told to silently count their inspirations from 1 to 10, continually repeating the counting.

Results Power spectral analysis and ODC analysis was done on the EEG. BC compared to pre-BC-resting significantly decreased power in delta, theta, and alpha1. Moreover, post-BC-resting compared to pre-BC-resting showed a significant decrease of power in delta and theta. ODC significantly increased from pre-BC-resting to BC, but showed no difference between pre- and post-BC-resting.

Conclusion The results showed that a single short application of BC treatment in headache patients produced a change of the measured EEG parameters towards normalization, during as well as immediately after the treatment. Further studies should examine the relation between BC effect on EEG

and on headache, study the duration of the resulting changes, and vary the duration of BC treatment.

References

Mehling et al. (2005)
Strenge et al. (2001)
Thomaides et al. (1996)

F009

Transcranial magnetic stimulation in migraine (TMS): high vs. low stimulation effects

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Objectives To determine whether there were significant differences between subjects receiving High stimulation intensities (50% maximum output [2 Tesla]) versus Low intensity (30% maximum output).

Methods 44 subjects were assessed. 23/44 received High stimulation (HS) and 21/44 Low stimulation (LS), mean age was 41.43 ± 11.45 yrs., 36 females. Pain was measured on a 5 point Likert-type scale with 5 being the most severe response. Each subject received 2 single pulses of TMS 5 seconds apart. Migraine was determined according to International Headache guidelines. 5/44 reported an aura, and 2/5 had an aura with pain.

Results No significant group differences were found for pain intensity. Both groups showed improvement after TMS. In the HS group 3/23 had an increase in pain immediately post stimulation versus 1/21 in the LS group. After 24 hours, 29% HS vs. 30% LS had no pain, 35% HS vs. 36% LS had severe pain and 35% HS vs. 36% LS reported mild-moderate pain. 40% did not take rescue medication. 3/5 subjects with an aura developed headache within 24 hours.

Conclusions TMS is an effective treatment for migraine. Optimal intensity levels must be determined and may be specific to individuals.

F010

Transcranial magnetic stimulation in migraine (TMS): single pulse adverse effects

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Objectives To determine whether there are significant adverse effects immediately post single pulse TMS for migraine and after 24 hours.

Methods 45 subjects, mean age 41.6 ± 11.78 s.d. years, 36 females, received 2 pulses of TMS, 5 seconds apart. Subjects were randomized into high (50% max output [2 Tesla]) and low (30%) levels of TMS. Pain intensity was measured on a 5 point Likert-type scale with 5 being the most severe pain. 3/5 had an aura with persistent pain and 2/5 had an aura only. 45 received 1 treatment (T1). 25/45 had T2, 12/45 T3, 5/45 T4, 3/45 T5, 1/45 T6, and 1 person had 7 treatments. Mean duration of headache before TMS was 11.51 ± 18.27 s.d. hours.

Results No unusual vomiting or new neurological signs were reported. 69% of subjects showed immediate improvement at

T1, 87% at T2, 82% at T3, 60% at T4&T5, and 100% after T6&T7. Mean time to show improvement was 15.21 ± 6.72 minutes. No significant differences were found between the high and low groups. Pain increased 1 level on the pain scale, post stimulation in 4/45 subjects after T1, 1/24 after T2, 0/12 T3, 1/5 T4, and after 24 hours post TMS pain increased in 26/45 T1, 14/24 T2, 4/11 T3, 2/3 T5.

Conclusions No significant adverse effects were found with single pulse TMS. Benefits of TMS outweigh the negative.

F011

Perceptions of suffering in migraine headache

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Objectives To determine whether the perception of suffering in migraine is an important clinical outcome measure separate from pain.

Methods Seventy-seven (77) patients with migraine were given a valid and reliable questionnaire (MASQ) to assess suffering. Items were scored on a 5 point Likert-type scale with 5 being the most negative response. Mean age was 42.9 ± 12.8 s.d. years, 66/77 were female. 30/70 had pain at the time of assessment.

Results Pearson correlation coefficients showed a weak relationship between pain intensity and total suffering scores: $r = 0.21$, $p = 0.06$ and between total pain (coping, belief items) and total suffering $r = 0.241$, $p = 0.20$. Mean differences were 1.69 ± 0.98 s.d. vs 2.69 ± 0.71 s.d. (total suffering vs. pain intensity). In the pain group, pain and suffering showed a non-significant inverse relationship, $r = -0.03$, $p = 0.86$.

Conclusions Suffering and pain are separate entities which are only sometimes related in migraine. Suffering is an important clinical outcome measure.

F012

Treatment of migraine and tension type headache in Croatia

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Objective The aims of this study were to assess the proportion of patients who are taking specific antimigraine therapy, number of tablets per month, proportion of patients taking prophylactic therapy, using alternative treatment methods and satisfaction with treatment.

Methods The design of the study was a cross-sectional survey. Self-completed questionnaires were randomly distributed to adults >18 years of age in Croatian population to contain a mix of urban, suburban and rural settings, and a spread of social class. Headache sufferers were classified into three groups for analysis: migraine (M), tension type headache (TTH) and probable migraine (PM).

Results A total of 616 questionnaires were analysed: 115 M, 174 PM and 327 TTH patients. For the treatment of migraine

35.7% of patients takes triptans and 21.7% ergotamines. The majority of M and TTH patients is taking 1 while patients with PM are taking 2 or more medications/attack. Prophylactic treatment has received 13.9% M and 6.9% PM patients. Less than 1/3 of patients has tried alternative treatment methods. More than half of TTH patients has never visited a physician. Patients with M more frequently visit a physician, regularly only 16.8%.

Conclusions Specific antimigraine therapy is currently taking half of patients with migraine, however, a relatively low percentage is taking triptans. Although the majority of patients needs only one tablet/attack, less than a third of patients is satisfied with treatment. Results of this study indicate that the treatment of primary headaches in Croatia should be improved.

F013

Gabapentin: effectiveness in headache prophylaxis

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Objective To assess the efficacy and safety of gabapentin in prophylaxis of different types of headache.

Methods A total of 25 out of 31 headache patients, 20 female, 5 male (19 migraine-M, 3 cluster headache-CH, 1 posttraumatic headache, 1 hemicrania continua-HC, 1 trigeminal neuralgia-TN) completed this prospective, open-label study. Patients were given 900–1800 mg of gabapentin in 3 doses; the follow-up period on average was 6 months. The reduction of days with headache, pain intensity and number of acute medications was assessed.

Results The mean number of migraine days/4 weeks was reduced from 15.8 (baseline) to 7.0, a reduction of 8.8 migraine days/4 weeks ($p < 0.0001$). Pain intensity was decreased for $>50\%$ in 7 patients and $>25\%$ in 2 patients. The mean number of headache days/4 weeks in patients with CH and TN was reduced from 28 (baseline) to 8.5, a reduction of 19.5 headache days/4 weeks; pain intensity was decreased from 25–75%. A reduction of acute medication use $>50\%$ was reported. No drug efficacy was reported by 3 patients (12%), 2 M patients and patient with HC. Adverse events (AEs) were reported by 12 patients (48%); in 8 patients (32%) the AEs led to discontinuation of the drug. The most frequently reported AEs were drowsiness, dizziness and constipation.

Conclusion If tolerated, prophylactic treatment with gabapentin is associated with significant reduction of headache days and decrease of pain intensity. Gabapentin could be offered as an efficient prophylactic drug in patients with migraine and cluster headache.

F014

PK and cardiovascular effects of a single tablet of Sumatriptan RT 85 mg/Naproxen Sodium 500 mg vs Sumatriptan RT 100 mg

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Background A direct comparison of sumatriptan bioavailability following a Fixed Single-Tablet of Sumatriptan 85 mg RT™ Technology with 500 mg Naproxen Sodium (SumaRT/Nap) and a Sumatriptan 100 mg RT™ Technology Tablet (SumaRT) was conducted to compare acute exposures [AUC(0-2)] and peak concentrations (Cmax). It was unknown whether the addition of naproxen would alter the acute cardiovascular effects compared to sumatriptan alone.

Objectives Compare sumatriptan pharmacokinetics during the first 2 hours and cardiovascular effects through 10 h post-dose following single oral doses of SumaRT/Nap and SumaRT.

Methods This was a randomized, open-label, 2-way crossover study in healthy volunteers (n = 32). Volunteers received single oral doses of SumaRT/Nap and SumaRT. Serial blood samples were analyzed for sumatriptan and naproxen concentrations, as applicable. Serial blood pressure (BP) measurements and 5-lead continuous telemetry were performed.

Results Following administration of SumaRT/Nap, sumatriptan peak concentrations (Cmax) and acute exposure [AUC(0-2)] were similar relative to SumaRT. The median of the differences indicated time to sumatriptan Cmax (tmax) occurred 53 minutes earlier for SumaRT/Nap relative to SumaRT though AUC(0-inf) was 15% less as expected from the difference in relative dose. No clinically relevant changes were noted in telemetry or BP following either treatment.

Conclusions Although SumaRT/Nap and SumaRT contain different amounts of sumatriptan (85 vs 100 mg), the sumatriptan pharmacokinetics, during the critical first 2 hours following dosing, were similar. The earlier sumatriptan tmax for SumaRT/Nap may produce more rapid onset of action and enhanced efficacy. Furthermore, the addition of naproxen did not clinically significantly increase the incidence of acute cardiovascular effects.

F015

Comparison between normal saline and 5% dextrose Water solutions in symptoms relief in acute migraine attacks

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Introduction Dehydration has been reported in acute migraine attacks, and fluid replacement therapy could relieve its symptoms. However, administered fluid composition may be effective in headache relief process in acute migraine attacks.

Materials and methods We selected 8 patients with known chronic migraine-type headaches referred to Emergency Department for acute attack of headache, and allocated them in two groups. The first group (N = 4, 2 males and 2 females, mean age = 29.0 years; mean headache duration = 11.4 years) administered with 500 ml of 0.9% sodium chloride solution infusion during 15 minutes. Second group (N = 4, 4 males, mean age = 27.2 years; mean headache duration = 7.2 years) received 500 ml of 5% dextrose solution infusion in 15 minutes. The patients were unaware of administered fluid type and they were monitored for their attack recurrence for up to 30 minutes after infusion completed.

Results The reduction in pain severity in all patients in Saline group was considerable and there was no need to use analgesics after about 30 minutes of infusion completion, while dextrose solution group need to take analgesic and anti-emetic therapy after 5 minutes of infusion completed. On the other hand, nausea and vomiting were the first symptoms relieved during Saline infusion, however, there was no improvement in nausea and vomiting condition in second group.

Discussion Our results could open new horizons in abortive therapy profile of migraine attacks and gleams to make new explanation to headaches pathophysiology. It seems that more clinical studies with greater sample sizes are yet needed in this era.

F016

Primary-type headaches associated with ribavirin plus interferon alpha2b in patients with chronic hepatitis C

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Objectives To evaluate new emerging headaches in patients with chronic hepatitis C under ribavirin plus interferon alpha-2b combination therapy.

Background Severe headaches are one of the most important problems in therapeutic process of chronic hepatitis C with ribavirin and interferon alpha-2b. There are few previous reports of migraine headaches triggered by ribavirin in combination therapy for chronic hepatitis C.

Methods We enrolled 54 (38 male and 16 female) patients with chronic hepatitis C and applied them with a headache diagnosis and status questionnaire according to IHS 2004 headaches diagnostic criteria. All patients were under combination therapy with ribavirin and interferon alpha-2b at least for 6 months.

Results A total of 18 (12 male, 6 female) patients had complaints from severe headaches. 6 migraine with aura-type, 1 migraine without aura-type and 2 tension type headache were seen with less than 1 year of duration, 2 patients were seen with tension type headache with duration of 1–5 years, and one female patient had chronic migraine with aura headaches.

Conclusions Our results showed increased rate of even migraine-type headaches with ribavirin plus interferon alpha-2b treatment of chronic hepatitis C patients, corroborating

previous studies. However, in our study the association of headaches with any of drugs is not clear. More clinical and experimental studies are to be needed to more clarify the association and possible underlying mechanisms.

F017

Botulinum therapy for headache attributed to craniocervical dystonia

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We examined the efficacy of Botulinum toxin type A for the treatment of headache attributed to craniocervical dystonia. Thirty-three patients were studied. Sixteen were male and 17 were female. The age ranged from 21 to 87 years old with the mean of 51.5 ± 18.1 . The history of dystonia was from 2 months to 33 years, with the mean of 4.7 ± 5.3 years. All patients showed headache as well as neck pain. The grade of headache was moderate in 13 cases and mild in 20. The postural abnormality of the neck was rotatocollis in 26 cases, laterocollis in 14, lateral shift in 4 and shoulder elevation in 10 including overlapping. Dose of Botox was from 20 to 80 units, and it was injected for affected muscles in each.

The effect for the pain was complete recovery in 3 cases (9.1%), remarkable decrease in 17 (51.5%), slight in 5 (15.2%) and not effective in 7 (21.2%).

There are more headaches than expected, and botulinum therapy certainly seems appropriate.

F018

Migraine – it's all in the cortex!

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Objective To determine whether TMS (transcranial magnetic stimulation) can be an effective treatment for severe, complex migraine.

Methods Two female patients were recruited for a study approved by the university ethics committee. Case 1, a 73-yr old former nurse, had a 52-yr history which began with attacks of acute vertigo, vomiting and occipital headache; later attacks included 'trigeminal neuralgia,' body pains, paraesthesiae, paralysis, hallucinations and coma. Case 2, a 46-yr old research scientist, began to have episodes of being 'off balance' with fatigue, headache and hypersomnia, 9 years ago. Her episodes subsequently included acute vertigo, diplopia with strabismus, severe orbital pain, paralysis and muscle spasms. Both patients had positive family histories and had been extensively investigated to exclude disorders other than migraine, and both had eventually become bed-bound because of their symptoms. Magnetic stimuli were applied over the cerebral cortex during migraine attacks, using Magstim 200 machines (Magstim Company Ltd, Whitland, Wales). Control observations were obtained by varying the sites and strengths of the stimuli. Case 1 has been treated on several thousand occasions, and Case 2 on over one hundred.

Results In both cases TMS abolished, or significantly reduced, contralateral pain, including headache, and there was also disappearance of vertigo, paralysis, paraesthesiae, and hallucinations (Case 1) and of strabismus (Case 2). No unwanted side-effects were apparent.

Conclusions TMS can be effective in severe, complex migraine, resistant to drug therapy. In addition, the results point to the cortex as the major source of migraine symptoms, including headache.

F019

The efficacy of repetitive prophylactic treatment in long term relief from migraine

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Objectives Observing migraine (M) attacks worsening within variable time after ending prophylactic treatment (PT), generated the idea that patients could benefit if repetitive doses of prophylactic medication were given at intervals after ending initial PT.

We called this repetitive PT for M. The aim of the study was to test its efficacy.

Methods Included in this retrospective study are 83 patients with M on PT, followed up for 24–36 months. 39 received repetitive PT for M whereas 44 didn't. Initial PT was similar for all 83 patients.

After initial PT, patients received no medication for 2 months. Then they performed the following scheme:

For 4 weeks patients received the maximum medication dose reached before interrupting initial PT. For another 2 weeks dose was reduced and then medication stopped. Patients then abstained from medication for 3 months. After that, they repeated the scheme again. For the remaining follow-up period the scheme was repeated once every 6 months.

Results All 39 patients who took repetitive PT maintained the result achieved by initial PT during the whole 24–36 month follow-up period. Among the 44 patients who didn't, rebound of M occurred with respect to attack frequency and intensity. The latter needed to start fulltime PT again.

Conclusion Patients on repetitive PT maintained for the result achieved by initial PT for 2–3 years. Among the rest, M either re-appeared or worsened within the same time. We are aware of no similar studies whereas further are needed to prove the efficacy of repetitive PT.

F020**Zolmitriptan nasal spray in the acute treatment of cluster headache – a double-blind study**

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Objectives To evaluate the efficacy and tolerability of zolmitriptan 5 mg and 10 mg nasal spray (ZNS) versus placebo in the acute treatment of cluster headache.

Methods We conducted a multicenter, double-blind, randomized, three-period crossover study using ZNS 5 mg, 10 mg and placebo. Headache intensity was rated on a five-point scale. Primary efficacy measure was headache response (pain reduced from moderate, severe or very severe at baseline, to mild or none) at 30 minutes. Logistic regression was used to account for treatment period effect as well as for cluster headache subtype effect.

Results A total of 52 adult patients treated 151 attacks. For the primary endpoint, both doses reached significance at 30 minutes (placebo = 30%, ZNS 5 mg = 50%, ZNS 10 mg = 63.3%). For headache relief, zolmitriptan 10 mg separated from placebo at 15 min (24.5% vs 10%). Zolmitriptan 5 mg separated from placebo at 20 minutes (38.5% vs 20%). For pain free status, zolmitriptan 10 mg was superior to placebo at 15 minutes (22% vs 6%). Both doses had higher pain free rates than placebo at 30 minutes (placebo = 20%, ZNS 5 mg = 38.5%, ZNS 10 mg = 46.9%). Side effects were mild and seen in 16% of those attacks treated with placebo; 25% of attacks treated with zolmitriptan 5 mg and 32.7% treated with zolmitriptan 10 mg.

Conclusions Zolmitriptan NS, at the doses of 5 and 10 mg, is effective and tolerable for the acute treatment of cluster headache.

F021**Zonisamide prophylaxis in refractory migraine**

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Objectives Zonisamide is a new anticonvulsant drug with multiple mechanisms of action, some of them may confer efficacy in the treatment of migraine headaches. We evaluated the efficacy and tolerability of zonisamide for migraine prophylaxis in refractory patients.

Methods Thirty-two patients, with International Headache Society-defined episodic migraine, were initiated on a 100 mg/day zonisamide dosage, which was titrated to 200 mg/day as tolerated. The patients had failed an average of 5.1 migraine prophylactic drugs prior to zonisamide. Headache frequency and severity before and after treatment initiation were compared. The average zonisamide daily dose was 182 mg and the average duration of treatment was 152 days.

Results Statistically significant improvements in headache severity ($P < 0.05$), and frequency ($P < 0.05$) were evident after 1 month of zonisamide therapy and persisted after 5 months of treatment. Zonisamide was well-tolerated and the most

common adverse events were drowsiness and difficulty in concentration. One patient discontinued because he developed a restless legs syndrome.

Conclusions These results suggest that zonisamide may be a safe and effective drug for migraine prevention and may be useful in refractory patients.

F022**Infratrocchlear neuralgia: treatment with botulinum toxin A**

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Objectives We report this case and discuss the suspected mechanisms of action for BTX-A therapy on the infratrocchlear neuralgia (IN).

Method (Case report) The patient in this case is a 28 year-old Asian female, without migraine or a history of other primary headaches. Her symptoms were characterized by shooting pain on the unilateral upper part of the skin of the nose, and the duration of the pain was short-lasting (from 10 s to 3 min). The frequency was more than four attacks per hour. Touch sometimes provoked the pain. The pain was so serious that it usually interfered with her daily activities. She did not have other associated symptoms. The pain was intractable to analgesics and anticonvulsants. The physical examination of the head and the findings of a brain MRI were normal. The patient was given a local injection of 25 units of Dysport. The patient noticed an analgesic effect 3 days after the injection and experienced a gradual decrease of pain throughout the following 14 days. Two months after the injection, the patient experienced nearly complete relief of the pain in the right infratrocchlear nerve distribution.

Conclusion The present case indicated that BTX-A could be used as an effective treatment in for IN. The mechanisms of action of BTX-A in IN might be the inhibition of peripheral and central sensitization, the chemodenervation of the motor endplate, and the anti-inflammatory effect of BTX-A.

F023**Influence of disease specific factors on adherence to migraine prophylaxis**

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Objectives The efficacy of mainly the more recently developed prophylactic treatments of migraine have been well established in a large number of randomised controlled trials. However, such trials tend to focus on the effects of the drug in an ideal setting and rather underestimate the impact of non-compliance, which generally escapes detection by the physician. This poorly understood phenomenon was further looked at in a naturalistic setting.

Methods A consecutive sample of 175 migraineurs (85% women, mean age 45 ± 12 , range 19–79 years) with a current

prescription of pharmacological prophylaxis were studied at a Swedish headache specialist clinic. Adherence was self-reported with the Medication Adherence Report Scale (MARS, possible range of scores 5–25). Logistic regression analysis was performed to analyze the association between MARS and frequency of attacks, number of days with migraine per month, attack duration, presence of prodrome (68%), presence of aura (41%, some or all attacks), mean intensity of pain, and recovery between attacks.

Results The mean frequency of migraine was 6.5 days/month, and 68% did not recover completely interictally. The mean MARS score was 22.5 ± 2.8 . One third (35%) was not highly adherent. Neither demographic characteristics, nor any of the studied disease specific variables were significantly associated with adherence.

Conclusion The full benefit of prophylactic migraine medication cannot be realised at currently achieved levels of adherence. Characteristics of the headaches per se are the starting point of patients' decision-making. However, the present study indicates that other factors play a more important role in this complicated process.

F024

Physical exercise in migraine – methodological considerations

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Objectives Little is known about physical exercise in migraine. Some patients avoid exercise due to fear of migraine attacks. The purpose of this study was to develop a method of physical exercise for migraine patients, which could improve exercise capacity without increasing the amount of migraine attacks.

Methods Six patients with migraine (diagnosed with and/or without aura, five women, mean age 45 range 34–61 years) were studied at a headache specialist clinic in Sweden. They were previously untrained with a documented high migraine attack frequency (2–6/month). The exercise programme was based on indoor-cycling using the Borg Scale for rating perceived exertion (RPE-Scale, maximum 19). Each training session consisted of 15 minutes of warming up (intensity: RPE-Scale: 11–13), 20 minutes of exercise (RPE-Scale: 14–16) and 5 minutes of cooling down (RPE-Scale: 11–13). The patients trained with a registered physiotherapist 3 times a week for 3 months. In case of absence, the subjects trained at home or at a local gym. Six patients have completed the training period. Headache diaries and maximum oxygen uptake ($VO_{2\max}$), measured using Åstrand's submaximal bicycle test, were used for evaluation.

Results $VO_{2\max}$ increased in four of the patients (in average $15 \text{ mL kg}^{-1} \text{ min}^{-1}$ ⁰⁰²¹). In two patients the frequency of migraine decreased, while in one patient it increased.

Conclusion Indoor-cycling is a promising exercise method in patients with migraine. It can increase $VO_{2\max}$ without increasing the frequency of migraine attacks. Further research is needed to prove this statement.

F025

Beliefs about medicines and adherence among Swedish migraineurs

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Objectives The aim was to analyse whether beliefs about medicines are associated with adherence to prophylactic medication among Swedish migraineurs.

Methods A questionnaire was distributed consecutively to migraineurs attending a tertiary clinic. All participants were prescribed prophylactic medication. The questionnaire comprised e.g. background questions, beliefs about medicines (BMQ), and self-reported adherence (MARS). The General BMQ comprises three subparts: General Harm, General Overuse, and General Benefit. The specific part of the BMQ has two subparts: Specific Necessity and Specific Concerns. For the BMQ Specific, a necessity concerns differential was calculated for each participant. A logistic regression analysis was performed to analyze the association between beliefs about medicines and adherence to prophylactic medication.

Results Of the 175 participants, 15% were male and more than half of the participants were aged 45 years and over. Fifty percent had a university degree. Sixty-four percent were considered adherent. There was no significant difference in adherence between gender, age groups, or by educational level. Respondents with only compulsory school were less concerned about the long-term effects of medications and had a higher necessity concern differential. In the logistic regression analysis, no variable was significantly associated with adherence.

Conclusions The present study showed no association between beliefs about medication and adherence. We recommend that lack of adherence to migraine prophylactic drugs should be considered more often, looked for, and addressed in order to identify sufferers with an unnecessarily high migraine-associated disability. This assumes greater attention to the problem amongst both physicians and researchers in all countries.

F026

Activation of the cortical pain network by soft tactile stimulation after injection of sumatriptan

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Objectives The anti-migraine drug sumatriptan often induces unpleasant somatosensory side effects, including a dislike of being touched. The aim was to study underlying mechanisms.

Methods With a double-blind cross-over design, we studied the effects of sumatriptan and saline on perception (visual analogue scale) and cortical processing (functional magnetic

resonance imaging) of tactile stimulation in six healthy subjects.

Results Soft brush stroking on the calf ($n = 6$) was less pleasant.

Conclusions One possible mechanism for the activation of pain processing regions by brush stroking is sensitization of nociceptors by sumatriptan. Another possibility is inhibition of a recently discovered system of low-threshold unmyelinated tactile (CT) afferents that are present in hairy skin only, project to posterior insular cortex, and serve affective aspects of tactile sensation. An inhibition of impulse transmission in the CT system by sumatriptan could disinhibit nociceptive signalling and make light touch less pleasant. This latter alternative is consistent with the observed reduction in posterior insular cortex activation and the selective effects of stimulation on hairy compared to glabrous skin, which are not explained by the nociceptor sensitization account.

F027

Effectiveness of Gore-San (Wuling San) for eliminating brain edema due to malignant brain tumors

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Objectives Glyceol, isosorbide and steroids can relieve headache and several focal neurological deficits due to perifocal edema produced by malignant brain tumors. Their side effects, however, sometimes prevent them from long-term use. The author has tried to reduce perifocal edema with one of the traditional oriental medical prescription, Gorei-San (Wuling San), which promotes diuresis and eliminates dampness. This prescription contains Polyporus 9 g, Rhizoma Alismatis 15 g, Rhizoma Atractylodis 9 g, Poria 9 g, and Ramulus Cinnamomi 6 g.

Methods Gorei-San were prescribed to 11 patients with malignant brain tumors (male 5, female 6, 35–82 years-old, mean 57.4). Five patients complained of headache, and other six patients complained of focal neurological deficits.

Results Ten patients showed acceptable relief of their symptom. Only one patient did not have a positive result from taking Gorei-San but he did not get a benefit from steroid either. No significant complications were recognized.

Conclusion Gorei-San can be used as a substitute for glycerol, isosorbide and steroids to decrease mild brain edema.

F028

Clinical effects of a behavioral training aimed at migraine prevention and delivered by migraine patient trainers

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Objectives To evaluate the effectiveness of a group behavioral training aimed at prevention of migraine attacks and delivered at home by migraine patient trainers.

Methods A RCT was conducted in the general population, in which migraine patients were randomly allocated to the

behavioral training (BT) or waitlist control group (WLC). BT consisted of 7 group sessions and aimed at physiological self-regulation skills, trigger-management and premonitory symptoms. Migraine patient trainers were selected after self-experience of BT and received supervision to provide BT to 4 fellow patients at home. Outcome measures (i.e. attack frequency, perceived control, quality of life) were registered at baseline and post-intervention with a 4-weeks headache diary and standardized questionnaires. Data were analyzed with co-variance and regression techniques.

Results Of the 264 screened subjects, 129 migraine patients were eligible and randomized (BT:61, WLC:68). Thirty-five percent of BT patients that completed protocol ($n = 52$) achieved a clinical significant improvement ($\geq 50\%$ decrease in attack frequency). Mean attack frequency significantly decreased from 3.1 attacks at baseline to 2.5 after BT. Headache improvement was less than expected but agreed with the clinical effects of group self-help programs in other chronic diseases. Internal control and self-efficacy in attack prevention significantly and substantially increased, but quality of life and other disease parameters did not change due to BT. Follow up results will be presented regarding mediators, moderators and predictors of clinical changes.

Conclusions A home-based behavioral training led by patient trainers can increase migraine patients' self-control and reduce attack frequency in a modest degree.

F029

Incidence and responsiveness of traditional and non-traditional migraine-associated symptoms

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Objective To evaluate the incidence of traditional T [nausea (N), vomiting (V), photophobia (PT), phonophobia (PN)] and non-traditional NT [sinus pain/pressure (SPP) and neck pain/discomfort (NPD)] migraine-associated symptoms pre and post treatment with a fixed-dose combination of sumatriptan and naproxen sodium (SumaRT/Nap) across up to 4 migraines. Neither T nor NT migraine associated symptoms have been studied in a controlled early intervention (EI) setting over multiple attacks.

Methods In two (S1: $N = 646$; S2: $N = 620$) identical, randomized, multi-center, double-blind, placebo-controlled, multiple-attack, EI, cross-over trials in adult migraineurs (ICHD-II) comparing SumaRT/Nap with placebo, 2 hr pain freedom (PF) and 2–24 hr sustained pain freedom (SPF) was consistently and significantly better than placebo across four attacks (Lipton 2006). Subjects were randomized to one of five sequence groups with interspersed placebo (PBO) and instructed to treat four migraine attacks. This secondary analysis used repeated measures techniques (GEE) across attacks for incidence of T (N, PT, PN) and NT (SPP, NPD) migraine-associated symptoms correcting for baseline variation and multiplicity.

Results Mean baseline incidence ranges for T and NT symptoms across 4 attacks were: N (27–33%), PT (69–74%), PN

(62–69%), V (1–3%), SPP (39–44%), NPD (59–61%). Across all attacks at 2 and 4 hrs, the incidence of N, PT, PN, SPP and NPD in Suma/RT treated patients was significantly less than PBO ($p < 0.005$) for both studies. (2 hr difference; S1: 6%, 22%, 18%, 14%, 10%; S2: 6%, 22%, 20%, 14%, 10%; 4 hr difference; S1: 16%, 26%, 24%, 16%, 16%; S2: 12%, 26%, 26%, 16%, 18%, respectively). In over 1100 patients treating over 3300 migraine attacks, SumaRT/Nap was generally well tolerated.

Conclusions Non-traditional and traditional migraine-associated symptoms were common at baseline, even in patients with mild pain, and consistently relieved by SumaRT/Nap in an EI paradigm.

F030

Therapeutic decisions in trigeminal neuralgia

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Introduction Trigeminal neuralgia is a frequent disease in a neurological pain unit. Pharmacological treatment is the first option and should be performed with the goal of pain free, with minimal side effects. In most cases this is the best choice. In fact, 5–8 years of treatment is generally good enough, counting the characteristic relapses and remissions of this neuralgic condition. Patients with a story of striking pain from the beginning, intolerance to drugs or lack of efficacy over the time, usually required a surgical procedure.

We aim to communicate that different surgical techniques either non-invasive or invasive, are useful if they are performed by experienced surgeons in a 'tailored made' indication.

Patients and methods

#35 patients were submitted to Thermolesion by Radiofrequency.

#7 patients were submitted to Microvascular decompression surgery.

#18 patients were submitted to Radiosurgery by Gamma Knife.

Results After 2 years:

*35 thermolesions: 2 relapses, 64% good control of pain

*7 MVD: 1 relapse, 6 good control of pain

*18 gamma -Knife: 5 relapses, 13 good pain control.

Conclusion An adequate patient selection, as well as different surgical techniques either invasive or not, can be optimal to improve quality of life in individuals with trigeminal neuralgia. None of these procedures are near 100% successful, an algorithm is proposed to a better approach for each case.

F031

How many migraine patients need prolonged (>1 year) preventive treatment? Experience with topiramate

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Background Usual recommended duration of preventive treatment for migraine is 3–6 months.

Objectives Our aim was to explore how many patients attending a specialised clinic need prolonged preventive treatment for longer than 1 year.

Patients and methods Eighty consecutive migraine patients who received preventive treatment with topiramate for 3 months with good response and tolerability were included in this observational study. All patients continued on topiramate until they had completed 6 months, when this drug was stopped. Topiramate was reintroduced if there was a worsening. Topiramate was kept for 6 more months and then discontinued again. Those patients whose headaches became worse after this second withdrawal received topiramate again and were followed-up for at least half a year.

Results Headaches did not worsen after the first withdrawal at 6 months in 40 patients (50%), while clearly worsened in the remaining 40 patients. At the end of the first year only two patients out of these 40 (5%) discontinued topiramate and did not notice an increase in headache frequency after 2 months.

Conclusion Around half of the patients attending a specialised clinic due to frequent headache need preventive treatment for more than one year. Our data suggest that the current practice recommending periods of preventive treatment of 3–6 months should be reconsidered for many patients.

F032

Currently marketed oral triptans: a systematic analysis on the comparative efficacy and tolerability

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Objective To update the efficacy and tolerability of marketed oral, non-overencapsulated triptan formulations versus placebo in the treatment of moderate-to-severe migraine attacks, also including early efficacy endpoints and trials published after Ferrari et al's metaanalysis.

Methods A systematic review of double-blind, randomised trials reporting data after a single attack was conducted. Results are shown using relative risk ratios with 95% CIs. A sensitivity analysis was also conducted.

Results After reviewing 202 publications, 37 were included. All triptans provided significant relief and/or absence of pain at 2 hours, and 1 hour relief when compared with placebo. After 30 minutes, fast-dissolving (FD) sumatriptan 50 and 100 mg, sumatriptan 50 mg and rizatriptan 10 mg showed significant relief over placebo, whereas FD sumatriptan 100 mg was the only oral triptan superior to placebo in the pain-free end point. FD sumatriptan 50 and 100 mg and eletriptan 40 mg showed a lower recurrence rate, whereas rizatriptan 10 mg was the only triptan with a recurrence rate greater than placebo. Adverse events of sumatriptan and zolmitriptan were significantly more frequent than those of the placebo group. The inclusion of trials with overencapsulated triptans in the analysis introduced minor changes.

Conclusion This analysis updates the comparative data available for the seven currently marketed oral triptans and clearly demonstrates their efficacy when compared to

placebo, even with stricter endpoints, such as efficacy at 30 minutes. No triptan exhibited better tolerability than placebo. Results are diverse, depending on the triptan, which probably is a reflection of heterogeneous pharmacokinetics.

F033

Effectiveness of topiramate and flunarizine for chronic migraine: a comparative case-series study

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Introduction Chronic migraine (CM) concept has been modified in the appendix of ICHD-2. Flunarizine and topiramate are considered as first-choice drugs in prophylactic treatment of migraine. When they were used comparatively as the initial drug in the prophylactic treatment, both drugs showed a high degree of effectiveness with no significant difference between them. Recently, topiramate has showed to be effective in CM.

Patients and methods Out of 395 patients receiving prophylactic treatment with flunarizine or topiramate as first-choice drugs, we selected patients fulfilling appendix ICHD-2 criteria for CM.

In both groups, the number of days with headache and with severe crisis of migraine within the month before starting treatment and after a four-month of treatment period as well as the response rate were determined.

Results Only 62 patients (36 on topiramate and 26 on flunarizine) were included in the analysis. In both groups were significant decrease ($p = 0.0001$) in mean number of severe attacks at fourth month, with significant difference between groups ($p = 0.0081$). The mean value for percentual reduction in number of migraines at fourth month was: 61.9% with topiramate and 41.1% with flunarizine ($p = 0.0336$). There was no significant difference between groups in terms of side effects or dropouts.

Conclusions Both drugs were effectiveness when used as the initial drug in the prophylactic treatment of CM according criteria of ICHD-2 appendix. Combination of topiramate with a triptan offered better results than flunarizine and triptan. Topiramate could be considered as a first-line treatment for CM prophylaxis.

F034

Gastroscintigraphic evaluation of gastric emptying and absorption of another conventionally formulated triptan

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Background A rapid onset of action is an important property of medications used to treat painful conditions such as migraine and rapid absorption can potentially allow a medication to more quickly reach its site of action. It was previously shown that conventionally formulated sumatriptan tablets disintegrate, empty the stomach and are absorbed more slowly than Sumatriptan with RTTM Technology in

migraineurs, both during and outside an active migraine attack. Repeating this evaluation with another conventionally formulated triptan would confirm that the differences in absorption are due to the formulation of the tablet.

Objectives To determine disintegration, gastric emptying and absorption characteristics of conventionally formulated eletriptan 40 mg (ELE) orally (IN) and interictally (OUT).

Methods This study evaluated ELE disintegration, gastric emptying and absorption in migraineurs (ICHD-II 1.2.1 or 1.1) following administration both IN and OUT. A radioisotope was incorporated in the ELE tablet to allow gastroscintigraphic evaluation. Times to 10% gastric emptying (10%GE) and 50% gastric emptying (50%GE) were determined. Blood samples were collected and analyzed to correlate the gastrointestinal behavior with concentration-time data.

Results 4 female migraineurs received radiolabeled ELE both IN and OUT. Mean times to 10%GE were slightly slower IN vs OUT (31 ± 13 vs 24 ± 10). Mean times to 50%GE were slightly slower IN vs OUT (77 ± 49 vs 61 ± 63).

Conclusions Conventionally formulated eletriptan exhibits disintegration, gastric emptying and absorption characteristics similar to those previously observed with conventionally formulated sumatriptan, but slower than those of sumatriptan with RTTM Technology.

F035

Clinical evaluation of headaches related to dental occlusion

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Disharmony of dental occlusion has not been considered a causal factor of headache in ICHD-II. However, we have found that occlusal treatment improves primary headache in many cases, and reported papers about the relationship between headache and dental occlusion entitled, (1) Headaches Due to Malocclusion, (2) Association between TMJ dysfunction, headaches and malocclusion, (3) Relationship Between Chewing Habit, Eccentricity of the Lower Jaw and Headache, at the 9th, 10th and 11th IHC meetings.

Purpose The aim of this study was to verify dental occlusion-related headache.

Method Twenty patients suspected to suffer from occlusion-related headache were examined (Female; 16, Male; 4, 11 y 8~62 y). Half of them and the other ten were diagnosed as migraine and tension-type headache by physicians, respectively. Four dental pathological factors: three dimensional shift of the mandible, interferences of dental occlusion, abnormal occlusal gravity and limitation of mandibular movement, were treated. When headache was completely or significantly cured, dental occlusion treatment was considered effective.

Results Dental occlusion treatment was effective for all the patients.

Conclusion The results indicate that dental pathological factors induce headache. Dentistry is a part of medicine. Facing treatment resistant headache, therefore, physicians should take account of dental occlusion-related.

F036

The efficacy of detoxification with intravenous magnesium sulfate in patients with medication overuse headache

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Various detoxification protocols have been proposed as treatment strategies for patients with medication overuse headache (MOH). Magnesium sulfate (MAG) has been shown efficacy in prophylactic and acute migraine therapy.

The aim of this study was to analyse the efficacy of 1 gram intravenous magnesium sulfate (MAG) treatment for detoxification of the patients with MOH at one-year follow-up.

The examined group consisted of 240 patients, diagnosed as MOH according to ICHD criteria. There were 182 (75.8%) females, aged 17–76 years, with mean MOH duration 4.8 years. Migraine was primary headache diagnosis in 161 (67.1%) and tension-type headache in 79 (32.9%) patients. Overused medications were nonsteroidal anti-inflammatory drugs, combination medications, opioids, ergot compounds and triptans.

Eighty seven (36.3%) patients were detoxicated with strong advise, while the others were admitted to hospital and treated with intravenous dihydroergotamine (DHE) infusions – 126 (52.5%) patients. Because the lack of DHE from October 2004 the detoxification with MAG was established – 27 (11.3%) patients. Preventive therapy is initiated during the detoxification. The examined groups did not significantly differ regarding demographic data, headache features and overused medications.

At 1 year follow-up, treatment success were obtained in 20 (74.1%) patients detoxified with MAG in comparison to 48 (55.2%) patients treated with advise and 69 (54.8%) with DHE, meanwhile, this difference was not significant ($p = 0.166$).

Although this study was not randomized and placebo-controlled, obtained results pointed to efficacy of detoxification with intravenous MAG and require further analysis.

F037

Topiramate in migraine prevention – analysis of the core phase of an open-label study in Germany

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Objective Migraine outcomes were observed in patients treated with topiramate in migraine prophylaxis allowing flexible dose titration (50–200 mg/d) according to patients needs.

Methods 403 patients (18–80 years) with diagnosed episodic migraine (using IHS-criteria) and three or more attacks/month were included in this open-label clinical trial

(TOPMAT-MIG-3004). Data from 360 patients were included in the ITT-analysis. Treatment was usually started with 25 mg/day TPM. Daily doses were increased in weekly increments of 25 mg/day up to individual maintenance doses kept stable (± 25 mg topiramate/day) in the last 4 weeks of the treatment-period. Patients reported their migraine attacks and intake of acute medication in a diary. In addition, quality of life (MIDAS, HIT-6) and patients' satisfaction were recorded. Primary efficacy parameter was the change in number of migraine days, assessed by comparing baseline-values to data after 24 weeks. Tolerability and safety were recorded by reporting adverse events (AE) and safety parameters (HR, BP).

Results Number of migraine days/28 days (mean \pm SD) decreased significantly from 8.3 ± 3.0 to 4.3 ± 3.0 ($p < 0.0001$). Days with intake of acute medication (mean \pm SD) decreased significantly from 6.9 ± 3.0 to 3.7 ± 2.8 ($p < 0.0001$). Quality of life and treatment-satisfaction improved significantly. The average topiramate-dose was 90 ± 43 mg/day. Observed AEs were consistent with the known safety-profile. Most frequent AE was paresthesia (45.6%). Safety parameters (HR, BP) remained unchanged between baseline and last value.

Conclusion Reductions in monthly migraine days and intake of acute medication similar to results reported from controlled fixed-dosed topiramate-trials were observed. In addition to satisfactory efficacy and tolerability, quality of life and treatment-satisfaction improved.

F038

Correlation between allodynia in periorbital region and potential zoster virus in trigeminal or occipital nerves

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Objectives To preliminarily argue on correlation between cutaneous allodynia in the periorbital region and exacerbation of migraine, and potential zoster virus in trigeminal or occipital nerves.

Methods A total of 100 or over consecutive International Headache Society migraineurs with 10 or over frequent and severe attacks were retrospectively observed clinical manifestations such as the onset of allodynia and the presence of ipsilateral migraine, efficacy of triptans, and calibrated antibody of zoster virus in advance prior to being orally administrated antivirus agent of zoster, valaciclovir, of TID for a week. The same manifestations as aforementioned items were observed 3 months later.

Results The frequency of attacks was declined and the severity of migraine was improved. The frequency of triptans' administration was likely to be decreased, compared with pre-use of the antivirus agent; whereas response to triptans was improved.

Conclusion Mathew reported that there is a higher chance for migraineurs with long history of the disorder and frequent attacks to develop central sensitization. In our argument, zoster virus may relate to develop allodynia as central sensitization in the trigeminal or occipital nerves was developed

due to activation by the virus. Botox is likely to have a prophylactic effect against attacks in recent argument, whereas it has an effect to inhibit the trigeminal nerve activated by the virus and administrate from the peripheral nerve. Antivirus agents are likely to have the same mechanism as Botox and the prophylactic effect against the development of cutaneous allodynia in periorbital region and high severity of attacks.

F039

Timing of triptan treatment in migraine attacks and treatment satisfaction

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The optimal timing of administering triptans to treat migraine attacks has not been established fully. Several studies suggest better efficacy when triptans are used early, when the pain is still mild, however definitive scientific evidence for this is lacking. Triptans have been shown to be less efficacious when taken during aura. In an earlier study we interviewed 214 patients to whom more than one type of specific antimigraine drug had been dispensed in a 1 year period. Patients were asked when they usually took their medication. Because these patients were selected for using two or more different drugs, 439 answers were given. Patients also were asked for their judgement on drug efficacy and speed of action. In this study we present the correlated data. Medication was usually taken during aura by 10 patients (17 answers, 3.9%). In only 38% patients judged positive on drug efficacy, versus in 72% for all other timing of drug intake ($p < 0.05$). For speed of action the results were comparable: 29% positive versus in 63% for all other timing ($p < 0.05$). In 46 cases (10.5%) patients postponed drug intake until their headache was severe enough. Their judgement on drug efficacy and speed of action was significantly better: 90% versus 68% ($p < 0.005$) and 78% versus 58% ($p < 0.05$) respectively. No significant differences were found for other timing of drug intake, including early treatment. These data confirm literature data that triptans should not be taken during aura. However, not confirmed is the expected deterioration of efficacy when treatment is postponed.

F040

Relationship between serum TSH levels and response to medication in patients with migraine

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Introduction The aim of this study was to examine a possible positive or negative association between pituitary function and response to medication for migraine.

Subjects and methods We selected 77 patients with migraine (12 men and 65 women, age: 40.6 ± 12.9 years, mean \pm SD). We determined levels of TSH (thyroid stimulating hormone) and PRL (prolactin) in serum, using enzyme immunoassay technique (EIA). We evaluated response to medication, preventive treatment and/or triptans on migrainous attacks. In the preventive treatment, we treated using 10 mg/day of lom-

erizine HCl, a standard Ca²⁺ blockade for migraine treatment in Japan. We divided the patients to two types good responder; headache frequency decreased half after the medication in two weeks, and poor responder; headache frequency did not decreased or worsened. On migraine attacks, we treated using sumatriptan or zolmitriptan. We also divided the patients to two types good responder; their headache improved in 1.5 hours, and poor responder; their headache improved in 1.5 or more hours.

Results The mean serum TSH levels were 1.37 micro U/ml in the good responders (GR), and 1.80 micro U/ml in the poor responders (PR). The PR showed significantly higher in the serum TSH levels than the GR. The serum PRL levels were no difference in the two groups.

Conclusion It was suggested that the serum TSH levels might be one of evaluators for response of medication in migraine.

F041

Impact of triptan formulation and timing of administration (early vs. late) on acute migraine therapy

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Objective To assess whether the formulation and timing of triptan administration affects migraine treatment outcome.

Methods In 3 different studies, patients received: sumatriptan injection ($n = 20$); zolmitriptan nasal spray [NS] ($n = 20$); or any oral triptan tablet ($n = 22$). Patients treated 4 migraine attacks in a crossover design; 2 attacks were treated early (as soon as possible) and 2 late (until pain became too much to bear) in the course of the attack. Efficacy was primarily evaluated in terms of mean time from treatment to relief of headache pain.

Results Mean pain scores at treatment administration were higher when treating late vs. early (average time to treatment around 7 h).

Conclusion For migraineurs who are not fully satisfied with existing oral triptan therapy, administering treatment earlier in the attack or switching from an oral to a non-oral triptan formulation (or a combination of formulations) may be beneficial.

F042

The development of analgesic use in Germany and in other countries from 1970 to 2005

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Objectives Pain-relieving therapy is generally symptom-induced. Doctor's intervention is usually not required for 'trivial', acute pain (e.g. episodic tension-type headache or migraine without aura), placing analgesics among the drugs most frequently used for self-medication. Reliable data on their use are hardly available. This study presents data for

Germany over 35 years and compares them with other countries.

Methods The pharmacies' purchases were evaluated by investigating the wholesales to the pharmacies together with a panel-sample of pharmacies. The data collected are internationally available as table-books and database ('MIDAS') under 'DPM'. The DPM-listed preparations were identified by composition – both country-specific and time-specific for the years between 1975 and 2005. They were grouped into nine different substance categories. The unit sales were converted into counting and standard units (StU). Per-capita use was calculated by dividing these counting units by the official population figures in the respective countries and years.

Results Per-capita use of antipyretic analgesics from 1970 to 2005 in Germany was stable with 48.8 to 49.7 StU. In France and Sweden, for example, use increased by nearly 50% (France: from 63.6 in 1980 to 141.5 in 2005; Sweden from 90.6 to 147.3). In the USA, use decreased from 75.5 StU 1986 to 60.7 StU 2005. Canada shows some increased use (42.8 StU 1980 to 81.3 StU 2005), which varies, however.

Conclusion Per-capita use of analgesics in Germany was surprisingly stable over the past 35 years. Compared to other industrialised countries analgesic use was partly 50% lower.

F043

Clinical relevance of efficacy endpoints in OTC headache trials based on the patient's global efficacy assessment

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Objectives Patient's global efficacy assessment is of particular importance in clinical trials with OTC medications for self-medication of headaches. The clinical relevance of the results obtained for the primary endpoints should therefore be reflected in a high correlation with the patient's global efficacy assessment.

Methods The 'Thomapyrin Study' showed the significant superiority of the fixed combination of acetylsalicylic acid + paracetamol + caffeine over the combination without caffeine, the single preparations, and placebo in the treatment of headache (Diener et al. 2005). For the 1734 patients included in the efficacy analysis, the correlation of patient's global efficacy assessment (PGEA) with the endpoint results of 'time to 50% pain relief', 'time to be pain-free' was investigated.

Results PGEA demonstrates a consistently close correlation with all examined endpoints. PGEA was 'very good' or 'good' at 'time to 50% pain relief' (medians; h : min) for 0:38 (n = 353) and 1:00 (n = 759), resp., and 'less good' or 'poor' for 2:19 (n = 412) and >4:00 (n = 210), respectively. PGEA was 'very good' or 'good' at 'time to be pain-free' (medians; h: min) for 0:59 (n = 353) and 1:56 (n = 759), resp., and 'less good' or 'poor' for >4:00 (n = 412) and >4:00 (n = 210), respectively. For parameter SPID% (sum of pain intensity differences%; mean) PGEA was 'very good' or 'good' for 85.5% (n = 353) and 73.7% (n = 759), resp., and 'less good' or 'poor' for 43.7 (n = 412) and 8.5% (n = 210), respectively.

Conclusion The clinical relevance of primary and secondary endpoints of headache studies can be demonstrated by investigating their correlation with the patient's global efficacy assessment.

Reference

Diener et al. (2005)

F044

The efficacy of sphenopalatine ganglion radiofrequency ablation in the management of chronic cluster headache

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Objectives Sphenopalatine ganglion block was shown to improve episodic cluster headache rather than chronic cluster. Here we report the efficacy of SPG radiofrequency ablation in 2 patients with intractable chronic cluster headache.

Case reports 2 patients with h/o episodic cluster headaches for 3–4 years whose headache lately lost its circannual pattern and continued without remission for the last 18–24 months. They became resistant to abortive and prophylactic medications.

They underwent a SPG block using the infratemporal approach with bupivacaine 0.5% (2 ml). This block was successful in aborting the headache in both patients. They remained headache free for only 3 weeks (1st patient) and 6 weeks (2nd patient). Subsequently they underwent radiofrequency ablation of the SPG at 80 degrees celsius.

Results The first patient was still headache free at 16 month follow up.

The second patient remained headache free for 9 months and then he developed cluster headaches that lasted for 12 weeks and he went into remission for another 6 months.

Discussion Chronic cluster headache accounts for about 10% of patients with cluster headache, it lacks the circadian pattern (episodic one) and patients are often resistant to pharmacological management.

Our 2 case reports showed that SPG radiofrequency is effective in the treatment for chronic cluster headache. One patient had complete relief of his headache for more than a year and the second one went back to an episodic form of cluster headache which was easily managed with the conventional pharmacological therapy.

F045**Conventional and atypical antipsychotic drugs in the treatment of chronic daily headache**

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Objectives Antipsychotics have long been used for headache treatment. In this study, we explore the efficacy of conventional and atypical antipsychotics in the treatment of Chronic Daily Headache (CDH).

Methods We reviewed the files of 20 patients with CDH (ICHD-II criteria were used). Ten were treated with perphenazine and another ten were treated with olanzapine for at least 3 months. Previous treatment with at least three preventive medications had failed for all 20 patients. t-test was used to measure efficacy by comparing headache days, duration and severity before and after treatment.

Results Treatment with perphenazine resulted in a statistically significant decrease in headache days per month, from 29 before to 6.2 after treatment. With olanzapine, headache days decreased from 27.5 before to 4.9 after treatment. Headache duration with perphenazine decreased from 15.4 hours before treatment to 3.5 hours after it. With olanzapine, duration decreased from 20.2 hours before treatment to 2.3 after it. Decrease in headache severity (0 to 10 scale) before and after treatment was statistically significant for perphenazine as well as for olanzapine.

Conclusion Our study involved a small patient group, was retrospective and patients had failed treatment with three previous preventive medications. We doubt that placebo effect significantly influenced our results.

Olanzapine may be more effective for patients with CDH than perphenazine. 4 patients in whom treatment with perphenazine failed were successfully treated with olanzapine.

Antipsychotics are effective for preventive treatment in CDH as second line medication.

F047**Race, treatment attrition, and treatment outcomes in headache specialty clinic patients**

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Objectives This longitudinal, naturalistic intervention study examined race differences in treatment participation and headache treatment outcomes in patients in headache treatment clinics.

Methods Participants (N = 264) were recruited through specialty clinics in Cincinnati, Columbus, Cleveland, and Toledo, OH. Participants provided data at baseline (BL) and 6-month follow-up (6-Mo FU). Participants (mean age = 36.8 years) were primarily female (88%) and Caucasian (57%). Sixty-eight percent were diagnosed with a mood disorder (i.e., depression, anxiety). African-Americans (79%) were more likely to

be diagnosed with comorbid psychiatric conditions than Caucasians (59%), X²(1) = 9.4, p < 0.01.

Results African-Americans (45%) were significantly more likely to discontinue treatment than Caucasians (31%), X²(1) = 4.7, p < 0.03. Main effects for 'Time' in repeated-measures ANCOVA, controlling for race-related differences in age, years of education, and the presence of a psychiatric comorbid condition, indicated that both African-Americans and Caucasians reported significant reductions in headache frequency, (African-Americans: BL = 17.6, 6-Mo FU = 12.7; Caucasians: BL = 17.7, 6-Mo FU = 12.6) F(1,87) = 28.6, p < 0.01; headache severity, (African-Americans: BL = 2.1, 6-Mo FU = 1.7; Caucasians: BL = 2.0, 6-Mo FU = 1.7) F(1,87) = 36.7, p < 0.01; and headache disability, (African-Americans: BL = 1.1, 6-Mo FU = 0.7; Caucasians: BL = 1.2, 6-Mo FU = 0.7), F(1,87) = 28.9, p < 0.01.

Conclusion While African-Americans were more likely to discontinue treatment for their headaches, those who remained in treatment demonstrated comparable improvements in headache characteristics as their Caucasian counterparts.

F048**Effectiveness of stellate ganglion block on chronic headache**

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Objectives Because the cause and etiology of chronic headache are not yet fully explained, the treatment is not simple and difficult. Chronic headache imposes considerable burdens on sufferer and society as well. Although stellate ganglion block (SGB) is usually used for the treatment of chronic headache, we evaluated and compared the effectiveness of SGB in treating chronic tension headache and migraine patients on pain alleviation and improving the quality of life after an 8 weeks treatment duration.

Methods Patients who experienced headache for more than 4 hours a day and more than 15 days a month were diagnosed as chronic headache and 46 subjects in total were enrolled in this study which were approved from University IRB. The patients were randomly classified into two groups, migraine group (MG, n = 26) and tension headache group (TG, n = 20). The patients of both groups were treated with only SGB twice a week for 8 weeks and evaluated effectiveness after 4 and 8 weeks of treatment, and 4 weeks after the end of treatment. The effectiveness of these treatments in two groups were analyzed using Visual Analogue Scale (VAS) pain scores and Brief Pain Inventory (BPI).

Results The VAS and BPI after 8 weeks of treatment showed significant differences compared with those of MG and TG before treatment and there were no differences between two groups.

Conclusions The above results suggested that SGB might be a useful modality for alleviating the pain and improving the quality of life in TG and MG patients.

F049**Neurophthalmological changes in migraine**Krisztina Benedek¹, M Janaky², J Tajti¹, L Vecsei¹¹Neurology, ²Ophtalmology, University of Szeged, Hungary

Objective The aim of this study was to evaluate latent visual disturbances in patients suffering from migraine with aura.

Methods Electroretinograms (ERGs), patterned electroretinograms (PERGs) and visual electrical responses (VEPs) of 20 patients were recorded and related to the ones of age-matched, healthy controls in terms of their disease duration.

Results Flash ERGs showed no characteristic differences between controls and migraineurs. However, the mean amplitude values of the first positive wave of oscillatory potentials (OPs) were significantly larger in migraine sufferers than in controls. However, a steady decrease of OP amplitudes was found in patients correlated with the time-course of the disease. Similarly, P100 amplitudes of VEPs were higher in the migraine population than in the controls ($p < 0.01$). Both N35/P50 and P50/N90 amplitudes of PERGs were larger in migraine than in controls ($p < 0.005$). Latency values of P50 also showed a positive correlation with the duration of migraine ($p < 0.01$).

Conclusion These electrophysiological changes in migraine could indicate a possible wearing out the initially hyperexcitable Ca^{2+} , Na^{+} and Cl^{-} channels in neurons along the visual pathway.

F050**Brain hyperexcitability can be reversed by topiramate in children with migraine**

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Objectives We have previously showed that in children with migraine the somatosensory system is hyperexcitable, as demonstrated by a shortened somatosensory evoked potential (SEP) recovery cycle (Valeriani et al., 2005). In the present study, our aim was to evaluate the effect of topiramate treatment on the headache clinical parameters and on the somatosensory hyperexcitability.

Methods Eleven children (mean age 11.5 years, range 8–15 years; 8 females, 3 males) were recruited. The somatosensory system excitability was assessed by calculating the SEP changes after paired electrical stimuli at 5 ms, 20 ms and 40 ms interstimulus intervals (ISIs), as compared with a single stimulus condition assumed as the baseline. Brain excitability was measured before the therapy and after a 3-month treatment with topiramate at the average dose of 1.3 mg/Kg/d.

Results In 9 patients, who had a significant reduction in headache frequency (>50%) with topiramate assumption, the recovery cycles of the parietal P24 and the frontal N30 potentials were slowed (two-way ANOVA, $P < 0.05$). On the contrary, in 2 migraineurs, who did not show any improvement, the recovery cycles of the cortical SEP components were even shortened after the pharmacological treatment.

Conclusion Our results showed that topiramate can reduce the somatosensory cortex excitability in children with migraine only when it is effective on the clinical parameters. This suggests that the brain hyperexcitability in paediatric migraine is strictly related to the pain attack frequency.

Reference

Valeriani et al. (2005)

F051**How are OTC headache remedies used? Results of a representative poll of 12,000 people in Germany**Bernhard Aicher¹, R Schneider¹, HC Diener²¹Boehringer-Ingelheim GmbH & Co.KG, ²Department of Neurology, University of Duisburg-Essen, Germany

Objectives The vast majority of headache patients treat their headaches with OTC analgesics without seeing a doctor. Only few data exist on the use of these remedies. This representative, first-time country-wide poll in Germany provides data of 11,897 people.

Methods A representative, multi-level random sample was taken by a random-route method from the basic population of German-speaking people aged >14 years living in private households in Germany. About 700 interviewers did computer-aided personal interviews (C.A.P.I.) in 2005; the interviewees did not receive any incentives. The data on actual analgesic use (without medical advice) included: number of treatment days, average daily dose, highest daily dose ever taken, longest (ever) treatment period, frequency of use as compared with previous years, type of medication used (brand), and personal and headache-related socio-demographic data.

Results Analysis includes the characteristics of use of active substances and brands, duration, severity and course of illness. 11,987 people were interviewed, 6027 (50.2%) thereof suffered from headache, and 3752 (62.3%) used the seven major analgesic brands. Average headache intensity of those was 5.1 cm (10 cm VAS(PI)). In the past 4 weeks analgesics were taken on 3.0 days at a mean dosage of 1.8 tablets/day. Compared with previous years, 19.1% of them reported higher frequency, 19.5% higher intensity, 18.6% lower frequency, and 13.5% lower intensity of their headaches. 11.0% saw a doctor for their headaches.

Conclusion This representative poll confirms the responsible use of OTC analgesics in headache self-treatment and complements data from patient files or clinical trials.

F052**Aspirin in tension-type headache treatment**

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Acetylsalicylic acid (ASA, Aspirin®) is among most used drugs worldwide. At present, Aspirin represents a quite versatile drug employed in the control of pain symptomatologies and in situations such as prevention of both ischemic stroke

and cardiovascular events. Aspirin causes inhibition of prostaglandin (PG) synthesis by inactivation of the cyclooxygenase (COX) enzyme. ASA constitutes the focus of new developments explaining more widely Aspirin's control of inflammation. The induction of lipoxins endogenous epimers (Aspirin-triggered 15-epi-lipoxins, ATLs) represents one of the most recent achievements. This particular feature of Aspirin is not shared by other NSAIDs. ASA is well-known as headache medication, figuring as possible treatment choice in tension-type headache but also in acute migraine attacks. Furthermore, a new aspirin formulation with a greater rapidity of action has been introduced. In conclusion, little information exists on the subject and more studies are required.

Reference

Farinelli I, Martelletti P. (2007) Aspirin and tension-type headache. *J Headache Pain* 8:1. DOI: 10.1007/s10194-006-0357-4

F053

Prophylaxis of chronic daily headache with Botulinum toxin type A

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Botulinum toxin type A (BoNT-A) has been recently suggested as prophylaxis therapy for the treatment of primary headache chronic forms. Several studies on its efficacy are available, but results are often contradictory and not univocal. BoNT-A has been investigated on chronic forms of both tension-type headache and migraine.

In this study we introduce our five-year long experience with BoNT-A (BOTOX®, Allergan, Irvine CA). The employed dosage has been of 100 U and the Fixed Sites – Fixed Doses (FSFD) protocol was used.

The period of study occurred between April 2001 and July 2006. About 1350 patients suffering from Chronic Daily Headache (CDH) have been under treatment.

We registered in these patients the number of headache days per month and observed their reduction in relation to the number of injections. The height has been reached after 12 months of treatment, with patients being free of attacks 23 days per month.

The BoNT-A treatment resulted safe and well-tolerated, since only 1.6% of patients reported adverse events which were all mild and transient.

In conclusion, BoNT-A therapy seems to appear an efficacious new therapeutic choice in the prophylaxis of CDH, especially for patients not responding to previous prophylactic treatments.

Reference

Farinelli I, Coloprisco G, De Filippis S, Martelletti P. (2006) Long-term benefits of botulinum toxin type A (BOTOX) in chronic daily headache: a five-year long experience. *J Headache Pain* 6:407–12

F054

Topiramate induced uveitis

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Case report We present a 29 years-old migraine sufferer with uveitis occurring after topiramate treatment for one month. Her previous history consisted of a 5 years-old common migraine, recurring 2–3 times weekly. Neurological examination was normal. No benefit was obtained from former medications with amitriptyline, flunarizine, propranolol or venlafaxine at effective doses and sufficient duration. Her cranial MRI revealed non-specific hyperintense millimetre gliotic lesions on T2 and FLAIR weighted images. Routine biochemistry, haemogram, thyroid function tests, B12 vitamin level, anticardiolipin IgG and IgM remained in normal ranges, whereas FANA and VDRL were negative. We started topiramate at 25 mg/day, increasing it gradually to 100 mg/day. Although her pain frequencies as well as pain intensity were controlled by the first month, she now complained of blurred vision on her left eye. Ophthalmologic consultation resulted in posterior uveitis with 100% vision loss on the left and 50% vision loss on the right eye. We repeated her cranial MRI with no changes in former findings. Her ESR and chest radiography was normal. RPR, rheumatoid factor, HLA B27 and B5 were negative. No infectious agent or immunologic finding was detected. Fluorescein angiography of the retina was normal.

Since no other evidence for uveitis could be identified, topiramate seems to be the suspected cause for uveitis in this case. We propose to inform patients of this potential risk.

F055

A randomized trial of IV dexamethasone for acute migraine in the emergency department

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Background It is not yet clear if corticosteroids are useful for the treatment of migraine. We determined the efficacy of 10 mg of intravenous dexamethasone as adjuvant therapy for patients presenting to an emergency department (ED) with acute migraine.

Methods This was a randomized, double-blind placebo-controlled multi-center trial. Subjects were randomized to dexamethasone 10 mg IV or placebo. As primary treatment for their migraine, all subjects received intravenous metoclopramide. Our primary hypotheses were the following: A greater percentage of migraine patients who received dexamethasone would (1) achieve a headache-free state in the ED and maintain it for 24 hours and (2) have no headache-related functional impairment after ED discharge when compared to placebo.

Results 656 patients were approached for participation and 205 were randomized. The persistent pain-free outcome was achieved in 25% of those randomized to dexamethasone and 19% of placebo ($p = 0.34$). No functional impairment after ED discharge occurred in 67% of those randomized to dexamethasone and 59% of placebo ($p = 0.20$). In the subgroup of subjects with migraine lasting longer than 72 hours, 38% of those randomized to dexamethasone were persistently pain-free versus 13% of placebo ($p = 0.06$). Side effect profiles were similar, with the exception of acute medication reactions, which occurred more commonly in the dexamethasone group.

Conclusion A moderate dose of intravenous dexamethasone should not be administered routinely for the ED-based treatment of acute migraine, although it might be useful for patients with migraine lasting longer than 72 hours.

F056

Anticephalic premedicated mask

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Objective A placebo-controlled double-blind study was performed to determine the efficacy of a topical anticephalic 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.

F057

Satisfaction with triptans in routine clinical practice

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Objectives Efficacy and tolerability of triptans in the treatment of migraine attacks have been well established in clinical trials. In clinical practice, triptans are widely used and most patients express satisfaction with this treatment.

However, little is known of the minority of migraineurs who find triptans unsatisfactory and choose not to use them.

Methods 29 migraine specialists enlisted 30 consecutive patients with migraine who had used a triptan at least once, excluding patients with chronic headache or/and medication overuse. Demographics, migraine characteristics, migraine severity (using HIT score), migraine prophylaxis, number of triptans used and psychological well being (using HAD score) were noted for all participants. Patients were asked about satisfaction with triptans, reasons of non-satisfaction were recorded, as well as the way triptans were used.

Results On a total of 663 migraineurs, 383 found triptans fully satisfactory (58.4%), 200 declared themselves only partially satisfied (30.5%) and for 73 patients, triptans were totally unsatisfactory and never used. For most unsatisfied or partially satisfied patients, lack of efficacy was the main problem, followed by inconsistency of response, recurrences, adverse effects and distrust generated by patients' doctors or pharmacists. Only 30% had used triptans to treat mild pain, most of them delaying treatment and/or using analgesics or NSAIDS first. Migraineurs who were unsatisfied with triptans tended to have a higher HIT score.

Conclusion Understanding the reasons of patients' non-satisfaction may help to overcome at least some of the obstacles to a better management of migraine attacks.

F058

Nociception-specific blink reflex: a double-blinded placebo-controlled pharmacological study in 21 healthy males

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Background The physiology and pharmacology of activation or perception of activation of pain-coding trigeminovascular afferents in humans is fundamental to understanding the biology of headache and developing new treatments.

Methods The blink reflex was elicited using a novel concentric electrode and recorded in four separate sessions, at baseline and two minutes after administration of ramped doses of diazepam (final dose 0.07 mg/kg), fentanyl (final dose 1.11 µg/kg), ketamine (final dose 0.084 mg/kg) and 0.9% saline solution. The AUC (area under the curve, µV*ms) and the latency (ms) of the ipsi- and contralateral R2 component of the blink reflex were calculated by PC-based offline analysis with custom written software programmed in Matlab. Immediately after each block of blink reflex recordings certain psychometric parameters were assessed.

Results There was an effect due to DRUG on the ipsilateral ($F_{3,60} = 7.3$, $P < 0.001$) AUC as well as on the contralateral ($F_{3,60} = 6.02$, $P < 0.001$) AUC across the study. A significant decrement in comparison to placebo was observed only for diazepam, affecting the ipsilateral AUC. The scores of

alertness, calmness, contentedness, reaction time and precision were not affected by the DRUG across the sessions.

Conclusion Previous studies suggest central, rather than peripheral changes in nociceptive trigeminal transmission in migraine. This study demonstrates a robust effect of benzodiazepine receptor modulation of the nociception specific blink reflex, without any μ -opiate or glutamate NMDA receptor component. The nociception specific blink reflex offers a reproducible, quantifiable method of assessment of trigeminal nociceptive system in humans.

F059

Efficacy of rizatriptan for ICHD-II pure menstrual migraine and menstrually related migraine

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Objective To examine the efficacy of rizatriptan for the treatment of pure menstrual migraine and menstrually related migraine, as defined by the 2004 revision of the International Classification of Headache Disorders (ICHD-II).

Methods The two protocols (MM1 and MM2) were randomized, parallel, placebo-controlled, double-blind studies. Adult patients with menstrual migraine defined by ICHD-II criteria were assigned to either rizatriptan 10-mg tablet or placebo (2 : 1). Patients treated a single menstrual migraine attack of moderate or severe pain intensity. This prospectively planned substudy pooled data from patients with a diagnosis of PMM. The primary substudy endpoint was 2-hour pain relief. Efficacy data was also summarized for patients with MRM.

Results Of the 707 (MM1: 357, MM2: 350) patients enrolled and treated in the study, 146 patients (MM1: 81; MM2: 65) had a diagnosis of PMM. The percentage of patients reporting 2-hour pain relief was significantly greater for rizatriptan than for placebo for the overall population (MM1: 70% vs. 53%, MM2: 73% vs. 50%, $p \leq 0.001$ for both studies) and for both the PMM (73% vs. 50%, $p = 0.006$) and MRM subgroups (71% vs. 52%).

Conclusion Rizatriptan 10 mg was superior to placebo for the treatment of pure menstrual migraine, as measured by 2-hour pain relief. Rizatriptan was also effective for the treatment of menstrually related migraine and for relief of migraine-associated symptoms and functional disability for both headaches subtypes.

F060

The novel oral CGRP antagonist, MK-0974, exhibits similar pharmacokinetics during and between migraine attacks

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Objective MK-0974 is a novel orally-bioavailable CGRP antagonist being developed for the acute treatment of

migraine. Migraine is associated with delayed gastric emptying which can potentially lead to a different pharmacokinetic profile during an attack than between attacks. This study investigated whether such an effect might be observed with MK-0974.

Methods In this randomized, double-blind, placebo-controlled, two-period fixed-sequence study in 23 migraineurs, 15 patients received 300 mg of Phase I formulation MK-0974 in both periods and 8 received placebo. In Period 1, patients attended a clinical research unit to receive study drug within ~2 h of the onset of a moderate to severe migraine attack, but at least 4 h after their last meal. In period 2, patients received study drug in-house after at least a 4 h fast, at a similar time of day to Period 1 dosing time.

Results No serious adverse experiences occurred in either period. MK-0974 was generally well tolerated. Geometric mean ratios during/between migraine attacks (90% CIs) for pharmacokinetic measures were as follows: $C_{max} = 0.89 \mu M$ (0.71, 1.11); $AUC_{0-4 h} = 0.94 \mu M h$ (0.77, 1.14); $AUC_{0-\infty} = 1.07 \mu M h$ (0.91, 1.25). The median T_{max} during a migraine was 1.5 h versus 1.0 h between attacks. The harmonic mean apparent $t_{1/2}$ was 8.5 h during a migraine versus 10.6 h between attacks.

Conclusions The values for MK-0974 pharmacokinetic parameters were generally similar during and between migraine attacks.

Funded by Merck Research Laboratories.

F061

Inhibition of capsaicin-induced increase in dermal microvascular blood flow by the oral CGRP antagonist, MK-0974

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Objective To evaluate inhibition of capsaicin-induced increase in dermal-blood-flow (DBF) following MK-0974, an orally-bioavailable CGRP antagonist being developed for treatment of migraine.

Methods Three-period crossover study in 12 healthy males. In each period, each subject received an oral dose of MK-0974 300 mg, MK-0974 800 mg, or placebo, followed by two topical doses of 300 and 1000 μg capsaicin/20 μL water-ethanol mixture, applied on the volar surface of the subjects' left and right forearms, at 30 min and 3.5 h post-dosing of MK-0974/placebo. DBF was assessed by laser Doppler perfusion imaging. Plasma samples were collected 30 min after each capsaicin administration. % inhibition was computed as $100 \times (1 - [\% \text{ increase active}/\% \text{ increase placebo}])$ where % increase is the percent increase in mean perfusion from baseline to postdose.

Results Geometric mean plasma concentrations after dosing with 300 mg and 800 mg MK-0974 were 745 nM and 1498 nM respectively at 1 h, and 609 nM and 2434 nM respectively at 4 h. The median % inhibition of DBF increase produced by MK-0974 300 mg was: 1 h = 86% (300 μg capsaicin), 84% (1000 μg

capsaicin); 4 h = 100% (300 µg capsaicin), 78% (1000 µg capsaicin). The median % inhibition of DBF increase produced by MK-0974 800 mg was: 1 h = 83% (300 µg capsaicin), 76% (1000 µg capsaicin); 4 h = 98% (300 µg capsaicin), 90% (1000 µg capsaicin).

Conclusion An 800 mg oral dose of MK-0974 resulted in higher plasma levels at 1 h and 4 h postdose than a 300 mg dose. However, both MK-0974 doses produced a robust inhibition of capsaicin-induced increase in DBF, that did not appear to differ between MK-0974 doses.

Funded by Merck Research Laboratories.

F062

Gabapentin for prevention of high-altitude headache: double-blind randomised clinical trial

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Objective In order to determine the impact of gabapentin prophylaxis on high-altitude headache (HAH) and acute mountain sickness (AMS) development within 24 hours of ascent, we designed a double-blind, randomised, clinical trial.

Methods A prospective, double blind, randomised, placebo controlled trial was carried out in Tochal mountain hotel at an altitude of 3500 meters above sea level during January 2007. Eighty-eight Iranian individuals (26 females/62males; average age: 30.10 ± 1.20 yr; range = 15–62 yr) randomly assigned (1 : 1) ratio to receive either gabapentin (600 mg) or placebo, after ascent. Mean time of HAH-free phase was considered as primary end point. AMS incidence measured by Lake Louise acute mountain sickness score ≥ 4 with headache and one other symptom. Secondary outcome measures included AMS incidence and severity of syndrome (Lake Louise scores ≥ 6).

Results Mean HAH-free period was 21.33 ± 0.94 (95% CI: 19.49–23.16) hours in gabapentin group that was significantly higher than placebo group with a mean HAH-free period of 17.65 ± 1.36 (95% CI: 14.98–20.31) hours ($p = 0.06$). AMS was more prevalent in placebo group (17 (38.6%)) than gabapentin group (9 (20.5%)); however, there was no significant statistical difference ($p = 0.06$). No association was detected between gabapentin prophylaxis and AMS severity.

Conclusion Gabapentin prophylaxis is effective in prevention of high-altitude headache development. Furthermore, our findings confirm that N-methyl-D-aspartic acid receptors and calcium channels in the central nervous system might play important role in HAH pathophysiology.

F063

Memantine for prevention of migraine: a retrospective review of 60 patients

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Objectives Based on our laboratory investigations, we identified memantine as a potential therapy for migraine

prevention, and we have now treated more than 100 patients with this medication. The objectives of this study are to evaluate the potential efficacy and tolerability of memantine as a migraine preventive therapy.

Methods UCLA IRB approval was obtained to review medical records and contact patients with questionnaires regarding their experiences with memantine. All patients had migraine with or without aura based on I.H.S. criteria. The majority had previously tried at least 2 first-line preventive therapies. Memantine was started at a dose of 5 mg. qd, and titrated as needed up to 10 mg. BID. Data collection is ongoing.

Results 54 out of 60 patients reviewed to date continued therapy for at least 1 month; the longest was 16 months. 35 out of 54 of the patients who took memantine for at least 1 month reported a 50% or greater reduction in the frequency of migraine. These patients also reported decreased overall medication use and improved sense of well being. The majority of patients reported no adverse effects associated with memantine therapy. Side effects included rash (2 patients), agitation (4 patients), insomnia (2 patients), and dizziness (2 patients).

Conclusion Although limited by its design, this study indicates that memantine holds promise as a well-tolerated, effective therapy for prevention of migraine. The results are particularly encouraging given the refractory patient population that was studied. A formal, placebo-controlled trial of memantine for migraine prevention is warranted.

F064

Physical therapy improves migraine without aura and chronic migraine

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Objective To study the effect of physical therapy with stretching tender muscles along their lengths (PTS) in patients with migraine without aura and chronic migraine.

Background The headache of migraine without aura (ICHD-II 1.1) and chronic migraine (1.5.1) is often caused by pain and tenderness coming from muscles and ligaments. PTS usually provides lasting relief in myofascial pain. This prospective pilot study evaluates the reduction of headache with PTS in migraineurs.

Methods 23 patients having 1.1 and 15 with 1.5.1 whose headaches were reproduced by the myofascial exam were offered PTS. The global percentage improvement of those who completed the course of PTS was compared to those who declined PTS.

Results In 1.1 patients, those completing PTS had an average improvement of 64%. Those not completing PTS had no improvement. 85% (11 of 13) of treated and 0 (of 5) of untreated 1.1 patients improved 50% or more ($p = 0.01$). The average improvement of patients with 1.5.1 who had PTS was 72%. 86% of treated patients had 50% or greater improvement. Of those who had no PTS, one reported a 50% improvement with the chronic use of fentanyl patches resulting for a mean group improvement of 10%.

Conclusion Physical therapy with stretching tender muscles along their lengths is effective treatment for migraine without aura and chronic migraine patients whose headaches can be reproduced by the myofascial examination.

F065

An open label study of levetiracetam in the prophylactic treatment of migraine

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Several antiepileptic drugs have been investigated for their efficacy in the prophylactic treatment of migraine. We performed a prospective, open, monocentre, non randomized study in order to evaluate the efficacy of levetiracetam in migraine prophylaxis with a treatment period of 12 weeks. Patients were treated with levetiracetam 1,000 mg bid as monotherapy. Migraine frequency was evaluated by a headache diary. The number of migraine attacks and the number of migraine days for every 4 week period (baseline and three periods of 4 weeks each) were primary efficacy parameters. In total, 50 patients entered the treatment period. 46.0% of the ITT population were responders in the last treatment period (52.3% of the PP population). The mean number of migraine attacks for the PP population were 5.2 ± 2.1 (baseline), 4.2 ± 2.4 (period 1), 3.5 ± 1.8 (period 2), and 3.4 ± 2.7 (period 3) and nearly identical to the data of the ITT population. The most frequently reported side effects were somnolence, nausea, and weight gain, all were mild and transient. This prospective open-label pilot study showed that levetiracetam 1,000 mg bid was effective in reducing migraine attack frequency by at least 50% in 46% of all patients. This rate is about in the range of responder rates known from other interventional migraine prophylaxis studies. Analysing the responders, it is suggested that those migraine patients who are not severely affected and those migraine patients with a migraine aura benefit most from prophylactic treatment with levetiracetam.

F066

Memantine in the acute treatment of migraine aura

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There is not established method for the acute treatment of migraine aura. The only substance shown to be effective in acute hemiplegic migraine aura was ketamine nasal spray. Based on the random observation of two patients reporting only mild migraine aura symptoms after the intake of memantine, we performed a small double-blind, placebo-controlled, crossover trial on the efficacy of memantine in the treatment of acute migraine aura. We enrolled 10 patients with pure migraine with aura (6 visual aura, 3 mixed aura, 1 hemiplegic aura) and advised them keep a diary for the next attack with aura. Then, they were asked to take 10 mg liquid memantine or liquid placebo in the next two migraine with aura attacks.

Eight of these patients treated at least one attack. After taking memantine, 6 patients reported a reduction of the aura duration of at least 50% as compared to the baseline aura and to the aura with placebo intake. All but one reported a decreased intensity of the aura symptoms. The headache following the aura was not influenced by the intake of memantine. There were no relevant side effects. We conclude that the NMDA receptor antagonist memantine might be an option for the treatment of acute aura and suggest a larger placebo-controlled trial.

F067

Stellate ganglion block: a new approach in the therapy of facial pain

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Stellate Ganglion Block (SGB) is an anaesthesiology procedure commonly used for the treatment of chronic pain. In the present study we verify the efficacy of SGD in the treatment of facial pain which can be found in different pathological syndromes such as traumas, iatrogenic issues, herpes zoster or neurological pathologies; and to examine whether the efficacy is dependent upon when this therapy is administered. Fifty patients were divided into 2 randomized groups ($n = 25$ each group), the first group was treated with a SGB by 10 administrations of 10 mg of Levobupivacaine given every other day, followed by one administration per month for six months thereafter. The second group was treated with Tramadol 100 mg/day and Gabapentin 1800 mg/day for 6 months, during the seventh month they were given SGB therapy using the same methodology as that described for the first group. Before treatment the mean visual analogue scale (VAS) pain score for the first group was 8.89; after the 10th SGB it was lowered to 0.2 and it remained at that reduced level for the 6th and 12th months. In addition, in the second group VAS value went from 8.83 to 4.1 after the 20th day on medication, 5.7 after 6 months and to 4.9 after the 12th months of medication. Thus, our results point out that SGB may be a new approach in the treatment of facial pain patients. Furthermore, this study indicates that patients must be treated with SGB therapy precociously to receive its full benefits.

F068

New antiepileptic drugs in migraine prophylaxis: an open-label study with levetiracetam.

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Objective To evaluate the efficacy of levetiracetam (LEV) as prophylactic treatment for migraine with and without aura.

Methods 30 migraine patients were included, at least 1-year after previous unsuccessful treatments with β -blockers and

calcium antagonists. After a 1-month run-in period for titration of drug (250 mg/day for the first week, increased by 250 mg/wk until a final dosage of 1000 mg/day), frequency, duration and severity of pain with VAS scale have been evaluated at 6 months with paired t test.

Results 3 patients reported one adverse event each: somnolence (2 patients), dizziness (1 patient). 2 patients dropped out because lack of compliance. MWO was diagnosed in 16 patients (6 men, 10 women) while MWA in 9 (2 men, 7 women) (mean age of 28.3 ± 4.6 years). At 6 months evaluation, in 76% of patients, headache frequency decreased from 4.7 ± 1 (before run-in period) to 1.2 ± 1.3 mean episode per month ($p < 0.001$), attack duration from 37.4 ± 13.3 to 17.6 ± 16.5 hours ($p < 0.001$) and pain intensity from 7.2 ± 1.2 to 5.7 ± 2.1 ($p = 0.0654$) by VAS. 9 patients were completely headache free at 6 months follow up. No statistically significant differences have been observed in relationship to age, sex, type of migraine and disease duration.

Discussion As previously reported in retrospective studies, LEV reduced the frequency and severity of both MWO and MWA with modest side-effects. These results may warrant a double-blind placebo-controlled trial of LEV in migraine prophylaxis.

F069

Pattern of triptans use in the population: why the sub-utilization?

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Objectives Studies performed in selected migraine patients, show that the use of triptans is low. Few studies on triptans use in the general population have been performed. Our study was aimed to establish the pattern of triptans utilization in a large population.

Methods The patterns of triptans prescriptions dispensed during 2006, in the population of 33 Italian Health Authorities were investigated. Previously, in one of these Authorities we performed an accurate analysis on the prescriptions of the 2005.

Results On a total population of 5549731 residents, patients receiving triptans treatment during 2006 were 32584 (0.6%), 22.3% males and 77.7% females. Males and females aged 15–44 received 51.4% of prescriptions, those aged 45–65 received 38.7% of prescriptions and over 65 years 7.8% of prescriptions.

In our previous study, in a Health Authority of 224065 residents the percentage of triptans utilization in the 2005 was 0.55% of the population, and also the age and sex distribution were the same of the analysis relative to the 2006. Oral and soluble tablets accounted of 94% of the prescriptions. In the 57.7% of triptans users only 1–2 packages were prescribed.

Conclusion This was a large study on the triptans use concerning about a tenth of the Italian population. Considering that the migraine prevalence in Italy is about 12%, our study shows a very low triptans utilization: only 5% of the migraine patients were treated with triptans. We should understand

why a small percentage of migraine patients use triptans and, when they do, in small amount.

F070

Prevalence and size of PFO in migraine with and without aura and cluster headache and relation with clinical phenotype

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Background and object To test the hypothesis that the link between cardiac interatrial patent foramen ovale (PFO) and migraine (both with and without aura; MA+/MA-) or cluster headache (CH) as well as migraine clinical phenotype are dependent on the size of the shunt.

Patients and methods Contrast enhanced transcranial Doppler examination with monitoring of the middle cerebral artery (MCA) was performed in a group of 260 consecutive patients with MA+, 74 with MA-, and 38 with CH, both at rest and after Valsalva maneuver. The size of the shunt was classified as small, medium or large, based on the number of spikes detected on MCA according to standard criteria.

Results Prevalence and size of PFO in each group were the following: 161 MA+ (61.9%), of which 86 (53.4%) small, 45 (27.9%) medium, 30 (18.7%) large; 12 MA- (16.2%), of which 8 (66.6%) small, 3 (25.0%) medium and 1 (8.4%) large; and 14 CH (36.8%), of which 11 (78.6%) small, 2 (14.2%) medium, 1 (7.2%) large. There was no significant association of clinical variables (prevalence of autonomic symptoms, intensity and frequency of pain, frequency of aura and its clinical presentation) with presence and size of PFO in each subgroup.

Conclusions Our findings confirm the relation between PFO and MA+, but do not support the hypothesis of a pathogenic link between presence and size of PFO and MA+, given that the clinical phenotype of the disease is independent on such an association.

F071

Successful preventive therapy in hypnic headache using hypnotics

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Objectives To report the case of a hypnic headache sufferer who consistently prevented his nocturnal headache attacks over many years using hypnotics at bedtime.

Methods Case report.

Results A 53-year-old man presented with a seven-year history of hypnic headache (meeting ICHD-2 criteria). Every night, without exception, a headache woke him up between 1:30 to 2:30 AM. If he took Unisom (doxylamine succinate 25 mg), Tylenol PM (acetaminophen 500 mg/diphenhydramine HCl 25 mg), or Lunesta (eszopiclone 2 mg) at bedtime he was able to sleep through the night without having the nocturnal headache wake him. On multiple occasions he did not take the sedative. Without exception on those nights, his usual

nocturnal headache recurred. He has been on these medications on a nightly basis for years successfully preventing his headaches.

The pathophysiology of hypnic headache is not entirely understood. In polysomnography studies, many hypnic headache attacks have the tendency to start during REM sleep, a period in sleep architecture where dorsal raphe and locus cerulei nuclei activity is absent. Ezopiclone is known to decrease total REM time, and REM density. Further, antihistamines that antagonize H1 receptors such as diphenhydramine and doxylamine are known to decrease the rate of REM sleep. By means of decreasing the density, rate, and/or total time of REM sleep, the hypnotics used by this patient may have prevented hypnic headache attacks.

Conclusions Other hypnic headache sufferers may benefit from prophylactic nocturnal doses of weak hypnotics, particularly those individuals with frequent or daily attacks.

F072

Usual headache locations and headache alterations in pregnant women exposed to short-term normobaric hypoxia

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Objectives To find out usual locations of headache in pregnant women and its alterations following short-term normobaric hypoxia exposures.

Methods 54 pregnant women (mean age 26.3 years, SD 4.9, range 19–39; mean gestational age 22.8 weeks, SD 4.5, range 13–33) experiencing headache immediately before hypoxic procedures (14–16% oxygen, 15 minutes) were studied. A headache location was asked prior to exposing. All the ladies were in no way informed on possible headache relief/shift.

Results There were 65 episodes of headache. Headache in the temporal region(s) was perceived in 35.7% of episodes; in 30.0%, headache was in the forehead, in 11.4% it was over the cranium vault, in the same percentage – over all the head, in 8.5% – in the occipital region, and in 2.8% – in a half of the head. After sessions, no headache aggravation took place. In 10.7%, the women reported no changes of pain. In 15.3%, a headache shift to another region appeared what was appraised by all the sufferers as a better situation. The rest 73.7% episodes were related to improving the headache status (50.7% of relief and 23.0% of disappearance).

Conclusions (1) Two thirds of pregnant women have headache in the temporal or frontal region; (2) only one sixth of pregnant women provided with normobaric hypoxia do report dislocating headache after exposures while three fourths of those ladies perceive headache relief or disappearance. Thus, frontal and temporal headache in pregnant women are most common, relatively easily alleviated, however hardly dislocated when exposing to normobaric hypoxia.

F073

Mobile internet support – a potential new tool in migraine management

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Objectives Development of protected and feasible online support of migraine management in real life and its testing in behavioural attack prevention.

Methods Online digital assistance (ODA) runs on clinical software connecting PDA's (or cell phones) with internet facility to a dedicated server, which manages the entry (log-in, password, patient nick names), the designing of electronic diaries (symptom monitoring) and the online execution of feedback or coaching (through tailored responses, emotions, graphics). The present application supports (1) early detection of migraine triggers and premonitory symptoms and (2) behavioural self-regulation in the premonitory stage of the attack. ODA feasibility was tested in 44 migraine patients with an average of 3.2 attacks at 4-week baseline in the last part of a 10-week behavioural training (BT).

Results The ODA application for migraine is safe and robust. Feasibility was confirmed convincingly regarding user-friendliness, usefulness versus burden, and intended support of ODA, and compliance established subjectively and objectively was high. Half of the respondents asserted that ODA can be inconvenient, but most participants appreciated that ODA imposed self-awareness (84%) and reinforced immediate action for attack prevention (73%). Preliminary results (N = 16) suggest a correlation between ODA support experienced subjectively and actual decrease in migraine attacks, and initial comparison with matched BT participants who did not receive ODA indicates that the significance of improvements in attack frequency and duration is stronger in the ODA group.

Conclusions ODA is feasible and well appreciated and may open new windows to migraine management and the outreach of patients.

F074

Repeated suboccipital steroid injections in cluster headache with poor response to preventive medication

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Objectives Ambrosini et al. (2005) demonstrated the efficacy of single suboccipital steroid injections in cluster headache (CH). We report our experience with repeated injections in a patient with severe CH.

Case report In 1998, this male patient developed CH which was chronic for 30 months, episodic for the following 5 years and thereafter chronic again. The attack frequency ranged between 2/month and 6/day with occasional constant pain. Cluster periods lasted 3–6 months and remissions 2–6 months. Treatment with prednisolon was effective only initially. Vera-

pamil at daily doses of up to 960 mg was inconsistently effective, nevertheless the patient continued to take verapamil 240 mg daily. Lithium and topiramate were not tolerated, other treatments were ineffective. In March 2006, the attack frequency increased to 5–6/day. Repeated injections with bupivacaine in the left suboccipital region at an anaesthesiological clinic decreased the frequency to 1–3/month. From December 1, 2006, the frequency increased to 2–3/day and constant pain occurred. On December 15 we injected 2.5 ml of a mixture containing betamethasone dipropionate, betamethasone disodiumphosphate and lidocaine without changing the dose of verapamil. Within 1 day the patient was free of attacks, the constant pain was milder but still present. Therefore, we repeated the injection 3, 5 and 6 days after the first one. Since then the patient has been pain-free for 5 weeks up to now. During 9 years of follow-up this was the shortest cluster period ever.

Conclusion Repeated suboccipital steroid injections might be useful in CH with poor response to preventive medication.

F075

Efficacy of zolmitriptan nasal spray according to migraine severity and timing of treatment

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Objective To explore whether the efficacy of zolmitriptan nasal spray (NS) is influenced by the severity of migraine and the timing of drug administration after headache onset.

Methods A pooled analysis was performed of 4 large international clinical trials of zolmitriptan NS (5 mg) in the treatment of adults with migraine. Efficacy according to migraine severity and timing of drug administration was evaluated: pain-free response at 2 h; relief of associated symptoms (nausea, photophobia and phonophobia) at 2 h; sustained pain-free response at 24 h (pain-free at 2 h and no recurrence or use of further medication within 24 h); and need for additional medication (second dose or escape medication).

Results High efficacy rates were apparent for zolmitriptan NS (n = 31,483) compared with placebo (n = 449). Response rates for mild attacks treated with zolmitriptan NS were 11–24% greater than for moderate attacks and 29–48% greater than for severe attacks, with 2-h pain-free rates as high as 80% when treating mild headaches. Some 42–49% of attacks were treated within 15 min and 56–64% within 30 min of headache onset. When 2-h pain-free response rates with zolmitriptan NS were analyzed, there did not appear to be any difference in response rates between attacks treated early or late in any severity subgroup. Similar findings were apparent for other efficacy endpoints.

Conclusion Zolmitriptan NS is highly effective for the acute treatment of migraine. Efficacy is very much influenced by the headache severity at the time of treatment, but not by time to treatment after onset of the attack.

F076

Thyroid function and trigeminal evoked potentials in migraine patients

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Objective To investigate the thyroid-stimulating hormone, thyroid hormones and trigeminal evoked potentials in migraine patients in accordance with clinical features of the disease.

Methods The levels of thyroid-stimulating hormone (TSH), T3, T4 and trigeminal evoked potentials (TEP) were investigated in an open-label study of 12 migraine (ICHD-II) patients aged 24–53 (average 38.54 years) interictally (the time period between the attack and the measurements not less than 72 h).

Results The levels of TSH, T3 and T4 were normal in all patients. The T4 levels positively correlated with the duration of the disease. No other correlations of TSH, T3, T4 levels with clinical features of migraine were found. The values of P1, N2 and N1-P1 (TEP) significantly increased in patients with lower levels of TSH and higher levels of T4. The values of TEP also straightly correlated with the disease duration and the frequency of attacks, and they inversely correlated with the length of the attacks.

Conclusions A dependence between thyroid function and trigeminal EP was found that may either suggest an influence of thyroid function on trigeminovascular system or reflect a role of hypothalamo-pituitary activity in trigeminal nociception in migraineurs. **Keywords:** migraine, thyroid, trigeminal evoked potentials.

F077

Transcutaneous temporal electrotherapy in chronic migraine: a pilot study of short term efficacy and mode of action

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Background Chronic migraine (CM, ICHD-II 1.5.1) is a disabling complication of migraine. TopMig® is a device delivering high frequency currents (up to 20 mA; 85 Hz; 130 µs) over the temples and claimed to be effective in headaches including migraine (<http://www.topmig.com/fr>). It is thought to act by blocking transmission at 2nd order trigeminal nociceptors.

Objectives To assess efficacy of TopMig® in 10 CM patients and its influence on pain perception and the nociception-specific blink reflex (nsBR).

Methods Ten CM patients applied TopMig® 3x/week 30 min up to the highest tolerable intensity. Treatment, headache frequency and intensity were monitored with diaries. Before and after electrotherapy, we measured perception and pain thresholds as well as the nsBR using a custom-built electrode. For comparison, we studied 10 healthy subjects of comparable age and sex distribution.

Results After 15 days, TopMig® decreased mean headache frequency ($p = 0.024$), intensity ($p = 0.038$) and duration (0.033). It had meaningful effectiveness in 50% of patients, as 5 of them continued the treatment after 30 days, while 2 preferred to interrupt it at 15 days and 3 at 30 days. TopMig® increased perception ($p = 0.03$), but not pain threshold ($p = 0.13$) at 15 days. It also reduced the AUC of the nsBR immediately after the 1st session ($p = 0.013$) and after 15 days ($p = 0.026$).

Conclusions This study suggests that TopMig® may be effective in disabled CM patients and that a larger controlled study may be worthwhile. Its mechanism of action could be acute and durable decrease of excitability in the nociceptive trigeminal system.

F078

Systemic rt-PA and sonothrombolysis in management of stroke associated with migraine – case report

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Introduction The association between stroke and migraine is highly complex. Several issues should be addressed: cerebral infarction occurring during the course of a typical migraine with aura attack (migrainous infarction), ischemic stroke during the course of a migraine without aura attack, coexisting stroke and migraine, stroke of other cause with symptoms resembling migraine with aura, migraine attacks triggered by cerebral ischemia, migraine as a risk factor for ischemic stroke.

Case description A case of 21-years old female, who suffered an acute ischemic stroke during migrainous attack without aura, is presented. The patient developed hemiplegia with hemihypoesthesia and right-sided hemianopsia 1 hour after the headache onset. Magnetic resonance imaging (diffusion weighted images) detected acute ischaemic lesion in the left occipital lobe. An occlusion of branches of posterior cerebral artery (PCA) was shown using MR angiography and transcranial color-coded sonography (TCCS) examination. A combined treatment with systemic thrombolysis with rt-PA and sonothrombolysis led to PCA recanalization, as visualized by TCCS examination. Further tests – screening for thrombophilias, ultrasound of cervical vessels, transoesophageal echocardiography and Holter electrocardiogram monitoring were normal. The patient was an active smoker and did not use oral contraceptives. A favorable clinical outcome was achieved after one month.

Discussion Stroke developing during a migraine attack is rare. If a thrombotic occlusion of intracranial artery is detected, systemic thrombolysis alone or in combination with another recanalization method, should be used to achieve early arterial recanalization in order to increase the chance for a good clinical outcome.

F079

Predictive factor for effectiveness of botulinum toxin treatment in migraine

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Objective To investigate the classic migraine symptoms that would differentiate responders from non-responders to prophylactic botulinum toxin type A (BTX-A) treatment in episodic migraine. Since the efficacy of BTX-A treatment in preventing migraine still remains controversial, there is an unmet need for identifying a predictive factor that will indicate responders from non-responders. Could quantitative sensory testing (QST) of cutaneous allodynia (CA) be useful is still not clear.

Methods Seventy patients with episodic migraine were enrolled in a randomized, double-blind, placebo-controlled, crossover study of 8 months duration. Patients were divided into two groups according to presence of CA assessed by QST. Both groups were injected at baseline and after 4 months with BTX-A (as BotoxR, Allergan, total dose 80 U) and/or placebo. Patients kept a home diary. The primary efficacy parameters were migraine frequency and headache days. Patients experiencing a >70% reduction in attacks frequency within 4 months of treatment were considered as responders.

Results A total of 30 patients with CA were included in group A, and 40 patients without CA were included in group B. No significant difference was found in the classical migraine symptoms. However, significant reduction ($P < 0.01$) of migraine frequency and number of headache days were found during BTX-A treatment compared to placebo only in patients with CA.

Conclusion Our results indicate that CA could be a predictive factor for responders and non-responders to BTX-A prophylactic therapy in migraine. These results should be followed to see if CA is a predictor of long-term efficacy.

F080

Lysine clonixinate vs. dipyrone for the acute treatment of severe migraine: a randomized and double-blind study

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Several nonsteroidal anti-inflammatory drugs (NSAID) are effective to treat migraine attacks. Lysine clonixinate (LC) and Dipyrone are NSAID proven effective for migraine attacks in its IV formulations. The aim of this study was to evaluate the efficacy and tolerability of the intravenous formulations of LC and dipyrone in the treatment of severe migraine attacks.

Methods Thirty patients (28 women, 2 men), ages 18 to 48 years (mean 31) with migraine according to the ICHD-II were prospectively studied. The patients were randomized into two groups (dipyrone or LC), when presenting to an emergency department with a severe migraine attack. The study was single-blind. Headache intensity, nausea, photophobia

and side effects were evaluated at 0, 30, 60 and 90 min after the drug administration.

Results All patients completed the study. At 60 and 90 min respectively, 2 and 5 patients from the dipyrone group and 11 (73.3%) and 13 (86.6%) patients from the LC group were pain free. Nausea was present at baseline in 12 patients of each group and photophobia in 15 of each group. At 60 min, 7 patients of the dipyrone group and 11 of the LC group were nausea-free. Photophobia was absent in 8 patients from dipyrone group and in 13 of the LC group at 60 min as well. Pain in the site of the injection was reported by 3 patients of the dipyrone group and in 13 patients of the LC group ($p < 0.0001$).

Conclusions LC is significantly effective and superior to dipyrone as well as reasonably tolerated in patients presenting severe attacks of migraine.

F081

Response to ayurvedic treatment in prevention of migraine: an update of multicentric observational clinical study

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Objective Migraine is characterized by various combinations of neurological, gastrointestinal and autonomic symptoms without any known etiopathophysiology. The present study is aimed to explore / establish preventive treatment of migraine using principles of ayurveda: the traditional Indian system of medicine.

Method A 30 months long pilot prospective clinical study on 104 migraine patients (Chandigarh – June 2002–Dec 2004) confirmed the findings of retrospective clinical experience of ayurvedic therapy in prevention of migraine. Ongoing confirmatory study since May 2005 is being carried at six centers in India (Bangalore, Bellary, Tumkur, Mysore, Warrangal and Aurangabad). Patients fulfilling IHS criteria for diagnosis of migraine were enrolled using central registry system and evaluated for frequency of migraine attacks, associated symptoms, pain intensity (VAS Score on 0, 30, 60, 90 days) and MIDAS score (on day 0 and day 90). These patients are treated with ayurvedic treatment protocol comprising indigenously prepared 4 herbo-mineral formulations along with regulated diet and lifestyle.

Results Patients who completed 90 days of Ayurvedic treatment protocol showed gradual and significant ($P < 0.05$) reduction in associated symptoms, frequency of attacks, pain intensity and mean MIDAS score. Ayurvedic treatment was well tolerated by the patients without any adverse events.

Conclusion The observation of the ongoing study indicated that Ayurveda has significant and sustainable effect in the prevention of migraine. The therapy should be developed further as a potential preventive treatment for migraine.

Note: Earlier findings have been published as poster abstract in *Cephalgia* Vol 26, No 11, 2006.

F082

Efficacy of rapid-release sumatriptan tablets in cluster headache: an open label preliminary study

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Subcutaneous administration of sumatriptan is the first choice for cluster headache attack due to the rapidity of the action compared to the duration of the attack. Oral administration of triptans are not effective. New fast-disintegrating/rapid-release sumatriptan tablets have a speedier absorption and a faster action on migraine attack. The present study evaluated the effect of the new formulation oral sumatriptan on cluster headache attacks. The study was carried out six patients (all men, mean age 42.12 ± 4.65) suffering from episodic cluster headache during a cluster period which had started from at least 10 days. The expected duration of the cluster period was at least 2 months. The patients were chosen because the long duration of the attacks (lasting minimum 120 minutes). The effect of three formulations of sumatriptan (subcutaneous, 50 mg and 100 mg oral tablets) were evaluated, administering each formulation for 5 attacks of every patients. Subcutaneous sumatriptan interrupt the attacks within 10 minutes; 100 mg tablets discontinued the headache within a period between 20 and 40 minutes, in 20 out of 30 monitored attacks. For 5 remaining attacks a decrease of the intensity was reported. The 50 mg tablets did not modify the duration but it improved the intensity of the attacks in 12 cases. The present findings, even if preliminary, confirm that rapid release oral sumatriptan shows a faster action also in cluster headache. Undred mg tablets could represent for some patients a suitable alternative to the subcutaneous administration.

F083

Effectiveness and safety of Rizatriptan Benzoate (MAXALT RPD®) in the treatment of acute migraine headaches

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Objective To assess the effectiveness and safety of Rizatriptan Benzoate for the management of migraine headaches in subjects not using a triptan-based treatment.

Methods Open-label, multi-center study. Subjects were adults with a ≥ 6 -month history of persistent migraines while on treatment with a non-triptan regimen. Subjects were treated with 10 mg Rizatriptan Benzoate for two consecutive migraine attacks. Outcomes were headache severity, time to resolution of pain, global satisfaction with treatment, and incidence of adverse events attributed to treatment.

Results 369 subjects qualified for the study, comprising 310 (84.0%) women and 317 (85.9%) Caucasians. The subjects were 40.5 ± 11.7 years old, and had suffered from migraines for 11.5 ± 11.1 years at a rate of 3.5 ± 1.8 migraines per month (means \pm SD). Of the 284 (77.0%) subjects experiencing at least one attack during the study, 204 (55.3%) endured two attacks. Two hours after rizatriptan administration, response and

pain-free were reported by 209 (73.6%) and 134 (47.2%) for the first attack and 157 (77%) and 110 (53.9%) for the second attack, respectively. Additional treatment to control the headache was used by 72 (25.4%) subjects for the 1st attack and 42 (20.6%) subjects for the 2nd attack. Satisfaction with treatment was reported by 61.6% subjects for the 1st attack and 65.7% for the 2nd attack. Discontinuation was reported by 72 (25.4%) subjects and there were 40 non-serious adverse events related to the treatment, predominately dizziness and somnolence reported by 27 (9.5%) subjects.

Conclusion Rizatriptan Benzoate is safe and effective for the management of migraine headaches in subjects who have been identified for a change to a triptan-based regimen.

F084

The incidence of headache among Jordanian school children

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Objective To show the incidence of migraine headache among school age children and how it relates to the climate of the living place.

Methods We used 2 groups in our study, group-1 randomly selected 1018 school children (391 male and 627 female) age from 13 to 18 years, living in Aqaba (hot climate) from 2 government female schools, 2 government male schools, and 2 private mixed gender schools. Group-2 is one of the private mixed gender school living in Amman (Mediterranean climate) randomly selected 256 children. In our study we used a special questionnaire data sheets fulfilled by the same child with the responsibility of the teacher of the classroom. We accepted the yes for headache if the headache attacks for more than 4 times a month and for longer than 3 months duration. We excluded secondary type headache from our study.

Results In group-1, 20.8% of male and 15.8% of female children suffer from different types of headache comparing with group-2, 17.3% male, and 12.4 female. 46.7% of children of the group-1 suffer from poor concentration comparing with 18.4% of group-2.

Conclusion we found that the incidence of headache and poor concentration are greater in those children who live in hot weather place (group-1) than those who live in cold place (group2), so we should investigate the cause of increasing incidence of headache among Jordanians in general and specifically in Aqaba.

F085

Efficacy of topiramate in patient populations with chronic migraine

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Objective Chronic migraine (CM) is the most common form of chronic daily headache. Few randomized controlled studies have been performed. Evidence for effective preventive treatments for CM is currently unavailable. To evaluate the efficacy and safety of topiramate for treatment of CM, 2 similar, randomized, placebo-controlled, multicenter studies were conducted in the United States (S1) and European Union (S2).

Methods Key distinctions exist between S1 vs. S2 trials, respectively: primary efficacy endpoints were change from baseline in mean monthly migraine/migrainous days over the entire double-blind phase vs. change from baseline in mean monthly migraine days to the last 28 days of the double-blind; $\geq 50\%$ migraine/migrainous vs. ≥ 12 migraine baseline headache days; disallowed vs. allowed concomitant migraine preventive therapy; permitted medication use ≤ 4 days/week vs. no restriction on medication overuse; topiramate target dose 100 mg/day vs. 100 mg/day up to 200 mg/day; ANCOVA methods vs Wilcoxon two-sample test for ordinal/continuous data.

Results ITT populations comprised 306 S1 patients (153 topiramate, 153 placebo) and 59 S2 patients (32 topiramate, 27 placebo). In S1, topiramate treatment vs. placebo resulted in a significant reduction in mean monthly migraine/migrainous days (-6.4 vs. -4.7 days, $P = 0.010$) and migraine days (-5.6 vs. -4.1 , $P = 0.032$). In S2, treatment with topiramate vs. placebo significantly reduced mean monthly migraine days (-3.5 vs. 0.2 days, $P = 0.02$). Topiramate was safe and generally well tolerated and the most common adverse event was paresthesia.

Conclusions In two similar studies topiramate was effective and generally well tolerated in patients with CM.

F086

Simvastatin in the treatment of migraine

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Objectives Statins have been proven to significantly decrease cardiovascular events in primary and secondary prevention of coronary heart disease and stroke. Statin's pleiotropic properties suggested it may exert beneficial effects on migraine. We thus decided to assess the value of statin in the treatment of migraine.

Methods We included 11 patients with migraine. All previously had preventive medications, but results were unsatisfi-

factory. We treated patients with simvastatin 40 mg for 3 months.

Results Treatment resulted in a statistically significant decrease in migraine frequency, from 6.3 ± 2.6 before treatment to 4.1 ± 2.4 after treatment ($p < 0.01$). The difference in headache severity (0 to 10 scales) before treatment (7.6 ± 2.2) and after treatment (3.5 ± 2.9) was also significant ($p < 0.01$).

Conclusion Simvastatin may be effective in patients with migraine. Future randomized prospective studies could provide a definite answer.

F087

Topiramate treatment in chronic migraine cohorts with medication overuse

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Objective Recent placebo-controlled, multicenter trials of topiramate in chronic migraine (CM), showed reductions in mean monthly migraine and migraine/migrainous headache days. Topiramate was safe and generally well tolerated. Enrollment criteria permitted medication overuse (MO) according to ICHD-2 definitions of medication overuse headache (ICHD-2 8.2). Topiramate vs. placebo treatment of patients with/without baseline MO from two CM trials in the United States (S1) and European Union (S2) was evaluated.

Methods Key inclusion criteria distinctions between S1 vs. S2 trials, respectively, were: $\geq 50\%$ migraine/migrainous vs. ≥ 12 baseline migraine days; disallowed vs. allowed concomitant migraine preventive therapy; permitted medication use ≤ 4 days/week vs. no MO restriction; topiramate target dose 100 mg/day vs. 100 mg/day–200 mg/day; primary efficacy endpoints: change from baseline in mean monthly migraine/migrainous days over entire double-blind vs. change from baseline in mean monthly migraine days to end of double-blind. Post-hoc analyses were performed to detect directional trends; subgroups not powered to detect clinically meaningful differences nor were results corrected for multiplicity.

Results ITT populations: 306 S1 (153 topiramate, 153 placebo), 59 S2 patients (32 topiramate, 27 placebo). In S1 MO patients (59 topiramate, 56 placebo, 37.6%), topiramate vs. placebo resulted in reductions in mean monthly migraine/migrainous days that approached statistical significance (7.6 vs. 5.3, $P = 0.059$). In S2 MO patients (23 topiramate, 23 placebo, 78.0%), statistically significant reductions in mean monthly migraine days were observed (3.7 vs. 0.9, $P < 0.05$).

Conclusions Topiramate may effectively treat CM patients with MO prior to detoxification. Randomized, placebo-controlled studies of preventive therapies in MO patients are warranted.

F088

The use of vitex – agnus castus in migraineous women with premenstrual syndrome

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Objectives Association between migraine and menstruation is well known, moreover headache is considered to be a part of premenstrual syndrome (PMS). A number of treatments were proposed for PMS, also with herbal medicines: among them the vitex, a derived from agnus castus (verbena), was reported to be very effective on PMS. We assess the influence on the headache frequency and duration of a prolonged vitex treatment on migraineurs women with PMS.

Methods Thirty-six women were enrolled in the study. Headache informations about previous 3 months were obtained by diary. The mean number of monthly headache attacks was $4.28 (\pm 1.9)$; the mean number of headache days per month was $7.55 (\pm 3.8)$. Each subjects received an in label treatment for PMS and/or dysmenorrhoea with vitex (40 mg/day) for 3 months.

Results All patients completed the study. The last month data, obtained by diary, were compared with the pre-treatment ones. A reduction ($>50\%$) of headache attacks was recorded by 13 women (36.1%), and a reduction $>50\%$ of headache days by 19 women (52.8%). No major side effects rose. After the treatment, the mean headache attack/month was $2.83 (\pm 1.71, p = 0.000003)$; the mean headache days/month was $4.08 (\pm 2.62, p = 0.00000005)$. A headache reduction was observed also in non-menstrual attacks.

Conclusion Vitex appear to be effective as headache treatment, in women with PMS. The effectiveness could be due to biological action of vitex, that is a dopaminergic, oestrogenic, and opiateergic agonist. Placebo-controlled trials on larger number of patients are necessary to confirm our findings.

F089

Topiramate (TPM) vs divalproex sodium (DVP) in the treatment of migraine: a prospective real-world study

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Objective To compare TPM and DVP for the prevention of migraine in a real-world setting.

Design/methods All episodic migraineurs (ICHD-II) from a tertiary center, who received TPM or DVP as their only preventive treatment, during a period of 12 months, were prospectively studied. Adherence, headache frequency (HF) reduction and side effects were evaluated after 3 months. The number of patients who were switched from one to the other was also evaluated.

Results One hundred twenty patients (104 women, 16 men, ages 18 to 68, mean 41.2 years) were included. At 3 months, 67.1% of TPM patients (mean dose 100 mg/day) and 60% of DVP (mean dose 800 mg/day) presented HF reduction greater than 50% ($p = \text{NS}$). The percentage of patients on TPM

and on DVP who did not return were, respectively 14.3% and 16%. Twenty percent of DVP patients were switched to TPM whereas 12.8% of the TPM group was switched to DVP. The most presented side effects by TPM patients who returned were weight loss (50%), paresthesia (46.7%) and cognitive disturbances (20%), whereas DVP patients reported mostly gaining weight, hair loss and gastrointestinal symptoms, which were presented by nearly 24% of the patients (for each adverse event).

Conclusions/relevance In a real-world setting, both TPM and DVP were effective and reasonably well tolerated in treating migraine preventively. In addition, the number of patients who were switched from one to the other was similar. Randomized controlled-studies are necessary to confirm these observations.

F090

Sumatriptan, nimesulide, trimebutine vs. the three together in the acute treatment of migraine: a controlled study

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Objective To compare the combination of sumatriptan plus nimesulide plus trimebutine (gastrokinetic drug without central penetration) with each of the drugs alone.

Patients and methods Twenty patients with migraine had to treat 4 moderate or severe attacks with 50 mg sumatriptan plus 200 mg nimesulide plus 200 mg trimebutine or with each of the agents plus placebo, in counterbalanced order. Attack severity, nausea and photophobia were compared after 1 and 2 h. Recurrence and adverse events were also contrasted.

Results Nineteen patients (17 women, 2 men) patients treated at least three moderate or severe attacks. Sixteen attacks were treated with sumatriptan, 15 with trimebutine, 14 with the combination and 14 with nimesulide (total 59 moderate or severe and 7 mild, not included). At 1 h, 7 attacks treated with the combination were pain free (50%), vs 21.4% in the nimesulide group, 12.5% in the sumatriptan group and 6.7% in the trimebutine group ($p < 0.01$). At 2 h, pain-free rates were 64.3% for the combination vs. 35.7% for nimesulide, 31.2% for sumatriptan and 26.7% for trimebutine alone ($p < 0.001$). With regard to nausea and photophobia, the combination was significantly more effective than sumatriptan, nimesulide and trimebutine as well. Recurrence was similar among the combination and the nimesulide groups but lower than sumatriptan and trimebutine (33.3% vs. 40% vs. 60% vs. 75%). Adverse events were similar among groups.

Conclusion The combination is more effective compared to each drug alone. Double-blind studies are necessary to confirm these observations and have been initiated.

F091

Effect of acute incubation with female sex steroids on CGRP-induced relaxations in human & porcine coronary segments

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Objectives The prevalence of migraine is 2–3 times higher in females than in males, and is intricately related to levels of female sex steroids. These might interact with calcitonin gene-related peptide (CGRP), a potent vasodilator implicated in the pathogenesis of migraine. We have shown that 17 β -estradiol significantly augments CGRP-induced relaxations in rat isolated arteries, as well as electrical stimulation-induced dilatations in a closed cranial model in rats. To establish the mechanism involved in 17 β -estradiol-mediated enhancement of relaxations to CGRP, we studied the rapid or non-genomic effect of female sex steroids on CGRP-induced relaxations.

Method Human and porcine distal coronary artery segments were incubated with vehicle or increasing concentrations of 17 β -estradiol or progesterone (1, 10, or 1000 nM) for 30 min. The artery segments were precontracted with KCl and cumulative concentration response curves to α -CGRP were constructed.

Results CGRP induced significantly higher maximal responses in human coronary artery segments obtained from females ($93 \pm 2\%$, $n = 25$) as compared to males ($85 \pm 3\%$, $n = 22$). There were no significant differences in CGRP responses between vehicle-treated artery segments or segments incubated with various concentrations of female sex steroids, either in human or porcine segments.

Conclusion Acute incubation with female sex steroids did not affect CGRP-induced relaxations in human or porcine coronary artery segments. The higher maximal responses obtained in segments from females as compared to males indicate that these enhanced responses may be due to genomic (slow) rather than non-genomic (rapid) effects of female sex steroids.

F092

Placebo controlled study to evaluate the efficacy of rizatriptan with acetaminophen for the treatment of migraine

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Objective To compare the efficacy of rizatriptan (R) with acetaminophen (A) to each of the components and placebo for treatment of migraine.

Methods Double blind, randomized, placebo controlled parallel trial of R10 mg with A 1000 mg to R alone, A alone or placebo (P) for a single moderate or severe migraine.

3 hypotheses based on 2 hour pain relief: 1st: R + A would be superior to P and if proved then; that R + A would be superior A and if proved then; that R + A would be superior to R.

Results Patients screened at 10 centers. 200 randomized to the 4 treatment groups. 28 failed to treat. Patients were 87.8% female, 79.7% white, mean age of 43.1 years. 82% treated at moderate and 18% at severe migraine pain. No statistical differences between the 4 groups. 2 hour pain relief results: R + A 89.6%, R 76.2%, A 69.8% and P 46.2%. Logistic regression analysis found R + A superior to P ($p < 0.0001$) and to A ($p = 0.023$). R + A was not superior to R ($p = 0.118$). There was no difference between groups for adverse events.

Conclusions The study demonstrated statistical superiority of R 10 mg + A 1000 mg for a single moderate or severe acute migraine versus P and A as monotherapies by 2 hour pain relief. The sample size allowed for at least a 16% difference to be declared significant. R + A was numerically superior to R. Given the efficacy rates in this model additional studies are warranted in a treat early model.

F093

Greater occipital nerve vs hypothalamic stimulation to treat drug-resistant chronic cluster headache

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Objective Surgery is considered when cluster headache (CH) has a chronic course and do not respond to drugs. Greater occipital nerve (GON) stimulation has been reported to improve drug-resistant chronic CH (DR-CCH). Aim of this study was to assess efficacy and tolerability of GON stimulation as a treatment for DR-CCH. Hypothalamic stimulation was performed if GON stimulation failed.

Methods Ten CH patients suffering from 4–9 attacks per day did not improve to all known effective preventative drugs alone or in combination and were considered for surgery. Mean age was 44 years, 8 men, duration of chronicity was 3.2 years (mean).

Results GON data: The median follow up was 4 months. The results are excellent in 3 (2 pain-free). The last implanted patient cannot be evaluated because just operated. In another patient the results are poor after 4 months. In six patients stimulation failed. We observed one infection of the IPG and one electrode migration.

Hypothalamic stimulation was performed in five out of the six patients in whom GON stimulation failed: two are pain free, a 70% reduction of headache frequency was observed in two and 60% in one.

Conclusions In DR-CCH patients suffering from multiple attacks per day, GON stimulation was effective in a small proportion of cases. Patients not-responding to GON stimulation improved during hypothalamic stimulation. GON stimulation may be considered as a surgical option before considering more invasive procedures.

F094

Intracisternal strychnine induced trigeminal neuralgia model

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Objectives We evaluated the possibility of introducing a strychnine-induced allodynia model of trigeminal neuralgia in the mouse and compared our findings with the well-known carbamazepine anticonvulsant model of analgesia for treatment of trigeminal neuralgia as well as to morphine, known to have less of an effect on trigeminal neuralgia, as part of a co-administration test.

Methods After brief halothane anesthesia, we injected 5 microliter of strychnine 200 micromol or artificial cerebrospinal fluid into the cisterna magna of mice (directly over the nucleus of the trigeminal nerve). To compare the effect of carbamazepine, the mice received carbamazepine 10, 11-epoxide 4 nanogram and strychnine or strychnine only intracisternally. To compare the effect of morphine, mice received morphine hydrochloride 3 mg per kg or saline subcutaneously 30 minutes before the intracisternal strychnine.

Results Our results showed that intracisternal strychnine resulted in behavioral abnormalities that may represent trigeminal allodynia. A high incidence of face scratching, flinching with wash stroke to touch, eye squinting and backward folding of the ears were observed. These responses continued for four to fifteen minutes after the strychnine injection, as a response to the stimuli only. Touching other areas produced no response, and unless the mice were touched they appeared normal.

Conclusions There was good correlation between the analgesic effects of carbamazepine on responses compared to the strychnine induced allodynia; however, morphine produced less pain relief for the allodynia. Therefore, this novel model may be used as a reliable method for trigeminal pain studies and new drug in mice.

F095

Patients' decisions to treat migraine: Influencing effects on zolmitriptan efficacy

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Objectives The objectives of this study were: assess if patients would use one form of Zolmitriptan earlier in their migraine and if earlier intervention influenced the time to pain free.

Background Early intervention both duration and pain intensity are determinants of treatment outcome. QST has a strong relationship to pain free treatment. At the time of the study, a standardized questionnaire to assess allodynia did not exist.

Methods This was an open-label crossover study of Zolmitriptan 5 mg oral tablets and oral dissolving tablets to treat migraine at the earliest time. They completed

questionnaires regarding migraine treatment. They treated two migraines early regardless of intensity of pain. Patients completed questionnaires including on allodynia. Times from headache onset, to treatment, to pain freedom were recorded.

Results 16 of 39 (42%) were pain free by 2 hours with the tabs and 60% with oral dissolving tabs ($p = 0.070$). Patients used oral dissolving tablet earlier than oral tablets ($p = 0.958$) with pain free occurring 90 minutes earlier ($p = 0.084$). There was a correlation between time from onset to time to pain free (tabs $p = 0.005$, oral dissolving $p > 0.001$).

Conclusions Patients may use oral dissolving tablets earlier in the course of a migraine. Treating earlier may be associated with an increase of pain freedom and of it occurring sooner.

F096

IV lidocaine for treatment of refractory migraines and headaches in the outpatient clinic

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Lidocaine has been used to treat neuropathic pain by virtue of its ability to block sodium channels and thus block neuropathic pain signaling. And all that area migraines or other headaches may be neuropathically mediated, we tried treatment of refractory migraines with this agent in the clinic.

22 patients were treated (19 female/3 male) [average age 40.8 yrs] for refractory headaches in the clinic. An IV line was started with pulse oximetry monitoring. Patients had failed at home treatment for their usual migraines. The beginning severity for migraines was 7.05/10 in severity before treatment and this was reduced to 2.18/10 in severity after treatment. 7 of 22 [32%] of patients had complete abolishment of their migraines. Average time of lidocaine infusion was 135 minutes and average dose was 334 mg of lidocaine. This resulted in a significant decrease in headache severity (p value of <0.001) for treatment of refractory migraines. There were 4 patients with transient nausea and dizziness during infusion, easily arrested by stopping or slowing the infusion rate. No other side effects were seen with treatment.

We conclude that IV lidocaine can be used in the clinic for treatment of refractory migraines and that sodium channel over activity may be playing a role in the maintenance or perpetuation of migraine headaches. Often, this allows choice of a sodium channel active agent for oral prophylaxis of migraines. The study also raises questions about mechanisms of aberrant neurotransmitter activity involving sodium channels playing a role in refractory migraine.

F097

IV tramadol for treatment of refractory headache in the clinic

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Tramadol is used orally for chronic pain in the USA, but no IV form is available. We decided to utilize an IV sterile prepara-

ration [IND applied for #73400], to treat refractory headaches, including migraines, in the clinic.

Tramadol, 50 mg per ml, was given IV in the clinic to patients with intractable migraines and other headaches. 38 patients were treated with IV tramadol, after placement of an IV line and with pulse oximetry monitoring. A 50 mg test dose was given and 50–100 mg was given every 7–10 minutes with monitoring of headache severity by the patient on a 0–10 scale.

All patients treated had response to IV tramadol. Average dose of tramadol was 397 mg (range 250–900 mg), given over 67 minutes in the clinic. Average reduction in severity (0–10 scale) was 6.66/10 to 2.89/10 in severity after treatment [$p < 0.001$]. No side effects other than transient drowsiness or nausea were noted. 10 patients were subsequently placed on oral tramadol. Headaches returned within 24 hours in 2 patients not treated with oral tramadol.

IV tramadol is effective in treating intractable migraines and mixed headaches acutely in the clinic. It has virtually no toxicity IV and can be the starting point for oral treatment. Typical dosage IV compares to daily oral dosing. Tramadol IV offers a new possibility in treating intractable migraines effectively and safely in the clinic and should be studied in a double-blind manner. The mechanism(s) for its effects are discussed.

F098

Effectiveness of IV treatment of refractory migraines in the clinic

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Aggressive headache treatment belongs in the specialty clinic, with greater cost- and time-effectiveness in treating intractable headaches and migraines. Compared with the emergency room, the clinic offers a wider range of treatments and better chance of maximum success. We have used IV treatment in the clinic since 1994 and presented data regarding effectiveness in 1998. This study continues documenting degree of success of outpatient IV treatment of headaches on an ongoing basis.

Total treated patients number over 2000 and 1074 were treated for refractory migraines/headaches. We utilized: IV magnesium sulfate, dexamethasone, valproate sodium, lidocaine, droperidol, dihydroergotamine, promethazine, propofol, tramadol, levetiracetam and ketamine.

Results are measured by successful resolution of symptoms, defined by at least a 50% decrease in severity of the presenting headache/migraine, or by return to work/regular activity. 62 patients from the total pool, and 22 from the headache pool (22/1074) [2%] had unsuccessful treatment that required re-treatment in the clinic, hospital ED or inpatient. This represents a 98% rate of effective treatment in the clinic.

We conclude that outpatient IV therapy of refractory headaches/migraines is highly successful with very low need for re-treatment, contributing to productivity in the workplace, at home and in personal life. Headache specialists should consider this method of treatment in the clinic.

F099**Prophylactic treatment of eletriptan conspicuously inhibits cluster headache**Hotaek Kim¹, Kunio Shimazu²¹Saitama Medical University, ²Neurology, Japan

Objectives Cluster headache is widely accepted as a refractory headache and a satisfactory treatment has not been established yet. Only triptans as the acute medication, can ameliorate the severe pain of cluster headache. Eletriptan is a longest-acting type of triptan that is available in Japan. We hypothesize that the prophylactic treatment of eletriptan would be able to inhibit cluster headache that usually occurs at the same time in every day during the cluster period. This study was designed to investigated the prophylactic treatment of eletriptan inhibits cluster headache.

Methods Nine patients with cluster headache were recruited for this study. Three were females and six were males. Mean age of the patients was 32.2 ± 5.4 (mean \pm S.D.) years old ranging 20 to 36. Mean cluster headache period was 1.9 ± 0.7 months. Mean duration of one attack was 2.0 ± 0.7 hours. Eletriptan (20 mg) was taken per os just before going to bed at night and/or just after waking-up in the morning everyday through the cluster period. No add-on therapy at the time of the induction of eletriptan. Results were semiquantitatively estimated using the headache diary written by each patient.

Results Two patients showed complete relief of the pain through the cluster period. Five showed improved extremely (over 50% reduction of intensity and frequency) and other two showed effective (over 30% reduction), respectively. No patients complained of any adverse effects.

Conclusion Prophylactic treatment of eletriptan conspicuously inhibits cluster headache with no adverse effects.

F100**Ziprasidone for prophylaxis of chronic daily headaches**Diane Cammarata¹, JC Krusz²¹Anodyne Headache and PainCare, ²Anodyne, USA

Ziprasidone is an antipsychotic agent with 5HT2 antagonist and dopamine blockade actions. Both mechanisms decrease headaches. We studied ziprasidone for suppression of chronic daily headaches (CDH) and chronic migraines (CM).

Other antipsychotic agents (quetiapine, olanzapine, risperidone) have utility in treatment of migraine headaches. Ziprasidone, is said to be less likely to cause weight gain.

Patients from a clinic population received ziprasidone as add-on therapy for CDH and CM. 36 patients were treated; 27 had co-existent migraines (75%). Dosing was started at 20–40 mg hs and increased weekly. Patients kept a diary of their headaches. 3 months' treatment was maintained after titration to 80–120 mg per day.

24/36 (66%) of treated patients reported improvement in CDH pattern with overall 60% reduction in frequency of CDH noted (22 days/mo to 8.8 days after treatment) [$p < 0.01$]. 6 patients reported a 32% reduction in CDH (22 days to 15.4 days) [$p < 0.01$]. 6 patients had minimal or no response. No side effects other than transient drowsiness the following

morning were reported. No akinesia was seen. 16/27 patients with chronic migraines reported a 35% decrease in migraine frequency (6.5 to 4.2/mo). 9 patients reported no change after ziprasidone. 28 of 30 responders (93%) reported a better sleep pattern with ziprasidone.

Ziprasidone is effective therapy for CDH and CM, difficult headache patterns to manage. Side effects are minimal. This study suggests that dopamine blockade is a strategy for treating CDH and CM. Ziprasidone should be studied in a double-blind manner.

F101**Simvastatin for migraine prevention and nitric oxide production**Marcelo Valença¹, F Medeiros¹, P Medeiros², W Reis³,J Antunes-Rodrigues³, D Dodick⁴¹Physiology, School of Medicine of Ribeirão Preto, Brazil, and ²Neurology, Mayo Clinic College of Medicine, USA, and ³Neuropsychiatry, ⁴Histology, Federal University of Pernambuco, Brazil

Objective To report the results of a prospective, active comparator study of simvastatin *versus* propranolol for the prophylactic treatment of migraine, correlating the results with plasmatic production of nitric oxide (NO).

Methods 25 women with more than 6 migraine attacks/month, received propranolol 60 mg daily for 3 months. In another group, 29 women with hyperlipidemia and over 6 migraine attacks/month received simvastatin 20 mg daily. All patients completed a daily headache diary over a 30-day baseline period and a 90-day treatment period. No migraine preventive medications were used during the 30-day baseline period. The primary endpoint was a reduction in migraine frequency during the last 30 days of the trial compared to the baseline period.

Results An increase in the plasmatic production of NO was observed during headache attack when compared with basal levels in the absence of headache (25.8 ± 1.4 vs 30.2 ± 1.4 $\mu\text{mol}/\text{ml}$, $p < 0.0001$). Simvastatin and propranolol significantly ($p < 0.05$) decreased not only the frequency of migraine attacks and the plasmatic concentration of NO (26.4 ± 2.2 vs 19.3 ± 1.0 and 25.8 ± 19.4 $\mu\text{mol}/\text{ml}$, respectively) during the last 30-day treatment period compared to the baseline phase, but also decreased migraine frequency within each month during the trial ($p < 0.05$). In the propranolol group, 88% of subjects had over 50% reduction in migraine frequency while the responder rate in the simvastatin group was 83% ($p = 0.7112$).

Conclusion These data suggest that simvastatin may be effective for migraine prevention, and raise the potential for a new therapeutic strategy.

F102**Memantine for migraine prophylaxis**Diane Cammarata¹, JC Krusz²¹Anodyne Headache and PainCare, ²Anodyne, USA

We studied the efficacy of memantine in treating migraines and tension-type headaches (TTH). This open label study

looked at reduction of frequency and severity of migraines. Secondary endpoints included reduction of TTH.

Memantine blocks NMDA glutamate receptors, thought to be intrinsic to pain transmission, windup, and central sensitization. Glutamate and its receptor subtype play a role in promoting pain. Blockade of NMDA might reduce central barrage of afferent signals that maintain migraine states. Agents whose activity impinges on the glutamate system are in use for migraine prophylaxis (ie, topiramate).

20 patients with chronic migraines unresponsive to prophylaxis measures were studied. They had an average of 9.2 migraines per month. 14/20 (60%) had TTH as well (average of 12.5 days per month). We added memantine 5 mg per day with weekly increases of 5 mg, up to a maximum of 20 mg per day, as tolerated.

Patients kept headache diaries for migraines and TTH as well. Evaluation were made after 1 month of therapy on 20 mg (or maximally tolerated dose) of memantine. Migraine frequency fell to an average of 4.1 migraines per month, or almost 56% less than at baseline, in 14 of 20 patients [$p < 0.01$]. Remaining migraines were rated as less severe and easier to treat. Acute migraine and rescue medication use dropped by two-thirds. TTH frequency fell by 62%, to 6 headaches per month [$p < 0.02$]. 6 patients saw no response to memantine. 4 patients reported dizziness and one nausea. 2 of these patients had betterment of their migraines.

F103

Investigation of GABA A receptors genes and migraine susceptibility

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Migraine is a neurogenetic disorder, affecting ~12% of Caucasian populations. Prior linkage studies have reported the localisation of a migraine genomic region to chromosome Xq24–28. This specific region contains a cluster of genes for GABA A receptors (GABRE, GABRA3 and GABRE) and also a Glutamate (GRIA 3) receptor gene. GABA and Glutamate neurotransmitters have been implicated in migraine pathophysiology and thus these genes are potential migraine candidates. The exact role of GABA, which predominantly serves as an inhibitory neurotransmitter in the brain, has not yet been established, although GABA receptor agonists have been the target of therapeutic developments. The aim of our research was to investigate the role of these Xq24–28 potential candidate genes in migraine susceptibility. In this study, we focussed on the subunit GABA A receptors type ε (GABRE) gene and its involvement in migraine. We performed an association analysis in a large population of Australian case–controls (275 unrelated Caucasian migraineurs versus 275 controls) examining a set of 3 single nucleotide polymorphisms (SNPs) located in the coding region (exons 3, 5 and 9) of the GABRE gene. Chi-square analysis of all tested SNPs within the GABRE gene did not show significant differences in allele frequencies for any of the tested variants ($P > 0.05$). Hence our study has not shown association between the 3

SNPs, localised within GABRE gene, in our Australian population sample. Further studies are however necessary to investigate the role of other GABA A receptor genes in migraine susceptibility.

F104

Deep brain stimulation of the posterior hypothalamus in chronic cluster headache – experience with two new cases

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Objective Recently, deep brain stimulation (DBS) of the posterior hypothalamus has been shown to be effective in the treatment of drug-resistant chronic cluster headache.

Methods DBS of the posterior hypothalamus was performed in two patients, one 55-year-old man with medically intractable chronic cluster headache since 1996, and one 31-year-old woman with a chronic form since 2002. Both patients showed continuous worsening headaches in the last years despite high dose medical treatment. Patients fulfilled the published criteria for DBS in chronic cluster headaches. Electrodes were implanted stereotactically in the ipsilateral posterior hypothalamus according to the published coordinates (2 mm lateral, 3 mm posterior, 5 mm inferior) referenced to the mid-AC-PC line.

Results The intra- and postoperative course was uneventful and postoperative MRI control documented regular position of the DBS electrodes. The current stimulation parameters at 12 months postoperatively were 0–; G+ 5.5 V; 60 µs; 180 Hz (Case 1) and 0–; G+ 3.5 V; 60 µs; 185 Hz at 6 months postoperatively (Case 2). Surgery- or stimulation-related side effects were not observed. Both patients showed initial pain reduction in the first days whereas 12 month follow-up did not show a significant reduction in attack frequency or intensity.

Conclusion Deep brain stimulation of the posterior inferior hypothalamus is an experimental procedure, should be restricted to selected therapy-refractory patients and should be performed in centres experienced in patient selection and performance of DBS as well as in cluster headache treatment. A multi-centre study is necessary to evaluate its effectiveness.

F105

Depression, anxiety, and menstrual migraine in patients treated with preventive frovatriptan

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Objective To assess whether short-term preventive frovatriptan impacts disability, quality of life (QOL), anxiety, or depression in women with difficult-to-treat menstrual migraine (MM).

Background MM incidence and severity are significantly reduced by short-term preventive frovatriptan (Silberstein, 2004), but effects on associated comorbidities such as depression and anxiety (Radat, 2005) are unknown.

Methods During three perimenstrual periods, women with difficult-to-treat MM (inadequate response to acute triptans) were administered 6 days of frovatriptan 2.5 mg (BID or QD) or placebo as previously described. Patients completed the Depression Anxiety and Positive Outlook Scale (DAPOS), Headache Impact Test Questionnaire (HIT-6TM), and Migraine-Specific QOL Questionnaire (MSQ v.2.1) before and after treatment. The Johnson-Neyman model was applied when homogeneity of regression lines was not obtained with analysis of covariance. Migraine impairment (HIT-6), anxiety, and depression interactions were evaluated by semipartial squared correlations.

Results 44 frovatriptan and 35 placebo patients completed QOL assessments. Only 9% of baseline variation in migraine impairment was associated with depression or anxiety, singly or combined. In difficult-to-treat women, baseline values for all QOL scales were elevated, indicating substantial impairment. With frovatriptan, HIT-6, MSQ v.2.1, and DAPOS scores trended toward improvement. Women with higher anxiety scores (baseline ≥ 5) had significant reductions in anxiety with preventive frovatriptan.

Conclusions Although 91% of baseline variation in migraine impairment was independent of depression and anxiety, patients with greater anxiety scores at baseline experienced significant reductions in anxiety with preventive frovatriptan. Additional studies are warranted to assess whether MM prevention improves psychiatric comorbidities.

References

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F106

Short-term frovatriptan for prevention of menstrual migraine: safety and efficacy over 12–15 months

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Objective Assess the efficacy and safety of short-term preventive frovatriptan for reducing the incidence of menstrual migraine (MM; occurring day -2 to +3 of menses) in women during 12 perimenstrual periods (PMPs).

Background Short-term preventive frovatriptan reduces MM incidence with good tolerability during double-blind treatment of two PMPs (Silberstein, 2004).

Methods Women initiated frovatriptan 5 mg BID 2 days before anticipated MM onset and continued frovatriptan 2.5 mg BID for 5 additional days. Incidence of MM and adverse events (AEs) were summarized for women completing treatment of 12 PMPs over 12–15 months.

Results Safety data for the 549 enrolled women were previously reported (MacGregor, 2006). The overall mean (standard deviation) age was 37.8 years (7.6) and MM onset was between days -2 to +1 in 82.1% of women. For the 308 women who treated 12 PMPs, MM incidence declined from 63.8% (PMP1) to 51.1% (PMP6) and 45.0% (PMP12). Migraine-

associated AEs declined from PMP1 to PMP11 (migraine [18.8% vs 12.0%]; dizziness).

Conclusions 6-day preventive frovatriptan was well tolerated by 308 women during treatment in 12 PMPs. MM incidence and migraine-associated AEs steadily declined over time. Rebound or delayed MM was not a significant problem in the overall population.

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F107

Efficacy of hyperbaric oxygen therapy in post-lumbar puncture headache

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Objective To determine the efficacy of hyperbaric oxygen therapy (HBO) in the patients with post-lumbar puncture headache (PPH).

Method This is a prospective, randomize, double blind, placebo controlled study. Twenty patients with PPH developed after spinal anesthesia were enrolled in the study. Patients were randomly assigned to the normobaric air breathing (1 ATA = 760 mmHg, the normal atmospheric pressure at sea level, 45 minutes, as placebo) and hyperbaric (2 ATA, 45 minutes) oxygen treatment. Treatments were performed in a hyperbaric chamber. All subjects evaluate their headache on a 100-mm visual analog scale (VAS) and 4-point scale (no, mild, moderate, severe), before and after each treatment.

Results All subjects well tolerated HBO therapy. Although the subjects did not benefit from HBO therapy immediately after the treatment, there was a reduction in the pain severity and duration later. The details of the results of HBO versus normobaric air breathing in the management of PPH will be discussed.

Conclusion Clinical importance of HBO treatment in various neurologic diseases (e.g. CO poisoning, cerebrovascular diseases, and migraine) is increasing. HBO, for the treatment of headaches (especially for vascular headaches) seems to be effective and safe. Its validity should be evaluated in comparison with other treatment modalities in future controlled studies.

F108

Acute frovatriptan for menstrual migraine improves pain-free response versus patients' usual care

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Objective Evaluate the effectiveness of frovatriptan administered early (International Headache Society [IHS] grade 1) in

a menstrual migraine (MM) compared with patients' usual treatment.

Background MM affects ~50% of female migraineurs and are reportedly more severe, of longer duration, and more resistant to acute treatment than non-MM. Because migraine treatment improves when triptans are administered early in an attack (Cady, 2004), we assessed early triptan treatment of MM.

Design/methods This open-label study had 2 phases; each included 1 menses. In the baseline phase, patients treated headaches with their current therapy. In the subsequent phase, patients treated all headaches at the mild stage (IHS grade 1) with frovatriptan (2.5 mg). Another dose could be administered after 2 hours. The primary endpoint was pain-free response 4 hours postdose in both phases. Adverse events (AEs) were monitored.

Results Patients (N = 153) had a mean \pm standard deviation age of 37.6 ± 8.4 years, 13.5 ± 6.8 MMs in the prior year, and a median 11-year migraine history. Most patients were white (88.2%), and 52% were taking a triptan as usual care. The 4-hour pain-free response was greater with frovatriptan (43.2%; 41/95) vs patients' usual care (30.5%; 29/95). More patients improved with frovatriptan (22.1%) than worsened (9.5%; P = 0.029). More patients (42.2%) preferred frovatriptan than previous treatment (34.8%); 22.2% had no preference (P = 0.015). Commonly reported AEs with frovatriptan were fatigue, nausea, upper respiratory tract infection, and paresthesia (1.2% each).

Conclusion Early treatment of MM with frovatriptan improves pain-free response relative to patients' usual care.

Reference

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F109

Effects of oral contraceptives to migraine headache in women

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Objectives Migraine, as a primary headache is often in the young women with reproductive period. Nowadays most women prefer to use hormonal contraception methods. It is known that using these hormone-contained tablets can influence headache course. In our clinical study we assessed the effects of combined oral contraceptives (COC) to migraine in Hungarian women.

Methods Own-made questionnaires were delivered to the patients by mail. Questions referred to menstrual cycle, to features of headache, and to the ways of contraception. One hundred questionnaires were sent out, and 63 were got back.

Results The response rate of the sent-out questionnaires was 63%. Based on data from 63 questionnaires, 14 women did not use COC. From 49 women migraineurs, who used COC, the migraine pain intensity and frequency, the concomitant symptoms and the duration of the migraine attack worsened in 33%

(16 cases), did not change in 59% (29 cases), and improved in 4 cases (8%).

Conclusion The response rate of the applied postal written interview was good (63%). In our study the effects of the combined oral contraceptives on the migraine headache were: mostly no change, in one-third of our patients worsening, and only in a few cases improving. Our results supported the findings of other clinical studies.

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F110

Acupuncture for migraine prophylaxis: methodological issues

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The objective of these trials were to evaluate the efficacy of acupuncture for migraine prophylaxis as well as to reach a best methodological design to a phase III trial. Subjects with migraine were randomized to the real or sham acupuncture groups in two different trials.

Distinctive treatment approaches were tested as being real acupuncture. In the first one, the individualized treatment was applied. Semi-standardized acupuncture treatment was evaluated in the second trial. All patients were treated with 16 acupuncture sessions in twelve weeks. Post-treatment follow-ups were done for 6-months. Primary endpoints adopted were the percentage of patients with reduction $\geq 40\%$ (study one) and $\geq 50\%$ in migraine attacks frequency (studies one and two) and the total of migraine days (study two).

Improvements with statistical significant differences appeared only in the study one. Real acupuncture group was superior to sham group in the second month of the treatment, when the percentage of patients with $\geq 50\%$ reduction in migraine attack frequency was evaluated (P = 0.021). The reported differences appeared as well, in two secondary endpoints: number of days with migraine per month (P = 0.007) in the second month of the treatment and in the first (P = 0.044) and second (P = 0.004) months of the treatment when the percentage of patients with a $\geq 40\%$ reduction in migraine attack frequency was measured.

The individualized treatment adopted in the trial one seemed to be the best approach to test acupuncture for migraine prophylaxis.

F111

Botulinum toxin type A in patients previously failing prophylactic treatment due to non-compliance

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Objective Examine efficacy, safety, and satisfaction with botulinum toxin type A (BoNTA; BOTOX®, Allergan, Inc., Irvine, CA, USA) treatment in migraine headache (HA) patients previously failing prophylaxis due to non-compliance.

Methods Randomized, double-blind, single-center, placebo (PBO)-controlled 3-month study, with a subsequent cross-over to open-label BoNTA treatment (months 4–6). Patients with disabling HA (IHS 1.1, 1.2, 1.7 or 2.1; HIT-6 scores ≥ 56), previously failing prophylaxis due to non-compliance, were enrolled. Patients were randomized 2:1 to BoNTA (139 units total; 17 sites/6 muscle groups) or PBO. After month 3, PBO-treated patients could receive BoNTA in an open-label period. Patients were evaluated using data from Headache Diaries

and HIT-6, MIDAS, and Migraine Impact Questionnaires (MIQ).

Results 61 patients (40 BoNTA; 21 PBO) were treated in months 1–3. 19/21 PBO-treated patients crossed-over to receive BoNTA after month 3. HA days and HA frequency were decreased from baseline at months 2, 5, and 6 in BoNTA but not PBO-treated patients. HIT-6 scores were also decreased in BoNTA-treated patients at all time points and in PBO-treated patients at months 1 and 3. Between-group comparisons were not significant except at month 3 for HIT-6 scores. BoNTA but not PBO-treated patients showed improvement in treatment satisfaction in MIQ at months 3 and 6. 18/40 BoNTA-treated and 5/21 PBO-treated patients reported AEs at month 3.

Conclusion BoNTA-treated patients showed improvements in HA frequency, impact, disability, and treatment satisfaction at multiple time points. BoNTA may be a useful treatment option for HA patients demonstrating poor compliance with oral prophylactic regimens.

LUNCH SEMINARS

LS7

Vertigo – when is it migraine and when is it not?

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Vertigo is not a typical migraineous symptom, although a substantial proportion of migraine patients complain of dizziness. By definition vertigo must include a sense of pseudo movement. This is a typical symptom in the extremely rare basilar type migraine. Seen from a vertigo clinic, the diagnostic spectrum does however look different. Here a number of patients have been described with migraine and vertigo and with no other cause of the vertigo. This has led to a suggested diagnosis of migraineous vertigo and other names have also been used. This seminar shall first present the views of the HIS classification committee, then data on basilar migraine and patients with basilar symptoms and lastly, the view from a vertigo clinic shall be presented. Hopefully the ensuing discussion will lead to a better understanding of the relation between migraine and vertigo.

LS9

Thunderclap headache is mainly a secondary headache

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Thunderclap headache is a warning symptom that may reveal a number of severe underlying causes, the most frequent being vascular disorders. The search for a cause should be

expedient and exhaustive. In the absence of an identified cause, the international headache classification suggests to consider the diagnosis of primary thunderclap headache, which remains controversial. In patients with a single thunderclap headache, investigations reveal a secondary cause in about 50% of the cases. In patients with multiple recurrent thunderclap headaches over a few days to a few weeks, the most prevalent underlying cause is a reversible cerebral vasoconstriction syndrome (RCVS). RCVS are characterized by severe sudden headache (often thunderclap headaches) with or without additional neurological symptoms and by reversible multifocal segmental vasoconstriction and dilatation of cerebral arteries. RCVS may occur spontaneously or in the setting of various conditions, the most common being postpartum and exposure to various vasoactive substances. In severe forms, the clinical features included seizures and/or acute neurological deficits revealing strokes. In milder forms, the clinical features consist of isolated recurrent thunderclap headaches. Diagnosis is based on the demonstration of vasospasms by cerebral angiogram. Magnetic resonance angiography (MRA) has an incomplete sensitivity, and the firm diagnosis may thus require a conventional angiography. Patients with recurrent thunderclap headaches with no visible vasospasm on MRA should be considered as having a probable RCVS and not primary thunderclap headaches. The long term prognosis of RCVS is still unknown. However, patients with proven RCVS, and the patients with recurrent thunderclap headaches but no visible vasospasms on MRA should be told to avoid exposure to vasoactive drugs or medications.

SCIENTIFIC SESSION

Scientific session 6: Developments and the future of treatments (acute and preventive)

ScS6-1

A randomized, double-blind, placebo-controlled study of Venlafaxine XR in outpatients with tension-type headache

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Objective Aim of this placebo controlled, prospective, randomized, double-blind study was to investigate the efficacy and safety of Venlafaxine XR, a serotonin and norepinephrine reuptake inhibitor, in the treatment of outpatients with Tension-Type Headache (TTH).

Methods Patients meeting the International Headache Society diagnostic criteria for TTH, recruited from Neurology and Headache outpatient clinics, were treated either with Venlafaxine XR (150 mg/day, n = 34), or placebo (n = 26). Treatment period was 12 weeks and study end point was the reduction in number of days with headache.

Results The Venlafaxine XR group displayed a statistically significant ($P \leq 0.05$) reduction in number of days with headache compared to the placebo group. At study end the number of days with headache declined by 44.8% in the Venlafaxine XR group and increased by 15.7% in the placebo group ($P = 0.023$). Secondary efficacy variables were not significantly different between the two groups. The number needed to treat for responders ($\geq 50\%$ reduction in days with headache) was 3.48.

Six patient in the Venlafaxine XR group discontinued therapy due to adverse events versus none in the placebo group. The number needed to harm was 5.58.

Conclusions Compared with placebo, Venlafaxine XR significantly reduced the number of days with headache in TTH patients. Tricyclic antidepressant amitriptyline is the only drug with prophylactic efficacy for TTH.

ScS6-2

Long-term migraine prevention with topiramate: a 12-month, placebo-controlled study (PROMPT)

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Objectives To evaluate the efficacy of topiramate beyond 6 months in migraine prophylaxis.

Methods After a 4–8-week baseline, patients entered a 26-week open-label phase, with titration from 25 mg/day topiramate to 100 mg/day in weekly 25-mg steps. The dose could be adjusted further (range: 50–200 mg/day), but was kept stable for the final 4 weeks. Patients were then randomised to continue this dose or switch to placebo for 26 weeks. The primary endpoint was change in number of migraine days (topiramate vs. placebo) during the last 4 weeks of the double-blind phase relative to the last 4 weeks of the open-label phase.

Results 559 of 818 patients (68.3%) completed the open-label period. Migraine days and use of acute medication decreased substantially, with improvement in quality of life (QoL). In the double-blind phase, there was an increase in migraine days per 4-week period in the placebo group (n = 254) compared with sustained reduction with topiramate (+1.2 vs. +0.1; $p < 0.01$) (n = 258). Similar results were seen for the change in MIDAS score (+6.1 vs. 0.0; $p < 0.01$), the physical component summary of the SF-12 QoL questionnaire (-3.1 vs. -0.6 ; $p < 0.001$) and days of acute medication use per 4-week period (+1.1 vs. +0.2; $p < 0.001$). Topiramate was well tolerated over 12 months of treatment, with adverse events consistent with those previously observed.

Conclusion Patients who continued topiramate after 6 months experienced a sustained reduction of migraine days, with benefits on QoL, while those discontinuing topiramate experienced partial, statistically significant loss of benefit.

ScS6-3**Within person Consistency across 4 migraine attacks of sumatriptan 85 mg RT Technology™ and naproxen sodium 500 mg**

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Objective To evaluate the within person consistency of response to a fixed-dose combination of sumatriptan and naproxen sodium (SumaRT/Nap) across up to 4 migraine attacks when treated in an early intervention paradigm.

Methods In two (S1: N = 646; S2: N = 620) identical, randomized, multi-center, double-blind, multiple-attack, early intervention trials in adult migraineurs (ICHD-II), subjects were randomized to five sequence groups. In four sequence groups, subjects treated 3 attacks with SumaRT/Nap and one with a randomly interspersed placebo. In the fifth arm, patients treated four migraine attacks with SumaRT/Nap. Summarizing across attacks, we reported that SumaRT/Nap was superior to placebo on 2 hr pain freedom (PF) and 2–24 hr sustained pain freedom (SPF) (Lipton 2006). Herein, we assess within person consistency of response.

Results Patient demographics were similar to other migraine studies. For Study 1 and Study 2 (S1/S2), 55%/52% of patients were PF at 2 hr for ≥2 of 3 attacks and 29%/29% for 3 of 3 attacks. At 4 hr, 80%/76% were pain free in ≥2 of 3 attacks and 55%/53% for 3 of 3 attacks. In patients treating 4 attacks with active drug, 2 hr PF rates were 53%/39% in ≥3 of 4 attacks and 28%/21% in 4 of 4 attacks. In patients PF at 2 hr for the first attack, 71%/71% were PF for the second attack. Corresponding 4 hr PF rates were 84%/84%. In over 1100 patients treating over 3300 migraine attacks, SumaRT/Nap was generally well tolerated [AE rate corrected for attack (SumaRT/Nap v PBO), S1: 9%v7%, S2: 13%v9%].

Conclusions SumaRT/Nap demonstrates consistent intra-individual pain free and sustained pain free response in an early intervention paradigm.

Reference

Lipton (2006)

ScS6-4**Zolmitriptan is effective for the acute treatment of cluster headache: a systematic review**

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Objective To assess the efficacy of zolmitriptan for the acute treatment of cluster headache.

Methods A systematic review of the medical literature and congress abstracts was completed to identify clinical studies of zolmitriptan for the acute treatment of cluster headache. Three randomized, double-blind studies were identified that

evaluated the efficacy of zolmitriptan nasal spray (NS) or oral tablet 5 or 10 mg vs. placebo. In these studies, patients treated at moderate, severe or very severe pain. One observational study of zolmitriptan NS, and one single-blind, placebo-controlled study, were also identified.

Results In the randomized, placebo-controlled studies (study A, n = 69; study B, n = 53; study C, n = 83 [episodic cluster headache patients only], ITT), 30-min headache response (primary endpoint) was significantly higher with zolmitriptan NS 5 or 10 mg (42% and 61%, respectively, in study A; 52% and 61%, respectively, in study B) and zolmitriptan oral tablet 10 mg (47% in study C) vs. placebo (23%, 34% and 29% respectively, p < 0.05 for all comparisons). Zolmitriptan NS was also superior to placebo at earlier timepoints (10–15 min post-dose). Both formulations were well tolerated.

Conclusion Zolmitriptan NS is effective and well tolerated for the acute treatment of cluster headache, providing patients with rapid relief from debilitating headache pain.

ScS6-5**Double-blind placebo-controlled trial of topiramate in SUNCT**

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Objectives Short-lasting unilateral Neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is one of the Trigeminal Autonomic Cephalgias along with cluster headache and paroxysmal hemicrania. These syndromes have responded in open-label trials of topiramate. This study compared the response of topiramate to placebo in SUNCT.

Methods Five male patients (aged 51–72) with SUNCT were randomised into a placebo-controlled, double-blind crossover trial of topiramate 50 mg twice daily. The primary endpoint was reduction in attack frequency by 50% for ten days at maximum dose compared to baseline. A secondary endpoint was reduction in 'attack load' in minutes of pain per day. The study was approved by the Ethics Committee. The results were analysed on an n-of-1 basis.

Results Two patients experienced beneficial response; one had complete cessation of attacks, and one had a 71% reduction in attack load. Of the remaining three patients, one had a placebo effect, and two patients had no benefit with either treatment. One patient each had side effects of peripheral paraesthesiae, and indigestion, whilst on active treatment, but this did not necessitate cessation of the drug.

Conclusion Topiramate had a good effect in 40% of patients. A previous study showed beneficial effects in 11/21 (52%) in an open label trial (1), although the doses were up to 400 mg daily. Given the trial's shortcomings of relatively low dose and short time at maximum dose, we advise the use of topiramate up to 200 mg daily as a preventive medication in SUNCT.

ScS6-6

PACAP-38 induces potent dilatations of dural arteries in closed cranial window model in rats

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Objectives Pituitary adenylate cyclase activating polypeptide-38 (PACAP-38) belonging to the secretin/glucagon/vaso intestinal peptide (VIP) family, is present in trigeminal perivascular nerve fibres in the brain. It is a potent dilator of various vascular beds in animals as well as in humans, like calcitonin gene-related peptide (CGRP). It activates PAC1, VPAC1 and VPAC2 receptors, belonging to PACAP/VIP receptor family. Dilatation of intracranial arteries, innervated with perivascular nerve fibers, is one of key events in migraine pathogenesis; therefore we studied the effect of this peptide on rat cranial vasculature.

Method We used intravital microscopy on closed cranial window in male rats (350–393 g) to study the effect of PACAP-38 on dural arteries at two different doses, 1000 and 3000 ng kg⁻¹, i.v. Mean arterial blood pressure was also measured simultaneously.

Results PACAP-38 dose-dependently induced dilatation of dural arteries, with 20 ± 6% and 51 ± 8% increase in the base line diameter, at 1000 and 3000 ng kg⁻¹ respectively. In addition, there was a dose-dependent decrease in the mean arterial blood pressure.

Conclusion PACAP-38, similar to calcitonin gene-related peptide (CGRP), induced dilatations of dural arteries in the rat model. Therefore, further studies with antagonists of PACAP/VIP receptor family might reveal potential novel anti-migraine targets.

ScS6-7

Efficacy and tolerability of a novel, oral CGRP antagonist, MK-0974, in the acute treatment of migraine

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Objective Calcitonin gene-related peptide (CGRP) is a neuro-inflammatory mediator believed to play a key role in the pathophysiology of migraine. This study evaluated the efficacy and tolerability of a novel oral CGRP antagonist, MK-0974, for the acute treatment of migraine.

Methods Randomized, double-blind, parallel-group, placebo and active-controlled clinical trial with a two-stage, adaptive, dose-ranging design. Patients were allocated to treat a moderate or severe migraine attack with oral MK-0974 (25 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg, 600 mg), or rizatriptan 10 mg, or placebo. The primary endpoint was the proportion of patients reporting pain relief (reduction to mild or none) at 2 h after dosing.

Results Per the adaptive study design, the four lowest MK-0974 groups (25, 50, 100, and 200 mg) were discontinued due to insufficient efficacy. For the remaining treatments, the estimated pain relief proportions at 2 h were: 300 mg (n = 38) 68.1%, 400 mg (n = 45) 48.2%, 600 mg (n = 40) 67.5%, rizatriptan 10 mg (n = 34) 69.5% and placebo (n = 115) 46.3%. The primary hypothesis testing, which compared the mean 2 h pain relief response proportion of the 300, 400, and 600 mg MK-0974 groups to placebo, was significant (p = 0.015). A similar pattern was seen on other endpoints including pain-freedom at 2 h and sustained pain-freedom at 24 h. MK-0974 appeared to be generally well tolerated and there did not appear to be an increase in adverse events with increasing dose.

Conclusions The novel, orally administered CGRP antagonist MK-0974 was effective and generally well tolerated in the acute treatment of migraine.

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