POSTER PRESENTATIONS

Scientific Session 1

Comorbidity

P1A1

The effect of i.v. L-NG methylarginine hydrochloride (L-NMMA: 546C88) on basal and acetazolamide (Diamox ®) induced changes of blood velocity in cerebral arteries and regional cerebral blood flow in man

Lisbeth Hjorth Lassen*[1], Bjoern Sperling[2] & Jes Olesen[1]
[1]*Danish Headache Center, Department of Neurology, Glostrup Hospital, Denmark,* [2]*Department of Clin. Phys. and Nuclear Medicine, Bispebjerg Hospital*

We have previously shown that the nitric oxide synthase inhibitor L-NMMA is effective in the treatment of migraine attacks without aura. Here we estimate the effect of L-NMMA on the diameter of the middle cerebral artery (MCA) and on regional cerebral blood flow (rCBF). Furthermore, we assess the effect of L-NMMA on acetazolamide induced increases in MCA blood velocity and rCBF.

In an open crossover design 12 healthy subjects attended the laboratory twice. At day one 6 mg/kg L-NMMA i.v. over 15 min preceded 1 g acetazolamide iv over 5 min. At day eight only acetazolamide was given. V_{mean} in MCA was determined with transcranial Doppler (TCD) and rCBF with Xe-133 inhalation SPECT at baseline, after L-NMMA, 25 and 55 min after acetazolamide infusion.

After L-NMMA the decrease in $rCBF_{MCA}$ was 6.8% (± 7.4)($P < 0.019, n = 12$), whereas V_{mean} was not affected ($P = 0.83, n = 8$). The change in MCA diameter was estimated to –1.3% ($P = 0.44, n = 8$). L-NMMA did not affect acetazolamide increases in Vmean ($P = 0.67, n = 8$) nor rCBF ($P = 0.29$; $n = 12$). The percentage increase of V_{mean} was 1.5 times that of rCBF ($n = 8$).

Our data suggests that the basal tone of the cerebral arterioles but not of conduit arteries is NO-dependent. The action of acetazolamide is not NO-dependent.

P1A2

Sleep patterns, major depression, and the risk for migraine

Peter Mattsson*[1]
[1]*Department of Neuroscience, Neurology, University Hospital, Uppsala*

Objective Few epidemiological studies have analysed the associations between sleep patterns and migraine.
Methods A neurologist clinically assessed 728 women aged 40–74 years attending a population-based mammography screening program. The assessment focused on the 1-year prevalence of migraine and major depression using modified IHS and DSM-III-R criteria. The participants' sleep patterns during the previous year were evaluated using a questionnaire. We used logistic regression to analyse age–adjusted associations.
Results Women complaining of bad sleep, women frequently experiencing difficulties falling asleep or daytime sleepiness, and women frequently sleeping less than 5 h per night had an increase in risk for migraine. Women using sleeping pills and women experiencing insomnia during the night were not at increased risk for migraine. There was no association between frequent snoring or the self-reported need for sleep, measured as the number of hours of sleep per night, and migraine. However, the larger the discrepancy between the self-reported need for sleep and length of sleep, the greater the risk for migraine. Major depression did not confound the significant associations between migraine and sleep patterns.
Conclusion In this cross-sectional study, women experiencing insomnia and sleep deficit had an increase in risk for migraine, which was independent of the risk for major depression.

P1A3

Impact of migraine and concomitant anxiety on economic and quality of life measures

Robert Shapiro*[1], Jacqueline Pesa[2], Birgit Eschmann[3] & Mary Lou Chatterton[4]
[1]*Department of Neurology, University of Vermont, College of Medicine, Burlington, VT,* [2]*AstraZeneca LP, Wilmintong, DE,* [3]*Consumer Health Sciences, Princeton, NJ,* [4]*MLG Consulting Services, Inc., Chadds Ford, PA*

Objectives While it is recognized that migraineurs have more anxiety, research has not investigated combined effects of these two conditions on economics and quality of life.
Methods Data were from a representative survey of 22 376 US adults. Analyses included the 1598 people diagnosed only with migraines, 692 only anxiety, 371 with both, and 2661 controls with neither. Multivariate models controlled for migraine frequency, severity, demographics, comorbidities, and depression. We modeled mental and physical well-being (SF-8), missed days of work and household activities, and doctor visits (past six months).
Results People with migraines only scored 50.6 for mental well-being, while those who also had anxiety scored lower: 35.2 ($P < 0.001$). Migraine-anxiety sufferers had more doctor visits: 9.1 compared to 4.4 for migraine only ($P < 0.001$). Both results held in multivariate analyses ($P = 0.007$; $p = 0.001$). Having migraines and anxiety alone were each associated with lower physical well-being and increased absenteeism, but having both conditions was not worse than the contribution of each condition separately.
Conclusion Additional direct and indirect costs accrue for migraineurs who also have anxiety. Further research is neces-

sary to assess whether disorders concomitant with migraine, such as anxiety or depression, contribute predominantly additive or synergistic effects on quality of life.

P1A4

Sleep disorders in primary nocturnal headaches: epidemiological data

Grazia Sances*[1], Natascia Ghiotto[1], Marianna Loi[1], Michele Terzaghi[2], Alberto Proietti Cecchini[1], Raffaele Manni[2] & Giuseppe Nappi[3,1]
[1]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH), Pavia, Italy,* [2]*Unit of Sleep Medicine and Epilepsy, IRCCS C. Modino Institute of Neurology, Pavia, Italy,* [3]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

The relationship between primary headache and sleep is well recognized but the exact nature of this association remains unclear. Our study was based on three stages: 1. Prospective epidemiological evaluation of headache outpatients to establish presence of nocturnal headache; 2. Patients with a high frequency of episodes during sleep underwent clinical evaluation of their headache according to the International Headache Society (HIS) classification. Moreover, we also included patients with hypnic headache, a new clinical entity that is to be included in the Second Edition of the IHS classification; 3. Investigation of the coexistence with sleep disorders by means of questionnaire and polysomnographic study in patients in whom there was a clinical suspicion of sleep disorder. 596 consecutive headache outpatients were screened and 65 (10.9%) of them found have nocturnal attacks with a frequency ≥50%. Thirty-nine patients (24 males; 15 female; mean age 54.51 years, range 19–85) agreed to participate in the study. Thirty-six patients were diagnosed with headache: 22 (61%) migraine without aura; 8 (22%) hypnic headache; and 6 (17%) cluster headache.

Sleep disorders were sleep apnoea, snoring, insomnia, restless legs syndrome, periodic limb movement disorder. Polysomnography was recorded in 16 patients and showed obstructive sleep apnoea in all of them. Our data suggest that nocturnal recurrence of headache may correlate with sleep disorders.

This study was supported by a grant from the Italian Ministry of Health (RF 2001/151).

P1A5

Impairment of CO2 cerebrovascular reactivity in CADASIL: a TCD study with breath holding index

Pasquale Marchione*[1], Patrizia Giacomini[1], Rita Restuccia[1], Ada Francia[2], Donatella Corigliano[1], Domenico Samà[1], Licia Finamore[2], Francesco Fattaposta[1] & Giuseppe Nappi[3,1]
[1]*Department of Neurology and ORL, University of Rome 'La sapienza', Rome, Italy,* [2]*Department of Neurological Sciences, University of Rome 'La Sapienza', Rome, Italy,* [3]*University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Modino Institute of Neurology, Pavia, Italy*

Introduction Despite advances in molecular genetics and biology of CADASIL, pathophysiology of migraine and cerebral ischemia is still unclear. The accumulation of Notch3 ectodomain within vessels wall seems to be the leading mechanism of vascular impairment. The aim of this study is to evaluate hemodynamic reserve and its relationship with clinical features.

Materials and methods We investigated the reactivity of mean cerebral arteries to hypercapnia by breath-holding index (BHI) in 11 CADASIL patients (5 men and 6 women, mean age 35,28 ± 2.8) vs. age and sex matched controls. 4 patients (2 men and 2 women) suffered from migraine with aura, stroke and dementia with wide distribution of lacunar infarcts at MRI. The other subjects (3 man and 4 women) referred only migraine with aura and have few neuroradiological features.

Results Mean flow velocities on middle cerebral arteries were lower in patients with strokes/dementia/migraine than in those with migraine only. BHI was lower in CADASIL patients than in controls without differences between fully symptomatic and migraineurs only subjects.

Discussion These results suggest an early dysfunction of cerebrovascular vasodilator stimuli response in CADASIL. The homogeneous impairment of hemodynamic reserve may account for the importance of vascular mechanisms in stroke/migraine comorbidity of CADASIL.

P1A6

Development of time-efficient procedures for assessing psychopathological aspects of medication overuse headache

Monica Silvia Verticale*[1], Alberto Proietti Cecchini[1], Natascia Ghiotto[1], Silvano Cristina[1], Caterina Biancardi[1], Giuseppe Nappi[1,2] & Grazia Sances[1]
[1]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia,* [2]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

DSM-IV/SCID-I substance dependence criteria do not entirely fit chronic headache with analgesic overuse and need to be adapted to cater for this condition. The aim of this study was: (a) to develop a new assessment tool for investigating this type of disorder (Interview for Medication Overuse and Dependence in Headache – IMODH); (b) to look for psychopathological aspects, other than neuroticism.

Over 16 months we investigated 369 patients (293 females, 76 males), admitted for analgesic overuse headache and detoxification treatment, using the SCID-I (clinical version). We also investigated a subgroup of 142 patients (106 females, 36 males) using the MMPI-2, and a subgroup of 67 patients (58 females, 9 males) using the IMODH.

Medication overuse was found in 293 patients (240 dependence and 53 overuse). Hysteria, Depression, Hypochondrias were significant, psychotic/borderline was not significant in MMPI-2 scores; IMODH interview founded warning behaviour in patients with analgesic overuse, including unauthorized dose escalations, procurement of medication from providers, reduced self-control regarding drug use, compulsive and continued use in spite of negative physical and

mental consequences; furthermore, subjects were found, in childhood, to have modelled themselves on their parents.

Application of our assessment procedure, investigating the patient's attitude towards medication, is suitable for chronic headache.

This study was supported by a grant from the Italian Ministry of Health (RC 2002).

P1A7

Comorbidity of migraine with Systemic Lupus Erythematosus (SLE): a metaanalysis of published studies

Dimos Mitsikostas*[1], Petros Sfikakis[1] & Peter Goadsby[2]
[1]*Athens Naval Hospital, Neurology Department, Athens, Greece,*
[2]*Headache Group, Institute of Neurology, Queen Square, London, U.K*

Objectives Controversy surrounding the occurrence of migraine among SLE patients, triggered us to search the literature by an evidence-based approach to investigate whether headache, and migraine in particular, were comorbid with SLE.
Methods We conducted an extensive Medline/Pub Medical search, using specific keywords. All reports published (>30 patients) were reviewed and classified into four classes (I, IIa, IIb and III) by the quality of their evidence.
Results Pooled data from eight studies that used the ÉÇS criteria show that 57.1% of SLE patients reported any type of headache (migraine 31.7% and tension-type headache 23.5%). Pooled data from seven controlled studies showed that the prevalence of all headache types, including migraine, was not different from controls. Insufficient evidence was found for the concept of 'lupus headache'. No particular pathogenetic mechanism of headache in SLE patients has been identified, nor an association between headache and the disease status, including the CNS involvement. There is no good evidence that headache is associated with anxiety and depression in SLE.
Conclusions We found no support in the literature for a comorbidity of migraine or tension-type headache with SLE.

P1A8

Effectiveness of a behavioral headache intervention among medication overusers

Justin Nash*[1], Rob Nicholson[1], Elyse Park[1], Amanda Graham[1] & Barbara Walker[1]
[1]*Brown Medical School/The Miriam Hospital, Providence, RI, USA*

Objectives To evaluate the effectiveness of behavioral group treatment in headache sufferers who overuse analgesics.
Methods Participants (n = 74) completed a 10-session behavioral group intervention while they continued with customary medical care. Participants were divided into those who overuse analgesics (n = 31) and those who do not (n = 43). Medication overuse was defined as self-reported analgesic use four or more days weekly. Measures included self-reported headache frequency, intensity (0–10), and duration (hours) during the previous month; type, amount, and number of days of analgesic use in last month; and depression (BDI) and quality of life (SF-36).
Results A repeated measures ANOVA indicated that medication overusers had a greater decrease in both medication use ($P < 0.001$) and depression ($P < 0.01$) following the intervention compared to those who did not overuse medication. Both groups showed comparable improvements in headache frequency and quality of life.
Conclusions Headache sufferers who use analgesics frequently may benefit from behavioral treatment. Addressing psychosocial factors may help to reduce excessive medication use and provide headache relief.

P1A9

Comorbid disorders in headache patients

Franco Mongini*[1], Andrea Deregibus[1], Luca Ferrero[1] & Tullia Mongini[1]
[1]*Section Headache-Facial Pain, Department Clinical Pathophysiology, University of Turin, Italy*

Objectives and methods To investigate the relevance of comorbidity in headache syndromes 409 patients (60 males, 349 females) were enrolled. They had (IHS criteria): episodic migraine (EM,190), chronic migraine (CM, 104), episodic tension type headache (ETTH, 51), chronic tension type headache (CTTH, 64). In 66 EM patients ETTH was also present.

Patient examination included history, structured interview, psychological assessment (DSM-IV), general, neurological and cranio-facial examination, muscle tenderness at palpation (score 0–3). Inter- and intragroup statistics included: 1) relationship between headache frequency, severity and duration, muscle tenderness score, presence of trigger points and psychosomatic symptoms (2) prevalence of depression and other psychiatric disorders, and (3) their relation to point 1 variables.
Results Depression was significantly ($P < 0.001$, Chi square) more prevalent in CM (CM = 74%, EM = 43%, ETTH = 41%, CTTH = 55%) and was in all groups associated with higher amount of trigger points and psychosomatic symptoms ($P < 0.001$, Student' t).

In the em group:1. depressed patients had higher tenderness score and pain duration ($P < 0.001$, Student' t); 2. tenderness score was significantly related to psychosomatic symptoms ($P < 0.001$, multiple regression).
Conclusions In headache patients depression is a frequent comorbid disorder. In EM depression might facilitate the worsening of the pain pathology and its consequent evolution into CM.

P1A10

Temporomandibular joint dysfunction in migraine and chronic migraine; a controlled study

Henrique Macedo*[1], Marcelo Bigal[2,3], Carlos Bordini[1] & Jose Speciali[1]
[1]*School of Medicine at Ribeirão Preto, University of São Paulo, Brazil,*
[2]*Albert Einstein College of Medicine, Bronx, NY, USA,* [3]*The New England Center for Headache, Stamford, CT, USA*

Background Pain from the temporomandibular joint (TMJ) is common. TMJ dysfunction (TMJD) is more prevalent in

migraineurs compared to controls; the relationship with chronic migraine (CM) is not determined.
Objectives To assess TMJD in subjects with migraine, CM, and controls.
Methods Participants with migraine ($n = 31$) and CM (m = 34) were selected in a headache ambulatory. Controls ($n = 28$) were subjects without any headache attack in the last 6 months. An effort was made to match all migraineurs with one CM case and one control, by age (±2 years) and sex. An experimented odontologist applied a protocol to assess the Helkimo index to TMJD.
Results CM sufferers had a higher Helkimo index when compared to both the migraine cases (39 vs. 22, $p < 0.001$), and controls (20, $p < 0.001$). Migraineurs had a higher index than controls ($P < 0.05$). Additionally, the severity of the TMJD was significantly higher in those with CM (62% had severe TMJD), compared to the migraine group (31%, $p < 0.01$) and to the controls (6%, $p < 0.001$).
Conclusions TMJD is more frequent and severe in migraine sufferers that in controls, and in CM sufferers than in migraine sufferers. TMJD may play a role in the migraine chronification process, beyond acting as a possible trigger in migraine.

P1A11

Familial occurrence of psychiatric disorders in headache, asthmatic, epileptic and healthy children: a control study

Federica Galli*[1], Vincenzo Guidetti[1], Maria Auricchio[1] & Milena Z. Ciccimarra[1]
[1]*Department of Child and Adolescent Neurology and Psychiatry, University of Rome 'La Sapienza*

The comorbidity of headache and psychiatric disorders (mainly anxiety and mood disorders) is high both in adults and children or adolescents. Analysing the occurrence of psychiatric disorders in relatives of headache patients add elements to explain the relationship between headache and psychiatric disorders. Our aim is analysing the occurrence of psychiatric disorders in parents of headache patients comparing three control groups
Material-Method One hundred parents of young headache patients seen in the Headache Center and parents of three samples (50 asthmatic, 46 epileptic and 100 healthy subjects referring for paediatric routine visits) have been interviewed for analysing the occurrence of headache (IHS criteria) and psychiatric disorders (DSM-IV criteria), by the mean of structured interviews. Student's T-test and χ^2 has been performed
Results Parents of headache and asthmatic patients showed the highest number of anxiety and mood disorders (about 60%) compared to the healthy and epileptic sample (about 15%). The parents of chronic daily headache patients have the highest number of psychiatric disorders compared to headache and not-headache patients.
Conclusion The implications need to be drawn. The etiology, the shared biological (genetical or environmental) mechanisms, the likely direction of influence are unknown, but a chance co-occurrence is ruled out.

P1A12

Migraine with aura, episodic cluster headache, and SUNCT syndrome consecutively in a patient: trigemino-vascular trinity

Monika Empl*[1], Peter J. Goadsby[1] & Holger Kaube[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London, UK*

We present a 59-year-old-priest, who developed consecutively migraine with aura, chronic cluster headache, and SUNCT syndrome in his life

From adolescence until the age of 33, the patient suffered occasionally from unilateral, typical migraine attacks with visual aura (MWA). After two headache-free years from 33 to 35, he developed severe, left temporal headache attacks with a duration of two to three hours accompanied by autonomic features, which occurred daily every year for five weeks around November, until the age of 43. These headaches were typical for episodic cluster headache (ECH). At the age of 44, the patient developed a constant, dull, boring, left-sided, temporal and facial pain, superimposed by short, very severe, stabbing, periorbital pain attacks occurring up to 150 times per day. These attacks last seconds to up to three minutes and are often accompanied by autonomic features. Serological investigations and neuroimaging were normal. The last headache suggests SUNCT syndrome. Only under gabapentin 3000 mg/day, the attack frequency dropped to 20 per day. Background pain intensity also decreased significantly. By random association, this coincidence would only be expected in less than $0.04\ (\text{MWA}) \times 0.004\ (\text{eCH}) \times 0.004\ (\text{SUNCT} < \text{eCH}) = 6.4$ in 10^7 subjects.

P1A13

Predictors of disability in a clinical population of patients with episodic and chronic migraine

Paolo Rossi[2], Alfonso Troisi*[1], Maria Grazia Malpezzi[1], Giorgio Di Lorenzo[1], Cherubino Di Lorenzo[2], Jessica Faroni[2] & Francesco Cesarino[2]
[1]*Psichiatry Unit, Department of Neuroscience, University of Rome 'Tor Vergata', [2]Headache Clinic, INI Grottaferrata*

Aim to assess the relative role of socio-demographic variables, migraine characteristics, and psychological factors in influencing migraine-related disability.
Methods The sample included 178 outpatients with episodic ($N = 122$) or chronic ($N = 56$) migraine. Measures included disability (MIDAS), adult attachment style (ASQ), depressive symptoms (BDI). Statistical analysis was based on a stepwise regression model using total MIDAS score as dependent variable and age, gender, type of migraine, medication overuse, duration of disease, number of migraine days per month, pain severity, BDI and ASQ scales as predictors.
Results The model was highly significant ($F = 6.96$, $P = 0.009$) and accounted for 25.4% of the total variance in disability. Depressive symptoms (beta = 0.23, $P = 0.002$), the presence of medication overuse (beta = 0.32, $P < 0.001$), and an insecure style of adult attachment (Confidence scale of the ASQ; beta = –0.20, $P = 0.009$) emerged as significant predictors of migraine-related disability.

Conclusions These findings show the relevance of personality and psychiatric factors in influencing the level of disability in patients with migraine.

Prospective studies are needed to clarify the causal relationship between such factors and disability, even though the development of attachment style in early life makes it unlikely the hypothesis of personality changes secondary to chronic pain syndrome.

P1A14

Relation of the Headache Impact test to depression, anxiety and stress: findings of the PAMINA study

Christian Wöber*[1], Karin Schmidt[1], Kadriye Aydinkoc[1], Evelyne Geuder[1], Robert Zingerle[1], Kathi Hanslik[1], Julia Holzhammer[1] & Çiçek Wöber-Bingöl[1]
[1]*Department of Neurology, University of Vienna, Vienna, Austria*

The aim of this study was to examine the relationship of the Headache Impact Test (HIT) to depression, anxiety and stress

We examined 373 migraine patients (87.7% females) aged 40.5 ± 11.8 years. All patients were recruited by articles in newspapers. They completed the HIT as well as the Self-rating Depression Scale (SDS), the Self-rating Anxiety Scale (SAS) and a stress questionnaire covering personal, environmental and task-related factors of stress. For statistical analyses we calculated Spearman correlation coefficients and multiple linear regression models.

The HIT score showed a strong relation to the SAS score ($r = 0.26$; $p < 0.001$), a weak relation to the SDS score ($r = 0.11$; $p = 0.39$) and it was related to the total stress score ($r = 0.21$; $p < 0.001$), as well as to the three subscales, i.e. personal ($r = 0.26$; $p < 0.001$), task-related ($r = 0.15$; $p = 0.004$), and environmental stress ($r = 0.11$; $p = 0.034$). In the multiple regression model, patients with high HIT scores were differentiated from those with lower scores by the SAS score ($P < 0.001$), the SDS score ($P = 0.006$) as well as the stress score ($P = 0.031$).

In conclusion, patients with high scores in the Headache Impact Test are at higher risk for anxiety, depression and stress.

P1A15

The study on migraine-using human lymphoblasts

Eiichiro Nagata*[1], Jun– ichi Hamada[1], Toshihiko Shimizu[1], Kyouko Gotoh[1], Yuki Katoth[1] & Yasuo Fukuuchi[1]
[1]*Department of Neurology, Keio University School of Medicine, Tokyo, Japan*

We have previously reported that the dysfunction of the autonomic nervous system occurs not only in the part of the brain, but also a whole body in migraine. It is also known that serotonin and neuropeptides have an important role in the pathophysiology of migraine. Based on those reasons, we have started to analyse a human cell line (lymphoblast) in migraine to investigate the mechanism of migraine. In this study we examined the characterization of a human lymphoblast.

Lymphocytes were obtained from peripheral blood of migraine and control subjects. To investigate serotonin receptors (5-HT1B, 1D, and 2 A) and CGRP receptor, we performed RT-PCR. Moreover, we measured the amount of 5?HT and 5-hydroxytryptophan (5-HTP) in lymphoblasts using HPLC.

The lymphoblasts had 5-HT1B, 1D, and CGRP receptors. Moreover, we could measure the amount of 5-HT and 5-HTP in human lymphoblasts.

These results will be useful to examine the response to serotonin and CGRP in migraine and this research system may have an important role to analyse the mechanism of migraine.

P1A16

Headache and specific learning disability in children: comorbidity and cofamiliarity

Renato Donfrancesco*[1], Sergio La Rosa[1], Andrea Dell'Uomo[1] & Giovanni Mazzotta[2]
[1]*ASL Roma/A Presidio,* [2]*University of Perugia*

Objectives This paper explores the possible existence of a cofamiliarity between headache and specific learning disability (LD).
Methods 116 LD children age 7–12, 37 female and 79 male, were recruited. All the children with at least one headache attack per month were interviewed using a structured interview exploring headache symptomatology according to IHS criteria. 372 parents and first grade siblings of the LD children were also interviewed. The control group consists of 87 children and their 250 parents and first grade siblings, and was recruited from the consecutive patients of a paediatric clinic. The children of the control group were 28 female and 59 male matched for age with the LD group.
Results LD children show a higher percentage ($P < 0.01$) of headache (27,58%) in comparison with the control group (12.64%). 8,88% of parents and sibling of the control group show headache, with a significant difference ($P < 0.01$) between control group and the group of the parents and sibling of the LD children with headache (28.15%) and (remarkably) of the LD children without headache (20.14%).
Conclusions Our data show that LD children have a comorbidity with headache and this comorbidity is probably due to a cofamiliarity.

P1A17

Evaluation of disease burden in subjects with migraine

Roger Cady*[1]
[1]*Headache Care Center, Springfield, MO, USA*

Objectives To evaluate baseline psychological and neurological functioning between attacks of migraine for a group of migraine sufferers, to determine the frequency, duration, and headache burden of their migraines, and to identify the association of headache with depression, anxiety, and other comorbid conditions and symptoms.
Methods 55 patients were randomly selected for testing and interviews from those seeking care at the Headache Care Center. They were stratified based on their Migraine Disability Assessment (MIDAS) scores. The participants completed

the following questionnaires: Headache Impact Test (HIT-6), MIDAS, Zung Depression Inventory, State-Trait Anxiety Scale, and Physical Symptoms (PHQ-15). A structured interview was conducted by the investigator for 30–45 min.

Results The patients' headache frequency averaged 4.36 headaches per month. The time from the onset of disabling headaches to the diagnosis of migraine was an average of 10 years. On the HIT-6, the burden of these headaches was severe for 60% of patients, moderate for 13%, mild for 11%, and no impact for 16%. By comparison, on the MIDAS, the impact was severe for 22%, moderate for 27%, mild for 16%, and no impact for 35%.Despite the frequency, duration, and burden of these headaches, only 5% of patients scored within the depressed range on the Zung. However, they reported other physical symptoms, most commonly mood alterations and nonheadache pain.

Conclusions As the migraine disability scores increased, there was a concomitant increase in the number of somatic, nonheadache complaints. While historically headache has served as the clinical marker of time for the neurological disruption of migraine transformation, this data suggest that other symptoms may also mark periods of advancing neurological dysfunction as migraine evolves to a chronic state.

P1A18

Different experience of anger and anxiety in depressed and not-depressed migraine without aura patients

Gianluca Coppola*[1], Giancarlo Fiermonte[2], Paolo Rossi[3], Giuliana Ricotta[2] & Francesco Pierelli[2,4]
[1]*Department of Neurology and ORL, University of Rome La Sapienza, Rome,* [2]*University Centre for Adaptive Disorders and Headache (UCADH), University of Rome La Sapienza, Rome,* [3]*Headache Clinic, INI, Grottaferrata, Rome,* [4]*IRCCS, NEUROMED, Pozzilli (IS)*

Objectives To clarify the relationship between depression, anxiety and anger in migraine without aura patients (MO) Methods 104 MO and 54 healthy volunteers (HV) completed these psychometric tests: Zung Self-Rating Depression Scale, State-Trait Anxiety Inventory and State-Trait Anger Expression Inventory.

The 95% of the confidence limits (CL) for Zung SDS index of HV was considered the cut-off value to divide the MO patients in two groups: depressed ($n = 77$) and not-depressed ($n = 27$).

Results In the not-depressed group only anger out scale was significantly increased with respect to HV. In the depressed group, moreover, state and trait anxiety, angry-reaction, anger-in, anger-out, and anger expression were significantly increased when compared to HV, and only anger control was significantly decreased.

Conclusions Our results suggest the existence of a distinct subgroup of MO patients in which depression, anxiety and migraine are closely linked and that they expressed more anger both outward and inward, and another subgroup of patients that yield a profile more similar to that of control subjects.

P1A19

Migraine caused by cerebral venous obstruction: increased Intrathoracic Pressure displayed by MRI/MRA in two Thoracic Outlet Syndrome (TOS) patients with herniated lung and jugular venous compression

Ernestina Saxton*[1], James D. Collins[2], Theodore Q. Miller[2] & Samuel S. Ahn[3]
[1]*Department of Neurology, UCLA School of Medicine, Los Angeles, CA, USA,* [2]*Department of Radiological Sciences, UCLA School of Medicine, Los Angeles, CA, USA,* [3]*Department of Vascular Surgery, UCLA School of Medicine, Los Angeles, CA, USA*

Background Cerebral venous distension may a source of migraine pain. Patients with TOS present with severe migraine, arm pain and paresthesias. Arm abduction- external rotation (AER) increases intrathoracic pressure, causes compression of the great veins and neurovascular bundles, and triggers TOS complaints and migraine.

Materials & Methods Two patients presented with intractable migraine, TOS symptoms and syncope. Imaging was on a 1.5T GE unit, 5.7 software, 4.0 thickness (Clin. Anat. 8 : 1–16), for bilateral coronal, transverse, oblique and sagittal T1-weighted, and MRA images. For AER sequence, the patient's arms were placed overhead and patient reintroduced into the gantry without changing position.

Results Lung herniation, and compression of the jugular vein and carotid sheath, respectively, was demonstrated in neutral position. In both patients AER MRI sequence demonstrated increased intrathoracic pressure with jugular and subclavian vein compression and cerebral venous congestion. There was further herniation of the lung through Sibson's fascia, and compression of the great veins and carotid sheath, respectively, and triggered migraine.

Conclusions Monitored MRI/MRA displays compression of the great veins and impaired venous drainage of the upper extremities, neck and brain in TOS patients with intractable migraine. The findings suggest that impaired venous flow is important in migraine pain mechanisms.

P1A20

Pharmacotherapy of migraine comorbid with epilepsy

Zarko Martinovic*[1], Maja Milovanovic[1], Nevenka Buder[1], Stanko Milic[2] & Valentina Jakovljevic[3]
[1]*Institute of Mental Health, Belgrade, Yugoslavia,* [2]*Neurology Clinic, Podgorica, Clinical Center Podgorica,* [3]*Health Center, Cuprija, Serbia and Montenegro*

The purpose of this paper is to define main principles of pharmacotherapy of migraine comorbid with epilepsy based on the prospective clinical study of 68 patients (age range 12–52 years).

The control of epilepsy was given the priority to the control of migraine. After 8 week baseline period, the severity of migraine in the group treated with valproate was compared with the group receiving other antiepileptic drugs. Also, in 28 patients with comorbid mood disorders, the subgroup treated with gabapentin was compared with controls.

Compared to controls, the severity and frequency of migraine headache was significantly reduced after 6, 9 and 12

months of treatment with valproate ($P < 0.01$). The use of sumatriptan, particularly subcutaneous, proved highly effective in the relief of postictal migraine-like headache in 75% of 12 patients.

In line with recent findings of valproate efficacy in migraine prophylaxis, our results suggest that valproate should be the drug of the first choice in the treatment of various associations of migraine with epilepsy. gabapentin may be indicated in migraine and focal epilepsy comorbid with dyshtymia and anxiety disorders.

P1A21

Description of characteristics of depression in a group of patients with Chronic Migraine (CM)

Cecilia Uribe-Valdivieso*[1], Maria Ximena Mejia[1] &
Fidel Ernesto Sobrino[2]
[1]*Insignis Psicologica Fundation Bogotá – Colombia,* [2]*Colsubsidio Headache Clinic Bogotá – Colombia*

Objective Describe the characteristics of depression in a group of patients with CM.
Background CM is characterized by episodic migraine that transforms into a more frequent and often less intense headache. Most patients are women. Depression is reported as a pathology that coexists with CM (80%); the explanations include common neurobiology mechanisms, effects between both diseases, and a random relationship.
Methods Total patients met revised criteria for CM. A total of 86 subjects (73 women and 13 men, mean age 37.4 years) completed Beck Depression Inventory (BDI).
Results BDI mean depression was 16.4. Women had higher levels of depression (32.8%), than men (7.6%).25 patients presented clinical depression, 72% were in productive work years. Independently of the BDI total score, the items that presented higher frequencies were related to disturbances associated with CM: tiredness, sleep problems, irritability, work difficulties and health worries.
Discussion We conclude that non necessary there is comorbidity between CM and depression, although they share similar symptoms suggesting that depression in these patients must be evaluated without the items related with CM symptoms, or with precaution because depression level must not reflect the real affective state, by the impact of CM in some aspects of patients' life.

P1A22

Prevalence of primary headaches in multiple sclerosis

Domenico D'Amico*[1], Andrea Rigamonti[1], Loredana La Mantia[1],
Nerina Mascoli[1], Susanna Usai[1], Clara Milanese[1] &
Gennaro Bussone[1]
[1]*C. Besta National Neurological Institute, Milano, Italy*

Previous investigations on the prevalence of headache in MS patients have lead to controversial results. No studies have been concerned specifically with the prevalence of headache in untreated MS patients using the diagnostic criteria of the International Headache Society (IHS. 1988).

The aim of the study was to assess the lifetime prevalence of primary headaches in MS. One-hundred-37 patients (42 males and 95 females; mean age 40.6 years) with clinically definite MS were studied All patients underwent a structured interview, taking into account the IHS diagnostic criteria.

Eighty-eight patients reported headache. After excluding 21 subjects who developed headache only after therapy with interferons, headache was present in 67 subjects (57.7%). Migraine was found in 25.0%; tension-type headache in 31.9%; cluster headache in one patient. Most migraine patients (19/29) had migraine without aura. These figures are higher than reported by most studies on MS patients, but in line with most recent reports (Rolak and Brown, 1990; Pollmann et al. 2002). Our study showed that primary headaches in general and migraine in particular are highly prevalent in MS patients. The reasons for this association are unclear; one speculative suggestion is that demyelinating lesions in the brainstem can provoke migraine-like headache.

P1A24

Headache in sleep apnea and periodic limb movements disorder

Maria Pia Prudenzano*[1], Mariantonietta Savarese[1], Bruno Brancasi[1],
Pietro Montesanti[1], Dhanpat Mohnot[1], A. Petruzzellis[1], R. Ambrosio[1]
& F. M. Puca[1]
[1]*I Neurologic Clinic, University of Bari, Italy*

Sleep apnoea patients often complain of headache. The pathogenesis of this type of headache is still discussed. An important role might be played by the hemodynamic effects of hypoxia and hypercapnia. The nocturnal sleep fragmentation might also play a causative or at least triggering role in sleep apnoea headache, since a similar headache is often complained also by patients with other disorders disrupting sleep such as the periodic limb movements disorder (PLMS). This study was aimed to examine headache occurrence in a sample of sleep apnoea patients vs. a sample of PLMS patients. Among patients successively referred to I Neurological Clinic. University of Bari during a two years period, two sample were selected, the first consisting of sleep apnoea patients and the second consisting of PLMS patients both polisomnographically diagnosed. A detailed medical history aimed to obtain information regarding occurrence and clinical features of headache was collected. Preliminary results show high rates of headache occurrence in both types of sleep disorders with higher percent in sleep apnoea patients. In most of the patients headache was bilateral and without associated symptoms. No difference was found in headache frequency between sleep apnoea patients and patients with the association of sleep apnoea and PLMS. These results confirm the comorbidity between sleep apnoea and headache and support the hypothesis of a major role played by hypoxia-hypercapnia mechanism in the pathogenesis of headache.

P1A25

Effect of depression and anxiety on the experience with precipitating factors of migraine: findings of the PAMINA study

Christian Wöber*[1], Karin Schmidt[1], Robert Zingerle[1], Kadriye Aydinkoc[1], Ludmila Zahlbruckner[1], Claudius Fazelnia[1], Andrea Böttcher[1], Thomas Hartl[1] & Peter Wessely[1]
[1]*Department of Neurology, University of Vienna, Vienna, Austria*

The aim of this study was to clarify whether the experience with precipitating factors of migraine differs in patients with depression and/or anxiety and subjects without these disorders

We examined 363 migraine patients (age: 40.6 ± 11.9; 85.5% female) recruited via newspapers. All subjects rated 52 potential precipitating factors on a five-point scale and they completed the Self-rating Depression Scale (SDS) and the Self-rating Anxiety Scale (SAS). We compared patients with normal SDS- and SAS-scores ($n = 223$) to those with increased scores in one scale ($n = 69$) and both scales ($n = 71$), respectively. The precipitating factors were grouped into 8 categories comprising psychological, physical, meteorological and other external factors, factors related to sleep and fatigue, nutrition, alcohol and smoking.

Patients with depression and anxiety gave the highest and subjects without these disorders gave the lowest ratings in all categories. Kruskal–Wallis tests revealed statistically significant differences in 7 categories. In a stepwise linear regression model, psychological ($P = 0.001$) and meteorological factors ($P = 0.05$) were included, whereas the other categories were excluded.

In conclusion, migraine patients with depression and anxiety experience precipitating factors more often than subjects without these disorders. This is particularly true for psychological and meteorological factors.

P1A26

Clinical features of migraine-related dizziness

Maurizio Versino*[1,2], Grazia Sances[3], Silvia Colnaghi[1,2], Claudio Albizzati[4], Giorgio Bono[5], Giuseppe Nappi[3,6] & Vittorio Cosi[1,2]
[1]*Department of Neurological Sciences, University of Pavia,* [2]*Eye Movement and Vestibular Laboratory, IRCCS C. Mondino Institute of Neurology,* [3]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH),* [4]*Casa di Cura Mater Domini, Castellanza,* [5]*Unit of Neurology, Circolo Hospital Varese and University of Insubria,* [6]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

We considered two groups of patients. The first group (G1) derived from 452 patients with balance problem referred to either a neurological or ENT outpatient consultation; 41 of them presented at least 5 attacks of vertigo/dizziness for which migraine was the most likely explanation. The second group (G2: 27 patients) derived from 75 migrainous patients who also presented with dizziness or vertigo.

In both groups the onset of dizziness was delayed of several months/years with respect to migraine onset (G1: 83.8%; G2: 92.3%). The balance problem more frequently consisted in dizziness (G1 : 68.3%; G2 : 77.7%) rather than in rotatory vertigo, and, within a single spell, might present not in association with headache (G1 : 30.6% always, 17.9% sometimes; G2: 26.9% and 11.5%). When associated with headache within a single spell, the balance problem usually occurred first (G1 : 51%; G2 : 52%). The occurrence and the duration of the spells showed a great variability, and some G1 patients reported that the disorder progressed to an almost constant feeling of dizziness.

Migraine is a complex disease, and the comorbidity with vertigo deserves special attention since according to the data from our and previous studies up to about 9% of dizzy patients may have migraine-related vertigo, and migraine would be the third cause of vertigo.

This study was supported by a grant from the Italian Ministry of Health (RC 2002).

P1A27

Chronic migraine associated with hysterical conversion

Ion Moldovanu*[1], Stela Odobescu[1] & David Dodick[2]
[1]*Neurology Department of the State Medical University of Moldova (Chisinau, Moldova),* [2]*Mayo Clinic Scottsdale, Arizona, USA*

Background The comorbidity of migraine with hysteria, especially with the hysterical conversion (HyC), is insufficiently studied.
Objective To delineate the clinical characteristics, presentation, and outcome of 3 patients with chronic migraine and HyC.
Methods Three patients underwent evaluation by Neurology, Psychiatry, and Neuropsychology. Each patient met the new IHS diagnostic criteria for chronic migraine (CM) and DSM-IV criteria for HyC.
Results All patients were females, ages 29, 37, and 44. Referral diagnoses were complicated migraine, migrainous stroke, and hemiplegic migraine. The duration of chronic migraine was 2, 4, and 14 years, respectively. During this period of chronification, associated affective and somatic symptoms became prominent such as anxiety, neck stuffiness, irritability, fatigue (patient 1); anxiety, insomnia, syncopes, irritable bowel syndrome (patient 2); depression, dysphory and polysubstance abuse (patient 3). All patients had a nonorganic left hemiparesis, astasia abasia, and a normal and extensive neurodiagnostic evaluation.
Conclusions HyC is an important diagnostic consideration in patients with chronic migraine. Accurate diagnosis avoids potentially harmful and enables appropriate therapy. The comorbidity of HyC and CM illustrates the potential influence of both psychogenic and behavioral mechanisms on the pathogenesis of CM. The role of hysteria as a possible factor in the transformation and maintenance of CM is still to be elucidated.

P1A28

Increasing headache frequency is associated with lower quality of life

Natalie Wiendels*[1,2], Arie Knuistingh Neven[2] & Michel Ferrari[1]
[1]*Department of Neurology, Leiden University Medical Centre, the Netherlands,* [2]*Department of General Practice, Leiden University Medical Centre, The Netherlands*

Objective To assess Quality of Life (QoL) in subjects with different headache frequencies in the general population.
Methods In 9 GP's offices, 2 questionnaires were sent consecutively to subjects with ages between 25 and 56 years. The first questionnaire screened for headache frequency. Subjects were classified into the following groups: (1) Chronic Daily Headache (CDH), headache on at least 15 days/month (2) Very Frequent Headache (VFH), headache on 8–14 days/month (3) Frequent Headache (FH), headache on 5–7 days/month (4) Episodic Headache (EH), headache on 1–4 days/month, and (5) No Headache (NH), headache on less than 1 day/month. A second questionnaire was sent to all subjects in groups 1 and 2 and to a random sample of subjects in groups 3–5. This questionnaire contained the RAND-36, a Dutch version of the SF-36, a generic QoL instrument.
Preliminary results Until now, the RAND-36 was completed by 842 subjects, 122 CDH, 104 VFH, 83 FH, 116 EH, 417 NH. With increasing headache frequency, QoL significantly decreases in each domain of the RAND-36.
Conclusion In the general population, increasing headache frequency is associated with lower QoL. The results of the completed study will be presented at the meeting.

P1A29

Migraine is not associated with cervical artery dissection but with cerebral venous thrombosis – two case-control studies

Esra Akova-Öztürk*[1], Sonja Schwaag[1], Achim Frese[1], Ingo-W. Husstedt[1] & Stefan Evers[1]
[1]*Department of Neurology, University of Muenster*

Several epidemiological studies have shown that migraine is associated with an increased risk of juvenile stroke in women. However, the mechanisms have not been clarified yet. A few observational studies have suggested that migraine is associated with cervical artery dissection. We therefore designed a larger case-control study to examine dissection as a possible cause of stroke in migraine patients. In addition, we performed a similar case-control study on cerebral venous thrombosis

We enrolled 148 patients with a proven dissection of cervical arteries and 58 patients with a proven cerebral venous thrombosis. Diagnosis was based on magnetic resonance imaging and history. We matched 148 and 58 healthy control subjects without any evidence for dissection or cerebral venous thrombosis, respectively. The history of migraine and vascular risk factors were evaluated in all groups.

The migraine life-time prevalence was 14.2% in patients with cervical artery dissection and 15.5% in the control group ($P = 0.744$). For cerebral venous thrombosis, the respective figures were 50% in the case group and 13.8% in the control group.

Our data clearly suggest that there is not significant association between migraine and cervical artery dissection but a significant association between migraine and cerebral venous thrombosis. The contradictive results in previous observational studies might be explained by different methodology, in particular by different control groups.

P1A30

Sleep quality and fatigue in migraine

Sara Gori*[1], Enrica Bonanni[1], Nicola Morelli[1], Michelangelo Maestri[1], Monica Fabbrini[1] & Luigi Murii[1]
[1]*Institute of Neurology, Department of Neurosciences, University Centre for Adaptive Disorders and Headache (UCADH), University of Pisa, Italy*

Strong clinical impression suggests that sleep duration and quality affect migraine, but little experimental data are available.

The aim of this study has been to assess sleep quality and daytime functioning parameters such as sleepiness and fatigue in migraine.

Ninety consecutive patients with migraine diagnosed according to IHS criteria (1988) were evaluated. The Pittsburg Sleep Quality Index, the Epworth Sleepiness Scale (ESS), the Fatigue Severity Scale (FSS), the Beck Depression Inventory scale (BDI) were applied.

Fifty-seven out of 90 patients (63%) showed a PSQI global score greater than 5 that is recommended as an indicator of relevant sleep disturbances, whereas only 5 out of 90 patients (5.5%) presented excessive daytime sleepiness.

Seventy-one patients (79%) had FSS scores greater than 27 which represents the cut-off defining fatigue. FSS scores correlated with BDI values ($P < 0.005$), however, also considering only patients without depression 41 out of 58 (70%) showed significant fatigue.

These data suggest that poor sleep quality and fatigue represent very common symptoms in migraine patients, the last one occurring even in absence of comorbidity for depression might be related to migraine pathogenesis mechanisms such as channelopathy or functional abnormalities in mithocondrial energy metabolism.

P1A31

The comorbidity of headaches and psychic disorders in the light of the complexity theory

Roland Woerz*[1]
[1]*Pain Center, Bad Schönborn, Germany*

The modern classification systems favour the phenomenological – descriptive approach both in algology (IHS) and psychiatry (ICD-10, DSM-IV) with the risk of neglecting causality. Comorbidity is a questionable term in the context of headaches with the associated phenomena of depression, anxiety, and substance abuse, for they are not a 'morbus' (Latin: disease) in the true sense of the word. Only in a minor-

ity of headaches is there a single cause i.e. morbific agent/trauma with a specific pathophysiology. Such pain states can be explained with the metaphor of a causal chain. The primary headaches must be principally differentiated from secondary headaches. Associations with depressions and interrelated anxiety disorders are important scientific and practical problems. In migraine and tension-headaches the life time prevalence of a panic disorder is significantly increased and vice versa. Both headache types can be regarded as features of dynamic systems with self-organisation.

Conclusion For the multifaceted constellations with psychic disorders the complexity approach instead of the model of nociception is suggested as a conceptual framework.

Table Simple vs. complex headaches

Simple	Complex headaches
Monocausal	Multifactorial
Stimulus–response	Interactions
Linear	Non-linear
Causal chain	Network
Deterministic	Nondeterministic

P1A32

Psychopathological features of chronic daily headache without analgesic overuse

Daniela Cologno*[1], Fernando Palma[2], Maria Matteis[1], Elio Troisi[1] & Carlo Caltagirone[1]
[1]*I.R.C.C.S. S.Lucia, Rome, Italy,* [2]*Epidemiology and Statistics Section of National Health Service's Local Unit 'ASL FG-1'-San Severo (FG), Italy*

Objective The majority of patients with chronic daily headaches (CDH) are burdened by a variety of neuropsychiatric comorbidities. The aim of this study was to evaluate alexithymia and mood and anxiety disorders in patients with two major forms of CDH: transformed migraine (TM) and chronic tension type headache (CTTH).

Methods During the 12 month-period (June 2001–May 2002), 53 CDH patients were selected among the population observed at the headache center (ASL-Foggia/1-Italy). Patients with analgesic overuse were excluded. Twenty-seven patients (19 females, 8 males) were affected by CTTH (IHS,1988) and 26 (21 females, 5 males) by TM (Silberstein's proposed diagnostic criteria – 1994). All patients underwent the Italian-language M.I.N.I. 4.4 version of the SCID interview**,** according to the 1994 DSM IV diagnostic criteria, to investigate mood and anxiety disorders, and to the Toronto Alexithymia Scale 20 to investigate the presence of alexithymia.

Results Patients with CTTH had significantly higher alexithymia scores ($P < 0.05$) when compared to TM patients. Depression and generalized anxiety were higher in CTTH patients although not significantly.

Conclusions When evaluating and managing these patients, both the higher frequency of mood and anxiety disorders, together with the higher alexithymic scores observed in CTTH patients should be taken into consideration. These psychopathological features could represent a more important role in the chronicity of pain in CTTH compared to TM.

P1A33

Depression in chronic daily headache and migraine

Ingrid Niedermayerová*[1] & Zdenek Kadanka[1]
[1]*Department of Neurology, University Hospital Brno, Czech Republic*

Background Common population suffer from depression in 10–15% and its occurrence in chronic disease may be higher.

Objective To evaluate the frequency of depression in patients with chronic daily headache (CDH) and migraine in ambulant practice and to find their relation to age and disease duration.

Methods Forty persons (30 female and 10 male) were studied. Twenty with CDH (17 transformed migraine, 3 chronic tension-type headache) and 20 migraine (minimal 1 attack of headache in one month) were investigated by Zung Self Rating Depression Scale and Beck Depression Inventary.

Results 62.5% of depressed patients (18 female and 7 male) were found in the whole group. Moderate or strong depression (60%) was more often diagnosed in CDH than minimal (15%), while in migraine minimal depression (35%) was more frequent than moderate or strong depression (15%). Depressed patients were significantly older ($P = 0.007$), have longer history of headache ($P = 0015$), and have more often CDH ($P = 0.003$) than nondepressed.

Conclusion Depression appears more frequently in patient with CDH than those with migraine. The occurrence of depression rises with duration of headache and age.

P1A34

Chronobiological features in episodic and chronic migraine

Mario Peres*[1,2], Alan Stiles[2], Charles Siow[2], Karl Dogramji[3], Stephen Silberstein[2] & Jose Cipolla-neto[4]
[1]*São Paulo Headache Center,* [2]*Jefferson Headache Center,* [3]*Jefferson's Sleep Disorders Center,* [4]*Instituto de Ciências Biomédicas, Universidade de São Paulo*

Introduction Hypothalamic dysfunction has been implicated in the pathogenesis of the migraine prodrome. Altered melatonin secretion and circadian, seasonal variations have been shown in migraine patients, but little is known about migraine chronobiological features.

Patients/methods Two hundred consecutive patients, 162 (81%) women and 38 (19%) men, 72 episodic migraine (36%), and 128 chronic migraine (64%) patients were studied.

Results Ninety-three patients (46.5%) reported headaches after changing their sleep schedule. Chronic migraineurs had more headaches after changing sleep schedule than episodic migraine patients, $p < 0.05$. Twenty-eight patients (14%) reported shift work, most (86%) had worsening headaches after shift work. Eighty six patients (43%) reported frequent traveling across time zones, and 79% had worsening of headaches when traveling. Patients significantly delayed their

sleep phase (22 : 46 h ± 01 : 20 h)vs.(22 : 22 h ± 01 : 17)$P <$ 0001. 108 patients (54%) shifted their sleep phase ranging from –2 : 30 h to +05 : 00 h. Most patients (75, 69%) delayed the sleep phase (stayed up too late), as opposed to 33 (31%) who advanced it (went to bed too soon). Patients shifting more than 02 : 00 h in both directions represented 12.5% of migraineurs.

Conclusion Our data supports the presence of chronobiological dysfunction in migraine patients. Jet lag, sleep, and work schedules, have to be assessed and addressed in migraine patients.

P1A35

Migraine Modular Theory; Part II: the aura

Leslie Kelman*[1]
[1]*Headache of Atlanta, Atlanta, USA*

Objectives To investigate in a large group of migraine patients aura characteristics, the relationship between aura and multiple variables, and the differences between migraine with and without aura; to explore the modular theory of migraine

Methods 952 migraine patients' (IHS 1.1–1.7) headache characteristics, medication responses, adverse effects, demographics, social, psychological, and personal characteristics, disability, sleep patterns, and women's issues were rated (from 0 to 3 or 0–10) at 1st visit. Aura frequency, percentage of headaches with aura, aura duration, time to headache and aura characteristics were analyzed and correlated.

Results Aura occurred in 35.5% of patients (36.8% females, 27.5% males) and differed by headache type. In aura patients, aura occurred in 19.7% of headaches. The average aura duration was 27.3min, was followed by headache in 10.4min, occurred before the headache in 67.4%, with visual aura present in 92.1%, numbness or tingling in 43.2%, speech difficulties in 30.2%, dizziness in 61.8%, blackouts in 8.4%, and aura without headache in 25.6%. Aura correlations with other variables and differences between migraine with and without aura were found.

Conclusions This study highlights some important aura correlations with the migraine attack and provides a framework for further analysis of the modular theory.

P1A36

ADHD, Subthreshold ADHD and migraine proneness

Maria Nicolodi*[1] & Federigo Sicuteri[1]
[1]*Interuniversity Headache Centre, Foundation 'Prevention and Therapy of Primary Pain and Headache', Florence, Italy*

Attention Deficit Hyperactivity Disorder (ADHD) consists in a pattern of inattention and hyperactivity/impulsivity. There are sparse data about hyperactivity and migraine. We evidenced a subtype of ADHD we named 'Sub-threshold ADHD' (SADHD). Our aim was to establish a possible comorbidity between headache proneness, ADH and SADHD.

We used HAVOD test for evaluating visceral/vascular hyperalgesia, a stigma of migraine proneness. DMS-IV criteria were used to diagnose ADHD. SADHD was diagnosed by a varied version of DSMIV where items were: -normal IQ,-normal neurological examination, -hyperactive/impulsive symptoms, -oppositional/defiant disorder, -externalizing behavior problems, -inattention, -memory deficit regarding school/peer-related activities, -low self esteem. Results indicate a comorbidity of pain proneness and SADHD in 1% of controls ($n = 268$, age range 4–11) and in 28% of 371 migraine prone children, matched for sex and age. ADHD syndrome occurred in 0.5% of the pain-prone subjects and in 0.8% of controls.

Results indicate (i) comorbidity of pain proneness and SADH (ii) no comorbidity between ADHD and pain predisposition. The comorbidity suggests a relationship regarding either genetic constellation or coheredity regarding peculiar psychological set-up and pain-proneness.

P1A37

Polysomnographic and plasma met-enkephalin studies in sleep and vigil state in primary headache patients

María de Lourdes Figuerola*[1,2], Jorge Leston[3], Carlos Medina[4], Osvaldo Bruera[2] & Marta Barontini[1]
[1]*CEDIE, CONICET, Htal De Ninos Ricardo Gutiérrez, Buenos Aires, Argentina,* [2]*Hospital de Clínicas José de San Martín, Buenos Aires, Argentina,* [3]*FLENI, Buenos Aires, Argentina,* [4]*Hospital de Pediatria P. Garraham*

Relationship between sleep disorders and headaches is complex and difficult to analyze. According to the International Classification of sleep disorders those sleep related headaches are migraine and cluster headache (CH). We studied 15 patients suffering from migraine without aura (M) ($n = 5$); chronic tension type headache (CTTH) ($n = 5$) and CH ($n = 5$). In order to evaluate sleep disorders polisomnography (PSG) studies were performed. Plasma met-enkephalin (ME) was determined (RIA; pmol/mL) before waking up, at waking up and after photostimulation. No abnormalities were found in PSG studies in any of the patients. In CH patients a significant increase of ME at the waking up moment (0.28 ± 0.07) was found when compared to the sleeping values (0.16 ± 0.03) ($P < 0.05$). M group presented a significant decrease of ME levels after photostimulation (0.22 ± 0.02) when compared to the waking up moment (0.32 ± 0.06) ($P < 0.05$). No significant differences in ME levels were found in CTTH at the different moments studied. In spite of the intragroup differences no significant differences in plasma ME levels were found among the groups in any of the three moments studied.

Plasma ME fluctuations may be related to clinical manifestations of these headaches such as the temporal pattern in CH or the trigger factors in M.

P1A38

Headache occurrence in psychiatric inpatients

Francomichele Puca*[1], Alfonso Tramontano[2], Angelo Bellfiore[2], Vittorio Cappa[2] & Maria Pia Prudenzano[1]
[1]*I Neurologic Clinic, University of Bari, Italy,* [2]*Villa Degli Ulivi, S.Leucio. Caserta. Italy*

Most of the clinical studies upon the association between mental disorders and headache had been conducted on

samples of headache patients. The aim of this study is to view this matter in a different light by studying a sample of patients hospitalised for a psychiatric disease to estimate the occurrence and the clinical features of headache. A sample of hospitalised psychiatric patients was enrolled, excluding the subject with cognitive deficiency, education shorter than 5 years, comorbidity with neurological diseases. The SCID interview was administered to obtain homogeneous diagnoses according to DSM-IV criteria and a clinical history specifically aimed at headache was collected. A statistical analysis was performed to correlate psychiatric features and headache occurrence. Preliminary results showed that about 60% of the psychiatric inpatients have a primary headache as comorbid disease. The most frequent form was the tension-type headache. When considering every single psychiatric disorder an elevated rate of headache was found in major depressive disorder, bipolar disorder, obsessive-compulsive disorder, generalized anxiety disorder, schizophrenia paranoid type The results of this study confirm the literature data concerning the existence of a comorbidity between anxiety disorder and primary headache as well as between mood disorders and primary headache. An innovative finding is the frequent association between schizophrenia and headache which is in disagreement with previous studies reporting a lower rate of pain and headache in schizophrenic patients.

P1A39

Cognitive evaluation in patients with migraine

F. Uzun*[1], M. Ozturk[1], Y. Altunkaynak[1], B. Guveli[1], F. Aysal[1] & S. Baybas[1]
[1]*Bakirkoy State Hospital for Neurologic and Psychiatric Diseases, 2nd Department of Neurology, Istanbul, Turkey*

In this study, we aimed to determine the cognitive deficits in patients with migraine during interictal, onset of attack and ictal period. The study group consisted of 25 migrainous patients and a control group consisting of age, gender, sociocultural and education level matched 25 subjects. Both groups were given Beck depression and Maudsley obsession scales before neuropsychometric evaluation. The neuropsychometric tests were given to the patient group twice, interictal and ictal periods, and once to the control group. The neuropsychometric battery included tests on memory, attention, language, frontal and visiospatial functions. The results of all modalities were lower in the patient group interictally, but the difference of two groups was not statistically significant ($P > 0.05$). Comparing the ictal results of the patient group with the control group revealed the values were significantly lower in the patient group ($P < 0.05$). Immediate memory, visual and verbal attention components were noticeably lower in the patient group.

When pain characteristics were investigated, only pain intensity and cognitive functions showed negative correlation in only attention and immediate memory ($r > 0.25$).

Conclusively, the patients with migraine have cognitive deficits, especially in attention and immediate memory components, during attack.

P1A40

Migraine-related stroke

Jera Kruja*[1], M. Rakacolli[1] & Edlira Harizi[2]
[1]*UHC 'Mother Theresa', Tirana, Albania,* [2]*Hospital de Durres, Durres, Albania*

The relationships between migraine and stroke are complex. We can distinguish some alternatives as coexisting stroke and migraine, stroke with clinical features of migraine and migraine induced stroke. We have described 9 our patients in the last category, hospitalized or visited at the outpatient center in the University Service of Neurology, UHC Mother Theresa of Tirana, during the last 4 years. There are 3 males and 6 females. The mean age at the stroke onset is 41.4 years old (range 28–55) and the mean duration of migraine history 18.3 years (range 1–35). The localization of infarct is supratentorial in 8 cases and infratentorial in one case. Other causes of stroke are excluded.

P1A41

The medically unrecognized migraine: a study on the effects of a sensitization campaign about migraine on both GPs and population

Vittorio Di Piero*[1], Gianluca Bruti[1], Claudio Mostardini[1], Rosanna Cerbo[1], Gian Luigi Lenzi[1], Giuseppe Conserva[2] & Tommaso Anzidei[2]
[1]*Departement of Neurological Sciences, University of Rome La Sapienza,* [2]*'Cooperativa dei Medici per il territorio' of the Casilino district*

A streaking feature of migraine is represented by the difference between the estimate of migraine prevalence and the actual number of migraineurs consulting their GPs.

Aim of the study is to estimate the impact of migraine in a large cohort of patients, living in a district of Rome, after a sensitization campaign in comparison with those resulting from the pre-existent data-bank of their GPs.

The study involves 14 GPs and a population of about 20 000 people which have been contacted by mail and posters located in the GP clinics.

All headache suffers have been invited to consult their GPs to be evaluated by: (a) a Three-item Self-administered Questionnaire for migraine (Lipton et al. 2003); (b) his/her GP, supported also by a computerized Headache Symptoms Questionnaire (based on IHS criteria for primary headaches and the common warning signs and symptoms for secondary headaches), and (c) a headache specialist, blind to the results of the GPs. Final results of the study will be available on next June.

Medically unrecognized migraine has a major social and economic impact and is frequently undertreated by self-administered OTC drugs. To sensitize population and GP on this disease could significantly improve the quality of life of migraineurs.

P1A42

Thrombophilic assessment in CADASIL: first evidences at basal screening

Licia Finamore*[2], Pasquale Marchione[1], Patrizia Giacomini[1], Ada Francia[2], Claudio Vento[1], Renzo Guglielmi[2], Tommaso Romeo[1], Donatella Corigliano[1], Domenico Samà[1] & Giuseppe Nappi[3,1]
[1]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy,* [2]*Department of Neurological Sciences, University of Rome 'La sapienza', Rome, Italy,* [3]*University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia, Italy*

Introduction Pathophysiology of subcortical lacunar infarcts and migraine in CADASIL is still unclear even if thrombotic phenomena on narrowed vessels have been suggested. We have investigated the presence of coagulation risk factors in CADASIL by screening test for stroke.
Methods Standardized routinary and specialized coagulation tests have been performed, studying prothrombin and partial thromboplastin time, protein C and S, antithrombin III, activated protein C resistance, lupus anticoagulant and anticardiolipin autoantibodies in 8 patients with CADASIL (3 men and 5 women, mean age 30.5 ± 2.5) and sex and age-matched controls. One patient presented stroke and migraine while others referred only migraine with aura.
Results Prothrombin and partial thromboplastin time was normal in both groups. Protein C, S, antithrombin III and anticardiolipin autoantibodies concentrations showed no differences between patients and controls. In all subjects, APC resistance and LAC factor were no present.
Discussion In basal conditions, we found no evidences of a thrombophilic status in CADASIL. The lack of association with this risk factor for stroke in young people could focus the attention on primary vascular mechanisms that lead to ischaemia. These results could contribute to elucidate pathophysiology of stroke in migraine. Since the small sample of this study, further observations are necessary.

Epidemiology

P1B1

Disability and health-related quality of life in strict migraine vs. probable migraine (migrainous headache) and control subjects within a health plan

Richard Lipton*[1], Nikil Patel[2], Ken Kolodner[2], Carol Leotta[2], Jennifer Lafata[3] & Marcelo Bigal[1,4]
[1]*Albert Einstein College of Medicine, Bronx, NY, USA,* [2]*Advance PCS, USA,* [3]*Henry Ford Health System, USA,* [4]*The New England Center for Headache, Stamford, CT, USA*

Objective To compare the health related quality of life (HRQoL) and disability in a case-control study of strict migraine and probable migraine (migrainous headache) sufferers vs. controls.
Design/methods Eligible subjects were individuals aged 18–55 enrolled in a mixed-model HMO. We used a validated telephone interview to identify strict migraine (IHS 1.1 and 1.2), probable migraine (PM) sufferers (migrainous headache, 1988 IHS 1.7), and controls (did not meet criteria for migraine or PM). Disability was assessed with MIDAS; HRQoL with SF-12.
Results From the 8579 survey respondents, we identified 1265 (14.7%) migraine sufferers; 1252 (14.6%) PM sufferers, and 960 randomly selected controls. HRQoL was significantly better in controls compared with the PM and strict migraine groups (Mental Health Scores: 53.1, 50.2, 48.2, $p < 0.0001$; Physical Health Scores: 51.2, 48.8, 46.8, $p < 0.0001$). Similarly, the disability was significantly higher in the migraine and PM groups compared to the control group (MIDAS III and IV: 31% vs.13% vs. 3%, $p < 0.0001$).
Conclusions Like strict migraine, PM produces decrements in HRQoL and increments in disability relative to controls. Probable migraine is a form of migraine and a worthy target for treatment.

P1B2

Prevalence of primary headaches in Italian elderly: preliminary data from the Zabút Aging Project

Rosolino Camarda*[1]
[1]*Department of Neurology and Rehabilitation, Institute of Neuropsychiatry, University of Palermo, Palermo, Italy*

Background Although primary headaches accounted for up to 66% of headaches in the elderly, population-based studies on this topic are limited.
Objectives To assess the 1-year prevalence of recurrent migraine headaches (MH), tension-type headaches (TTH), and other headaches (OH) in a rural elderly population.
Methods A door-to-door two-phase survey was conducted on all elderly (= 65 years) residents of a little village in southern Italy. Participants underwent a two-phase screening including a validated semistructured questionnaire for headaches based on IHS criteria, and a neurological evaluation. Recurrent headache was defined as two or more attacks of headache within the past 12 months.
Results Two hundred and twenty-five (21.8%) out of 1031 subjects evaluated suffered from headache. One-year prevalence rates for recurrent headaches were, respectively, 4.6% for MH, 16% for TTH, and 1.3% for other headaches. For MH (χ^2 test, p .002) and TTH (χ^2 test, $p < 0.03$), but not for OH, prevalence rates were higher for female than for men. Only for MH (χ^2 for trend, $p < 0.0001$), prevalence rates decrease with increasing age.
Conclusions In our population, about one-fifth of elderly subjects suffered from recurrent primary headaches. Prevalence rates were higher in women, and tended to decline with increasing age.

P1B3

Long-term prognosis of migraine in adolescents: a 10-year follow-up

Roberto Monastero*[1], Cecilia Camarda[1], Carmela Pipia[1], Lawrence Camarda[1], Valentina Baiamonte[1], Vincenzo Raieli[1] & Rosolino Camarda[1]
[1]*Adult Headache Center, Department of Neurology and Rehabilitation, Institute of Neuropsychiatry, University of Palermo, Palermo, Italy*

Objectives To evaluate the long-term prognosis and clinical correlates of migraine headaches in an adolescent population over a fixed 10-year period using IHS criteria.
Subjects and methods Fifty-five out of 80 subjects with migraine headaches (mean age 22.2 ± 1.1) selected in a previous epidemiological survey participated to the study. Of these, 28 (50.9%) had migraine without aura (MWOA), 14 (25.5%) had migraineous disorder (MD), and 13 (23.6%) had nonclassifiable headache (HnC). The criteria of IHS were used both at baseline and at 10-year follow-up.
Results Over the 10-year period, all migraine headaches showed an high tendency to remit (MWOA = 35.7%; MD = 42.9%; HnC = 46.1%). Only 25% of subjects with MWOA persist in the same one-digit IHS diagnosis after 10-year, while MD and HnC changes their characteristics over time. Migraine headaches changed to episodic tension-type headache in 16.4% of cases, while remitted and restarted in 12.7 of subjects. Adjustment for potential confounders, family history for headache was significantly related to the persistence of migraine headaches (OR 6.4; 95% CI 1.4–28.6, $P = 0.02$).
Conclusions Migraine headaches in adolescence had basically a favourable long-term prognosis, remitting in more than 40% of cases. In our population, the tendency to persist probably reflects a genetic predisposition.

P1B4

The one-year period prevalence of strict migraine, probable migraine (migrainous headache), and the full spectrum of migraine within a health-plan population

Marcelo Bigal*[1,2], Nikil Patel[3], Ken Kolodner[3], Jennifer Lafata[4], Carol Leotta[3] & Richard Lipton[1]
[1]*Albert Einstein College of Medicine, Bronx, NY, USA,* [2]*The New England Center for Headache, Stamford, CT, USA,* [3]*Advance PCS, USA,* [4]*Henry Ford Health System, USA*

Objective To use a validated telephone interview to assess the prevalence of strict migraine (IHS 1.1 and 1.2), probable migraine (migrainous headache, 1988 IHS 1.7) and the full spectrum of migraine (IHS 1.1, 1.2, 1.7) within a health plan.
Design/methods Eligible study subjects were individuals aged 18–55 enrolled in a mixed-model HMO receiving care from a large multispecialty group. We used a validated telephone interview to identify migraine and probable migraine sufferers.
Results Of the 8579 survey respondents, two-thirds were female, almost 60% were 40 years of age or older, and two-thirds were Caucasian. The one-year prevalence of strict migraine was 14.7% (19.2% in women and 6.5% in men, adjusted gender PR = 2.66). The one-year prevalence of probable migraine was 14.5% (19.6% in women, 13.1% in men; PR = 1.39). The full spectrum of migraine had a one-year prevalence of 29.2% (38.8% in women and 19.6% in men; crude PR = 1.9).
Conclusions Strict migraine (IHS 1.1 and 1.2) and probable migraine (IHS 1.7) have similar one-year period prevalence within a health-plan. Probable migraine has a similar age profile but a lower female preponderance than strict migraine. Men are over-represented in the probable migraine group reflecting gender differences in symptom profiles or symptom reporting.

P1B5

Is there a change in prevalence of migraine and tension-type headache?

Ann Lyngberg*[1], Rigmor Jensen[2], Birthe Krogh Rasmussen[3] & Torben Jørgensen[1]
[1]*Research Centre for Prevention and Health (RCPH), Copenhagen University Hospital, Glostrup, Denmark,* [2]*Department of Neurology, Copenhagen University Hospital, Glostrup, Denmark,* [3]*Department of Neurology, Hilleroed Hospital, Hilleroed, Denmark*

Few studies have re-evaluated the prevalence of primary headache disorders by replicating a prior study. The present study is a cross-sectional study of primary headaches in a general population and replicates the methods of a prior study from 1989. The aim of the study is to compare the prevalence of primary headaches in 2001 with the prevalence from 1989.

A new cohort of 300 randomly chosen subjects aged 25–36 years were invited to participate in a structured interview and examination or a telephone-interview, and compared with prevalence data from a similar cohort of 221 subjects examined in 1989. The IHS-criteria were used.

The participation rate in 2001 was 69.7% ($N = 207$) and in 1989 72.5%.

The one-year prevalence of migraine was 15.5% in 2001 and 11.3% in 1989 ($P = 0.21$).

The male:female ratio changed from 1 : 2 to 1 : 4 ($P = 0.3$).

The one-year prevalence of tension-type headache was 86.5% in 2001 and 78.8% in 1989 ($P = 0.04$).

The male : female ratio changed from 7 : 10 to 9 : 10.

When re-evaluating the prevalence of primary headaches after 12 years, we found a significant increase in the one-year prevalence of tension-type headache, but not of migraine.

Unexpectedly the male:female ratio of migraine increased, but not significantly.

P1B6

Analgesic overuse among subjects with headache, neck and low-back pain. The Head-HUNT Study, Norway

John-Anker Zwart*[1], Grete Dyb[2], Knut Hagen[1], Lars J. Stovner[1], Sven Svebak[2] & Jostein Holmen[3]
[1]*Department of Clinical Neuroscience, Section of Neurology, Faculty of Medicine, The Norwegian University of Science and Technology, Trondheim, Norway,* [2]*Department of Psychiatry and behavioural medicine, Faculty of Medicine, The Norwegian University of Science and Technology, Trondheim, Norway,* [3]*HUNT Research Centre, Faculty of Medicine, The Norwegian University of Science and Technology, Trondheim, Norway*

Few population-based studies have evaluated the association between chronic headache and analgesic overuse. The main objective of the present large cross-sectional population-based study was to examine this relation with regards to chronic pain (i.e. headache, neck or low-back pain). In the Nord-Trøndelag Health Study 1995–97 (HUNT 2), a total of 51 383 subjects responded to headache questions (Head-HUNT), out of which 51 056 completed questions related to musculoskeletal symptoms and 49 064 questions regarding the use of analgesics. The prevalence of analgesic use increased with age, especially among headache sufferers and among women. The prevalence of medication overuse headache (MOH, i.e. headache = 15 days/month and analgesic overuse) was 1% (1.3 for women and 0.7% for men). Chronic headache (headache = 15 days/month) was more than seven times more likely among those with analgesic overuse than those without. For the respective headache subgroups analysed separately, the association with analgesic overuse was strongest for chronic migraine, intermediate for chronic nonmigrainous headache and lowest for chronic neck and chronic low-back pain. The association increased for all groups with increasing duration of reported use of analgesics, and was most evident among those with headache, especially those with migraine.

P1B7

One-year prevalence of chronic daily headache in a population of German and Turkish adults

Ilker Kavuk*[1], Zaza Katsarava[1], Andreas Stang[2], Volker Limmroth[1], Hans-Christoph Diener[1], G. Gueneyli[1], M. Araz[1] & M. W. Agelink[3]
[1]*Department of Neurology, University of Essen, Germany,* [2]*Institute of Medical Informatics, Biometry and Epidemiology, University of Essen, Germany,* [3]*Department of Biological Psychiatry and Neuroscience, The Evengelical Clinics, Ruhr-University of Bochum, Germany*

In this study we wanted to investigate the prevalence and the risk factors of chronic daily headache (CDH) in a population with Turkish immigrants and German adults. Employees of a big textile company in a little township in Germany were asked to participate at the study. A total of 523 people were interviewed. Participants with headache were clinical examined by a neurologist. Diagnostic criteria for each headache type were based on those of the International Headache Society (IHS). CDH was diagnosed if the subjects had headache = 15 days/month with a duration of = 4 h each day. Also CDH was further classified into chronic tension-type headache (CTTH) and CDH with migrainous features (CDH-MF). 35 participants (7.4%) fulfilled the criteria of CDH. The prevalence of CDH was higher in Turkish immigrants (10.7% vs. 3.6% in the German group). The prevalence of CDH with medication overuse was significant higher in the group of Turkish immigrants (7.9% vs. 0.9%). Only 1.7% of the Turkish people had consulted a neurologist or a physician for their headaches in the previous year (German people: 24.2%). A pharmacological treatment in headache prophylaxis was higher in German migraine sufferers (14.7% of migraine sufferers). Nobody of Turkish headache patients had got a prophylaxis. A further risk factor for developing a CDH was that Turkish headache sufferers had often consulted a hoca (an Islamic religious membership) for their headaches in the previous year. We could show three main predictors (low consulting rate to a neurologist or a physician; no preventive therapy and the higher nonmedical treatment rate with consulting a hoca as a nonspecialist for headache) for the reason of a higher prevalence of CDH in Turkish immigrants.

P1B8

Epidemiology of chronic daily headache with analgesic overuse

Rafael Colás[1], Pedro Muñoz[1], Rosario Temprano[1], Cándido Gómez[1] & Julio Pascual*[1]
[1]*Health Center of Santoña, Primary Care Management Unit and Service of Neurology, University Hospital Marqués de Valdecilla (UC), Cantabria, Spain*

Objectives To analyse the prevalence of chronic daily headache with analgesic overuse (CDHAO) in the general population.
Patients and methods The study population was 9984 inhabitants aged 14 or more. We interviewed 4855 subjects. Those referring to analgesic intake >10 days/month and analgesic use were given a headache diary for one month. Then, subjects were classified or not into CDHAO subtypes.
Results Headache >10 days with analgesic consumption was admitted by 332 subjects. Seven were diagnosed as secondary headache. Seventy-four (prevalence 1.41%, 95% CI 1.1–1.8) fulfilled CDHAO criteria. Prevalence in women (2.6%) was higher than in men (0.19%). Mean age was 56 years (range 19–82). Mean duration of primary headache was 35 years and the mean duration of near-daily drug intake 11 years. Transformed migraine was diagnosed in 49 (prevalence 0.9%), chronic tension-type headache in 20 (0.4%) and new daily persistent headache in 5 (0.1%). 35% overused simple analgesics, 22% ergotics, 12.5% opioids and 2.7% triptans, while 27.8% overused combinations.
Conclusions CDHAO is a common disorder with a prevalence of 1.5%. This prevalence reaches its maximum during the fifties, when 5% of women fulfil its criteria. Three-quarters meet transformed migraine criteria and two-thirds consume simple analgesics or/and ergotics.

P1B9

Sensitivity and predictive value of trigger factors and premonitory symptoms in migraine

G. G. Schoonman*[1], D. J. Evers[1] & J. G. van Dijk[1], M. D. Ferrari[1]
[1]*Department of Neurology, Leiden University Medical Center, Leiden, the Netherlands*

Objectives To study the sensitivity and predictive value of trigger factors and premonitory symptoms in migraine.
Methods Twelve trigger factors (TF) and 16 premonitory symptoms (PS) were studied in 460 migraine patients (outpatient clinic) by means of a questionnaire. The sensitivity (how often is a migraine attack preceded by the TF or PS) and predictive value (how often is a TF or PS followed by an attack) were categorized in 4 groups (never, less than 1/3, 1/3–2/3, and more than 2/3 events). We defined sensitivity and predictive value as positive if present in more than 2/3 of the events.
Results In total 78% (364/460 patients; 290 females) responded; mean age 48 years (±11.2). The three main TF (based on positive sensitivity) were menstruation (31% of patients), sunlight (20%) and stress (17%). Tiredness (46%) was the most frequently reported PS followed by phonophobia (36%) and a stiff neck (35%). In this subgroup of main TF and PS, between 68% and 90% of patients reported a positive predictive value.
Conclusion Sensitivity in the group main TF and PS is positive at maximum in 46%, but in this subgroup the predictive value is positive in 68% or more.

P1B10

Incidence of migraine in a Danish population-based follow-up study

Ann Lyngberg*[1], Rigmor Jensen[2], Birthe Krogh Rasmussen[3] & Torben Jørgensen[1]
[1]*Research Centre for Prevention and Health (RCPH), Copenhagen University Hospital, Glostrup, Denmark1Research Centre For Prevention and Health (RCPH), Copenhagen University Hospital, Glostrup, Denmark,* [2]*Department of Neurology, Copenhagen University Hospital, Glostrup, Denmark2Department of Neurology, Copenhagen University Hospital, Glostrup, Denmark,* [3]*Department of Neurology, Hilleroed Hospital, Hilleroed, Denmark3Department of Neurology, Hilleroed Hospital, Hilleroed, Denmark*

Despite the high prevalence of primary headache disorders, only few incidence studies have been published. The present study is a follow-up of a cross-sectional epidemiological study from 1989. We here report the incidence of migraine in a general population.

All eligible participants ($N = 673$) in the 1989 study (25–64 years) were re-invited to participate in a structured interview and examination, or a telephone interview using the IHS-criteria. All interviews were done by the same resident (AL).

The participation rate was 81.6% (549/673).

Of the 453, who did not have migraine in 1989, 42 had developed migraine, leaving an annual incidence of 0.8%. The annual incidence in females was 1.5% and in males 0.3%.

Male: female ratio 1 : 5.7. In both genders, the highest incidence was found in the youngest age-group (age 25–36 years in 1989 and 37–44 years in 2001).

In a longitudinal epidemiological study of migraine incidence we found an overall incidence of migraine of 0.8%, with the highest incidence (2.0%) in young females.

Table Migraine incidence according to age and gender

Age groups in 2001	Total	Males	Females
37–44 years	1.3	0.7	2.0
45–54 years	0.9	0.4	1.6
55–64 years	0.6	0.0	1.4
65–76 years	0.4	0.1	0.7
All ages	0.8	0.3	1.5

P1B11

Analgesic use as a predictor of chronic pain and medication overuse headache. A prospective study of 32 067 adults in Norway. The Head-HUNT Study

John-Anker Zwart*[1], Grete Dyb[1], Knut Hagen[1], Sven Svebak[1] & Jostein Holmen[2]
[1]*Department of Neuromedicine, Faculty of Medicine, The Norwegian University of Science and Technology, Trondheim, Norway,* [2]*HUNT Research Centre, Faculty of Medicine, The Norwegian University of Science and Technology, Trondheim, Norway*

There are few large population-based studies, assessing the association between analgesic overuse and the subsequent risk of chronic pain and headache. The main objectives of the present study was to examine the relation between analgesic use at baseline and the subsequent risk of chronic pain (= 15 days/month) and the risk of chronic pain associated with analgesic overuse. In the county of Nord-Trøndelag, Norway, two population-based epidemiological studies have been performed (The HUNT studies). In total 32, 067 adults reported the use of analgesics in 1984–6 and at follow-up 11 years later (1995–7). The risk ratios (RR) of chronic pain and RR of chronic pain associated with analgesic overuse in the different diagnostic groups (i.e. migraine, nonmigrainous headache, neck and low-back pain) were estimated in relation to analgesic consumption at baseline. Individuals who reported use of analgesics daily or weekly at baseline showed significant increased risk for having chronic pain and chronic pain associated with analgesic overuse at follow up. The risk was most evident for chronic migraine, intermediate for chronic nonmigrainous headaches and lowest for chronic neck or chronic low-back pain. The results indicate that overuse of analgesics strongly predicts chronic pain and chronic pain associated with analgesic overuse 11 years later, especially among those with chronic migraine.

P1B12

Headache prevalence in a general population based study

Samuel Díaz-Insa[1], Sandra García[2], Teresa Turró[2], Mónica Roig[2], Cristina Soriano[1], Esther Romero*[2] & José Manuel Soler[2]
[1]*Neurology Section, Hospital Francesc de Borja de Gandía,* [2]*CS Tavernes, Tavernes de la Valldigna, Valencia, Spain*

Objectives To describe and analyse the headache's prevalence and characteristics in a general population.

Methods Personal interview and structured data pick-up about headache in ≅ 10% of all 16 000 Tavernes de la Valldigna inhabitants. We describe age and gender of nonsufferers and sufferers and, in the last, also IHS type of headache, exhaustive headache characteristics in localisation, quality, intensity and accompanying symptoms, drug intake, time suffering headache and all data related.
Results We interview 1539 persons, 426 of them (27.68%) with headache; mean age 50.07 years, being 87.79% women and 12.21% men. Episodic Tension-Type Headache (ETTH) is the most frequent (37.09%), following episodic migraine (30.75%), Chronic Daily Headache (CDH) with 28.64%, 2.58% of mixed headache, 0.47% Cluster Headache (CH) and 0.47% unclassifiable. These results in general population would mean 10.24% ETTH, 8.51% episodic migraine and 7.93% CDH with gender differences.
Conclusions The present study allows to describe headache in general population, which is different from the usual pattern seen in neurologists' series. ETTH is the most prevalent type followed by migraine, but it's a bit surprising the great amount of CDH sufferers, half of them with Chronic Tension-Type Headache (CTTH).

P1B13

ID Migraine TM: a three-item self-administered questionnaire to identify migraine sufferers in primary care

Richard Lipton*[1,2], Jayasena Hettiarachchi[3], David Dodick[4], Richard Sadovsky[5], Kenneth Kolodner[2], Jean Endicott[6] & Wilma Harrison[3]
[1]*Albert Einstein College of Medicine,* [2]*IMR, a Division of AdvancePCS,* [3]*Pfizer Inc,* [4]*Mayo Clinic,* [5]*SUNY Downstate Medical Center,* [6]*New York State Psychiatric Institute*

Objective To validate a simple, brief, self-administered screening questionnaire to help identify migraine patients in primary-care settings.
Methods Patients seeing primary-care physicians for any reason who had a history of disabling headaches or wanted to talk to a physician about their headaches completed a written screening questionnaire. The initial screener contained 9 items, 8 paralleling IHS criteria for migraine and 1 assessing disability. Headache specialists, blind to screener results, evaluated and diagnosed patients based on IHS criteria. Each screener-item alone and all items combined were assessed using specialists' diagnoses as the gold standard. A 3-item screener was designed using questions with greatest discriminative validity for migraine.
Results Of the 550 patients who completed a screening evaluation in primary care, 451 (82%) completed a clinical evaluation by a headache specialist. Of 9 questions, 3 items (disability, nausea, photophobia) provided optimal performance using the specialist's diagnosis as the gold standard. When responses to 2/3 or 3/3 items were positive, the 3-item screener had a sensitivity of 0.81, specificity of 0.75 and positive predictive value of 93%. Test-retest reliability was good ($\kappa = 0.68$). Sensitivity and specificity of the 3-item screener were similar, regardless of sex, age, comorbid headaches or previous headache diagnosis.
Conclusion The key features for migraine screening were disability, nausea and photophobia. The simplicity, ease of use and operating characteristics suggest that ID Migraine™ could significantly improve migraine recognition in primary care.

P1B14

Prevalence and burden of migraine: a survey in a cohort of university employees

Michel Vandenheede*[1], A. Fumal[1] & J. Schoenen[1]
[1]*Headache Research Unit, Department of Neurology, University of Liège, CHR Citadelle*

Objective To assess 1-year prevalence, current management and economic burden of headache in a cohort of employees.
Methods A structured questionnaire was sent to 1500 nonacademic employees of the University of Liege.
Results The questionnaire was returned by 1467 subjects. 85.5% (1255) had no headache in the preceding year. Among 212 headache sufferers, 77% had migraine, 113 fulfilling all, 50 all but one IHS criteria; 19% had migraine with aura. Twelve subjects (6%) had chronic daily headache. Acute antimigraine treatment was taken by 98% of migraineurs (triptans 9%), more than 2x/week by 29%. Although 35% of migraineurs reported more than 2 attacks/month, 3% only took a prophylactic treatment. During attacks 12% of migraineurs stopped working and 48% were less productive. The financial cost of work loss due to migraine was evaluated at 300.000 ¤/year. After the survey, 15% of headache sufferers attended an information session organized for them and 5% only filled in prospectively a headache diary for 3 months.
Conclusion This study highlights that at least 1/3 of migraineurs are inadequately treated at a substantial cost to the community. It also suggests that sufferers themselves are part of the barriers to optimal migraine management.

P1B15

A door-to-door survey of migraine in Japan: the Daisen Study

Takao Takeshima*[1], Kumiko Ishizaki[1], Yoko Fukuhara[1], Tamami Ijiri[1], Masayoshi Kusumi[1], Yosuke Wakutani[1], Hisanori Kowa[1] & Kenji Nakashima[1]
[1]*Department of Neurology, Tottori University Faculty of Medicine*

To determine prevalence and characteristics of Japanese migraineurs, and to investigate the pattern of medical use, and in addition, to investigate food preference and possible association with risk of migraine. Structured questionnaires were given all 5758 adult residents (male; female = 2,681: 3077) in Daisen, which is a rural town located in western Japan. Second questionnaires, specified to headache, were given to 1628 headache sufferers. An additional telephone survey was also carried out. Data were analysed by SPSS statistical packages.

The one-year prevalence of migraine was 2.3% (migraine with aura; MA, 0.4% and without aura; MO, 0.9%) in male and 9.1% (1.0% and 8.1%) in female. Overall prevalence of

migraine was 6.0% (95% CI: 5.4–6.6%) in Daisen. Only 7.3% of MA and 5.3% MO sufferers have consulted physicians, and 61.0% of MA and 71.8% MO never visited a medical doctor for their headache.

Migraineurs consume significantly more fatty/oily foods and coffee/tea than nonheadache subjects of the same community. Migraineurs consume significantly fewer fish than nonheadache residents. We concluded that only a few Japanese migraineurs receive benefits of medical services and recent advance of headache medicine. Public education concerning headaches is one of the most urgent issues in Japan.

P1B16

A population-based study of chronic headache in Florianopolis, Brazil

Luiz Paulo Queiroz*[1], Nelson Blank[1] & Liselotte Barea[1]
[1]*University Hospital, Universidade Federal de Santa Catarina, Florianopolis, Brazil*

Objectives To estimate the prevalence of chronic headache (CH) and to compare some epidemiological characteristics of chronic and episodic headache, in a representative sample of the population of Florianopolis, Brazil.
Methods This is a cross-sectional, door-to-door, population-based study. 625 subjects, aged 15–64 years, responded to a structured questionnaire. The analysis was done with 502 subjects who had headache within the last year and reported the frequency of their headache. Comparison of proportions was done through the qui-square test.
Results The 1-year prevalence of CH was 6.4% (males: 2.1%; females: 10.1%). Forty subjects had CH 32 (80%) had 'chronic migraine' and 8 (20%) had chronic tension-type headache. Only 10% were on prophylactic treatment. Comparing chronic and episodic headache groups, subjects with chronic pain significantly ($P < 0.001$) sought more assistance, had more medical consultation ever and last year and had more diagnostic investigation than subjects with episodic pain. The use of medication was similar in both groups. The MIDAS scores were significantly ($P < 0.001$) higher in subjects with chronic headache.
Conclusions The prevalence of CH in Florianopolis was high. The utilization of the health care system and the disability was significantly higher in subjects with CH than with episodic headache.

P1B17

Cluster headache prevalence in the Italian general population

Paola Torelli*[1,2], Ettore Beghi[3] & Gian Camillo Manzoni[1,2]
[1]*Headache Center, Unit of Neurology, Department of Neuroscience, University of Parma, Parma, Italy,* [2]*University Centre For Adaptive Disorders and Headache (UCADH),* [3]*'Mario Negri' Institute, Milano, and Neurological Clinic, University of Milano-Bicocca, Italy*

The conflicting results of the few studies published on cluster headache (CH) epidemiology are probably due to method inconsistencies. We calculated CH lifetime prevalence in a sample representative of the Italian general population aged over 14 years. 'Possible CH' cases according to the International Headache Society classification (1988) diagnostic criteria were investigated in 10 071 patients (5311 female and 4760 male, mean age 50.4 ± 19.7 years) of seven GPs in the city of Parma using a previously validated, specially designed self-questionnaire. A total of 7522 people (74.7%, 3971 female and 3551 male, mean age 50.8 ± 19.0 years) responded to the questionnaire in their GP's office ($n = 3338$, 1885 female and 1453 male) or at home by mail ($n = 1914$, 1030 female and 884 male) or by Tel. ($n = 2270$, 1056 female and 1214 male). Of the 111 identified 'suspected cases' (77 female and 34 male), 53 have been seen to date by a neurologist who confirmed CH in 12 (seven female and five male), including seven already followed at our center for CH. Our preliminary results point to a higher CH lifetime prevalence than was previously reported.

Supported by GSK – Italy.

P1B18

Migraine patterns among hospital nurses in Spain

Valentín Mateos*[1] & Lourdes Jiménez-Blanco[1]
[1]*Neurological Department. Central Hospital of Asturias, Oviedo, Spain*

Objectives To assess the clinical-epidemiological characteristics of migraine in hospital nurses and the burden of migraine on their work absenteeism and productivity.
Background Little is known about the prevalence, treatment patterns and burden of migraine among nurses in Spain.
Methods A three-part self-administered survey was mailed to all of the nurses in the Hospital ($N = 1083$). Respondents were invited to participate in an interview with the neurologist.
Results There were 286 (26.4%) nurses who completed the survey and 173 of them (60.4%) answered YES to some questions of the screening test. The most frequently used drugs for acute treatment were NSAIDs (42.1%). Triptans were reported as first option in only 5%. Preventive treatment was reported by 13.2% and 61% had never consulted a doctor. Migraine affected presence and performance at work, 27.2% reported being absent from work due to migraine during the last year.
Conclusions Migraine sufferers were more motivated to complete the survey. Undertreatment of migraine among hospital nurses in Spain is not uncommon. The burden of migraine on work absenteeism and productivity in nurses is high. Early intervention and stratified care with more expanded use of triptans were the neurologist's main recommendations.

P1B19

Hereditary pattern of Belgrade University female students with menstrual and other subtypes of migraine

Eleonora Dzoljic*[2], Hristina Vlajinac[1], Sandra Sipetic[1], Jelena Marinkovic[3] & Vladimir Kostic[2]
[1]*Institute of Epidemiology, School of Medicine, Belgrade University, Belgrade,* [2]*Institute of Neurology, School of Medicine, Belgrade University, Belgrade,* [3]*Institute of Social Medicine, Statistics and Health Research, School of Medicine, Belgrade University, Belgrade*

Objective Was to estimate hereditary pattern of our female students with menstrual and other subtypes of migraine.
Methods The prevalence study conducted in Belgrade comprised randomly selected female students (1943 students) of the School of Medicine and the School of Pharmacy of University of Belgrade, Serbia and Montenegro. Diagnoses were assigned according to the criteria of the International Headache Society and MacGregor's stricter definition of 'menstrual migraine'.
Results In this paper hereditary patterns of female students with menstrual migraine (30 subjects) and other subtypes of migraine (215 subjects) were compared. There were no significant differences in the proportion of students with various subtypes of migraine who reported one relative with migraine as well as in the proportion of those who had first-degree relatives with migraine. However, ≥2 relatives with migraine was most frequently reported in students with menstrual migraine, the difference being significant in comparison with students suffering from menstrually associated migraine ($P < 0.05$), menstrually changed migraine ($P < 0.05$) and menstrually unrelated migraine ($P < 0.01$). Second-degree relatives with migraine also were the most frequently reported by students with menstrual migraine.
Conclusion. Is that students with menstrual migraine have stronger evidence for heredity of migraine comparing to students with other subtypes of migraine.

P1B20

Impact of headache among hospital workers measured by means of MIDAS questionnaire: preliminary results

Piero Meineri*[1], Fiorella Mondino[1], Chiara Baima[1] & Enzo Grasso[1]
[1]*Department of Neurology, A.S.O. 'S. Croce e Carle', Cuneo, Italy*

Objective To study epidemiology and impact of migraine among hospital employees (Cuneo Hospital, Italy) by means of MIDAS questionnaire.
Methods Every hospital employee (1791–585 males, 1206 females) was asked whether he had suffered from headache during the previous three months. Then, all the headache sufferers were carefully interwiewed. People meeting IHS diagnostic criteria for migraine completed MIDAS.
Results Among 1639 (91.5%) responders, 1207 (73.6%) had suffered from headache during the last three months. Migraine was diagnosed in 290 (17.7%) (M 61, F 229, M/F = 1/4.9, mean age 39.2, range 21–64). In 46.3% frequency of attack was low (1–3/month), in 18.6% moderate (4–6/month), and in 35.1% high (> 6/month). MIDAS showed a grade IV disability in 25.2%, III in 29.1%, II in 17.4% and I in 28.3%. Nurses and caregivers were the most affected (22.0% and 27.7%). No significant differences in prevalence were observed between shift and nonshift workers (18.8% vs. 17%), however, shift workers showed a higher disability (MIDAS grade III + IV) than nonshift workers (62.3% vs. 37.7%).
Conclusions Our preliminary data indicate that migraine prevalence is higher among people working closed to patients. Working in shifts has no influence on migraine prevalence, but is a worsening factor.

P1B21

MEDEMIG (I): prevalence, clinical characteristics and effect of migraine in French medical population

Michel Lanteri-Minet*[4], Hélène Massiou[1], Pierre Clavelou[2] & Christine Chaffaut[3]
[1]*Neurology, Lariboisière Hospital, Paris, France,* [2]*Neurology, Clermont-Ferrand, France,* [3]*AstraZeneca France, Rueil-Malmaison, France,* [4]*Pain Department Hôpital Pasteur CHU de Nice, France*

Objective Aim was to determine prevalence and clinical features of migraine among French general practitioners (GPs) with impact on migraine management.
Methods A telephone survey (algorithm based on IHS criteria, 76 item questionnaire, CATI system) was carried out from May to June 2002: 1077 GPs representative of the French medical population were included. Prevalence of migraine (IHS 1.1) and migrainous disorder (IHS 1.7) were estimated. GPs thinking themselves to have migraine (GPs/M) were compared to those who did not know that they had (GPs/nM). GPs with migraine (1.1 and 1.7) were compared to GPs without migraine in terms of migraine management. Student's test was used for statistical analysis.
Results 108 GPs had migraine (10,96%) and 82 GPs had migrainous disorder (7,61%). GPs/M proportion was, respectively, of 86% and 59%. Compared to GPs/nM, GPs/M described significantly older and more severe headaches. No significant difference was found between GPs with migraine and GPs without migraine in terms of migraine management.
Conclusions Migraine prevalence in French medical population is near of general migraine prevalence. knowledge of his own migraine is associated to age and severity of headaches. The fact to be a migraine sufferer does not increase his skill.

P1B22

Occurrence of recurrent headache in Sweden by subtype and gender

Dan A. Svensson*[1], Karl Ekbom[2], Nancy L. Pedersen[3] & Elisabet Waldenlind[2]
[1]*Neurotec Department, Division of Neurology, Huddinge University Hospital, Sweden,* [2]*Department of Neurology, Huddinge University Hospital,* [3]*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden*

The occurrence of recurrent headache in Sweden was examined using a nationwide twin register. Quantitative genetic studies is the major application of the twin register, however, it may also be used as an epidemiological base register. A life history of recurrent headache was evaluated in 25490 subjects

aged 41–64 years (76% participation frequency) applying structured telephone interviews on the International Headache Society criteria. The lifetime prevalence of recurrent headache was 26.1% and totally 16 diagnostic subgroups were distinguished. The lifetime prevalence was 5.5% for migraine, 8.7% for tension-type headache, and 4.7% for migraine plus tension-type headache. The corresponding female-to-male ratios were 3.4 (95%CI: 3.0, 3.9), 1.2 (95%CI: 1.1, 1.4), and 3.5 (95%CI: 3.1, 4.0). A higher risk of recurrent headache in women than men was strengthened by, respectively, accompanying migraine symptoms and pain features of tension-type headache. In terms of symptom clustering, phenotypes of migraine and tension-type headache were more severe in women than men. Co-existing migraine exaggerated some pain features of tension-type headache, while chronic tension-type headache was more common in migraine-free subjects.

P1B23

Migraine may spoil your day, but seldom your life

Jan Passchier*[1] & J. A. M. Hunfeld[1]
[1]*Department of Medical Psychology and Psychotherapy, NIHES, Erasmus Medical Centre, Rotterdam, the Netherlands*

From previous studies we know that chronic headache is positively associated with life events, i.e. stressful intrusions in life that require a lot of adaptation. But does chronic headache, in particular migraine, *cause* such events, like divorce or losing your job? Or does the migraine cause only minor stressors? In order to answer these questions, 129 migraine patients from the Dutch Society of Headache Patients completed standardized questionnaires on intrusive life events and on daily hassles. About one third of the patients reported that one or more life events in the past year were caused by their migraine, while about half reported this for daily hassles in the previous 2 months. From all stressors experienced, 10% of the life events and 25% of the daily hassles were attributed to their migraine. Major life events, such as the loss of a job, divorce, or becoming disabled, were seldom mentioned as being caused by their migraines. This information can be provided as an antidote to those migraine patients who catastrophize their migraine.

P1B24

Headache in the emergency room: patients and headache characteristics

Esther Romero[1], Samuel Díaz-Insa*[2], Cristina Soriano[2], Mónica Roig[1], Gemma Amer[1] & Juan Carlos Martín-Baena[1]
[1]*Emergency Department, Hospital 'Francesc de Borja' de Gandía, Gandía, Spain,* [2]*Neurology Section, Hospital 'Francesc de Borja' de Gandía, Gandía, Spain*

Objectives To describe and analyse the patients and their headache characteristics attended in the Emergency Room (ER).
Methods During 4 months we evaluated all patients attending ER with headache as prior symptom. We considered age, gender, IHS type of headache, time with headache till ER arrival, previous treatment taken or not, time staying in the ER, treatment received, outcome, use of complementary diagnostic techniques and discharge. Patients under 17 years were excluded. When comparing groups, statistical differences with $p < 0.05$ were considered.
Results 315 patients attended ER with headache. Mean age 40 years with a distribution women/men 2.8 : 1 (232/83). IHS headache type: tension-type headache 33.02%, migraine 26.98%, secondary headaches 13.02%, chronic daily headache 10.48%, . . . and 7.3% unclassifiable. 50% of patients arrived before 24 h with headache. 78.72% had taken drugs before arriving to ER. The mean time staying in the ER was 2 h 26min. Diagnostic techniques were used in 36.51% of patients. 68.75% were discharged to Primary Health Care and just 3.31% hospitalised.
Conclusions The most frequent users of ER with headache are medium age women, with various primary headaches. Most of them had taken drugs previously. Time in ER is quite short and few diagnostic techniques are needed.

P1B25

Sumatriptan exposure during pregnancy: what have we learned about the risk of birth defects?

Sara Ephross*[1]
[1]*GlaxoSmithKline, Worldwide Epidemiology, RTP, NC*

Objective At drug approval, little information is available about use during pregnancy. Sumatriptan is the only triptan with published postmarketing pregnancy data.
Methods In 1996, GlaxoSmithKline established an international registry monitoring outcomes of reported prenatal sumatriptan exposures. Four additional studies have been published: prospective exposure registration (Shuhaiber 1998) and open-label (O'Quinn 1999) studies and two studies using birth registry data (Olesen 2000; Källén 2001).
Results Through October 2002, the sumatriptan registry prospectively obtained 376 pregnancy outcomes. Among 334 first trimester exposures, birth defects were reported in 10 live births, 1 stillbirth, and 1 induced abortion. No defects were reported in 286 live births, 3 stillbirths, 22 spontaneous, and 11 induced, abortions. The proportion with birth defects (12/298, excluding abortions without birth defects) is 4.0% (95% CI 2.2–7.1%), not significantly different from the expected general population proportion. There was no consistent pattern among reported birth defects. The occurrence of defects ranged from 0 to 2.7% (95% CI 1.6–4.3) in the four other studies.
Conclusion While sample sizes remain insufficient to draw definitive conclusions, five studies using different methodologies suggest no increased risk of birth defects associated with sumatriptan. Although use during pregnancy cannot be encouraged, data are reassuring regarding inadvertent exposure.

P1B26

Some lifestyle habits of Belgrade University female students with menstrual and other subtypes of migraine

Sandra Sipetic*[1], Hristina Vlajinac[1], Eleonora Dzoljic[2], Jadranka Maksimovic[1], Vladimir Kostic[2] & Jelena Marinkovic[3]
[1]*Institute of Epidemiology, School of Medicine, Belgrade University,* [2]*Institute of Neurology, School of Medicine, Belgrade University,* [3]*Institute of Social Medicine, Statistics and Health Research, School of Medicine, Belgrade University*

Objective was to estimate some lifestyle habits of our female students with menstrual and other subtypes of migraine.
Methods The prevalence study conducted in Belgrade from February to June 2000 comprised randomly selected female students (1943 students) of the School of Medicine and the School of Pharmacy of University of Belgrade, Serbia and Montenegro. Diagnoses were assigned according to the criteria of the International Headache Society and MacGregor's stricter definition of 'menstrual migraine'.
Results In this paper some lifestyle habits of female students with menstrual migraine (30 subjects) and other subtypes of migraine (premenstrual migraine-30 subjects, menstrually associated-119, menstrually unchanged-52 and menstrually unrelated migraine-27) were compared. Students with menstrual migraine did not significantly differ in their lifestyle habits (average number of meals per day, frequency of missing meal per month, average number of sleeping hours, sleep duration shorter or longer than usual) in other to other subtypes of migraine. The percent of ever smokers was significantly ($\chi^2 = 7.66$, $p = 0.006$) higher among female students with menstrually unrelated migraine (66.7%) than among students with menstrual migraine (30.0%). Among students with menstrual migraine 33.3% of them smoked less than 10 and 66.7% ≥ 10 cigarettes per day.
Conclusion Students with menstrual migraine did not significantly differ in their lifestyle habits except smoking in other to students with other subtypes of migraine.

P1B27

Knowledge and management of migraine in primary care: influence of functional impairment appreciated by Headache Impact Test (HIT) score

Emmanuelle de Villaume de Diego[1] & Michel Lantéri-Minet*[1]
[1]*Pain Department Hôpital Pasteur CHU de Nice, France*

Objective Aim was to study management of migraine in primary care with focus on headache disability.
Methods Study population consisted of 696 patients seen in the waiting room of 50 GPs. Questionnaire was administered to inform on existence of migraine (IHS 1.1) or migraine disorder (IHS 1.7) and headache-induced disability (HIT scale). Patient questionnaire was coupled to a doctor questionnaire to know if the GP considered the patient as a migraine sufferer and if he specifically managed him. Chi-2 and Fisher's tests were used for statistical analysis.
Results 176 (25.29%) patients were migraine sufferers according to IHS criteria (HIT 59.08 ± 8.77). They were 78 (11.21%) code 1.1 (HIT 61.12 ± 8.31) and 98 (14.08%) code 1.7 (HIT 57.49 ± 8.82). Only 71 of them (40.34%) were known as migraine sufferers by their GP: 50 with specific management (28.41%) and 21 (11.93%) without such a management. Disability was greater in patients known as migraine sufferers (63,38 ± 8.5 vs. 56.26 ± 8.03, $p < 0.05$) but identical in patients with management (HIT 63.39 ± 8.18) compared to those without (HIT 63.05 ± 7.57).
Conclusion Results confirmed an underdiagnosis and under management of migraine in primary care.

P1B28

Patterns of specific antimigraine drug use. A study based on the records of 18 public pharmacies

Joseph J. H. M. Lohman*[1], Monique M. van der Kuy-de Ree[2], Group of Co-operating Pharmacists Sittard-Geleen & its environs
[1]*Department of Clinical Pharmacy, Maasland Hospital, Sittard, the Netherlands,* [2]*Pharmacy Susteren, Susteren, the Netherlands*

This study was executed to characterize the patterns of use of specific antimigraine drugs, and to identify patients with more than one specific antimigraine drug. Data were collected from 18 public pharmacies over one year.

In a population of approximately 168 000 people 2343 (1.4-%) patients were identified with specific antimigraine medication.

The total number of prescriptions for specific antimigraine drugs was 7,542, a mean of 3.2 prescriptions per patient per year. Notably, 986 patients (42%) had only one prescription in one year, possibly indicating a low number of migraines, patients were not satisfied with their medication, and/or were not diagnosed correctly.

Tablets were prescribed mostly (54%), disintegrating tablets in 23%, subcutaneous injections in 10%, rectal suppositories in 7% and nasal sprays in 6%. Almost half (48%) of the number of dosage units were sumatriptan, 24% rizatriptan, 10% zolmitriptan and 8% naratriptan. Ergotamine was prescribed in 4.6% and the number of dosage units per prescription was 20.9, significantly higher than for the triptans (6.2–13.2 per prescription).

We identified 292 patients (12.5%) with more than one drug. These patients were slightly older and had used significantly more subcutaneous injections and less orally disintegrating tablets, more sumatriptan, eletriptan and almotriptan, and less rizatriptan.

P1B29

Headaches in obese patients

Mario Peres*[1], Daniel Lerario[2], Artur Garrido[3] & Eliova Zukerman[2]
[1]*São Paulo Headache Center,* [2]*Albert Einstein Hospital,* [3]*Hospital Beneficiencia Portuguesa, Garrido Institute for Obesity*

Introduction Obesity is a major public health problem worldwide contributing to increased morbidity and mortality. The prevalence of obesity varies from 7% in France to 32.8% in Brazil. Headache and obesity have been linked in idiopathic intracranial hypertension, but little is known about headache disorders in obese patients.

Patients/methods Seventy-four consecutive obese patients from the obesity surgery service at the Hospital Beneficiencia Portuguesa and the obesity clinic at the São Paulo Federal University were studied.
Results Mean age was 38,4 (61 women, 13 men), mean body mass index was 43, 5 patients overweight, 12 patients with obesity I, 10 obesity II, and 47 obesity III. Thirty-six patients (48%) had incapacitating headaches. Only 10 patients had morning headaches. The mean epworth sleepiness scale was 7.4, 26 patients (35%) had the score higher than 10, indicating daytime sleepiness. Fifty-six patients (75%) had a headache diagnosis, 49 migraine (66%), 7 tension-type headache (9%), 35 had migraine without aura (47%) patients, 5 migraine with aura, 7 chronic migraine, 1 menstrual migraine, 1 migrainous disorder, 2 chronic and 5 episodic tension-type headache.
Conclusion Headaches are common and incapacitating in obese patients, migraine is the most prevalent primary headache disorder.

P1B30

Impact of headache on quality of life

Maurizio Evangelista*[1], Selena Arena[1], Sara Sabato[1], Edoardo Tasciotti[1] & Domenico Camaioni[1]
[1]*Università Cattolica del Sacro Cuore Istituto di Anestesiologia Rianimazione E T, Rome, Italy*

Objectives Aim of this study is to evaluate how and how much chronic pain (headache) impacts on quality of life(Q.o.L.)of person affected and to compare with those without headache.
Material and methods: Data about Q.o.L. have been collected using Short Form Questionnaire 12 (SF 12) that has been administered to a sample of 47 (39f-8 m) patients with headache according to the IHS criteria.The data obtained have been compared with those available into 'Indagine ISTAT 1999–2000' on the state of Italians health; in order to make the sample homogenous, the data have been ulteriorly uniformed for sex and classes of age (18–44; 45–64; 65–85). The comparison between the two groups has been lead using median and quartiles.
Results Pertaining to the age bands 18–44 and 45–64 of female headaches, we have founded low PCS and MCS score strongly reduced vs. control group (respectively): PCS (18–44:median 41.7/55.5, 1° quartile 33.2/53.4, 2° quartile 47.5/56.4; 45–64: median 29.1/54, 1° quartile 19.2/47.9, 2° quartile 49.1/55.7); MCS (18–44: median 37.9/52.7, 1° quartile 26.7/46.4, 2° quartile 44.3/56.7; 45–64: median 24.5/51.6, 1° quartile 16.8/42.1, 2° quartile 35.8/55.8).
Conclusion This is an ongoing study but preliminary results suggest that, as headache impacts strongly on patients Q.o.L., there is still urgent need for greater attention by health care providers.

P1B31

New characteristics of children's headache in Rome

Davide Moscato*[1], A. Falasconi[1] & F. Bochicchio[1]
[1]*Childhood Headache Center, Saint Charles IDI, Rome, Italy*

The Italian social and environmental changes may have affected childhood headache. The aim of this study was to prove this.

The research was made on a territory in Rome ASLRME (550 000 people 350 km^2), representative of Italian children. 3973 (1980 M; 1993 F; age range 5–18 years) children were included in the study (questionnaire + interview). The statistical evaluation was made by χ^2 with Yates continuity correction and cross tabulation with SPSS.

Headache incidence was 34.5%. This increased in families with 4 or more children ($P = 0.04$). An important variable is the extra-community parents 8.4%; 3.3% with one foreign parent and 4.9% with both. The incidence is 52.5% in children with one foreigner($P = 0.000$), 38% with both.

Headache arises in 40% 8–11 age range, 7.3% of the boys are younger than 5 ($P = 0.000$), more frequent in families where both parents work.

Diagnoses MWoA 26.3%; MWA 0.5%; M disorder not fulfilling 8.2%; ETTH 37%; CTTH 5.7%; TTH not fulfilling 8.%; Idiopathic Stabbing Headache 5.3%; Missing 9%.

The use of symptomatic drugs is 60%, 8% in all the crises; use more by children with both parents foreign.

58.5% Headache Sufferers use drugs vs. 67% of children with two immigrants ($P < 0.05$).

Drugs are often self-prescribed.

Headache is one of the most widespread pathologies in development age, with the onset of new characteristics of immigration, as to early onset and early risk of drug abuse.

P1B32

Rizatriptan 10 mg reduces the impact of migraine on work and productivity compared to usual care in clinical practice (I-MAX migraine disability assessment program - Spain)

G. Nocea*[1], M. Torres[2], V. Baos[3], C. Bertral[4], M. Caloto[1] & W. Gerth[5]
[1]*Outcomes Research, MSD, Madrid, Spain,* [2]*C.S. Buenos Aires, Madrid, Spain,* [3]*C.S. Collado Villalba, Madrid, Spain,* [4]*C.A.P. Cardona, Barcelona, Spain,* [5]*Worldwide Outcomes Research, Merck & Co., Whitehouse Station, NJ, USA*

Objectives To evaluate the impact of rizatriptan 10 mg (wafer) on paid work and productivity relative to nontriptan treatment.
Background Migraine often reduces work productivity due to absenteeism and reduced effectiveness at work.
Design Observational study in Spain with 118 patients (≥18 years, triptan-naïve, met IHS migraine criteria, provided informed consent). Patients completed a diary for 3 consecutive attacks: 1st & 3rd treated with rizatriptan; 2nd with previous nontriptan therapy. It contained questions on migraine-specific absenteeism, work effectiveness, difficulty working for pay, and hours worked with symptoms. Work and productivity analyses were performed only in employed patients.

Results 33 patients were employed and scheduled to work for pay across the three attacks. Over two-thirds (69.7%) were female and the mean age was 34 years. Previous migraine treatment included NSAIDs (46.9%), analgesics (25%), ergotamines (18.7%) and combinations (9.4%). In attacks treated with rizatriptan, there were significantly less hours missed from work ($P = 0.005$), more hours at work ($P = 0.04$), greater effectiveness while at work with migraine ($P = 0.01$) and less difficulty to work ($P < 0.05$) compare to nontriptans.
Conclusions Migraine attacks, in patient previously naïve to triptans, treated with rizatriptan compared to nontriptan therapy reduced absenteeism and improved the amount and quality of time at work.

P1B33

Does a questionnaire facilitate the screening of migraine in primary care?

Salvador Tranche[1], Maria Jose Arbesú[1], Alba Riesgo*[1], Mounir Al Fayad[1], Julio Alonso[1] & Eduardo Hevia[1]
[1]*Centro de Salud El Cristo, Oviedo, Spain*

Objective To validate, in Spanish, a questionnaire designed for screening of migraine.
Methods Descriptive and cross-sectional study developed between March and July of 2002 in a district.

Four questions were formulated 'Have you ever had migraine?'; 'Have you ever had severe headache accompanied by nausea?'; 'Have you ever had severe headache accompanied by hypersensitivity to sound and light?'; 'Have you ever had visual disturbances lasting 5–60 min followed by headache?'. The questionnaires were followed by a structured clinical interview.
Subjects Two populations were selected by simple random sampling: patient diagnosed of migraine and general population.
Results 200 people were interviewed (107 patients and 93 of general population), of 42 ± 15 years, 27% men. They answered affirmatively some question 144 (72%). In the general sample, sensitivity was of 100% (IC, 95%:95–100) and the specificity 57.7% (IC,95%:47–67%); the question with the greatest sensitivity was the first (S:98.1%) and specificity, the fourth (E:95.9%). In general population sensitivity reached the 100% (IC, 95%:73–100) and the specificity 63% (IC, 95%:50–73%), with a positive predictive value of 32,6 (IC,95%:19,6–48.7) and negative 100 (IC, 95%: 91.1–100).
Conclusions Because of its high sensibility, this questionnaire can be used as a method of screening of migraine in primary care.

P1B35

Drug-induced headaches

Carlos Alberto Fontes Ribeiro*[1], Francisco Batel Marques[1], Germano Ferreira[1], Paulo Carrola[1], Luis Santiago[1] & Frederico Teixeira[1]
[1]*Department of Pharmacology, Faculty of Medicine, University of Coimbra, Portugal*

Data about drug-induced headaches can be gathered from spontaneous reports of adverse reactions (ADR) to Pharmacovigilance Systems (PhV). The NFC is a regional centre of the portuguese PhV, created in 2000. Until 2002, we received 716 ADR reports, 5.5% of them related to headaches. Drugs involved were not primarily for headaches and no one was related to withdrawal. ADR were not exacerbations of preexisting headache disorders. Applying WHO criteria, 33 were at least possibly caused by the drug (compatible time to onset, suggestive course of the reaction when the drug is stopped, semeiological criteria, no other explanation). There was no preferential distribution for age. Besides headache there was another clinical signal or symptom (90%) and patients were taking another drug (75%). Eleven of these adverse syndromes were unexpected and 7 serious (WHO criteria). Antiinflammatory drugs and psychoanaleptics were the most frequent involved agents; clearly, the majority of drugs was not vasodilatator, does not cause water and salt retention or intracranial hypertension. In conclusion, these headaches are in general part of a syndrome, occur when a patient is taking more than a drug and at a specified time after drug intake, disappear with drug suspension, and are induced by unspecified mechanisms.

P1B36

Epidemiological study of migraine among women suffering from Chernobyl disaster in Belarus

Halina Naumova*[1] & Marina Klimava[1]
[1]*Vitebsk Regional Diagnostic Center, Vitebsk, Belarus*

The aim of our investigation was to carry out an epidemiological study on migraine among women suffering from Chernobyl disaster in Belarus.
Methods We performed a population-based case ascertainment of all available sources of medical care (including the State Belorussian Register of people who were subjected to radiation exposure resulted from Chernobyl disaster) since May, 1986 till December, 2002. A number of women under study were 68 450. Females of all ages were analysed. HIS criteria were used.
Results Prevalence rate of migraine among women suffering from Chernobyl disaster in 1986–2002 varied from 17.8 to 31.2 per 100 000 of population. Analysing an average prevalence profile of migraine according to the age, we noticed, that: Bimodal distribution of the cases with age had two maximums: at the age of 10–15-year-old-and at the age of 30–35 years old. At the age of 15–35-year-old-prevalence rate of migraine was steady high. We have no patients using triptans in Belarus, because there is no official pharmaceutical registration of these medicines till now.
Conclusion The incidence rates of migraine among women in Belarus were similar to those reported by other developed countries.

P1B37

Drug use to treat headache in a general population based study

Teresa Turró[1], Samuel Díaz-Insa*[2], Mónica Roig[1], Sandra García[1], Cristina Soriano[2], Rosana Espinosa[1] & Manuel Galofre[1]
[1]*C. S. Tavernes, Tavernes de la Valldigna, Valencia, Spain,* [2]*Neurology Section, Hospital 'Francesc de Borja' de Gandía, Gandía, Spain*

Objectives To describe and analyse the pattern of drug use to treat headache in a general population based study.
Methods Personal interview and structured data pick-up about headache in ≅10% of all 16 000 Tavernes de la Valldigna inhabitants including drug intake in people with headache. We also describe the drug intake in each headache type and look for statistical differences.
Results We interview 1539 persons, 426 of them (27.68%) with headache; mean age 50.07 years, 87.79% women and 12.21% men. 33 people with headache (7.75%) don't take any drug or cannot remember. Resting 393 with headache (92.25%), which would mean 25.54% of general population, take drugs to treat headache. 44.53% of them just one drug, and the rest (55.47%) more than one. Paracetamol is used by 53.69% of headache sufferers taking drugs, NSAID's in 35.37%, metamizol in 28.50%, 13.74% take ergotamine compounds, 6.87% take triptans and 22.39% other drugs and mixed compounds.
Conclusions The great majority of headache sufferers take drugs to treat their pain. More than a half take two or more different drugs, which varies depending on the headache type. Simple and smooth analgesic paracetamol is taken broadly. Triptans are still less used than ergotics for migraine.

P1B39

I. Study of prevalence and physician consultations for headache among Spanish Mail Service Employees

Mª Teófila Vicente-Herrero*[1], Miguel JALáinez[2], Samuel Díaz[3] & Correos Headache Study Group[4]
[1]*Médico Área de Salud Laboral Correos, Valencia,* [2]*Servicio de Neurología, Hospital Clínico Universitario, University of Valencia.,* [3]*Servicio de Neurología. Hospital San Francisco de Borja, Gandia, Valencia.,* [4]*Correos Headache Study Group*

Objective To know the prevalence of headache, physician consultation and satisfaction levels with this consultation between the employees of the Spanish Mail Services.
Material and methods A survey was sent in 2001 with the salary containing 3 questions: Prevalence of headache, medical demand and satisfaction obtained. Results were evaluated by age groups, jobs involved and geographical distribution.
Results 61.665 post office employees were involved in the study, from 47 Spanish provinces, aged between 18 and 65 years, 63% males, 34% female. Geographical distribution was 35% in cities and 65% in the rural areas. The response rate was 16%,(9832 people), responder rate was higher between women (53%) over men (47%), mean age was 40 years for women and 44 for men.

Prevalence of headache was 34%, women 53% and men 47%. Demand for medical care was 61%, women 72% and men 57%. 35% of employees were satisfied with the medical care obtained, 65% were not.
Conclusions In relation to the prevalence obtained, the rate of consultations is still low, and rate of insatisfaction high among patients. In our labour medical circle, it is necessary to improve medical care and information given to the employees.

P1B40

II. Headache conditions in the Spanish Mail Service Employees: characteristics of the pain and population affected

Mª Teófila Vicente-Herrero*[1], Miguel JALáinez[2], Samuel Díaz[3] & Correos Headache Study Group[4]
[1]*Médico Área de Salud Laboral Correos, Valencia.,* [2]*Servicio de Neurología, Hospital Clínico Universitario, University of Valencia,* [3]*Servicio de Neurología, Hospital San Francisco de Borja, Gandia, Valencia.,* [4]*Correos Headache Study Group*

Objective After to send a headache survey to 61.665 Spanish Mail Service employees, we selected 446 workers with migraine and we studied on them: the characteristics of patients with migraine, associated symptoms and changes noted in their crisis, during and observational period of time.
Material and methods After a positive reply to our survey, we selected 446 employees, from 20 Spanish provinces, who requested treatment for migraine. Initial visits were made, monitoring during 6 months with formation and information, together with autocheck lists.
Results 66% were females, 34% male. 73% were married and came from all departments of the company. Average age 44 male, 40 female. 67% of those surveyed had family members with record of headache problems, 20 years of evolution and 3 migraine attacks per month. 76% were migraines without aura and 24% with aura. 51% suffered headache 15 or more days per month with abuse of medication: 44% analgesics and anti-inflammatory pills, 28% combinations, 6% ergot and 4% triptanes. Only 48% control or partially control their crisis with this medication.
Conclusions Percentage of patients with chronic headache conditions was much higher than expected, due to abuse of medication, although much less so with ergots in comparison with other studies in our country.

P1B41

An assessment of headache prevalence at work place

Marius Laur Birlea*[1] & Marcelo E. Bigal[2]
[1]*Department of Neurology, County Hospital of Zalau, Romania,* [2]*Department of Neurology, Albert Einstein College of Medicine, Bronx, New York, USA; The New England Center for Headache, Stamford, CT, USA*

Objective To estimate the prevalence and disability of chronic headaches on the employees of a Romanian textile factory.
Method Enrolled employees were evaluated by the same neurologist (MLB). They had their headaches assessed by

headache calendars (1 month) and by the Head-HUNT and MIDAS Questionnaires. Grossly, two groups of workers were evaluated: Group I those whose job required high levels of heat, noise and repeatability, and Group II with less heat and noise but more stressful, according to previous social-professional studies.

Results Our sample consisted of 400 subjects (96% women, mean age of 32). The response rate was 67%. Lifetime prevalence of headache was 96.3% with 82.2% prevalence for the last year. Episodic migraine was diagnosed in 52 patients (19.4%). The prevalence of chronic daily headache was 21.6% (12.4% in Group I vs. 32.5% in Group II). MIDAS grades were distributed as follow: grade I: 35.1%; grade II:13.8%; grade III:13.8%; grade IV:37.3%. Asked about the therapeutic needs, 27.6% of subjects considered preventive medication necessary.

Conclusion The high prevalence of headache, especially chronic forms, in this population suggest an important social-economical impact. This is the first epidemiological study for headache at work place in Romania.

P1B42

Shift work and headache: observations in a group of hospital workers

Ennio Pucci*[1], Francesco Matozzo[1], Giorgio Sandrini[1], Alfredo Costa[1], Antonietta Citterio[2] & Giuseppe Nappi[1,3]
[1]*University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia,* [2]*Neuroepidemiology Unit, IRCCS C. Mondino Institute of Neurology, University of Pavia,* [3]*Department of Neurology and ORL, University of Rome La Sapienza, Rome*

Work shift, involving 33% of employed population in Europe, affects physical health and facilitate the development of disease. To clarify its role in headache, we studied 228 subjects working at our Institute. Using a dedicated questionnaire, headache was reported by 42 of 157 patients clinically examined (26.7%), namely migraine without aura (21), with aura (1), tension-type headache (18), episodic cluster headache (2). In 50%, work shift (14.00–22.00 hours, 7.00–14.00 hours, 22.00–07.00 hours) was a major risk factor. Prolonged PC use, excess responsibility/reduced visibility among the working group, and social and familial problems were other factors. Among the 21 shift workers with headache, 12 had episodic tension-type (57.1%), 8 migraine without aura (38.1%) and 1 episodic cluster headache (4.8%). Thus, shift workers often suffer from headache, mainly of the tension type. In this case, following intense and/or prolonged precipitating factors (altered biological rhythms, psycho-physical stress, etc.) the increased nociceptive afferents may affect the pain control processes and result in headache. In migraine, hormone fluctuations, changes in sleep-wake cycle, stress, anxiety and depression may act on a state of latent disexcitability triggering cortical spreading depression, activation of the trigeminovascular system, and thus attack onset.

P1B43

Relation of the Headache Impact test to biographic data and headache: findings of the PAMINA study

Christian Wöber*[1], Karin Schmidt[1], Robert Zingerle[1], Evelyne Geuder[1], Natalie Hattinger[1], Andrea Böttcher[1], Ludmila Zahlbruckner[1] & Çiçek Wöber-Bingöl[1]
[1]*Department of Neurology, University of Vienna, Austria*

The aim of this study was to investigate the relationship of the Headache Impact Test (HIT) to biographic data and various characteristics of migraine.

We examined 373 patients (87.7% females) aged 40.5 ± 11.8 years suffering from migraine according to the IHS criteria. All patients were recruited by articles in newspapers. They underwent a semistructured interview and completed the HIT. For statistical analyses we calculated Spearman correlation coefficients and multiple linear regression models.

The HIT-score was not related to age, gender and the number of children, but it showed an increase with decreasing levels of education ($r = 0.15$; $p = 0.004$). Among 12 headache characteristics, 8 were related to the HIT score and 4 (including the duration of attacks without and with medication) were not. In the multiple regression model, patients with high HIT-scores were differentiated from those with lower scores by 5 variables, i.e. nausea, intensity, frequency, photophobia and aggravation of pain by physical activity.

In conclusion, this study agrees with previous findings showing that migraine is more severe in patients with a low level of education and it demonstrates that many migraine characteristics are reflected in the HIT-score, but that this is not true for the duration of attacks.

Scientific Session 2

Paediatric headache

P2C1

Levels of nitrites and sensory neuropeptides in salivary secretions of young migraine patients during attacks

Beatrice Gallai*[1], Giovanni Mazzotta[2], Francesca Coppola[2], Francesca Floridi[2] & Paola Sarchielli[2]
[1]*Department of Child and Adolescence Neurology and Psychiatry, University of Rome La Sapienza, Italy,* [2]*Neuroscience Department, University of Perugia, Italy*

Aim of the study The study was aimed to verify the changes in the calcitonin gene-related peptide (CGRP) and neurokinin A (NKA) levels, as well as those of the end-products of nitric oxide, the nitrites, in the salivary samples of 12 (8 females and 6 males-age range = 7–11 years) with migraine without aura with usual attacks lasting at least 2 h.

Methods Salivary samples were collected at the beginning of the attack, at the 1st and 2nd hours from the onset and 2 and 24 h from the end of the attack. The levels of CGRP and NKA were determined by RIA methods, those of nitrites by HPLC.

Results Significantly higher levels of both CGRP and NKA were found compared with the headache-free period ($P < 0.001$ and $p < 0.02$, respectively). Their peak was reached at the first hour. A similar trend was observed for nitrites whose higher levels were detected at the first and second hours.

Discussion The present study confirms the activation of trigemino-vascular system and increased NO synthesis in young migraine patients as in the adults. Salivary secretions offer therefore an alternative to peripheral or jugular venous blood for measuring biochemical changes in migraine (1). This is particularly relevant in young patients, where the possibility to carry out serial blood drawing is limited, especially during attacks.

P2C2

The habituation of the nociceptive trigeminal laser evoked potentials in childhood migraine

Marina De Tommaso*[1], Lucia Margari[2], Massimiliano Valeriani[3], Luciana Losito[1], Olimpia Difruscolo[1], Marco Guido[1], Giuseppe Libro[1], Michele Sardaro[1] & Francomichele Puca[1]
[1]*First Neurologic Clinic, Psychiatric and Neurologic Department, University of Bari,* [2]*Childhood Neuropsychiatric Section, Psychiatric and Neurologic Department, University of Bari,* [3]*Neurologic Department, Bambin Gesu' Hospital, Rome, Italy*

A lack of habituation of trigeminal nociceptive laser evoked potentials (LEPs) was observed in adult migraine without aura patients (Valeriani et al. 2003). The aim of the present study was to extend the study in childhood migraine during the headache-free phase, in order to clarify if the reduced cortical habituation to nociceptive inputs may be a phenomenon predisposing to headache and intrinsic to migraine pathogenesis. Twenty migraine without aura patients (MA), aged 12–15, and 15 age matched control subjects, were evaluated by LEPs obtained by the stimulation of the skin of the dorsum of the hand and the supraorbital zone. Three trials of 20 laser stimuli were delivered. The N-P complex peak-to-peak amplitude was computed and the amplitude variation of the 20 responses within the single trial and of the averaged responses between the three trials was evaluated in patients and controls. MA patients showed a tendency toward a N-P complex amplitude increase within the single trial and a clear lack of LEP amplitude suppression in the third repetition, in comparison with control subjects, when the supraorbital zone was stimulated.

The reduced habituation of cortical responses to nociceptive trigeminal input may be a phenomenon intrinsic to migraine pathogenesis, predisposing to the persistence of pain during migraine attack.

P2C3

Sleep and headache in adolescents

Liisa Metsähonkala*[1], Pirjo Anttila[2], Minna Aromaa[3], Katri Laimi[3] & Matti Sillanpää[1]
[1]*Department of Neurology, Turku University Hospital, Turku, Finland,* [2]*Turku City Hospital, Turku, Finland,* [3]*Department of Public Health, Turku University, Turku, Finland*

Objective To compare quality and quantity of sleep in adolescents suffering from different types of frequent headache.
Study setting A randomly selected population-based study.
Methods As the first step of the study, a structured questionnaire concerning headache was filled up by the whole age group of 12-year-old-schoolchildren ($n = 1409$, response rate 81%). As the second step, totally 304 children with different headache types (migraine, tension-type headache, other headache and no headache) were randomly selected to a clinical examination. After the examination, children with at least monthly headache episodes were asked to fill in a questionnaire on their sleep during a period of two weeks (duration and quality of sleep, daytime tiredness, headache episodes). 98 children returned an acceptably completed questionnaire (migraine 31, tension headache 36, other headache 29).
Results Adolescents with migraine did not differ from those with tension headache in the duration of sleep, the quality of sleep or in the number of headache episodes but they reported more often day-time tiredness than adolescents with tension headache.
Conclusions Sleeping problems contribute to recurrent headache. However, in the present study, the sleeping habits did not differ between adolescents with migraine and adolescents with tension type headache.

P2C4

Headache: what do the child and mother want from their physician? Methodological issues and preliminary data

Vincenzo Raieli*[1], Gian Luca Eliseo[1], Girolama La Franca[1], Michela La Vecchia[1], Eleonora Pandolfi[1], D. Puma[1], D. Ragusa[1], M. Eliseo[1] & G. Santangelo[2]
[1]*Department NPI 'L.Biondo' Osp. Ingrassia-A.U.S.L. 6-Palermo.,* [2]*Divisione NPI-Osp. Civico-Palermo*

Objectives Aim of this study has been focused on cephalalgic child and mother's expectations about the diagnostic and therapeutical approaches to headache from paediatrician and neuropsychiatrist.
Methods Our aim has been to select consecutive children with headache, admitted at first time to our department. We have given independently a questionnaire, constituted by several questions about their fears, their expectations and opinions about the use of pharmacological therapy, to the children older than 10 years and to mothers.
Results We show the preliminary data about n°40 children, n. 40 mothers. The principal reasons of the visit are the frequency and severe intensity of pain (52.5 and 27.5%). The more important mother's expectations are the explanations about headache and reassurances about their fears (57.5% and 52.5%), while the most of the fears is that her child suffers much for the headache. The children's answers show that 90‰f children want a pain relief, 60% doesn't fear his headache and 32.5% thinks that the visit has carried out by the parent's fear.
Discussions These preliminary data confirm that the main child and mother's expectations are the explanation of headache and the reassurance about it and not the prescriptions of drugs or medical tests.

P2C5

Chronic and continous headaches in children younger than 6 years of age

Vincenzo Raieli*[1], Domenico Puma[1], Gian Luca Eliseo[1], Donatella Ragusa[1], Mario Eliseo[1], G. La Franca[1], M. La Vecchia[1], E. Pandolfi[1] & G. Santangelo[2]
[1]*Department NPI 'L.Biondo' Osp. Ingrassia-A.U.S.L. 6-Palermo,* [2]*Department NPI- Osp. Civico – Palermo*

Objectives Aim of this study has been to review our prescholar population with headache to outline the principal features and to classify them according the IHS criteria.
Methods We have included only the children, that were younger than 6 years of age to our first observation between 1997 and 2001. The headaches were classified according to IHS criteria. We excluded children with less than 5 headache attacks or less than 15 days of daily headache.
Results Subjects consisted of n. 67 children, about 6.1% of all population (n.1088) with headache. The mean age was 4.8 y. (range 1.8–5.11 years). Males were 41, females were 26. The classified headaches has been: 31.3% migraine, 22.3% episodic tensive headache, 4.4% chronic daily headache, 13.4% idiopathic stabbing headache, 29.8% post-traumatic headaches, 5.9% other secondary headaches and 4.4% unclassifiable headaches.
Discussion Our study shows some differences about headaches in this population vs. scholar children. In fact in this age the migraine is the more common headache, but we also find a increase of secondary causes among the chronic/recurrent and daily headaches, especially post-traumatic disorders and the most prevalence of the stabbing headache in comparison with other ages.

P2C6

Wafer Rizatriptan in the treatment of children's migraine

Davide Moscato*[1]
[1]*Childhood Headache Centre. Saint Charles IDI Hospital, Rome, Italy*

Objective Evaluate the effectiveness of wafer Rizatriptan, chosen for its easy use in the treatment of migraine in children and adolescents.
Methods The study was performed 'in the open' on our patients. With the consent of the parents, the following children/adolescents were treated: MWoA (IHS 1988), headache for over 6 months, more than two crises per month, medium-strong intensity, long duration, age range 10/17, weight over 35 kg. Treatment: 1 tablet of Rizatriptan (Maxalt RPD10. Merck), another after 2 h, if the first had no effect, symptomatic drugs if necessary. Duration: one month. Main outcome measure: headache response at 1.2 h after initial dose. Secondary endpoints: 4-h headache response, reduction of the associated symptoms.
Results 35 patients enrolled, 4 dropped out, 2 for no crises, 2 not responding. So, 31 were included, 67 migraine crises were treated. Only two took the second dose (2 girls with menstrual migraine). Side-effects: heavy tiredness in 4 subjects for a few hours and in 2, muscular contractions in the neck. Headache response occurred at 1 h 36%, 2 h 51.7% ($P < 0.05$), at 4 h 71%. Nausea ceased in 39.6%, vomiting in 62.7%, dizziness in 66%, abdominal pain 53%.
Conclusions Wafer Rizatriptan is an effective treatment against migraine crisis during development age, though not completely useful for all symptoms.

P2C7

Self-reported illness behaviour in headache and migraineous children's families

Vincenzo Guidetti*[1], Federica Galli[1], Glenda Tripicchio[1], Paolo M. Russo[2] & Cristiano Violani[1]
[1]*Department of Developmental Neurological and Psychiatric Sciences, University of Rome 'La Sapienza',* [2]*Department of Psychology, University of Rome 'La SapienzaObjectives:*

Objective Evaluate self reported behaviours related to illness in headache sufferers' parents and healthy children parents.
Methods Fifth-five parents (43 mothers and 12 fathers) of children referring to the Headache Centre (Headache Parents) and a group of 52 control parents (37 mothers and 15 fathers) participated to the study. All parents filled in the Italian version of the Illness Behaviour Questionnaire (IBQ), a self reported questionnaire developed for assessing different attitudes and behaviours related to health.
Results The multivariate test evidenced a difference between groups [Wilks $\lambda = 0.62$; $p < 0{,}001$]. In particular, parents of headache's sufferers obtain higher scores, compared to control group, for the following scales: General Hypochondria, Disease conviction, Psychological vs. somatic focusing, Affective disturbances and Irritability. Considering headache subtypes, parents of migraineous children report higher level of Irritability than parents of not migraineous headache sufferers.
Conclusions Parents of headache patients are characterized by particular illness-related behaviors. The potential effect of these behaviours on their children is discussed.

P2C8

The HSQOL-C: a new instrument for measuring the Impact of Headache on quality of life in children and adolescents

Vincenzo Guidetti*[2], Cristiano Violani[1], Paolo M. Russo[1], Giulietta Capacchione[1] & Federica Galli[2]
[1]*Department of Psychology, University of Rome 'La Sapienza',* [2]*Department of Developmental Neurological and Psychiatric Sciences, University of Rome 'La SapienzaObjectives:*

Objectives Validate a new questionnaire, the HSQOL, assessing the negative impact of headache on daily activities, avoidant behaviours and self-reported well being in juvenile headache sufferers.
Methods HSQOL was completed by 272 (158F, 114M) migraineous and non migraineous headache sufferers (Age 9–15), recruited half in educational and half clinical settings. A short version of HSQOL was completed by their parents.
Results The HSQOL scales yielded consistent factorial structures and satisfactory reliability coefficients. The Impact scale

differentiates children with different degrees of disturbance severity and between treated/not treated subjects. Younger children reported more avoidance behaviours aimed to prevent the attack. Females reported higher scores in the Well-being Scale. Parents-Children agreement is significantly higher for 'objective' aspects (e.g. number of attacks in the last month) than for subjective ones (impact on daily activity).
Conclusions The HSQOL scales can be a useful tool for both clinicians and researchers interested in assessing different health related QOL aspects in juvenile headache sufferers.

P2C9

Actigraphic monitoring of sleep in migraineous children

Vincenzo Guidetti*[1], Oliviero Bruni[1], Paolo M. Russo[2] & Cristiano Violani[2]
[1]*Department of Developmental Neurological and Psychiatric Sciences, University of Rome 'La Sapienza*, [2]*Department of Psychology, University of Rome 'La Sapienza'*

Objectives In order to analyse the relationship between sleep-wake cycle and migraine's attacks, young headache sufferers were monitored with diaries and actigraphic recording for two weeks.
Methods subjects Eighteen migraineous children (10M, 8F) and 17 age matched controls. Children (Age 7–12) daily completed a sleep-wake and headache diary. Sleep parameters were measured through actigraph using the Sadeh algorithm.
Results Fifth-three attacks were reported in 248 days of monitoring. Compared to attack free nights, the intranight motor activity indexes were lower in the nights of the attack, in the nights following the attack, with the lowest values in the nights before the attack. When attack-free nights are considered, no differences between migraine and control group have been found for any of the actigraphic sleep parameters (total sleep time, sleep efficiency, wake after sleep onset, sleep onset latency).
Conclusions The observed reduction of intranight motor activity could be related to imbalance between noradrenergic and serotonergic systems, known to fluctuate in function of the occurrence of the migraine attack.

P2C11

Quality of life and migraine disability in pediatric and adolescent patients: the relation of PedsQL to PedMIDAS

Andrew D. Hershey*[1,2], Scott W. Powers[1,2], Marielle A. Kabbouche[1,2], Ann Segers[1], Susan L. LeCates[1] & Anna-Liisa B. Vockell[1]
[1]*Children's Hospital Medical Center, Cincinnati, OH,* [2]*University of Cincinnati, Cincinnati, OH*

Objective Characterize the impact of migraine on children attending using a general QOL measure (PedsQL) and a migraine specific measure (PedMIDAS).
Methods Patients attending the Cincinnati Children's Headache Center were completed. PedsQL and PedMIDAS at their initial evaluation. PedsQL has been validated for healthy children and measures physical and psychosocial factors. PedMIDAS measures migraine disability and mirrors the adult MIDAS.
Results 575 patients (mean age 11.6 ± 3.5; male : female ratio 1 : 1.3) completed both questionnaires. The mean frequency was 13 ± 10 headaches per month; mean severity was 6.7 ± 1.8 out of 10; and a mean duration was 9.4 ± 16.1 h. 90.4% met the IHS criteria for migraine. School effort was decreased to 42 ± 27% effort with 3.7 ± 6.7 days missed per semester. Mean PedMIDAS score was 40 ± 47.3. Mean PedsQL for patients and parents were 72 ± 15. The Pearson correlation for PedMIDAS:patient PedsQL was –0.33, while the correlation with parent PedsQL was –0.34. The parent:patient PedsQL correlation was 0.77.
Conclusion Migraine headache significantly impacts children's lives. The combination of a nonspecific (PedsQL) and migraine specific (PedMIDAS) instrument may increase our understanding of this impact and help monitor treatment responses.

P2C12

Treatment patterns of new and follow-up patients attending tertiary pediatric headache clinics

Paul Winner*[1], Andrew D. Hershey[2], Marielle A. Kabbouche[2], Jack Gladstein[3], Steven L. Linder[4], Scott W. Powers[2] & Donald W. Lewis[5]
[1]*Palm Beach Headache Center, W.P.B., FL,* [2]*Children's Hospital Medical Center, Cincinnati, OH,* [3]*University of Maryland School of Medicine, Baltimore, MD,* [4]*Dallas Pediatric Neurology, Dallas, TX,* [5]*Children's Hospital of the King's Daughters, Norfolk, VA*

Objective Assess the pattern of headache treatment in the pediatric tertiary care.
Methods 191 patients(13 ± 3.3 years – 70 new:121 follow-up) and 177 parents (66 new:111 follow-up) at four tertiary headache clinics completed a survey assessing current treatment, satisfaction with treatment and desired treatment.
Results Ibuprofen was the most commonly used medication (67%) followed by triptans (22.5%) and acetaminophen (18%). Acetaminophen was used more often (36%) and triptans less often (11%) in new patients, while in follow-up patients, ibuprofen (71%) and triptans (29%) use increased and acetaminophen (7.4%) decreased with a resulting increase in patient's satisfaction. New patients were not happy (21.4%) or very unhappy (20%) with current treatment, while follow-up patients were very happy (38%) or somewhat happy (31.4%). 88% prefered to treat their headaches with a pill when given the choice of pill, nasal spray or shot, with 53% listed nasal spray as their second choice.
Conclusion Pediatric patients are frequently not satisfied with current medications. Tertiary headache care improves this overall satisfaction, by optimizing nonspecific (NSAIDs) and specific (triptans) headache care. Future development of oral forms of therapy would best meet patient's desired treatment, although many are amenable to nasal formulations.

P2C13

Consultation patterns of patients presenting to pediatric tertiary headache clinics

Andrew D. Hershey*[1], Paul Winner[2], Marielle A. Kabbouche[1], Jack Gladstein[3], Steven L. Linder[4], Scott W. Powers[1] & Donald W. Lewis[5]
[1]*Children's Hospital Medical Center, Cincinnati, OH,* [2]*Palm Beach Headache Center, W.P.B., FL,* [3]*University of Maryland School of Medicine, Baltimore, MD,* [4]*Dallas Pediatric Neurology, Dallas, T,* [5]*Children's Hospital of the King's Daughters, Norfolk, VA*

Objective This study assesses patient consultation pattern, timing of visit and diagnosis.
Methods 191 patients (13 ± 3.3 years) and 177 parents at 4 headache clinics completed a survey assessing healthcare providers seen, when last seen and diagnosis.
Results 70% of the patients saw a healthcare provider for their headaches – pediatrician or general physician (92%), ophthalmologist (29%) and allergist (13%). 33% of visits for all patients occurred within the last 3 months, while for new patients 71% had occurred within the 3 months. 91% of all patients were diagnosed with migraine, however, only 62% of new patients had been diagnosed with migraine. Reasons for not being seen were: my medicine works (39%), headaches not severe (30%) and nothing available (30%). Parents reported a higher perception of medicine working (67%). 26% had stopped seeing a physician with the most common reason listed as a perception that the physician was not helping the headaches (49%).
Conclusion Pediatric patients have often been seen by other healthcare providers, diagnosed with migraine but frequently without complete satisfaction in the evaluation and management. The consultation pattern, awareness and receipt of effective acute treatment in this population needs continued study.

P2C14

A multicenter study on quality of life in juvenile patients with primary headache

Pier Antonio Battistella*[1], Silvia Polvara[1], Livia Nicoletta Rossi[2], Stefano D'Arrigo[3], Stefano Soriani[4], Elisabetta Tozzi[5], Giovanni Mazzotta[6], Magda Verdecchia[7], Graziella Di Meo[8], Luigi De Carlo[9], Davide Moscato[7], Guiseppe Santangelo[10], Vincenzo Raieli[10] & Angelo Vecchio[10]
[1]*Department of Pediatrics, University of Padova, Italy,* [2]*Department of Pediatrics, University of Milano, Italy,* [3]*IRCCS 'C. Mondino', University of Pavia, Italy,* [4]*Pediatric Clinic, University of Ferrara, Italy,* [5]*Department of Experimental Medicine, Pediatric Clinic University of L'Aquila, Italy,* [6]*Headache Centre, University of Perugia, Italy,* [7]*Centre for juvenile, Roma, Italy,* [8]*Headache Center, University of Chieti, Italy,* [9]*Pediatric Hospital of Rovigo, Italy,* [10]*Institute of Neuropsichiatry, University of Palermo, Italy*

Objectives To evaluate the quality of life (QoL) in a large sample of juvenile out patients suffering from primary headache in Italy.
Material and methods Group A: 351 subjects, 157 m and 194 f, aged 10–18 year (12,7 years, SD 2,1) 66.4% of them affected by migraine (59.3% without aura, 7.1% with aura) and 33.6% by tension-type headache (23.9% episodic and 9.7% chronic) referred to 13 Juvenile Headache Centres of Italy, diagnosed according to the IHS criteria (1988). Group B: 351 headache-free, age and sex-matched subjects (control group), selected by schools of North Italy.

'QoL headache in youth' questionnaire (Langeveld 1996), adapted and validated in Italian version (Nodari E. 1999, Favero *C*. 2001), included 46 items, divided over 9 subscales to cover 4 QoL domains (functional status, psychological, social and physical functioning).
Results (in process). (1) comparison between QoL of patients and headache-free subjects. (2) relationship between QoL and type of headache, the gravity of the headache pattern and the other variables considered.

P2C15

What causes new daily persistent headache in children?

Kenneth Mack*[1]
[1]*Mayo Clinic, Rochester MN, USA*

Objectives This study sought to identify the initiating factors in the development of new daily persistent headache (NDPH).
Methods Children with chronic daily headache (according to HIS criteria) were prospectively identified at the Mayo Clinic from October 2001 to March 2003.
Results A total of 163 patients were identified as having chronic daily headache and seen by the author. Of these patients, 41 (25%) with NDPH were identified. These patients had no significant prior headache history. Fifteen patients (36%) had the onset of their symptoms during a viral infection. Of these postviral patients, 60% had positive EBV serology at the onset of symptoms. Eight patients (20%) had minor head injuries at the onset of their symptoms, yet had a normal exam and neuroimaging. Symptom onset was also associated with surgery (3 patients) and high altitude camping (1 patient). In 5 patients, no specific etiological stressor could be identified. There were 4 patients of the 41 who were initially identified as having idiopathic intracranial hypertension, yet their chronic headache persisted despite the normalization of their intracranial pressure. After the onset of symptoms, the characteristics of NDPH patients were not significantly different than other patients with chronic daily headache.
Conclusions In children, the onset of new daily persistent headache is strongly associated with a physiologic stress such as a viral infection, head trauma or postsurgery.

P2C16

Short migraine attacks in children: the results of a prospective diary-based study

Ishaq Abu-Arafeh[1] & Mary Callaghan*[1]
[1]*Headache Clinic, Fraser of Allander Neurosciences Unit, Royal Hospital for Sick Children, Yorkhill, Glasgow, UK*

The IHS's diagnostic criteria of headache in children (1988) provoked a debate on the appropriateness of defining migraine attacks as lasting for at least 2 h. Many authors proposed reducing the lower limit to 1 h and others proposed

further reduction to 30 min This study aims to clarify the issue.

Among the 720 children who attended our specialist headache clinic, over a period of 6 years, 231 had migraine with or without aura fulfilling the IHS criteria. Further 15 children reported headache attacks typical of migraine, but of duration less than 2 h. They were asked to fill prospective headache diaries in order to determine the duration of their headache attacks with certainty.

Ten children (67%) provided prospective fully analysable headache diaries recording 120 headache attacks; 66 (55%) were less than one hour each, 30 attacks (25%) between 1 and 2 h and 24 attacks (20%) over 2 h. Three of the 10 children had consistently headache attacks lasting less than 1 h. Three children had some attacks lasting for at least 1 h and 4 had some attacks lasting at least 2 h.

This study shows that headache attacks in children with migraine can be variable, but attacks less than one-hour duration are rare. The diagnostic criteria should therefore, acknowledge such variation and accept attacks lasting for at least 1 h.

P2C17

The drawing of a young headache sufferer, a diagnostic guide

Davide Moscato*[1] & M. I. Peracchi[1]
[1]*Childhood Headache Centre, Saint Charles IDI Hospital, Rome, Italy*

A child can describe the characteristics of his headache (1); as he uses drawings to show his feelings. We tried to assess his ability to describe headache with a drawing.

At the first entry in the DH the children drew 'their headaches'. The drawings were compared at random with the subsequent medical diagnosis.

161 patients were evaluated (78m, 83f, range 5/17 years, MWoA-36 m29f.; ETTH-20 m 28f., CTTH-22 m 26f.).

The diagnoses made from the drawings: the type of pain, localization, associated symptoms; the intensity comparing with the McGrath scale of faces (2).

The diagnostics were rather accurate: MwoA 77%, ETTH 58%, CTTH 70%. Diagnostic accuracy is not linked to the child's age, it is higher when the headache lasts more than one year.

The drawing consistency with age was compared with the scale of pain of Bibace and Walch (3); in this case, adherence exceeded 80%.

Due to its characteristics of precision and simplicity, we believe that 'headache drawings' may be a very useful instrument to the child to freely describe his situation, and for better understanding to the physician.

References

1 D. Moscato. Abstract IV Int Cong headache in childhood and adolescence. Turku 1999:66.
2 McGrath, P.A., DeVeber L, Hearn M. Advances in Pain research and Therapy.New York: Raven Press 1988.
3 Bibace R., Walsh M. Illness and bodily functions. Jossey- Bass. San Francisco CA 1981:31–48.

P2C18

Thaumaturgical effect of the drug in the young headache sufferer. A few hypotheses from an epidemiological study

Davide Moscato*[1], Annibale Bertola[2], A. Falasconi[1] & F. Bochicchio[1]
[1]*Childhood Headache Centre. Saint Charles IDI Hospital. Rome Italy,*
[2]*International School of Research in Clinical Psychology and Psychoteraphy IDI, Rome, Italy*

From an epidemiological study on 3976 children emerged that the use of symptomatic drugs exceeded 60%. We tried to explain the possible reasons.

Drug use is a typical reaction of parents. 60% of the children take drugs, 8% say they take drugs 'every time they have a headache'.

The analysis of the psychological variables from that data led us to 'read the drug as mediator of identification mechanisms with the sick parent and his style of response to the illness. Through this identification, a child can, allegedly, defend himself from paranoid anxieties and from the feeling of guilt triggered by the parent's pathology; the use of the same drug, to which in the fantasy a thaumaturgical valence would be ascribed, would take up reparation and idealization valences. We believe the results of this process can be inferred, both from a clinical and psychological standpoint. Firstly, the attitude of fatalist resignation towards the pathology would facilitate an early conduct of drug abuse, with consequent risks of addiction and chronic use. From a psychological standpoint, identification with the parent may represent the starting point of successful defence mechanisms such as regression to the parent's role, often disturbances are seen in narcissistic personality and in hypochondriac mechanisms, focusing on organs having a great symbolic value.

P2C19

A global diagnostic intervention: day hospital for children's headache

Davide Moscato*[1]
[1]*Childhood Headache Centre. Saint Charles IDI Hospital, Rome, Italy*

A child suffering from headache is brought to the centre when his headache is disturbing the family circle. The request of the family is to solve the problem as soon as possible. The first intervention is to help the family understand that psychophysical stress situations and altered rhythm in the child's life are main headache triggers. This is often difficult with a series of interventions in the clinic.

We implemented a diagnostic therapeutic course including some days of DH, during which the entire family lived together.

After routine checks and psychological evaluations, we observed how they acted. This enabled the family to become aware of possible altered mechanisms of reciprocal behaviour.

The study was performed on 118 patients (without prophylaxis therapy, followed by us both in the clinic, and patient of DH) with an evaluation of Pain Index (DxF) at the first check, and after 6 months.

	Sample		
	Sex	Age	Diagnosis
60 DH	27 m , 33f	range 3–17	MwoA 27 MwA 3 ETTH19 CTTH11
58 Amb	28 m , 30f	range 3–16	MwoA 24 MwA 4 ETTH21 CTTH 8

We found considerably lower data for DH (117.5–67.7) vs. Clinic (133.7–93) ($P < 0.05$) with no differences in the diagnosis and between sexes.

During the age of development, when family characteristics affect children in a more considerable way, the DH of headache offers a good management tool.

P2C20

Home-based behavior therapy vs. drug treatment for adolescent migraine: preliminary data

Kenneth Holroyd*[1], Constance Cottrell[1], Jessica Gibson[1] & Francis O'Donnell[2]
[1]*Ohio University College of Osteopathic Medicine, Athens, OH, USA,* [2]*Headache Treatment & Research, Westerville, OH, USA*

This study asked if (1) behavioral treatment could be effectively administered in a home-based treatment format where behavioral headache management skills were learned at home aided by telephone consultations with a counselor, and (2) if home-based behavioral therapy (HBT) was as effective as 'triptan' drug therapy (TT). 34 adolescents (12–17 year. old; 56% female; 94% Caucasian) with an IHS diagnosis of migraine (mean = 3.3 migraines/month) were enrolled. Following neurological and medical evaluation adolescents were randomly assigned to receive TT (5 mg Rizatriptan® or alternative triptan if indicated) or HBT. HBT included instruction in relaxation, trigger identification, effective medication use, thermal biofeedback, and cognitive coping. Diary data (migraine days, duration, pain severity), total and partial disability hours, and quality of life (Migraine Specific Quality of Life Questionnaire: MSQ 2.1) scores served as the dependent variables.

HBT produced significant ($P < 0.01$) improvements (relative to baseline) on total number of migraines, total disability, quality of life and number of migraine days. TT produced significant ($P < 0.01$) improvement on average duration of migraine and total disability. Both triptan therapy and home-based behavioral therapy appeared to be effective treatments for adolescent migraines. Additional studies with larger samples and additional comparison groups are indicated.

P2C21

What do parents and patients presenting to pediatric tertiary headache clinics want in headache treatment

Andrew D. Hershey*[1], Paul Winner[2], Marielle A. Kabbouche[1], Jack Gladstein[3], Steven L. Linder[4], Scott W. Powers[1] & Donald W. Lewis[5]
[1]*Children's Hospital Medical Center, Cincinnati, OH,* [2]*Palm Beach Headache Center, W.P.B., FL,* [3]*University of Maryland School of Medicine, Baltimore, MD,* [4]*Dallas Pediatric Neurology, Dallas, TX,* [5]*Children's Hospital of the King's Daughters, Norfolk, VA*

Objective Optimizing headache treatment necessitates an understanding of patient's expectations. This study assesses patient satisfaction and expectations.
Methods 191 patients (13 ± 3.3 years) and 177 parents at 4 headache clinics completed a survey assessing satisfaction and problems with treatment/evaluation rated from least important (1) to most important (5).
Results Incomplete (patients 3.9 ± 1.1, parents 3.8 ± 1.0) and inconsistent (3.8 ± 1.2, 4.0 ± 1.2) treatment were the most common complaint, while side-effects were least (1.7 ± 1.2, 1.9 ± 1.3). Complete relief of pain was the most important expectation (4.1 ± 1.1, 4.4 ± 0.9). New patients rated fast relief next (3.7 ± 1.1, 3.8 ± 1.2). The most important reason to see a doctor was to learn to eliminate headaches (4.2 ± 1.0, 4.3 ± 0.9, p = 0.36). The patients biggest current problem was medicine not working (3.6 ± 1.5), while parents rated missing school (3.9 ± 1.2).
Conclusions Pediatric patients want rapid, complete relief of headaches without relapse. Lack of side-effects and ease of use are lower priorities. They want to be taught by their doctor how to effective eliminate their headaches, while addressing their current concern with medicine not working and missing school.

P2C22

Psychological factors in headache among Finnish adolescent twins

Ruut Virtanen*[1], Minna Aromaa[1], Markku Koskenvuo[1], Matti Sillanpää[1,2], Lea Pulkkinen[3], Liisa Metsähonkala[4], Sakari Suominen[1], Richard Rose[5], Hans Helenius[6] & Jaakko Kaprio[7]
[1]*Department of Public Health, University of Turku, Finland,* [2]*Department of Paediatric Neurology, University of Turku, Finland,* [3]*Department of Psychology, University of Jyväskylä, Finland,* [4]*Department of Paediatric Neurology, University of Helsinki, Finland,* [5]*Department of Psychology, Indiana University, Bloomington, USA,* [6]*Department of Biostatistics, University of Turku, Finland,* [7]*Department of Public Health, University of Helsinki and National Public Health Institute, Finland*

Objective To examine the association of psychological factors with headache among Finnish adolescent twins.
Methods Data were collected from 1995 to 1999 from a nationwide sample of Finnish families with 11–12-year-old twins born between 1983 and 1987 ($n = 5393$) and again at age 14. Psychological factors were measured by parents' and teachers' MPNI (Multidimensional Peer Nomination Inventory).
Results The prevalence of frequent headaches (>1/month) was 60% at age 11–12 years and 65% at age 14. At age 11–12 of children headache was associated with behavioral, emo-

tional and adjustment problems assessed by the parents, but only with behavioral problems assessed by the teachers. The results were similar at age 14. The incidence of frequent headache between the ages of 11–12 and 14 years was predicted by behavioral problems, poor constructiveness and poor compliance. In headache discordant pairs the behavioral and emotional problems were more common among the headache sufferers than among headache-nonsufferers. Among discordant monozygotic pairs, only behavioral problems were associated with headache.

Conclusions The occurrence of adolescents' headache is associated with different psychological factors, especially with behavioral problems.

P2C23

Efficacy and tolerability of the selective COX-2 inhibitor Parecoxib as escape medication in children with refractory migraine attacks

Michael A. Ueberall*[1]
[1]*Institute for Neurological Sciences, Algesiology and Pediatrics, Germany*

Objectives Parecoxib. the first selective COX-2-inhibitor available for parenteral use, is a potent nonopioid which combines analgesic and anti-inflammatory properties. In clinical studies, parecoxib was characterized by a powerful pain relief, a fast onset (7–10 min) and a long lasting action (up to 24 h). Due to these characteristics, parecoxib seems to be a potent candidate for the rescue/escape-treatment of migraine attacks. Several open studies demonstrated high and sustained response rates in adults. This is the first report on its efficacy and tolerability in pediatric migraine patients, suffering from severe migraine attacks refractory to commonly used antimigraine therapies.

Materials and methods In an open design 24 children/adolescents (mean: 10.4 year., range 6–16) suffering from refractory migraine attacks with/without aura according to IHS-criteria were treated with 0.5 mg/kgBW parecoxib i.v. Headache intensity (0 = none, 1 = mild, 2 = moderate, 3 = severe) as well as accompanying symptoms and AEs were documented in a special diary card at baseline and after 10, 20, 30, 45, 60, 90, 120 min and 4, 8, 12, 24 h post treatment.

Results Mean pain intensity at baseline was 2.8; significant relief was reported at 30, 45, 60, 90 and 120 min postdose by: 50%, 83%, 92%, 92% and 96%; total relief was seen in: 13%, 25%, 54%, 75% and 83%. Four hours postdose 23 out of 24 children were pain free. Headache recurrence was not seen.

Conclusions I,v, parecoxib proved to be an highly efficacious and well tolerated rescue/escape medication for the treatment of severe migraine headache attacks in children and adolescents.

P2C24

Migraine and tension-type headache in children under six years of age: a follow-up study in 14 subjects

Umberto Balottin*[1], Francesca Nicoli[1], Giovanni Pitillo[1], Oreste Ferrari Ginevra[2], Cristiano Termine[1], Marta Quadrelli[1] & Giovanni Lanzi[3]
[1]*Child Neuropsychiatry Unit, University of Insubria, Varese, Italy,* [2]*University of Pavia, IRCCS Fondazione C. Mondino, Pavia, Italy,* [3]*Department of Child Neuropsychiatry, University of Pavia, IRCCS Fondazione C. Mondino, Pavia, Italy*

Objective To investigate the clinical features of idiopathic headache with early onset and the influence of environmental and psychological factors.

Methods Prospective longitudinal evaluation of 14 children with at least 4 years follow-up (mean duration: 5 years and 3 months; range: 4 years and 1 month–7 years) selected from a sample of 35 consecutive patients presenting with headache (onset before the age of six) referred to the Neuropsychiatry Departments of the Universities of Varese and Pavia (mean age at first observation: 4 years and 1 months; range: 12 months–5 years and 11 months). All patients were assessed by a semistructured interview, playing sessions, clinical observations, interview with parents to detect early developmental disorders, interictal somatic disorders, affective functioning styles and to evaluate the role of psychosocial factors at the onset and in the course of headache.

Results Early developmental disorders were detected in 7/14 children; interictal somatic disorders in 10/14, psychosocial components in 6/14. Findings of the follow-up study will be illustrated.

Conclusions We suppose that a better clinical definition of headache in very young affected children allow to plan more effectiveness therapeutic interventions, taking into account environmental and psychological factors. Our follow-up results will be discussed.

P2C25

Evaluation of migraine aura at onset in a group of children and adolescents and long-term follow up

Giovanni Lanzi*[1], Oreste Ferrari Ginevra[1,2], Cristiano Termine[3], Stefano D'Arrigo[1], Maura Rossi[1], Matteo Ferri[3], Alexis Mongelli[1] & Ettore Beghi[4]
[1]*Department of Child Neurology and Psychiatry, IRCCS C. Mondino, University of Pavia,* [2]*Don Gnocchi Foundation, Centro S. Maria al Castello, Pessano C.B., Milan,* [3]*Child Neuropsychiatry Unit, University of Insubria, Varese,* [4]*Neurological Clinic, University of Milano-Bicocca, Monza and Mario Negri Institute, Milan*

Differences in the evolution, over time, of migraine with aura have been interpreted according to a variety of hypotheses: subjects' different personality structures, neurobiological maturation factors, the presence of migraine in family members, and the possible presence of psychiatric comorbidity.

In a long-term, follow-up study, we examined the natural history of early onset migraine with aura. We reviewed the clinical records of all the subjects admitted to our department between January 1st 1980 and December 31st 1996 and discharged with a diagnosis of migraine with aura. We therefore

restricted our study to cases presenting the specific characteristics needed to confirm a migraine with aura diagnosis according to the IHS criteria (1988).

Applying these inclusion criteria, we selected 96 subjects (53 females and 43 males – from 5 to 17 years and 9 months) and for each subject, in addition to the headache characteristics, we collected detailed anagraphical data, family and medical history.

All subjects were contacted and re-assessed in order to ascertain the long term evolution of their migraine with aura (follow-up ranged from 5 to 21 years). We discuss correlations between the evolution of the clinical picture and factors relating to the disease semiology, family and physiological history, and previous illnesses.

P2C26

Cyclic vomitting in twins: ElectroEncephaloGraphic (EEG)-clinical evolution from early childhood to adulthood

Zarko Martinovic*[1]
[1]*Institute of Mental Health, Belgrade, Yugoslavia*

This paper describes the clinical and EEG evolution of cyclic vomiting in two twin sisters who were followed-up by neurologic and pediatric assessments and EEG recording from the age of 4–23 years.

Dyzigotic female twins were born at term, after a normal pregnancy and delivery. Their growth and mental development was normal. From the age of 4.1 years til the age 14 years, first sister manifested 42 and the second twin 39 episodes of cyclic vomiting, maximally 6 per year, lasting from 4 to 18 h each. The most common associated symptoms were prostration, fatigue and abdominal pain Migraine-like headache occurred only in 1/6 of episodes. The EEG during 24 episodes recorded abnormal bilateral delta activity and slight slowing often persited between the episodes. Epileptiform EEG abnormalities were never recorded. Complete EEG normalization occurred at the age 14 years. Other findings of gastrointestinal investigations and brain neuroimaging were normal in both twins.

Although cyclic vomiting in these twin sisters occasionally involved symptoms of migraine-like headache, the long-term follow-up has not shown its evolution into migraine.

P2C27

Clinical characteristics of migraine in children and adolescents – a population based study in Belgrade (Yugoslavia)

Maja Milovanovic*[1] & Zarko Martinovic[1]
[1]*Institute for Mental Health, Belgrade, Yugoslavia*

Objective To evaluate clinical features of migraine in the defined population of children and adolescents, and to study agreement between clinical migraine diagnosis and diagnosis based on the International Headache Society (IHS) criteria.
Methods The sample was drawn from a total of 5268 subjects (1663 schoolchildren aged 7–14 and 3605 school students aged 15–19 years). From the sample of 413 subjects with recurrent headaches, diagnosis of migraine was made by clinical interview with neurological examination.
Results Clinical diagnosis of migraine was made in 187 subjects: 56 aged 7–14 and 131 aged 15–19 years. Using the clinical diagnosis as the gold standard, the IHS criteria had sensitivity of 44.8% in younger and 54.5% in older subjects. Migraine with aura was diagnosed in 55 (29.9%) subjects. The most frequent aura symptoms were: visual in 67.9%, oculomotory-vertiginous in 60.7%, sensory-motor in 17.8% and aphasic in 7.1% patients. Compared with adolescents, children aged 7–14 years had a significantly higher frequency of migraine attacks, shorter duration of attacks, frequently nonpulsatile quality of pain and bilateral frontal pain ($P <$ 0.05–0.01).
Conclusion Clinical features of migraine in children are different than in adolescents. The IHS criteria are not highly sensitive in these age groups.

P2C28

Long-term use of Sumatriptan Nasal Spray (SNS) is well-tolerated and effective in adolescent migraineurs

Mary Richardson*[2], Shankar Natarjan[1], J. T. Jabbour[1] & Christopher Webster[2]
[1]*Pediatric Neurology, La Bonheur Children's Hospital, Memphis, TN, USA,* [2]*GlaxoSmithKline, Research Triangle Park, NC, USA*

Objectives To assess the long-term tolerability and efficacy of SNS 20 mg in a population of migraineurs aged 12–17 years.
Methods Adolescent migraine sufferers (meeting IHS criteria 1.1 or 1.2) treated an unlimited number of migraine attacks with SNS for up to 12 months in this open-label, observational study (SUM40276). Subjects started treatment with 20 mg SNS; down-titration of dose to 5 mg was permitted to optimise tolerability and efficacy needs. Adverse events (AEs) were recorded and efficacy data were also collected via an interactive voice-response system. ECG and laboratory evaluations were performed.
Results 484 subjects treated a total of 4718 attacks with SNS. Only 42 attacks were treated with 5 mg SNS. Taste disturbance was the most frequently reported AE. No subject experienced any drug-related changes in ECG, vital signs or nasal assessments. When treated with 20 mg SNS, headache relief was experienced in 43% and 59% of attacks at 60 and 120 min, respectively, and 44% of attacks were pain-free at 120 min Headache recurrence was reported for only 7% of attacks.
Conclusions SNS is well-tolerated and effective during long-term use by adolescent migraineurs.

P2C29

Epidemiology of children headache in Vojvodina

Marija Knezevic-Pogancev*[1]
[1]*Institute for Child and Youth Health Care, Novi Sad, Yugoslavija*

Headache is the mean cause for first visit in primary medical care in 6–23% of all children. Migraine is to most often type of recurrent headache.

The objects of study was to present rate and types of recurrent headaches in Children of Vojvodina.

24035 children aged 3–16 years have been examined. The examination was conducted by a carefully constructed and standardized questionnaire and by interviewing directly children and parents of the children who had recurrent headaches.

The migraine syndrome shows in 3.87% of children aged 3–7 years, and in 8.63% of children aged 3–16 years. The migraine syndrome appears as the migraine with aura in 25.55%, migraine without aura in 67.21% and other migraine syndromes in 7.23%.

The presence rate of the migraine syndrome increases with age from 2.65% to 11.72% in boys and from 2.71% to 15.86% in girls. The migraine with aura shows a continuos linear rise from 1.8% to 32.7%, whereas the migraine without aura reaches its peak at prepuberty stage. Migraine equivalents reach their peak at the age of five (67.3% of migraine syndromes).

P2C30

The MIDAS questionnaire in juvenile headache patients: an Italian pilot study

Licia Grazzi*[1], Domenico D'Amico[1], Susanna Usai[1], Frank Andrasik[2], Massimo Leone[1], Andrea Rigamonti[1] & Gennaro Bussone[1]
[1]*C. Besta National Neurlogical Institute, Milan, Italy C. Besta National Neurlogical Institute, Milan, Italy,* [2]*Institute for Human and Machine Cognition, University of West Florida, Pensacola, Florida, USA*

Objective To determine the suitability of the Migraine Disability Assessment (MIDAS) questionnaire for assessing disability in juvenile headache patients; to obtain preliminary information about disability in different primary headaches.
Methods Ninety-five patients aged 7–17 years with tension-type headache (TTH), migraine or both completed the validated Italian form of the MIDAS questionnaire on two occasions. Test-retest reliability was assessed by Spearman's correlation test. Internal consistency was assessed by Cronbach's alpha. The patients answered questions about the adequacy of the questionnaire.
Results Cronbach's alpha was 0.8. Correlation coefficients were generally high for overall MIDAS score and for the items investigating disability in school and in family/leisure activities; they were lower for the items about household work. All primary headaches had a considerable impact on daily activities, but patients with migraine tended to have lower headache frequencies and lower total disability time, while those with TTH suffered more days in which activities although performed were substantial impaired.
Conclusions The MIDAS questionnaire is useful for assessing disability in juvenile patients with different primary headaches. Minimal changes in the phrasing and content of the items would be sufficient to render MIDAS specific for young sufferers.

P2C31

Treatment of migraine in children and adolescents: a review of efficacy data with sumatriptan nasal spray (SNS)

Andy Dowson*[1], Mirja Hamalainen[2], Christopher Webster[3], Laura Lisk[4] & Martin Jones[4]
[1]*King's Headache Service, London, UK,* [2]*Hospital for Children and Adolescents, University of Helsinki, Finland,* [3]*GlaxoSmithKline, Research Triangle Park, NC, USA,* [4]*GlaxoSmithKline, Greenford, England, UK*

Objectives Efficacy of oral triptans is difficult to demonstrate in young migraineurs. These prospective studies aim to establish the efficacy of SNS in this population.
Methods Efficacy data from 7 studies, in children and adolescents are evaluated.
Results 782 patients aged 12–17 years were enrolled in 2 controlled studies. In SUM40019, headache relief (HR) at 2 h was achieved by 64% (SNS) vs. 39% (placebo), respectively ($P < 0.05$). In SUMA3005, HR at 1 h was reported by 47–56% (SNS) vs. 41% (placebo), respectively ($P < 0.05$).

5 smaller studies enrolled 172 patients aged under12 years. In the 2 controlled studies, HR at 2 h was achieved by 86% and 64% (SNS) vs. 43% and 42% (placebo), respectively. In the 3 uncontrolled studies, HR at 2 h was reported in 77%, 86% and 78% of patients receiving SNS.

Taste disturbance was the most frequently reported AE.
Conclusions SNS was significantly more effective than placebo in all 4 controlled studies and provided good headache relief in 2 uncontrolled studies. SNS is effective and well tolerated in the acute treatment of migraine in those aged under 17 years. SNS allows the benefits of triptan therapy to be extended to children and adolescents.

P2C32

The Family Drawing Test as a tool to evaluate individual psychopathological features and relational dynamics in children with headache aged 7–9 years

Maria Pia Prudenzano*[1], Teresa Francavilla[1], Francesca Cuonzo[1] & Francomichele Puca[1]
[1]*I Neurologic Clinic, University of Bari, Italy*

Both individual psychological features and familial relations might play an important role in the onset and the course of children headache. The family drawing test allows to define both child's feelings about his life role and his thoughts about himself and the others family members. This study was conducted to evaluate individual features and familial dynamics by means of the family drawing test in headache children. A sample of children aged 7–9 years, suffering from headache and referring to Headache Centre of the I Neurological Clinic, University of Bari were enrolled. Their siblings not suffering from headache formed a sex and age matched control group. A nonheadache, nonsibling, age and sex matched sample of children was enrolled as control group. All of them were asked to draw a fancied family Then the drawings were classified according to standardized parameters such as the position on the sheet, the typology and the single components. A more elevated rate of a rational typology (hierarchical order

of figures, static positions, lack of environmental elements and plenty of personal details) was found in the headache siblings than in non headache ones and non sibling controls. These results confirm the existence of specific psychological features in children suffering from headache and show the usefulness of a comprehensive individual and relational evaluation to identify possible dysfunctions might interfere with the success of treatment.

P2C33

Impact of trigger avoidance in childhood and adolescent migraine headaches

M. V. Francis*[1]
[1]*Headache and Migraine Research Centre, Kerala, South India*

Objective To assess the impact of trigger avoidance in migraine headaches in children and adolescents
Materials and methods Retrospective study .4900 children and adolescents were diagnosed as migraine during a period of 9 years and 1800 were followed up for a duration of 4 years. IHS, IHS R and IHS RR 2001 Modified(revised) criteria were strictly applied in diagnosing migraine headaches.

All triggers were recorded and common triggers were identified. Parents and teachers were advised regarding measures to avoid common triggers.
Results The common triggers were exposure to sunlight 60%(1040), daytime bus travelling 42%(756), strenuous physical exercises 23%(414) and tension anxiety situations 21%(378).Two or more triggers were reported by 41%(738)of all patients studied. 52% (936) reported more than 50% improvement in the severity and frequency of their migraine headaches by avoidance of common triggers (hat with a wide brim, wrap around sunglasses, umbrellas, avoiding sun exposure during school assembly sessions and physical training programmes, etc.). Prevalence of migraine headaches among parents also were high. 85% mothers and 12% fathers were migraine sufferers and their triggers were also similar.
Conclusion Avoiding common migraine triggers will have a tremendous impact on the course of migraine headaches

P2C34

Diagnostic flow chart to differentiate episodic tension type headaches and episodic migraines in children and adolescents

M. V. Francis[1]
[1]*Headache and Migraine Research Centre, Kerala, South India*

Objective To design a diagnostic flow chart to differentiate episodic tension type headaches from episodic migraine headaches in children and adolescents
Background HIS episodic tension type headache and episodic migraine diagnostic criteria have more than one overlapping statements. No significant study has been done to clearly differentiate between the two entities
Methods 617 children and adolescents who initially presented with IHS episodic tension type headaches(2.1 and 2.3) were identified later when they presented with migraine features (IHS 1 (1.1 and 1.2), IHS R, IHS RR 2001 modified). Parenteral migraine history and common migraine triggers were the most helpful differentiating features. Migraine trait symptoms were also helpful in some.
Results (The diagnostic flow chart – details in the text.) The important features are recurrent headpain, activity affected or not, autonomic symptoms present or not. Common migraine triggers, migraine parents and migraine trait symptoms were also considered.

Common migraine triggers – exposure to sunlight,day time traveling, strenuous physical exercises, lack of sleep, hunger and tension anxiety situations.

Migraine trait symptoms – motion sickness, dizzy spells precipitated by common triggers, common migraine triggers other than tension anxiety situations precipitating activity affected headpain without autonomic symptoms.
Conclusion The diagnostic flow chart is the most simple way of clinically differentiating episodic tension type headaches from episodic migraine headaches in children and adolescents.

P2C35

Attentional and pain intensities in nursery and primary school children

Gabriele Gerda Ostkirchen*[1] & Petra Petersen[2]
[1]*University Clinics Essen, Department of Neurology, Essen, Germany,*
[2]*Seminaraus ggmbh, Mülheim, Ruhr, Germany*

Objectives Pain is not a bare expression of organic damage; whose intensity is proportional to the degree of the damage; it rather is a result of complex information processing procedures modulated by attentional processes. In order to intensify the pediatric pain research, this study aims in deriving empirically based knowledge about the development of subjective headache-experiences combined with basic attentional concepts.
Methods 87 healthy children (male = 44; female = 43), 5–10y., participated up to now. The participants estimated the imagined pain intensity of a child on a picture suffering from headache as well as the degree of a subjectively experienced headache-intensity (VAS1–10). Furthermore, alertness reactions were registered according to ABBA-design (TAP: A = without signal; B = with signal) and analysed in relation to age, gender and developmental stage.
Results Intensity-dimensions for headaches and for short-term attentional performances do not correlate (nonsignificant Pearson correlations). Analysis of variance show no sex-differences for the raised intensity measures. Attentional and imagined pain intensities differ with age (e.g. $F = 9.010$, $p = 0.000$). Pain intensities basing on experienced headaches show no age-effect. Additional developmental effects can only be found for attentional measures ($F = 13.367$, $p = 0.000$).
Conclusions At this point of analysis, more questions are raised than answers given. Considerable intra- and individual differences impede the interpretation of the driven data. Important hints are expected from more detailed analysis of the pain interviews and from the outstanding comparison of

the healthy groups with children who suffer from regularly appearing headaches.

P2C36

Migraine prophylaxis with flunarizine in children

Anannit Visudtibhan*[1], Apasri Lusawat[1], Surang Chiemchanya[1] & Pongsakdi Visudhiphan[1]
[1]*Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Objective To determine the effectiveness of flunarizine in migraine prophylaxis in children.
Patients and method Children aged more than 6-year-old-with migraine headache who met indication for prophylactic treatment were recruited in a prospective study at the Department of Pediatrics, Ramathibodi hospital, between January to December 1999. After verbal consent obtained, flunarizine was administered at 5 mg or 10 mg per day for 2–3 months. Serial evaluations for severity of migraine including duration, intensity, and frequency were determined every 2 weeks.
Results Twenty-one children (10 boys, 11 girls) with mean age 11.3 ± 2.48 years (range 7–16 years) enrolled in the study. There were 10 children with aura and 11 children without aura. Flunarizine was initiated in 19 patients at 5 mg daily and at 10 mg daily in the other two. The dosage was increased to 10 mg per day after two weeks in 5 patients. Improvement was observed in 14 patients (66%). Among these patients, 13 received flunarizine 5 mg daily. Five patients (23%) had no recurrence. Nine patients (42%) had more than 50% reduction of frequency of migraine. Shorter duration or less intensity of attack was observed in 3 patients. No severe adverse effect was detected.
Conclusion Flunarizine is one of the drugs which may be considered for migraine prophylaxis in children.

P2C37

Headache and psychopathologic symptoms in young subjects

Luigi Mazzone*[1], Diego Mugno[1], Liliana Ruta[1], Maria Cristina Scoto[1], Ilenia Cancemi[1] & Domenico Mazzone[1]
[1]*Department of Pediatrics – University of Catania, Italy*

Aim of our study is to evaluate psychopathological characteristics of a group of infants and adolescents suffering from different types of headache.

Patients and methods 80 patients, aged 6–15 years: 26 suffering from tension-type headache (A group), 39 suffering from migraine without aura (B group) and 15 with aura (C group).

The following tests were used for the neuropsychological evaluation: CBCL, CDI, MASC, Conner's Scales and EAS.
Results CBCL internalizing subscale was high in 11 (42.3%) A group and in and in 19 (48.7%) B group patients. CDI's score was high in 5 (19.2%) A group and 5 (12.8%) B group patients. MASC's total score was high in 8 (30.8%) A Group, and in 14 (35.9%) B Group patients. Conner's scales score was high in 6 A group (23.1%) and in 6 B group (15.4%) patients. EAS scale in A group indicated higher excitability, hyperactivity and reduced sociability.
Conclusion A Group and B group have a remarkable psychopathological vulnerability, concerning in particular with the internalizing aspects of behaviour. Hyperactivity, excitability, and low sociability are more frequent temperamental features in group A. The patients of group C are characterised by a lower psychopathological vulnerability.

P2C38

The risk for tension-type headache in children with neuropsychiatric disorder

Renato Donfrancesco*[1] & Andrea Dell'Uomo[1]
[1]*Presidio La Scarpetta ASL RM/A*

Objectives Some papers, concerning adult people, shows a higher prevalence of tension-type headache than migraine among people with psychiatric disorders. The aim of this paper is to verify these data among children with psychiatric disorder.
Methods A structured interview, concerning headache symptomatology, was used with 158 children, all psychiatric consecutive patients of 3 child neuropsychiatrists of a primary health care unit. A control group of 105 subjects was recruited among the consecutive patients of 2 paediatricians of the same primary health care unit. Data are collected on children from age 5 to 14. The two group were matched for age. Diagnosis was performed according the IHS criteria.
Results Children visited in the neuropsychiatry primary care had more headache (22.78%) than children of the paediatrician clinics (9.90%, $p < 0.05$). 10.12% of psychiatric population had a tension-type headache and 8.22% a migraine. Among the control group 5.96% of the children had tension-type headache and 3.96% a type of migraine. No statistic difference were found between the ratio migraine/tension-type headache of the two groups.
Conclusions Children with psychiatric disorders have more frequently headache than children of the paediatric clinics but tension-type headache is not a specific feature of this association.

P2C39

Anamnestic and clinical comparisons of childhood migraine with and without aura

Fulvio Sorge*[1], Cristina Cerruti[1], Anna Chiacchio[1], Francesca Cipollone[1] & Benedetto Speranza[1]
[1]*Dipartimento Di Neuroscienze E Scienze Del Comportamento. Sezione Di Psichiatria. Centro Per Lo Studio Delle Cefalee In Età Evolutiva Ed Adolescenziale. Università Degli Studi Di Napoli*

Objectives To evaluate if childhood migraine with aura has a different clinical pattern compared to migraine without aura.
Material and methods 85 children referred to the 'Headache Study Centre' of the Psychiatric Clinic at the University Federico II of Naples (Italy) were assessed by a neurologist and the diagnosis were made according to the IHS criteria. Children with migraine and aura (16 male, 19 female, middle age 10.2 ± 2.3) were considered cases and children with migraine

but without aura (25 male, 25 female, middle age 11.3 ± 2.89) were classified as controls.

We investigated familiarity for migraine; over-reactivity during the first six months of life; allergic diathesis, cyclic vomiting; recurrent abdominal pain; migratory limbs' pain; sleep disorders; kinetosis; presence, frequency, duration and severity of headache; nausea, vomiting, photophobia and phonophobia during migraine attack.

The statistical significance and strength of association were calculated using Odds Ratio and 95% confidence interval of Odds Ratio.

Results Our study showed no significant difference between migraine with or without aura respect to any variable considered.

Comments Our date support thesis that migraine with or without aura are similar in their clinical characteristics but we steel don't know if therapy and prognosis are similar too.

P2C40

Incidence of migraine in criminal adolescents and correlation with other neurological findings

Pamela Blake*[1], Julio Cantero[1], Maureen Sheehan[1] & Jeffrey Canceko[1]
[1]*Georgetown University*

We have noted an increased incidence of headache in the juvenile aggressive and violent population. We studied this population in more detail to correlate the findings on the neurological exam and the prevalence of ADHD with the occurrence of migraine headache in this group.

Thirty-four adolescent male criminals were referred from the juvenile justice system for neurological examination. Complete headache histories were obtained. Fifteen subjects met IHS criteria for migraine headaches; 19 subjects had no headaches. Complete general and neuropsychiatric histories were obtained and complete neurological examinations were performed.

The incidence of headache that met IHS criteria for migraine in this group of criminal adolescents was 56%, significantly higher than reported rates of 5% in control populations (Deubner, 1977). The incidence of neurological abnormalities on examination was 53% in the headache group and 52.6% in the headache free group. Abnormal findings were most commonly related to frontal lobe dysfunction, consistent with previous reports (Blake et al. 1995). There was a trend to lower rates of ADHD in the migraine group, with ADHD present in 53% of the headache group and in 68% of the nonheadache group. The incidence of migraine in children is about 4–5% according to epidemiologic studies.

P2C41

Chronic daily headaches in children and adolescents: a study of clinical characteristics

Jose Luiz Dias Gherpelli*[1] & Sandro Blasi Esposito[1]
[1]*Department of Neurology, University of Sao Paulo*

The clinical characteristics of chronic daily headache (CDH) were studied in 40 children and adolescents as well as the associated factors responsible for the maintenance of the headache continuous pattern. The study of the headache clinical characteristics, showed a female preponderance (75%), mean age at the first consultation of 11 years old, and headache symptomatology onset at a mean age of 8.5 years old. The average time interval for the evolution of sporadic headache into CDH was 1.4 years, and psychosocial stressors were present acute or chronically, during the period of headache frequency increase, in 47% of the children, the most common being school (failure, change), detected in 6 patients, and domestic problems (frequent parent's fight, parental illness), in 5. Anxiety, depressive and quality of life questionnaires results showed that 27% patients had scores that suggested a depressive trait, 19.5%, scores that revealed a high anxiety status, and 31.5%, low scores in the quality of life questionnaire. No difference between sexes were observed regarding headache characteristics, or psychological traits, or quality of life evaluation. Headaches were classified as transformed migraine (65%), mixed pattern (17.5%) and chronic tension-type headache (17.5%). Sixty percent of the patients had mothers with migraine. Data regarding common analgesic use showed an average intake of 11.2 days/month.

P2C42

Attachment and headache

Umberto Balottin*[1], Giorgio Rossi[1], Oreste Ferrari Ginevra[2,3], Gea Drumbl[2] & Francesca Bonforte[2]
[1]*University of Insubria, Macchi Hospital, Varese,* [2]*Department of Child Neurology and Psychiatry, IRCCS C. Mondino, Pavia,* [3]*Don Gnocchi Foundation – Centro S. Maria al Castello, Pessano C.B., Milan*

The literature contains numerous studies of mechanisms at work within the families of headache patients, and each has adopted different methods and procedures.

The symptom of headache, which can also be interpreted on a psychosomatic level, appears to be correlated with and perpetuated by certain types of family system. Therefore, it could be useful to consider the structure of the subject's family and the relationships that are formed within it.

Of the various tests cited in the literature, we selected the PBI (Parental Bonding Instrument) of Parker et al. (1979), a questionnaire that examines, through two variables, overprotection and care, the style of the parent-child bond.

Our sample includes 34 patients (aged 9–17 years) with diagnoses of tension-type headache, migraine without aura, and migraine with aura. We recruited a group of 56 controls (aged 11–18 years).

The aim of our study was to evaluate whether, and to what degree, parental care and protectiveness towards children can influence the pathological picture, and whether the style of attachment within a family is passed from generation to generation.

We hypothesise that overprotection could be more prevalent in the families of headache subjects, strengthening the mechanisms responsible for the same.

P2C43

Evaluation of the efficacy and the safety of Flunarizine (Sibelium) for prophylaxis of pediatric migraine

Iliyana Pacheva*[1]
[1]*Medical University, Department of Pediatrics and Genetic Diseases*

Introduction Migraine is not rare in childhood and adolescence and may be a disabling disease. In the recent years Flunarizin is wide used for prophylaxis of Migraine in adults. But in Pediatric migraine there is a little experience.
Aim To evaluate the efficacy and the safety of Flunarizin(Sibelium) for prophylaxis of Pediatric migraine
Materials and methods Fourteen patients (aged 8–15 years) with proved Migraine (3-with aura, 11-without aura) were included in the study. The inclusion criteria were frequent or very severe attacks, impairing patients 'daily activities. Sibelium was administered 5 and 10 mg, respectively, in patients under and above 13 years of age for 6 months. All characteristics of migraine attacks and side-effects were registered in headache-diaries. Patients were examined every three months and followed for 1-year.
Results During prophylaxis 10 of 14 patients (71.43%) were free of migraine attacks, 3(21.43%)-with reduction more than 50% and 1(7.14%)-with the same frequency, but less severity. In 3 of the 10 patients the attacks reappeared after stopping Sibelium, but with less frequency and intensity. In all other cases the effect remained the same. No significant side-effects, except transitory drowsiness in 2 patients, were reported.
Conclusions Sibelium as prophylactic medication for Pediatric migraine showed excellent therapeutic results and no serious side-effects.

P2C44

Successful treatment of chronic daily headache by sonography-guided injections of botulinum toxin A in muscular trigger points

Steffen Berweck*[1], Anette Schwerin[2], Urban Fietzek[1] & Florian Heinen[1]
[1]*Dr Von Hauner's Children's Hospital, University of Munich,* [2]*Children's Hospital, Wedau Hospital, Duisburg*

Headache is the most common reason for children and adolescents to request medical help. Most pathophysiological concepts of headaches mention the role of hypertense musculature as to trigger or to sustain the pain, but muscle tension relaxing treatments have produced controversial results up to now. We report the successful analgesic treatment of six adolescents using sonography-guided injections of botulinum toxin type A (BTA) into muscular trigger points (TP).

Within a two-year period (2001–2) we evaluated 180 patients at our headache clinic. Among those were six patients who suffered from (i) chronic headache for at least 6 months (mean duration 1.9 year.) (ii) had TP in cervical and/or shoulder muscles, and (iii) treatment failed with analgesics and physical therapy incl. relaxation techniques. Four week prior to treatment the mean frequency was 27 days per month, the mean severity 6.6 (range 6–8) on the VAS. The six patients underwent sonography-guided BTA injections in one or two TP (10–25 U Botox® per TP). Four weeks after BTA injections, all patients had a decrease in frequency (mean 4.8 days per month) and severity (VAS mean: 2.4, range 0–5). Following successful treatment children regained the ability to fully participate in schooling and social activities.

Further controlled investigations are necessary to evaluate the reliability and validity of this preliminary data.

P2C45

Migraine and epilepsy in pervasive developmental disorders

R. Canitano*[1] & A. Luchetti
[1]*General Hospital of Siena, Division of Child Neuropsychiatry, Siena, Italy*

The association between epilepsy and pervasive developmental disorders is well documented. As well migraine and epilepsy in children are frequently co-occurring in various association. The incidence and the characteristics of headache in this selected population are undetermined.
Objective To examine the prevalence of migraine and epilepsy in a group of children and adolescents with pervasive developmental disorders.
Methods 101 subjects, mean age 10,1 ys SD ± 4.3, with a diagnosis of Autism or Pervasive Developmental Disorders according to DSM IV criteria were consecutively evaluated, the presence of paroxysmal disorders were specifically investigated at history taking and clinical workup.
Results 8 children were suffering from epilepsy (9%), 6 having seizures yet and 2 with a long lasting seizures free period, all of them were under anticonvulsants treatment. 3 patients were suffering from migraine (3%), one child had both seizures and migraine attacks, anti migraine medications were administered as preventive treatment or symptomatic.
Conclusion Headache was relatively rare in our patients, epilepsy rate was in the low range of percentage reported in pervasive developmental disorders. The clinical features of migraine were similar of those observed in children without developmental disorders, in spite of communicative impairment there were not major difficulties to recognize a migraine attack.

P2C46

Clinical studies of sinus headache in Korean Children

Changwoo Lee*[1], Jong Ryul Kim[1], Hoil Bang[1], Yeon Gyun Oh[1], Hyang Suk Yoon[1] & Jong Duck Kim[1]
[1]*Department of Pediatrics, Wonkwang University College of Medicine*

Purpose Headache is a common reason for children to seek medical care. There are many causes of headache in children, such as migraine and its variants, tension, intracranial masses, and sinusitis. A high frequency of diagnosis of sinus headache, which specialists consider to be relatively rare, raises the possibility that migraine and other headache types are sometimes mistaken for sinus headache. This report studied the clinical characteristics of sinus headache in the pediatric population.

Methods We analyzed the clinical manifestations of 25 patients who had sinusitis in 97 children whose chief complain was headache. The clinical manifestation involved location, type, frequency and associated symptoms of headache, frequency of upper respiratory tract infection(URI), and family history of migraine.

Result: 1 There were 8 cases of organic headaches, which were 2 cases of brain tumor, 2 cases of arachnoid cyst, 1 cases of Moyamoya disease, 1 cases of brain abscess and 2 cases of eye problems.

2 The mean age of patients who had sinus headache was 8.2 years. The most common group of age was between 6 and 11 years(76%).

3 The most common location of sinus headache was frontal area in 10 cases(40%). And the most common pattern of headache was dull and steady pain in 16 cases(64%).

4 The most common associate symptom of headache was gastrointestinal symptom such as nausea, vomiting and abdominal pain in 13 cases(52%).

5 The number of patients who had no history of frequent URI were 13(52%). And number of patients who had family history of migraine was seven(28%).

Conclusions Consider in aggregate, the data show that the occurrence of sinus inflammation associated with a headache should neither trigger a diagnosis of sinus disease nor exclude a diagnosis of migraine. It should prompt diagnostic consideration of both conditions.

P2C47

Diagnostic-therapeutic guidelines of juvenile headache: perspective multicenter study on the applicability of a flow-chart

Giovanni Mazzotta*[1], Francesca Floridi[1], Elisabetta Cittadini[1], Alessia Mattioni[1], Paola Sarchielli[1] & Beatrice Gallai[1]
[1]*Dipartimento Di Neuroscienze, University of Perugia, Italy*

After the publication of Diagnostic Guidelines of Juvenile Headache (1), a perspective multicenter study was conducted to verify the feasibility of application of a diagnostic flow chart in clinical practice.

Until now 23 Italian Juvenile Headache Centres participated to the study. A structured questionnaire was used for data collection. A 12-month observation period was established.

Preliminary data related to the first observation semester are reported (from September 1, 2002 to February 28, 2003).

1963 young patients (1033 females and 930 males), complaining of first time headache, were included. 5.8% of these were diagnosed with non classifiable headache according to IHS Criteria., 75.2% had a primary headache diagnosis, 10.1% had combined primary headache forms. The remaining 8.8% were classified with a secondary headache.

In all patients without risk factors for secondary and threatening headache, clinical history was collected, general and neurological examinations were performed and a headache diary was given. All the additional investigations indicated in the flow chart were done in patients with positive risk factors for secondary headaches. Arterial blood pressure measurement was done in 90.5% of patients, patient-family therapy in 82.8%, ocular visit in 71.8%, EEG in 64.2%, blood exams in 58.8%.

Although the above results are preliminary, the diagnostic flow chart proposed have received a large consensus among Italian experts of Juvenile Headache, thanks to sensitization and diffusion of recently published Guidelines.

Classification of headaches

P2D1

'Pseudomigraine' with temporary neurologic symptoms and CSF lymphocytosis (or HaNDL) is pathophysiologically similar to migraine with aura: results from an evoked potential and single fiber EMG study

Arnaud Fuma1[1], Michel Venheede[1], Laura DiClemente[1], Julie Jacquart[1], Pascuale Gerard[1], Alain Maertens de Noordhout[1] & Jean Schoenen[1]
[1]*Departments of Neurology and Neuroanatomy, University of Liège, Hospital Citadelle, Liège, Belgium*

Background Pathogenesis of HaNDL, so-called 'pseudomigraine', is not known, but the clinical phenotype resembles migraine with aura.

Objective We performed in a HaNDL patient an electrophysiological study searching for pathophysiologic features usually found in migraineurs: deficient interictal habituation of cortical evoked potentials, which can be corrected by high frequency repetitive transcranial magnetic stimulation (rTMS), and impairment of neuromuscular transmission on single fiber EMG (SFEMG).

Methods Using previously published methods, we performed the following studies: pattern-reversal visual evoked potentials (PR-VEP) before and after 10 Hz rTMS over the occipital cortex; intensity dependence of cortical auditory evoked potentials; and SFEMG in forearm muscles.

Results There was a clear potentiation of PR-VEPs (+22%) before rTMS, which was reversed to habituation (–28%) after rTMS. IDAP was markedly increased (ASF slope: 3.49 μV/10dB). On SFEMG the averaged MCD was abnormal (37.1 μsec) and 20% of fibers had a jitter superior to 40 μsec.

Conclusions This HaNDL patient presented electrophysiological abnormalities which are usually found in migraineurs, and for SFEMG chiefly in migraine with prolonged aura. Taken together, these results favour the concept that HaNDL is a migraine with aura variant and that it may be a channelopathy.

P2D2

Validation of criteria for migraine with aura in the IHS Classification 2nd Edition

Malene Kirchmann Eriksen*[1], Lise Lykke Thomsen[1] & Jes O1esen[1]
[1]*Danish Headache Center, University of Copenhagen and Department of Neurology, Glostrup University Hospital, Glostrup, Copenhagen, Denmark*

Objectives The diagnostic criteria for migraine with aura (MA) have been revised in the 2nd. edition of the International

Headache Classification. Here we present the study underlying the revision.

Materials and methods We tested several selected sets of diagnostic criteria on 141 MA patients with visual aura (IHC 1988) and 59 patients with other reversible visual disturbances. The diagnoses made according to the selected criteria were compared to the diagnoses according to the IHC 1988. The criteria with the highest sensitivity and specificity were chosen and they were validated on 137 MA patients with visual aura (IHC 1988).

Results The presence of at least two of the following characteristics were positively correlated to definite visual migraine aura 1) Homonymous visual symptoms including positive features (i.e. flickering lights, spots, lines) or negative features (i.e. loss of vision). 2) At least one symptom develops gradually over ≥5 min and/or different symptoms occur in succession. 3) Each symptom lasts ≥5 min and ≤60 min The sensitivity is (118/141) 84%(95% CI 79–89%), the specificity is (57/59) 97%(95% CI 95–99%). In the validation sample the sensitivity was 96%.

Conclusion The analysis resulted in a set of diagnostic criteria with high sensitivity and specificity compared to the IHC 1988. The criteria were subsequently included in the IHC 2nd Ed.

P2D3

Kinesophobia

Isabel Pavão-Martins*[1], Raquel Gi 1-Gouveia[1], Elsa Parreira[2] & Susana Borges[3]
[1]*Centro De Estudos Egas Moniz, Avenue. Professor Egas Moniz, Hospital De Santa Maria, Lisboa, Portugal,* [2]*Serviço de Neurologia, Hospital Fernando da Fonseca, Amadora, Portugal,* [3]*Serviço de Psiquiatria, Hospital Júlio de Matos, Lisboa, Portugal*

Objectives Patients with migraine often complain of intolerance to several sensory stimuli, namely smell and movement. We compared the impact of these stimuli in migraine.

Methods Consecutive patients whose headache fulfilled IHS Criteria for migraine were questioned concerning the impact of several stimuli (noise, smells, light, movement) on their migraine crises. An analogical scale(0–11.5 cm) was given to report the degree of intolerance to each stimulus during attacks.

Results Preliminary results were obtained in 57 patients(7 males) with an age average of 37 years. Most patients suffered from migraine without aura(68.4%) and the remaining 18 patients had migraine with aura.

The average scale scores were 9.2 cm for light intolerance and 9.8 cm for sound intolerance. Smell intolerance scored 7.4 cm and cough 6.2 cm. Head movements had high average scores with leaning forward scoring 9.5 cm and turning the head (slow shaking movement) scoring 9.8 cm, as much as sound intolerance. Responses to noise, light and head movements were highly correlated in the same patient.

Conclusions Aggravation of headache by head movements is a sensible symptom of migraine attacks and can be compared to classical photo and phonophobia. Kinesiophobia might be used as independent diagnostic criteria.

P2D4

Non-Infectious Sinus Headache (NISH): evidence for a new primary headache disorder

Eric Eross*[1] & David Dodick[1]
[1]*Mayo Clinic Scottsdale, AZ, USA*

Objective The objective of this study is to classify the headache types that self-diagnosed 'sinus-headache' sufferers experience.

Methods One-hundred subjects participated in this descriptive clinical study. All patients who believed they suffered from 'sinus headache' and were over 18 years-of-age were enrolled without exclusion. A detailed history and exam was performed in each patient, and patients were given a headache diagnosis based on the current IHS criteria.

Results Of the 100 self-diagnosed 'sinus headache' sufferers, 63% actually had migraine, 22% had migrainous headache, 1% had cluster, 1% had hemicrania continua, 3% had headache secondary to acute rhinosinusitis, and 10% had 'headaches not classifiable'. The 'headaches not classifiable' were characterized by a bilateral facial pressure of mild to moderate intensity associated with at least one cranial autonomic feature. Features suggestive of migraine were absent in all 10 cases.

Conclusions The majority (85%) of patients who believe they suffer from 'sinus headache' are actually suffering from either migraine headache or migrainous headache. Ten percent of patients suffer from a headache type, which is unclassifiable by the current IHS criteria. NISH is characterized by bilateral facial pressure, mild to moderate intensity, cranial autonomic symptoms, and the complete absence of migraine features.

P2D5

New diagnostic criteria for retinal migraine

Seymour So1omon*[1] & Brian Grosberg[2]
[1]*Headache Unit, Montefiore Medical Center,* [2]*Albert Einstein College of Medicine, Bronx, New York, USA*

Review of the literature reveals only 5 cases that fulfilled IHS criteria for retinal migraine. We recently reported 2 cases of prolonged (hours/days) fully reversible monocular defects during attacks of migraine with aura. Of the 37 cases of retinal infarction associated with migraine and sometimes referred to as retinal migraine, 34 occurred in patients who had migraine with aura. In the light of these data we propose the following change in the classification of retinal migraine.

1.4.1. Transient fully reversible monocular visual defects
- A. At least 2 attacks fulfilling B-C
- B. Fully reversible strictly monocular visual loss lasting:
  1. Less than 60 min
  2. More than 60 min

Confirmed by examination during attack or by patient's drawing of monocular field defect during attack.

- C Headache temporally associated with visual symptoms

D Normal ophthalmological examination outside of attack. Other causes of transient visual defects ruled out by appropriate investigations.

1.4.2. Permanent monocular visual defects induced by migraine.

A At least 2 prior attacks of migraine with aura

B Migraine with aura temporally associated with monocular visual symptoms.

C Permanent visual field defect confirmed by ophthalmologic examination.

D Other causes of retinal infarction ruled out by appropriate investigations.

P2D6

Phenotypic characterisation of the headache associated with pituitary tumours

Miles Jonathan Levy*[1], Manjit S. Matharu[1], Michael Powe11[2], Karim Meeran[3] & Peter J. Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square London UK,* [2]*The National Hospital for Neurology and Neurosurgery, Queen Square London UK,* [3]*Department of Endocrinology, Charing Cross Hospital, Loncon, UK*

Objectives To describe the range of phenotypic presentations of pituitary tumour-related headache.

Methods Patients presenting with pituitary tumour-related headache were assessed by a single headache specialist. Headache was classified according to IHS diagnostic criteria and the response to treatment observed.

Results Eighty-seven patients presenting with a range of tumour subtypes were included(63 females, 24 males). Prolactinomas(36%) and acromegalics(31%) were the commonest tumour types. Headache was unilateral in 72% of cases. Twenty-one tumours invaded the cavernous sinus, with 14(67%) reporting ipsilateral headache.

Pain was frontal in 87% and occipital in 25%. An IHS diagnosis of migraine was recorded in 78%. Other phenotypes included cluster headache ($n = 4$), SUNCT ($n = 3$), hemicrania continua ($n = 1$), idiopathic stabbing headache ($n = 1$) and tension-type headache ($n = 1$). Ten patients had unclassifiable phenotpyes and were labelled as secondary headache. Hypophysectomy improved headache in 55%. Somatostatin analogues relieved headache in 9 acromegalics. Dopamine agonists altered headache severity in 13 prolactinoma cases(8 improved, 5 exacerbated).

Conclusions Headache may be a prominent feature of pituitary tumours. This group of patients may lead to insights into the role of the cavernous sinus and Hypothalamic-pituitary axis in primary headache.

P2D7

Clinical characteristics of migraine in an Australian research registry: prospects for genetic studies

Rod Lea*[1,3], Dale Nyho1t[2], Sharon Quin1an[1] & Lyn Griffiths[1]
[1]*Genomics Research Centre, Griffith University,* [2]*Genetic Epidemiology Laboratory, Queensland Institute of Medical Research,* [3]*Institute for Molecular Systematics, Victoria University*

The Genomics Research Centre (GRC) in Australia has been recruiting volunteers to participate in molecular genetic studies of migraine since 1994. To date, our clinical registry includes 1306 subjects diagnosed with migraine based on the IHS criteria. Of this clinic-based group, 76.3% have been diagnosed with migraine with aura (MA), whilst 20.3% suffer migraine without the aura (MO). Utilising data from a headache survey of 6265 Australian twin individuals, Nyholt et al. used latent class analysis (LCA) to identify three major classes of headache (mild, moderate and severe) (1). Interestingly, the LCA migrainous phenotype (i.e. moderate and severe classes) was shown to have an increased heritability over the IHS-affected phenotype(0.41 vs. 0.33). Moreover, the relative risk for the 'severe' latent class of migraineurs in DZ twins (RR = 2.16) was larger than the risk for MA (RR = 1.77). Using data from the population-based twin sample we re-diagnosed (phenotyped) our GRC clinical sample under the new LCA criteria. This analysis showed 98.5% of the IHS-diagnosed migraineurs as being affected with migraine under LCA, with 78.5% being classified as 'severely' affected. Members of this 'severe' migraine class(868 MA and 157 MO) form a valuable target group for molecular genetic studies into this important disease.

References

1 Nyholt DR, Gillespie NA, Heath AC, Merikangas KR, Duffy DL, Martin NG 2003 Latent class analysis does not support migraine with aura and migraine without aura as separate entities. *Ann Neurol* (under review).

P2D8

Migraine disorder (IHS 1.7): an analysis of a large clinical sample in primary care

Michel Lanteri-Minet*[1], Christian Lucas[2] & Dominique Valade[3]
[1]*Pain Department Hôpital Pasteur CHU de Nice, France,* [2]*Neurology CHU de Lille, France,* [3]*Emergency Headache Center – Hôpital Lariboisière, France*

Objective Aim of this work was to study importance and characteristics of migraine disorder in primary care.

Methods Initial sample consisted of 2304 'migraine sufferers' seen in primary care. Structured questionnaire was administered to obtain information on diagnostic according to IHS criteria, headache history, medical history and medication use. Migraine disorder (IHS 1.7) patients were compared with migraine without aura (IHS 1.1) patients. Chi-2, Fisher, Student, Mann–Whitney tests were used for statistical analysis.

Results Among 'migraine sufferers', 2237 (97.1%) were migraine sufferers according to IHS criteria: 1737 with code 1.1 (77.6%) and 500 with code 1.7 (22.4%). Comparison of both groups indicated: lesser female predominance (75.5% vs. 81.3%, $p < 0.01$), lesser high blood pressure association (8.7 et 12.9%, $p < 0$; 01) lesser migraine familial antecedents (52% vs. 59.2%, $p < 0.01$) and lesser severity (frequency, intensity, functional impact) in 1.7 group. Medication use (acute and prophylactic) comparison indicated that the groups did not significantly differ.

Conclusion Prevalence of migraine disorder was high in migraine sufferers who consulted their GP. Contrast between

lesser severity of migraine disorder and absence of management difference between 1.1 and 1.7 groups could be related to the global undermanagement of migraine.

P2D9

Headache Spectrum: insight from the Landmark Study

Carl Dahlof*[1], Andy Dowson[2], Larry Newman[3] & Stewart Tepper[4], Ba'. Pham[5]
[1]*Gothenburg Migraine Clinic, Sweden,* [2]*Kings College Hospital, London, UK,* [3]*St. Lukes Roosevelt Hospital Center, New York, USA,* [4]*New England Headache Center, Stamford CT, USA,* [5]*GlaxoSmithKline, Missasagwa, Ontario, Canada*

Objective To examine the relationship between an individual's IHS diagnosis and her/his headache spectrum.
Methods Subjects presenting to primary care with a new history of migraine completed headache diaries over three months. An expert panel reviewed the diaries and assigned IHS diagnosis to each headache and each participant.
Results The assigned overall IHS diagnoses and headache spectrum of 377 patients with complete diaries are below.

Overall Diagnosis n(%)/HA types within overall Dx*	IHS1.1 176 (47%) %	IHS1.2 112 (30%) %	IHS1.7 67 (18%) %	IHS2.1 11 (2%) %	IHS13.0 11 (2%) %
IHS1.1	73	25	0.6	0	0
IHS1.2	0.5	58	0.5	0	0
IHS1.7	21	12	73	0	0
IHS2.1	4	3	20	93	3
IHS13.0	1	2	6	7	97

*Derived from multivariate analysis.

For headaches classified, respectively, as (IHS1.1,1.2,1.7), the percentage of headaches with moderate or severe pain at onset was (81%,75%,76%), with nausea or vomiting (70%,61%.9%), with sensitivity to light and sound (69%,55%.6%), aggravated by physical activities (77%,67%,46%), and headaches lasting >24 h (12%.5%.9%).
Conclusions The majority of patients presenting to primary care with headache have migraine. These patients each suffer a spectrum of headaches consisting mainly of different migraine types.

P2D10

Diagnostic value of pain characteristics and associated symptoms in the differential diagnosis of facial pain

Christian Wöber*[1], Karin Zebenholzer[1], Marion Vigl[1], Peter Wessely[1] & Çiçek Wöber-Bingöl[1]
[1]*Department of Neurology, University of Vienna, Vienna, Austria*

The aim of this study was to assess the sensitivity, specificity, positive and negative predictive value (PPV, NPV) of pain characteristics and associated symptoms in trigeminal neuralgia and primary ('atypical') facial pain.

We examined 97 consecutive patients referred for facial pain to a neurological tertiary care centre including a broad spectrum of disorders. We applied the IHS criteria and considered a sensitivity, specificity, PPV and NPV of ≥0.7 as clinically relevant.

We diagnosed trigeminal (or other types of cranial) neuralgia in 38%, primary facial pain in 27% and other disorders in 35% of the patients. In trigeminal neuralgia, the sensitivity and the NPV were ≥0.7 in all but one of 14 features, whereas the specificity was sufficient in three features (duration <2 min; quality sudden, intense, sharp; distribution along divisions of the trigeminal nerve) and the PPV in one feature (duration < 2 min) only. In primary facial pain, sensitivity and NPV were ≥ 0.7 in 12 and 14 of 16 features, respectively, whereas specificity was sufficient in six features only and PPV in none.

In conclusion, the majority of diagnostic criteria of trigeminal neuralgia and primary facial pain shows good sensitivity and NPV, but poor specificity and PPV.

P2D11

Prevalence and demographics of migrainous headache adults in a primary care setting: data from the Landmark Study

Stewart Tepper*[1], Carl Dahlof[2], Andy Dowson[3], Larry Newman[4] & Timothy A. Kuhn[5]
[1]*New England Headache Center, Stamford CT, USA,* [2]*Gothenburg Migraine Clinic, Gothenburg, Sweden,* [3]*Kings College Hospital, London, United Kingdom,* [4]*St. Lukes Roosevelt Hospital Center, New York, USA,* [5]*GlaxoSmithKline, Research Triangle Park, NC, USA*

Objective To characterize the adults meeting 1988 IHS criteria for migrainous headache.
Methods Adults with episodic headache presenting to primary care completed the HIT-6 and a headache survey. Physicians diagnosed patients as previously diagnosed migraine, newly diagnosed migraine (NDM), nonmigraine primary headache (NMPH), or secondary headache. NDM and NMPH subjects completed diaries for up to 6 headaches over a 3-month period. An expert panel reviewed the diaries and assigned an IHS diagnosis.
Results Of the 272 NDM subjects, diaries indicated that 31 (11%) met criteria for migrainous headache. Of the 105 NMPH subjects, 36 (34%) met criteria for migrainous headache. Of the 67 migrainous headache subjects, 47 (70%) were women, mean (± SD) age was 40 years (12), mean (± SD) HIT-6 score was 61 (8). Of the headache features recorded, 62% included at least 2 of the IHS pain features and only 8% included IHS associated symptoms.
Conclusions 34% of adults with episodic headache presenting to primary care met criteria for migrainous headaches but received a nonmigraine diagnosis. Demographics and headache impact of adults with IHS migrainous headache are consistent with those of migraine. Failure to report traditional IHS pain features and associated symptoms may account for the missed diagnosis.

P2D12

Different headache patterns of chronic migraine based on clinical data

Jasna Zidverc-Trajkovic*[1], Milija Mijajlovic[1], Aleksandra Pavlovic[1], Zagorka Jovanovic[1] & Nadezda Sternic[1]
[1]*Institute of Neurology, Clinical Center of Serbia, Belgrade, Serbia and Montenegro*

Chronic migraine is primary disorder that usually evolves from an episodic form. Although labeled by the same diagnosis, chronic migraine patients present by different headache patterns.

We analyzed headache features of 150 patients with chronic migraine. Based on patients' diaries and collected data, three different clinical subtypes were recognized. In the first subtype were 40 (26.7%) patients with frequent attacks. In the second subtype group 46 (30.7%) patients had continuous headache with several severe attacks monthly. The continuous headache without attacks were recorded in 64 (42.7%) patients thus forming the third group subtype. Statistical analysis underlined the differences between these three subtypes, especially in the second subtype. In this group chronic headache disorder started eight years earlier, the headache intensity was 2 points higher and the hemicrania with pulsatile pain and associated symptoms were more frequently recorded in comparison to other two groups.

The results of statistical analysis confirmed clinical impression of different headache patterns in our group of chronic migraine patients. Based on clinical data, it is hard to estimate the exact meaning of this difference. Further studies are necessary to highlight the possibility of different receptors or transmitters presented by different headache patterns of migraine transformation.

P2D13

Trigger factor headaches or migrainous disorders – a modification to IHS 1.7 diagnostic criteria

M. V. Francis*[1]
[1]*Headache and Migraine Research Centre, Kerala, South India*

Objective To propose a modification to I H S 1.7.
Methods 411 patients aged 20–40 years were studied over a period of 8 years. Most of them presented with recurrent attacks of activity affected headaches lasting less than 4 h and precipitated by 5 common I H S migraine triggers of this region and without I H S migraine diagnostic autonomic symptoms.
Results The common migraine triggers were Exposure to sunlight(357), Daytime bus travelling(204),Tension anxiety situations(84),Hunger or missing a meal at the right time(79) and Sleep disturbances(78).Associated autonomic symptoms were phonophobia alone in 127 and photophobia alone in 93. Activity was affected throughout the duration of headpain in 248 and for a short duration in 163. 342 patients had one of the parents or other siblings with migraine origin pain precipitated by same triggers. 89 reported motion sickness either at the time of consultation or sometime in the past. 41 had dizzy spells again precipitated by same triggers.
Conclusion This study concludes that recurrent activity affected headaches of less than 4 h duration precipitated by common I H S migraine triggers of a particular region without current I H S migraine autonomic symptoms with one migraine parent or sibling with one other migraine trait (motion sickness or dizzy spells) to be diagnosed as I H S 1.7.

P2D14

Basilar/sporadic hemiplegic migraine complicated by bilateral thalamic infarction in a young man: the concept of 'trinity' applied to headache?

Grazia Sances*[1], Carla Uggetti[2], Natascia Ghiotto[1], Maria Grazia Egitto[2], Cristina Tassorelli[1], Maurizio Versino[3,4], Filippo Maria Santorelli[5] & Giorgio Sandrini[1]
[1]*Headache Treatment and Diagnosis Centre, University Centre for Adaptive Disorders and Headache (UCADH), Pavia, Italy,* [2]*Department of Neuroradiology, Pavia, Italy,* [3]*Eye Movement and Vestibular Laboratory, IRCCS C. Modino Institute of Neurology, Pavia, Italy,* [4]*Department of Neurological Sciences, University of Pavia, Pavia, Italy,* [5]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

Literature data suggest that many patients with familial hemiplegic migraine (FHM) also fulfil International Headache Society (IHS) criteria for basilar migraine. Migraine with aura-affected 42-year-old-man case report. His mother suffered from migraine without aura. He developed typical basilar symptoms consistently associated with right hemiparesis lasting 30–60 min and followed by impairment of consciousness for at least 2 h, followed by a diffuse throbbing headache lasting 24 h (4 attacks/month). Blood tests (including the more common prothrombotic risk factors), EEG, transcranial Doppler and transthoracic echocardiography were normal; however, cerebral MRI showed a left hypothalamic ischemic lesion. In 2000 he developed a typical attack, accompanied by a downward gaze paralysis, which persisted after pain resolution. Ocular motility study demonstrated an alteration of the rostral interstitial nucleus of the medial longitudinal fasciculus and cerebral MRI showed a bilateral thalamic infarction. Transesophageal echocardiography was normal and cerebral angiography revealed normal basilar and posterior cerebral arteries. Search for mutations for FHM1, CADASIL and MELAS was negative.

Our patient was originally diagnosed as suffering from basilar migraine. According to the preliminary drafts of the second edition if the IHS classification, most of his attacks will be classifiable as 'sporadic hemiplegic migraine'. The appearance of bilateral thalamic infarction following a headache attack adds a third diagnosis: migrainous infarction.

This study was supported by a grant from the Italian Ministry of Health (RC 2002).

History of headaches

P2E1

Cluster headache from a historical perspective

Giorgio Zanchin*[1,2], Filippo Dainese[2], Federico Mainardi[2], Carlo Lisotto[2] & Ferdinando Maggioni[2]
[1]*Section of History of Medicine, Department of Neurosciences, University of Padua, Italy,* [2]*Headache Center, Department of Neurosciences, University of Padua, Italy*

Although the identification of this headache is relatively recent and the term 'cluster headache' (CH) dates back to 1952, its first descriptions may possibly be traced back more than two hundred years. However, until the XIX century very rare reports could have been diagnosed as CH. This has prompted the present study. We analyzed 6708 clinical records of our Department between the years 1932–50; among the 242 diagnosis of headache, no CH were identified. Since in those time CH patients could have received such diagnosis as Sluder's or Charlin's syndrome, we also reviewed the clinical records (n = 6594) of our ORL Department. Out of 69 patients with diagnosis of headache, only 2 cases were fitting with the CH diagnosis. Furthermore, a sample review (years 1949–50) of clinical records of Internal Medicine (n = 1690) and of Ophthalmology (n = 984) yielded no CH cases. Considering the limited diagnostic facilities of that time, it is highly improbable that a CH patient would not be admitted to the ward. Our investigation, along with the recent and noticeable gradual change in the male/female ratio from 6.2 : 1 before 1960 to 2.1 : 1 during the nineties, poses the question whether CH could be connected with life-style modifications or other changes that have mostly occurred during the two last centuries.

P2E2

The migraine personality: American headache research in the early 20th century

Joanna Kempner*[1]
[1]*Department of Sociology, University of Pensylvania, Philadelphia, USA*

In the early to mid 20th century, migraine was understood as a vascular and psychosomatic condition prominent in women, the intelligentsia, and others who 'overused' their mind. Using a variety of materials, including published medical literature of the era and archives of prominent migraine researchers, this historical analysis examines how researchers conceptualized migraine patients as a certain type of person, embodying a 'migraine personality.' The male migraine personality was described as ambitious, successful, perfectionist and efficient. The migraine personality was less favorable when applied to women, who were often described as unwilling to accept the female role, sexually frigid, or even psychopathic. This presentation examines the social and intellectual environment of the time, including the research of Harold G. Wolff, the increasing acceptance of psychology, metaphorical qualities associated with the vascular system, efficacy of ergotamine, and class and gender norms. Theories of migraine personality declined in influence in the 1960s as researchers discovered underlying biological correlates with the condition and improved treatment. Population based studies also failed to support theories of a migraine personality. This analysis demonstrates how early 20th century theories of migraine reflected other issues of importance during the time.

P2E3

Leao's spreading depression – 60 years: from a serendipic and mysterious experimental event to a fashionable hypothesis for some neurological disorders

Hélio A. G. Teive*[1], Pedro Andre Kowacs[1], Elcio Juliato Piovesan[1] & Lineu Cesar Werneck[1]
[1]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil*

LSD was described by Aristides Leao, a Brazilian neurophysiologist at Harvard University in 1943, under supervision of Professor Hallowell Davis and Dr Arturo Rosenblueth. Dr Leão and Dr Rosenblueth were studying the electrical activity in the brains of rabbits under anaesthesia. Dr Leão started the experiment and, following the stimulation of the cortex, there was a most unexpected and contradictory result: '*the activity at the nearest pair of recording electrodes did not increase but ceased almost entirely*'. Dr Davis was called in consultation and he said: . . . '*nothing resembles a new phenomenon as much as a good artifact*'. In 1944 Leao published the seminal paper titled 'Spreading depression of activity in the cerebral cortex' (Journal of Neurophysiology, 1944, 7:359–390), becoming internationally known and the phenomenon was called 'Leão's spreading depression'. In 1945, Leão and Morrison suggested that cortical spreading depression could be involved in the pathophysiology of migraine. This suggestion has been corroborated by other researchers in the last few years. Currently several studies on LSD confirm that this phenomenon plays an important role in some neurological disorders including migraine, transient global amnesia, cerebrovascular disorders and head injury.

P2E4

Evolution of diagnosis and disability in a headache sufferers cohort over time

Fatima Nachit-Ouinekh*[1,2], Jean-Francois Dartigues[2], Patrick Henry[3], Virginie Chrysostome[2], Christophe Sourgen[2] & Abdelkader El Hasnaoui[1]
[1]*GlaxoSmithKline Laboratory, Marly Le-Roi, France,* [2]*INSERM U593, Bordeaux, France,* [3]*Pellegrin Hospital, Bordeaux, France*

Background Despite clear and precise criteria for the diagnosis, migraine and other episodic headache are still a heterogeneous disease.
Objective To describe the evolution of self reported headache symptoms, of the diagnosis and of the quality of life over time.
Methods Hemicrania cohort is a subproject of Gazel cohort study conducted on 20 000 volunteers working in 'Electricité et Gaz de France' company. In 1993, 2500 headache and 2500 non headache sufferers were randomly chosen from Gazel to constitute Hemicrania cohort. Those who participate in 1993,

were contacted again in 1994 and in 2003. A mailed questionnaire comprising socio demographic, self reported headache symptoms and quality of life were sent to all the subject. The diagnosis of headache was based on the IHS criteria. The diagnosis will be evaluated at the 3 date point and the stability will be measured by a kappa coefficient. The evolution of quality of life will be studied.
Results In 1993, 2053 (82%) headache sufferers and 1757 (70%) non headache sufferers participated, 1735 (69%) headache sufferers and 1541 (62%) non headache sufferers participated in 1994 and 1295 (75%) headache sufferers and 1158 (75%) non headache sufferers participated in 2003.

P2E5

Relationship between chewing habit, eccentricity of the lower jaw and headache

Shoji Nakamura*[1], H. Tamagawa[2], T. Sasaki[2], S. Nakamura[2], A. Kyuma[2], H. Suzuki[2], K. Nagahara[3], J. Teramoto[4], H. Nagasaka[1], T. Matsukubo[1] & T. Ishikawa[5]
[1]*Department of Epidemiology and Public Health, Tokyo Dental College, Tokyo, Japan,* [2]*Bio-Occlusion Research Center,* [3]*Department of Orthodontics, Aichi-Gakuin University,* [4]*Teramoto Neurology Clinic, Nagoya, Japan,* [5]*Department of Operative Dentistry, Tokyo Dental College, Tokyo, Japan*

Objective This study investigated whether an unilateral chewing habit is related to the occurrence of a headache.
Methods We used 1596 patients who were visiting a dental clinic. Chewing habits were classified into unilateral chewing on the right, unilateral chewing on the left and bilateral chewing. The eccentricity of the lower jaw to the maxillary medial line was classified into the right-side eccentric position (EP-R), the left-side eccentric position (EP-L), and the N-L position. The medical specialist diagnosed the headaches and classified them into migraine or tension headaches. The existence of a headache was taken as the self-report within the past year.
Results Patients with either right- or left-side eccentric position showed a significantly higher frequency unilateral chewing ($P < 0.001$). Patients with unilateral chewing had significantly more headaches than patients with a bilateral chewing habit, and the frequency of migraine headaches was higher than tension headaches ($P < 0.001$). Only the N-L patients had more tension headaches, while patients with EP-L or EP-R reported more migraine headaches irrespective of the existence of the eccentricity of the medial line.
Conclusion These results suggest that unilateral chewing is related to both migraine and tension headaches.

P2E6

The migraine of Giorgio de Chirico

Ubaldo Nicola*[1] & Klaus Podoll[2]
[1]*Chair of Philosophy, Pavia. Italy,* [2]*University of Technology, Aachen, Germany*

The Italian painter Giorgio de Chirico (1888–1978), founder of the style of 'metaphysical art', suffered from migraine and used migrainous visual hallucinations as inspiration for some of the more striking details of his work. An analysis of his iconography from a neurological point of view demonstrates that several peculiar features of his metaphysical style bear a striking similarity to the phenomenal features of migraine with aura, namely the headache of the acute migraine attack, photophobia, scotomas, elementary geometric and complex visual hallucinations, visual illusions and somesthetic symptoms such as macrosomatognosia and out-of-body experiences.

Education for doctors or patients

P2F1

MIDAS questionnaire pitfalls

Andrew Blumenfeld*[1] & Marie Tischio[1]
[1]*Kaiser Permanente, San Diego, CA, USA*

Background MIDAS questionnaires have become the standard for assessing disability and outcomes in patients with primary headache disorders. The methodology for completing this self-administered form is key to accurate data collection.
Objective To determine if patients are able to accurately complete this questionnaire and to assess which questions produce errors in completion.
Methods A prospective review for accuracy of self-completed MIDAS questionnaires was performed, in 130 patients with a primary headache disorder undergoing assessment in a headache clinic.
Results 61 (47%) were inaccurately completed. Of these inaccurate questionnaires 39 (64%) underestimated the number of headache days only counting their most severe headache days; 16 (25%) double counted the days in questions 1 and 2 and/or questions 3 and 4; and 6 (10%) had inadequate data to complete all the fields of the form.
Conclusions There are too many errors to allow patients to self-administer this questionnaire. Patients have difficulty in comprehending the questions that are mutually exclusive and recording all of their headache days. Headache diaries are essential to accurately complete the questions. The MIDAS questionnaire is useful only if the provider reviews the data with each patient and clarifies the entries.

P2F2

Depacon and P.O Depakote ER for treatment of status migrainosis and prevention of episodic migraine

Charles Popeney*[1]
[1]*Fort Bend Neurology, Sugar Land, Texas, USA*

Objective To assess the efficacy and safety of I.V Depacon (Valproate Sodium) to abort Status Migrainosis.
Design/methods 31 consecutive patients ((27/31) female (4/31) male) were included in this retrospective study. All patients met the IHS criteria for status migrainosis. All patients received 1000 mg I.V Depacon over 5–10 min Pain free status was assessed. Those patients that did not achieve

pain free status over the time of infusion were given additional Depacon 500 mg I.V. q. 8 h for 5 additional doses. Adverse events and side-effects were recorded.

Results 71% of patients received pain free status after one time 1000 mg Depacon or additional 5 Depacon doses as outlined in our protocol. 2 patients had recurrence of their status migrainosis. There were no adverse events seen with I.V. Depacon.

Conclusions Depacon I.V is safe and effective for treatment of status migrainosis. Using the Depacon protocol we chose was highly efficacious.

P2F3

A single question that can provide a rough index of MSQOL

Sadayoshi Ohbu*[1], Hisaka Igarashi[2], Hiroyuki Okayasu[3], Fumihiko Sakai[2], Joseph Green[4], Richard F. Heller[5], Shunichi Fukuhara[6] & Donald L. Patrick[7]
[1]*Department of Neurology, Yokohama Municipal Citizen's Hospital,* [2]*Department of Medicine, Kitasato University,* [3]*Division of Neurology, St.Luke's International Hospital,* [4]*Graduate School of Medicine, University of Tokyo,* [5]*School of Epidemiology and Health Sciences, School of Medicine, University of Manchester,* [6]*Department of Epidemiology and Health Care Research, Kyoto University Graduate School of Medicine and Public Health,* [7]*University of Washington, Seattle*

Quality of Life among patients with migraine can be measured with the MS-QOL, aan instrument with 20 questions. While testing the Japanese version of that questionnaire, we found that responses to a single question about the eoverall effects of headaches were closely associated with responses on the equestionnaire. eWe studied 57 patients with a definite diagnosis of migraine. With their tinformed consent, all were interviewed and completed the MS-QOL. And we also fasked the patients to summarize the effect of their headaches by responding kto a single question: 'How different would your life have been without fheadaches?' (In Japanese, the question clearly refers to both the past and athe present, but not to the future.) They chose one of five options: ecompletely different, very different, somewhat different, not much mdifferent, and not at all different. Their total scores on the MS-QOL ranged lfrom 3.33 to 83.3, and their responses to the single question were closely oassociated with their MS-QOL scores (ANOVA, $P < 0.001$).

We believe that patients' responses to this single question can provide a arough index of headache-related quality of life, which may be particularly uuseful during the initial evaluation of patients thought to have migraine.

P2F4

Migraine disability in the workplace

Charles Popeney*[1] & Joe Simmons[2]
[1]*D.O.PA., Sugarland, TX, USA,* [2]*BS*

Objective To assess the burden, diagnosis, and treatment of headaches in the workplace.

Methods A 20-question survey was completed. 67 participants were queried. Disability questions included: Disabling headaches? Function at 100% or 50% with your headaches? Seen a doctor for your headaches? Think you have sinus headaches? Neck pain? Participants asked if they took triptans and their response.

Results 56 migraines with or without aura, 11 nonmigraine. Results tabulated on migrainous participants:

Average years with headaches 9.5 years
Severity scale (1–10) average: 5
Average duration 28 h
Average headaches monthly 6
82% cannot work adequately
89% function less than 50%
14% to ER
44% headaches were disabling
58% saw physician specifically for headache
69% attributed headaches to sinus
59% 'sinus headache' increased to severity that reduced their functioning
27% tried a triptan
93% triptan helped

Conclusion A disparity exists between high disability and low percentage of participants seeking care. (Majority of patients did not see a physician specifically for headache) This mismatch accounts to lost productivity in the workplace. The majority of participants had 'sinus headache' and neck pain which may lead to incorrect self-diagnosis. Direct awareness endorsed by the employer has the potential to correct the above disparity.

P2F5

Expanding headache awareness in Italy

Paolo Martelletti*[1]
[1]*Italian League of Headache Patients*

The Italian League of Headache Patients (LIC) is a lay, nonprofit organization (Registered charitable organization No. AC/CF8498–9 February 2002) created in February 2000 by a group of headache sufferers and researchers involved in this area of clinical medicine.

LIC is affiliated with Italian Society for the Study of Headache (SISC, http://www.sisc.it) and is member of World Headache Alliance (WHA, http://www.w-h-a.org).

The mission of the Italian League of Headache Patients is:

- To heighten the awareness of headache disorders within the general population, emphasizing the importance of taking care of headache patients (prevention of habit risk factors) and not just treating them (drug therapy).
- The dissemination of information on the availability of specialized headache centres on a regional level and increasingly direct patients towards them.
- To increase media awareness through press conferences on the social impact of headache disorders.
- Provide financial support towards training for young doctors in the clinical management of headaches.

- Raise the awareness of politically relevant individuals within the field of health or in institutions responsible for the management of bodies dedicated to headache.

Main Objectives

- To increase social awareness of headache disorders through national information campaigns on the risk of headaches and the pathologies of painkiller abuse and to de-incentivate the 'miracle cure' type information which minimalises the importance of headache disorders in the eyes of the public and the scientific world taking on the appearance, in fact, of a commercial message without concern for community health.
- Influence the national scientific world so that resources and programs can be redirected from the area of headache physiopathology to that of disability, of direct and of intangible costing, of pharma-economy, of a large epidemiological evaluation of workplace loss of productivity. All factors related or caused by headache disorders. In brief, the definition of 'Global Headache Risk'.
- Increase the awareness of pharmaceutical companies and invest resources in new programs for perfecting new and effective drugs for headache prophylaxis, particularly for migraine and chronic daily headaches. The failure of therapy or the presence of unbearable side-effects from currently available drugs represents one of the most frequent causes of patient distancing from the medical area.

P2F6

Outcomes measurement and assessment of an innovative education program for headache management

Meenal Patwardhan*[1], Gregory Samsa[1] & David Matchar[1]
[1]*Duke Center for Clinical Health Policy Research, Durham, USA*

Background Despite the burden of migraine and availability of effective treatment, the management of migraine remains suboptimal. In this context the American Headache Society (AHS) has developed a continuing medical education (CME) program for primary care providers headache management. This education effort addresses barriers to optimal headache care using a multimedia format. It is intended to enhance physician performance, and improve patient outcomes.
Objectives The objective is to assess physician performance in headache care, the degree to which participation in the CME increases conformance of belief, knowledge, and action, and to examine the durability of education effects.
Research design Using a prospective case-control research design, we will evaluate 100 attendee and 100 nonattendee physicians through the US, and 100 attendee and 100 nonattendee physicians in North Carolina.

Outcome measures Questionnaires and vignettes will assess physician knowledge at baseline, and post-CME: immediately, 3 months, and 9 months. Standardized patients (patient actors) will evaluate physician interaction with patients 9 months after the CME. They will also assess prescription patterns and serve as a proxy for patient satisfaction.

Data analysis We will compare questionnaire/vignette data from attendees and nonattendees, pre and post-CME – immediately and over time, and compare questionnaire responses with SP data at 9 months.

P2F7

Focused migraine educational intervention improves the impact of migraine and quality of life in a provider group setting

Timothy Smith*[1]
[1]*Mercy Health Research, St. Louis, MO, USA*

Objective To demonstrate the value of a complete migraine educational intervention in a provider group setting.
Methods Patients having headache/migraine medical claims were enrolled in a migraine education program. Baseline, 3-month, and 6-month assessments included questions on patient satisfaction and headache impact (HIT-6™). Quality of Life was assessed using the Migraine Specific Quality of Life Questionnaire (MSQ) at Baseline and 6-months.
Results Results reflect interim analysis to quantify the impact of the initiative. Of the 283 enrolled, 199 patients reported data at Baseline, 3-months and 6-months. More patients reported satisfaction with care at 6 months than baseline (65.1% vs. 30.2% $p < 0.0001$; $n = 189$); headache impact was reduced with mean HIT-6 scores decreasing from 62.4 to 58.4 (Baseline to 6 months $p < 0.0001$; $n = 199$). Each dimension of migraine quality of life showed clinical and statistical improvement from Baseline: Role Restrictive 56.45–67.45, Role Preventive 73.14–81.01, and Emotional 61.98–72.56 ($P < 0.0001$; $n = 199$).
Conclusion A focused migraine educational intervention conducted in a provider group setting is effective in improving outcomes for headache patients.

P2F8

One-year follow-up of a self-administered intervention for headache management: a self-efficacy approach

Dale Bond*[1], Susan Baggaley[2], Kathleen Digre[2], Carla Rubingh[2] & Lynne Durrant[3]
[1]*Community Health Education, Virginia Commonwealth University, Richmond, Virginia,* [2]*Neurology, University of Utah, Salt Lake City,* [3]*Health Promotion and Education, University of Salt Lake City, Utah*

Objective To evaluate the longitudinal impact of a videotaped program designed to strengthen self-efficacy related to four headache management behaviors: (1) headache diary use; (2) limiting medication overuse; (3) relaxation techniques; and (4) stretching exercises.
Methods Primary headache disordered patients by IHS criteria ($n = 38$), randomly assigned to one of 3 groups: (1) self-efficacy videotape treatment (SET; education + behavioral skills training) (2) information-only videotape treatment (IOT; education), and (3) waiting-list control (WLC; no treatment), were mailed questionnaires completed one year prior at 1-month postintervention. Current follow-up data regarding self-efficacy, behaviors, quality of life, disability, abortive

medication usage, and headache activity were compared to previous data using repeated measures ANOVA.

Results SET participants reported both higher self-efficacy scores than the IOT participants ($P = 0.006$) and more frequent use of the headache diary and relaxation techniques as compared to the IOT ($P = 0.009$ and 0.05) and WLC ($P = 05$ and .02) groups, respectively. No other time-related effects were observed.

Conclusions Although SET was effective in comparison to both the IOT and WLC regarding headache-management self-efficacy beliefs and related behaviors over time, single exposure may be insufficient to effect long-lasting behavior change and concomitant changes in headache activity.

P2F9

Feasibility of patient-to-patient support in the nonpharmacological prevention of migraine attacks

Saskia Mérelle*[2,1], Marjolijn Sorbi[2] & Jan Passchier[1]
[1]*Department of Medical Psychology and Psychotherapy, Erasmus Mc, Rotterdam, the Netherlands,* [2]*Department of Health Psychology, Utrecht University, Utrecht, the Netherlands*

Behavioural treatments for migraine are efficacious to reduce attack frequency and may assist in the preventive treatment of migraine (Campbell et al. 2000). Home-based behavioural treatments are strongly advocated and cost-effective (Penzien et al. 2002). Studies with 'lay leaders' (Lorig et al. 2001) indicate that such an intervention is strengthened by the feedback and motivational assistance of experienced patients. Our pilot study demonstrated that a home-based group training, focused on neutralising migraine triggers by proactive application of relaxation and other lifestyle changes, is feasible. It also showed that migraine frequency was reduced in the majority of the patients (>60%) and quality of life improved. Five patients were selected based on their skills in preventing migraine attacks and their abilities to coach a group member. First results of those patient trainers confirm that migraine patients can successfully coach their fellow patients. The pilot also detected important qualities of successful patient trainers for our RCT.

P2F10

Rationale for migraine prophylaxis in headache specialist daily practice

Dominique Valade*[1], Anne Aubertin[1], Jean François Doubrère[1], Philippe Baud[1], Serge Iglesias[1], F. Dubas[1], Alain Serrie[1], Alain D. Tehindrazanarivelo[2] & Jean Marc Visy[1]
[1]*Emergency Headache Center, Lariboisiere Hospital,* [2]*Service de Neurologie Hôpital Lariboisière, Paris, France*

Rationale Management of migraine prophylaxis is a frequent cause of referral from GP to headache specialist.

Objectives To identify the rationale for: (1) introduction, change and continuation of migraine prophylaxis; (2) drug choice.

Design and setting Cross sectional descriptive study in outpatient clinics from 2 areas (Paris and Champagne Ardennes), in university hospital ($n = 3$), General hospital ($n = 3$), and private practice ($n = 3$).

Participants 9 neurologists and 173 consecutive patients (44 ± 14.13 years, 126 female and 47 male, MwoA = 144, MwA = 29).

Main outcome measures Frequency distribution of prophylaxis decision, criteria for each decision, and criteria for drug choice.

Results 114 (65.89%) were under prophylactic treatment. It was continued for 76 (66,66%), mainly because of good efficacy (69/76), and modified for 38 (33.33%), mainly for lack of efficacy (27/38). Among the remaining 59 patients, prophylaxis was introduced in 55 (93.22%), mainly for high frequency (47/55). Drug choice was based on specialist preference for 96/169 (56.80%), comorbidity in 50 (29.58%) and associated condition in 20 (11.83%).

Conclusion Referral to headache specialist for migraine prophylaxis was generally appropriate.

Introduction changes and continuation of prophylaxis were based on scientific rationale. Drug choice depends mainly to specialist preference, which scientific rationale needs further investigations.

P2F11

Women and gynecologists: do they talk about migraine?

Joao Jose Carvalho*[1]
[1]*Hospital Geral de Fortaleza, Neurology Department, Fortaleza, Brazil*

Objectives Migraine disproportionately affects women and recent advances highlight the advantage of an early therapeutic approach. Unfortunately women with migraines are diagnosed after almost 5 years of crises when they had had at least four gynecologist consultations. This study analyses how women and gynecologists approach the migraine subject in their routine appointments.

Methods We interviewed 140 women with migraine without aura (IHS88). Age, headache characteristics, number of times patient complained spontaneously about her pain, reasons for complain or not and gynecologist attitude, were record.

Results Visiting gynecologists every 13.7 months, only 37% of the patients had complained about migraine and only 3% of their gynecologists had asked about headaches or migraine. The reasons for complain were: association of headaches with menstrual cycle (25%), headache intensity (18%) or association of headaches with contraceptives (4%). The explanations for never complain were: lack of relationship between gynecologists and headaches (70%), not judging necessary to talk (7%) or because they were never asked about (6%).

Conclusions The majority of women doesn't speak about their migraines with gynecologists and vice versa. This emphasize the urgent need of effective educative actions toward women and gynecologists, aiming to anticipate the migraine diagnosis and the early therapeutic approach.

Tension-type headache

P2G1

Patterns of experimentally induced pain in pericranial muscles in patients with tension-type headache and matched controls

Peter Thede Schmidt-Hansen*[1], Peter Svensson[2], Troels Staehelin Jensen[3], Thomas Graven-Nielsen[4] & Flemming Winther Bach[5]
[1]*Department of Neurology, Hospital of Viborg, Viborg, Denmark,* [2]*Danish Pain Research Center and Department of Neurology, Aarhus University Hospital, Aarhus, Denmark,* [3]*Department of Clinical Oral Physiology, Dental School, University of Aarhus, Aarhus, Denmark,* [4]*Department of Maxillofacial Surgery, Aarhus University Hospital, Aarhus, Denmark,* [5]*Center for Sensory–Motor Interaction, Aalborg University, Aalborg, Denmark*

Aim Investigation of experimentally induced pain patterns in episodic (ETT), chronic tension-type (CTT) headache patients and control subjects.
Methods 24 ETT, 22 CTT patients, and 26 age- and gender matched control subjects participated. 0.5 mL hypertonic (5.8%) saline was injected into masseter, temporalis and anterior tibialis muscles. Headache patients were examined twice; with and without headache; controls were also examined twice. Pressure-pain thresholds (PPT), perceived pain intensity on electronic visual analogue scale (VAS) and drawings of saline-evoked pain areas were used for quantitative assessment. Data were analysed with ANOVAS.
Results PPTs, saline-evoked VAS pain scores and pain areas were significantly different between headache patients and controls ($P < 0.001$). Headache patients demonstrated significantly lower PPTs, higher VAS pain scores and greater pain areas in all the tested muscles ($P < 0.05$). There were no differences between ETT/CTT patients and no differences with or without headache. Analyses indicated significant gender differences for PPTs in all groups ($P < 0.05$) and CTT patients VAS pain scores ($P < 0.05$).
Conclusion The study demonstrated gender differences in deep pain sensitivity and generalized muscular hyperalgesia, unrelated to actual headache status in ETT/CTT patients.

Supported by Viborg Amt, Vestdansk Sundhedsvidenskabeligt Forskningsforum, Rosa and Asta Jensens Fond.

P2G2

Increased muscular pain sensitivity in cephalic region but not in extremity in patients with chronic tension-type headache

Sait Ashina*[1], Ludmilla Babenko[1], Rigmor Jensen[1], Messoud Ashina[1], Walter Magerl[2] & Lars Bendtsen[1]
[1]*Department of Neurology and Danish Headache Center, Glostrup Hospital, University of Copenhagen, Glostrup, Copenhagen, Denmark,* [2]*Institute of Physiology and Pathophysiology, Johannes Gutenberg University, Mainz, Germany*

Objectives We aimed to assess and compare mechanical and electrical pain thresholds in trapezius and anterior tibial muscles between patients with chronic tension type headache and healthy controls.
Methods Twenty patients and 20 controls were included. Local tenderness was assessed by pressure-controlled palpation, mechanical pain thresholds by algometry and intramuscular electrical pain thresholds by needle electrodes. Three types of electrical stimulation were used: single pulses, 2 Hz and 100 Hz.
Results Pain thresholds to three types of electrical stimulation in trapezius muscle were significantly lower in patients than in controls (ANOVA, $P = 0.04$), while there was no difference between groups in anterior tibial muscle (ANOVA, $P = 0.99$). Post-hoc analysis did not show any significant interaction between patients and controls in relation to each type of stimulation. In trapezius muscle, local tenderness score ($P = 0.007$) and pressure-pain thresholds ($P = 0.03$) were significantly lower in patients than in controls. In anterior tibial muscle, there was no difference between groups in either local tenderness ($P = 0.34$) or pressure-pain thresholds ($P = 0.19$).
Conclusions This study demonstrates increased intramuscular pain sensitivity in cephalic region but not in extremity in patients with chronic tension-type headache.

P2G3

Glyceryl trinitrate may trigger endogenous nitric oxide production during immediate experimental headache in patients with chronic tension-type headache

Messoud Ashina*[1], Henrik Simonsen[2], Lars Bendtsen[1] & Jes Olesen[1]
[1]*Department of Neurology and Danish Headache Center, Glostrup Hospital, University of Copenhagen, Glostrup, Copenhagen, Denmark,* [2]*Department of Clinical Biochemistry, Statens Serum Institute, Copenhagen, Denmark*

Objectives To investigate plasma levels of citrulline and arginine as markers of NO production after infusion of the NO donor, glyceryl trinitrate (GTN).
Methods We recruited 16 patients with chronic tension-type headache and 16 healthy controls. The subjects were randomly allocated to receive 0.5 μg/kg/min GTN or placebo over 20 min Patients were examined on headache free days. Blood samples were collected at baseline and 60 min after start of infusion.
Results Both patients and controls developed stronger immediate headache on the GTN day than on the placebo day ($P < 0.05$) and the headache was more pronounced in patients than in controls ($P = 0.02$). Plasma levels of citrulline increased significantly 60 min after start of GTN infusion compared to placebo infusion in patients ($P = 0.01$) but not in controls ($P = 0.50$). Plasma levels of arginine were unchanged in both patients and controls ($P > 0.05$).
Conclusions We suggest that GTN induced immediate headache in patients with chronic tension-type headache is due to stimulation of endogenous NO synthesis and that immediate headache could be explained by direct effect of NO on perivascular sensory afferents or NO-induced arterial dilatation, or both.

P2G4

Muscle strain is involved in tension-type headache

Merete Bechmann Christensen*[1], Lars Bendtsen[1] & Rigmor Jensen[1]
[1]*Danish Headache Center, University of Copenhagen and Department of Neurology, Glostrup University Hospital, Copenhagen, Denmark*

The aim of the present study was to investigate the impact of static contraction of the shoulder- and neck muscles in tension-type headache patients.

Twenty patients with episodic tension-type headache and 20 controls were examined using a placebo-controlled, cross-over design. The active procedure consisted of 30 min of static contraction (10% of maximal force) of the trapezius muscle and the placebo procedure consisted of a similar contraction of the anterior tibial muscle. Tenderness scores, pressure pain detection thresholds and headache were evaluated before and after the static work.

Pericranial tenderness increased significantly more in patients than in controls after the active procedure ($P < 0.04$) but not after the placebo. Pericranial tenderness was higher after the active procedure than after the placebo in both groups (patients, $P < 0.08$, controls, $P < 0.07$). Sixty percent of the patients and 20% of controls developed headache after the active procedure, and 50% of the patients and none of the controls after the placebo. There was no significant difference between the two procedures in patients ($P < 0.73$) or in controls ($P < 0.13$).

Tension-type headache patients are more liable to develop shoulder- and neck pain in response to static work in this region than healthy controls, indicating increased pain sensitivity in the cranial region.

P2G5

Episodic tension-type headache (ETTH): evidence of prolonged disability from a placebo-controlled comparison of aspirin and paracetamol

Timothy Steiner*[1], Ralph Lange[2] & Michael Voelker[2]
[1]*Division of Neuroscience, Imperial College London, London, UK,* [2]*BG Consumer Care, Bayer AG, Leverkusen, Germany*

It is generally believed that ETTH is rarely disabling. It does not, usually, provoke medical consultation but is self-treated with OTC analgesics.

In a double-blind RCT, 638 adults with ETTH (but not migraine) by IHS criteria were recruited from the general population. They treated one moderate or severe episode with aspirin (ASA) 500 or 1000 mg, paracetamol (PAR) 500 or 1000 mg, or placebo (PLA). The primary efficacy analysis is published elsewhere ($N = 542$ ITT). Amongst secondary variables was functional impairment at baseline (from 0 [normal] to 3 [cannot do anything]) and over 24 h post-treatment.

Mean baseline headache intensity was 57–61 mm on 100-mm VAS with 72.0% of subjects ($n = 390$) reporting functional impairment (ASA1000: 77.7%; ASA50: 73.0%; PAR1000: 69.4%; PAR500: 75.2%; PLA: 65.2%. Time-to-recovery to normal function, recorded by 311 subjects (79.7%), was 11.9 h overall (mean; [9.4 median]) and treatment-dependent: ASA1000: $n = 63$ (9.9 [4.0]); ASA500: $n = 58$ (11.8 [9.9]); PAR1000: $n = 55$ (11.2 [5.7]); PAR500: $n = 61$ (13.6 [13.5]); PLA: $n = 74$ (13.8 [10.1]). Distributions were skewed by a few subjects reporting times of 37–54 h.

Thus at least 28% of subjects with ETTH remained functionally impaired for 9.4 h, even with rescue medication allowed after 2 h (taken by 15.5–16.2% on ASA, 19.8–25.7% on PAR, 29.5% on PLA).

P2G6

Migraine and quality of life: a comparison with tensional-type headache

Xiomara Betancourt*[1], Alix Padron[1] & Miguel Lainez[1]
[1]*Clínica de Cefaleas, Unidad de Neurología, Hospital Universitario de Los Andes (HULA), Mérida, Venezuela*

Objective To compare the quality of life (QoL) of migraineurs and people with tensional headache (TTH).
Methods Three groups were selected, migraine, TTH and a healthy control group. They completed the SF-36 survey.
Results The comorbility with depression was high in the migraineurs (16.3%) and people with TTH (33.3%) in comparison with the healthy group (2.3%). Those with migraine and TTH had lower scores in all the domains of the SF-36 survey when compared with the healthy group. In 6 of the 8 domains, the TTH group scores lower than migraineurs. When establishing the percentage of subjects with a poor QoL, there were no significant differences between the group with migraine and that with TTH. Depression was seen to produce significant differences when comparing the two groups with headache and the healthy group.
Conclusion The TTH was proved to have an impact as important as that of migraine patients on the QoL. The comorbility of depression with these conditions was established and, as expected, depression contributed decrease the QoL of these subjects.

P2G7

Blindness and validity in clinical trials for headache

Kenneth Holroyd*[1], Gregg Tkachuk[1], Francis O'Donnell[2] & Gary Cordingley[1]
[1]*Ohio University College of Osteopathic Medicine, Athens, OH, USA,* [2]*Headache Treatment & Research, Westerville, OH, USA*

Objectives To examine treatment blindness, factors associated with blindness penetration, and any resulting bias in a headache clinical trial.
Method Participants ($n = 169$) were treated with either a tricyclic antidepressant or placebo in a randomized parallel groups trial. Neurologists and participants ratings and daily diary recordings of improvement, side-effects, as well as participants' and neurologists' 'guesses' about treatment condition were assessed after three months of treatment.
Results Neurologists' correctly identified treatment assignment for 86% of participants receiving antidepressant therapy ($P < 0.001$) and 67% of patients receiving placebo ($P = 0.004$); 67% of participants receiving active medication ($P < 0.001$),

but only 45% receiving placebo ($P = 0.054$) correctly identified their own treatment assignment. Participants correctly identified by neurologists as receiving antidepressant medication had higher neurologist ratings of improvement ($P < 0.001$), greater daily diary improvements ($P < 0.001$), and more severe side-effects ($P = 0.002$) than misidentified participants. Participants tended to overestimate (9%), and neurologists underestimate (–5%), patient improvements compared to headache index, but these measures of 'bias' did not differ across conditions.

Conclusion Neurologists penetrated the double blind for both conditions after three months of treatment; patients did so only for the antidepressant condition. The integrity of the blind cannot be assumed; it must be assessed.

P2G8

Headache severity and psychiatric comorbidity as predictors of response to treatments for chronic tension-type headache

Kenneth Holroyd*[1], Peter Malinoski[1], Francis O'Donnell[2] & Gary Cordingley[1]
[1]*Ohio University College of Osteopathic Medicine, Athens, OH, USA,* [2]*Headache Treatment & Research, Westerville, OH, USA*

Tricyclic antidepressant therapy (AMT) and cognitive-behavior therapy (CBT) are each moderately effective in treating chronic tension-type headaches (CTTH). However, information about patient characteristics that might predict response to treatment is unavailable.

169 patients (125 females; mean age 38) with an IHS diagnosis of CTTH (mean 26 headache days/month) were randomized to one of four treatments [Placebo (PL), AMT, CBT + PL, CBT + AMT]. Primary outcome measures were the Headache Index (average daily pain rating taken 4 times per day) and the Headache Disability Inventory (HDI) that assesses the impact of headaches on psychosocial and affective functioning.

AMT showed the greatest advantage over PL when headache activity ($P = 0.001$) and disability ($P = 0.013$) were severe, and when a comorbid mood ($P < 0.001$) or anxiety disorder ($P = 0.027$) was present. Similarly, CBT showed the greatest advantage over PL when headache activity ($P = 0.003$) and disability ($P < 0.001$) were severe, and when a comorbid anxiety disorder ($P = 0.009$) was present. In general, both AMT and CBT showed greater benefit (relative to PL) with more severe headache disorders and when a comorbid mood or anxiety disorder was present.

P2G9

Effects of acetylsalicyclic acid on sensoric, motoric and vascular muscle reagibility

Hartmut Göbel*[1], Axel Heinze[1], Marianne Petersen-Braun[2] & Uwe Gessner[2]
[1]*Kiel Pain Clinic, Kiel, Germany,* [2]*Bayer Vital Gmbh, Bayer, Germany*

Objectives According to recent studies 50–60% of all patients suffering from tension-type headache present with increased pericranial tenderness according to IHS-criteria. If headache episodes recur within short periods a constant sensitisation of myofascial tissue may result. This study investigated for the first time whether Acetylsalicylic acid has direct effects on muscle tenderness and may thus influence proposed mechanisms of tension-type headache chronification.

Methods In a placebo-controlled, randomised double-blind study 60 patients with episodic tension-type headache with increased pericranial tenderness according to IHS-criteria were treated with either 2×500 mg Acetylsalicylic acid or placebo. Investigated parameters were effects on muscle tenderness, EMG-activity, muscle stiffness, exteroceptive suppression of temporalis muscle activity, submaximal effort tournique-test and muscular tender-points.

Results Compared to placebo acetylsalicylic acid lead to a significant reduction of both muscle tenderness and muscle resistance within 60 min.

Conclusions In tension-type headache Acetylsalicylic acid may not only relieve headache but also may reduce muscle tenderness and muscle stiffness. Muscular mechanisms relevant for possible chronification may thus be opposed.

P2G10

Headache in intracerebral hemorrhages is associated with molecular markers for inflammation

Rogelio Leira*[1], José Miguel Lainez[2], José Vivancos[3], José Egido[4], Miguel Blanco[1] & José Castillo[1]
[1]*Hospital Clinico Universitario Santiago,* [2]*Hospital Clinico Universitario Valencia,* [3]*Hospital La Princesa Madrid,* [4]*Hospital Clinico Madrid*

Objectives Headache presents early in 30–60% of ICH, but the mechanism of this symptom is not well understood. This study considers the clinical and biochemical factors associated with the development of headache in ICH.

Patients and methods From a multicenter series of 266 ICH cases, we included 189 patients with primary hemispheric ICH of less than 24 h evolution. The study protocol included the collection of 65 clinical, laboratory and neuroimaging variables at the time of inclusion. The monitoring period was 3 months, at the end of which a control cerebral CT was carried out, while the patients' clinical condition was evaluated by means of the CSS and the Modified Rankin Scale.

Results Sixty-five patients (34.4%) presented headache at ICH onset. The univariate study demonstrated that the patients with headache had a more extensive history of infections ($P = 0.009$) and of inflammatory processes ($P = 0.045$) in the days prior to the ICH, higher body temperature ($P = 0.021$), a greater number of leukocytes ($P = 0.038$) and a higher ESR ($P = 0.011$). The concentration of IL-6 (26.7 ± 12.7 vs. 15.1 ± 6.4 pg/mL, $p < 0.0001$) and of TNF-á (18.2 ± 12.4 vs. 10.5 ± 7.7 pg/mL, $p < 0.0001$) was greater in those patients with headache.

Conclusions Headache in ICH is associated with clinical and biochemical inflammatory markers.

P2G11

Platelet ultrastructure and aggregation in chronic tension-type headache

Rakesh Shukla*[1], G. Umashankar[1], V. K. Bajpai[2], S. P. S. Gaur[2] & D. Nag[1]
[1]*Department of Neurology, CSM Medical University (Upgrade KGMC), Lucknow, Uttar Pradesh, India,* [2]*Central Drug Research Institute, Lucknow, Uttar, Pradesh, India*

Several studies have reported abnormalities in platelet serotonergic mechanisms in tension-type headache (TTH). Serotonin (5-hydroxytryptamine, 5-HT) is stored in the dense granules of the platelets. The present study has been undertaken to evaluate platelet ultrastructure and aggregation in patients of chronic tension-type headache (CTTH). Thirty patients of CTTH (diagnosed by IHS criteria) attending the Neurology OPD and 25 healthy controls were the subjects of the present study. The mean age was 29.5 ± 9,02 years and there were 9 males and 21 females. Platelet aggregation was done by the turbidimetric method of Born using the automated dual chamber aggregometer. Electron microscopy was done using the 410 LS electron microscope. Spontaneous platelet aggregation was significantly high in CTTH but ADP induced aggregation at different concentrations of ADP did not show any significant difference. Sex of the patient, positive family history and headache index did not have any correlation with the increased spontaneous platelet aggregation. Platelet ultrastructure did not show any significant change in any of the morphologic parameters (shape change, dense bodies, alpha granules, deep tubular system, open canalicular system). So, it can be concluded that there are no structural changes in platelets of CTTH patients and the reported abnormalities in 5-HT in TTH are due to functional alterations.

P2G12

Refractory chronic daily headache. Response to Botulinum Toxin A and psychological factors

Carles Roig*[1], Isabel Sala[2], Pilar Otermin[1], Carmen García[2] & Jaime Kulisevsky[1]
[1]*Neurology Department, Hospital Sant Pau, Autonomous University, Barcelona, Spain.,* [2]Neuropsychology Unit, Hospital Sant Pau, Autonomous University, Barcelona, Spain

Objectives To evaluate the effectiveness of botulinum toxin A (BT) on refractory chronic daily headache (CDH) and its psycopathological associations.
Methods Fifteen refractory CDH women with painful cranial points explored manually (9 points by hemicranium). Doses of BT were 5–10 units by point depending on pain score. Evaluations (basal, one, two, three months after treatment) included: pain (PAS), anxiety and depression analogue visual scales, and Lettinen test.

Psychological evaluation included anxiety (STAI), depression (Beck), obsessions scales and MMPI test. Comparisons were made with a control group without headache and 38 nonrefractory CDH patients.
Results PAS improved significantly after BT (1st month, p = 0.007; 2nd month, p = 0.003; 3rd month, p = 0.035; ANOVA). Lettinen test score was better at 2nd and 3rd month ($P < 0.01$). Six patients did not change after BT (NR group) and nine had strong significant improvement in all scores (R group). NR group scored significantly worse than controls on STAI and Beck scales and MMPI neurotic triad (hypochondria, depression, hysteria). R group differed from controls on STAI and MMPI conversive profile (hypocondria, hysteria). No differences were observed between BT and CDH non-BT treated groups.
Conclusions Patients without response to BT have higher depression score and a neurotic MMPI profile.

P2G13

Validity and reliability of Migraine Disability Assessment (MIDAS) questionnaire in Turkish patients with tension type headache

Umit Gedikoglu*[1], Serap Ucler[1], Ozlem Coskun[1], Tugba Tunc[1], Ufuk Emre[1], Hulya Yildiz[1] & Levent Inan[1]
[1]*Ministry of Health, Ankara Research Hospital, Department of Neurology, Ankara, Turkey*

Background The Migraine Disability Assessment (MIDAS) questionnaire is a brief, self administered questionnaire designed to quantify headache related disability over a 3-month period.
Materials and methods: We have tested Turkish version of the Migraine Disability Assessment (MIDAS) questionnaire, instrument patients with tension type headache.

In this study our aim was to evaluate validity and reliability of MIDAS questionnaire in tension type headache. 32 patients who had a chronic tension type headache included this study. All of the patients were recorded in a 90-day diary. The day diary and the MIDAS questionnaire were compared.
Results We found that cronbach's alpha 0,82 and had good reliability.
Conclusions Our findings suggest that this questionnaire which was designed for migraine patients may also be used in patients with tension type headache.

P2G14

Topographic analysis of cerebral event-related potentials following painful CO2 laser stimulation in chronic tension-type headache

Marina De Tommaso*[1], Giuseppe Libro[1], Marco Guido[1], Luciana Losito[1], Olimpia Difruscolo[1], Raffaella Massafra[1], Roberto Bellotti[1] & Francomichele Puca[1]
[1]*Neurological and Psychiatric Science Department and Center of Innovative Technologies for signal detection and processing, University of Bari, Italy*

Central sensitisation plays a primary role concerning the pathophysiology of tension-type headache (TTH) and its related pericranial muscle tenderness. Laser-evoked potentials (LEPs), an objective tool for the assessment of pain perception, can be used to investigate this phenomenon (de Tommaso et al. 2003).

In the present study we examined topographic features of LEPs in relation to the tenderness of pericranial muscles in

TTH with pericranial muscle disorder, during a pain-free phase.

Ten patients with TTH and 10 controls were studied.

The dorsum of the hand and the cutaneous zones corresponding to pericranial muscles were stimulated by a CO2 laser pulse. Two responses, N2a and P2, were considered: the absolute latency and the peak-to-peak amplitude were measured in order to calculate the amplitude maps of N2a-P2 at pain threshold. Dipolar sources of the responses N2a and P2 were computed by a program called Advanced Source Analysis (ASA).

Preliminary results show that the amplitude maps of the N2a–P2 complex elicited by stimulation of pericranial zones are greater in TTH patients than in controls, as well as light anomalies concerning the dipoles' orientation of the N2a–P2 components.

These findings could suggest the presence of a greater pain-specific cortical hypervigilance, related to possible changes of LEPs dipolar generators.

P2G15

Psychological aspects of episodic tension-type headache in children

Anna Olszewska*[1]
[1]*Developmental Neurology Department Medical University of Gdansk, Gdansk, Poland*

Objectives The aim of the study was the evaluation of the role the psychological and psychosocial factors in episodic tension-type headache (ETTH), which may be identified as stressors or resistance resources.

Methods The study investigated 60 schoolchildren with ETTH (30 girls, 30 boys) hospitalized in the Developmental Neurology Department and 30 children without headache. The questionnaires, semistructural interviews, tests for evaluated temperament, emotionality, intellectual ability, attributional style, reactivity to stress, family factors (structure, parenting styles), and social relationships with peers were administered to both groups (children and mothers).

Results No difference was found in relations with family and peers between both groups. The children with tension-type headache differed in temperamental trait, emotionality, attributional style and type reaction to stress.

Conclusions The results showed that children with ETTH are not great exposure to stressful events in its environment but have a different way of perception and reacting to stress.

P2G16

Long-term efficacy and safety of Botulinum toxin type A in refractory chronic daily headache

A. Kemal Erdemoglu*[1] & Ayhan Varlibas[1]
[1]*Department of Neurology, Faculty of Medicine, Kirikkale University, Turkey*

Objective To asses and observe the long-term effect the efficacy and safety of botulinum toxin type A (BTA) in refractory chronic daily headache sufferers (CDH).

Methods and patients This study was conducted as open label, prospective study, at the Department of Neurology, Kirikkale University. Twenty-eight participants, 20 women, aged 26–47, were enrolled in the study. Each patient had the diagnosis of moderate or severe CDH, refractory to the usual preventive medications. Each patient received BTA injections for the pericranial muscles.

Main outcome Headache frequency was recorded according to headache diary. Response was scored as complete partial, improvement and nonresponders. Follow-up exceeded three years.

Results Headache frequency and severity were decreased significantly ($P < 0.05$). Sixty-four percentage of patients had a complete relief of headache, only 7% of patients were continued to have CDH in the follow-up of 36 months. Adverse effects were transient and local but there was not any long-term side-effect.

Conclusion BTA is found to be potent agent in the treatment of CDH. The effect of BTA might be mediated via decreasing myofascial factors and peripheral sensitization, resulting in improvement on headache severity and frequency, and preventing the development of central sensitization.

P2G17

Botulinum toxin type A treatment reduces acute analgesic costs in chronic tension type headache

Paolo Martelletti*[1], Gabriella Coloprisco[1], Sergio De Filippis[1] & Pier Giorgio Santi[1]
[1]*Department of Internal Medicine, Service of Internal Medicine and Headache Centre, II School of Medicine, Rome University 'La Sapienza', Sant'Andrea Hospital, Rome, Italy*

Objective The aim of this study was to investigate the impact of botulinum toxin type A (BoNT-A: BOTOX®, Allergan, Inc) preventive treatment of chronic tension type headache (CTTH) on analgesic expenditure and use.

Design This was a prospective, single center, 1 years, open-label study of the effect BoNT-A treatment on acute analgesic costs in CTTH patients.

Methods A headache questionnaire, which included capture of medication costs, was completed by CTTH patients attending a specialist headache clinic in Rome prior to BoNT-A injections. Repeat injections were administered every 3 months for up to 1 years. Patients were required to complete the questionnaire prior to each injection cycle.

Results 300 questionnaires were distributed with 98% completed. The study population was 67.8% female and had a mean age of 46.7 ± 16.1 years. Median monthly acute medication costs decreased steadily over the study period of BoNT-A treatment. Acute analgesic costs were a median of ¤24.30 at baseline vs. ¤7.20 at 9 months ($P < 0.001$).

Conclusions BoNT-A treatment reduced significantly analgesic costs and use, with repeated injection associated with cumulative improvements. Thus BoNT-A treatment may reduce the risk of acute medication overuse and its associated disability and indirect costs.

P2G18

Treatment of chronic tension-type headache with an intraoral orthosis

Elliot Shevel*[1]
[1]*Headache Clinics International, Johannesburg Branch, Houghton, South Africa*

Tension-type headache is the most frequently occurring primary headache. There is a strong association between tension-type headache and presence of pericranial muscle tenderness. There are indications that prolonged nociceptive stimuli from the pericranial myofascial tissue sensitise the central nervous system and, thereby, lead to an increased general pain sensitivity. From experimental research and clinical studies, it appears that myofascial nociception is important in episodic tension-type headache; however, central mechanisms (i.e. central sensitisation) are preponderant in the pathophysiology of chronic tension-type headache (CTTH). The presence of central sensitisation does not necessarily, however, preclude the possibility that myofascial nociception may play some part in the pathogenesis of CTTH. The use of intraoral appliances has been shown to significantly reduce pericranial muscle tenderness. Preliminary studies on the use of palatal appliances in the treatment of painful dysfunction of the craniomandibular muscles have shown encouraging results. The aim of the present investigation was to ascertain whether reduction in myofascial nociception by means of an intraoral orthosis would be of value in the treatment of CTTH. Pre- and post-treatment quality of life scores were obtained from 91 CTTH patients, who were treated with a speech adjusted subpalatal intraoral orthosis. Post-treatment quality of life scores were significantly better than pre-treatment scores.

P2G19

Cerebral vasomotor instability in cases of tension-type headache

Galina Baltgaile*[1] & Tatiana Timofejeva[1]
[1]*Rigas Stradina University, Depart. of Neurology, Riga, Latvia*

The role of vascular factor in a genesis of tension-type headache (TTH) is still unclear although signs of autonomic nervous system disorders accompanied by cerebral vasomotor instability had been often found in young people with TTH.

With the aim to detect changes in cerebral circulation and a function of cerebral arterial wall in young people with headache, 97 patients aged 17–35 years with episodic TTH and 25 controls had been observed used transcranial colour coded duplex sonography (TCCD) examination. Carotid arteries wall's moving during systole-diastole had been measured used M-mode additionally to routine examination by 4,5–7 MHz linear probe as well as usual measurements of cerebral flow by 3,5 MHz sectoral probe (HDI 5000, ATL).

The most of young patients with TTH (78%) had ultrasonological patterns of autonomic dysregulation of cerebral vessels wall's tone manifested as an increase of carotid artery's wall dilatation during cardiac cycle (mean on 0,07 ± 0,03 cm) with the increase of pulsative index (1,96 ± 0,67); flow acceleration in normal sized or dilated middle cerebral arteries (Vmax ± s/d136 ± 15,6 cm/ s) with the presence of vascular bruits in arterial branching (in 52% of cases) and the dilatation of vertebral and basal veins ($P < 0,05$).

P2G20

The therapeutic effect of botulinum toxin on tension-type headache: a multicenter, randomized, double-blind, placebo-controlled study

Wilhelm J. Schulte-Mattler*[1] & Paul Krack[2]
[1]*Klinik und Poliklinik für Neurologie der Universität Regensburg, Universitätsstr. 84, 93053 Regensburg, Germany,* [2]*Klinik für Neurologie des Klinikums der Christian-Albrechts-Universität zu Kiel, Niemannsweg 147, 24105 Kiel, Germany*

A beneficial effect of botulinum toxin on tension-type headache was reported in open-label studies but scientifically rigorous clinical studies are lacking. Therefore we conducted a prospective, multicenter, randomized, double-blind, placebo-controlled trial. Multiple pericranial muscles of 113 patients with pure tension-type headache were treated either with 500 mouse units of botulinum toxin (Dysport®) or with placebo. The diagnoses were made strictly following the IHS criteria. Co-existence of migraine was an exclusion criterion. Injections were made following a fixed scheme and not adjusted to the patient's symptoms. Patients kept a headache diary that was used to calculate the area under the headache curve of 6 weeks before and after the treatment as the main outcome variable. The last patient has been included and data will be unblinded in April The results of this trial will be reported.

P2G21

Efficacy of Neurotropin for tension-type headache

Toshiki Shimizu*[1] & Jun Teramoto[2]
[1]*Souma Hospital, Kyouto, Japan,* [2]*Teramoto Clinic, Nagoya, Japan*

Neurotropin, an extract from cutaneous tissue of rabbit inoculated with vaccinia virus, has been used in Japan for the treatment of various painful disease[s.] In the present study, we examined the efficacy on tension-type headache using this drug. Thirty-five patients were investigated in this study. Thirteen cases were male and 22 were female, The age ranged 29–84-year-old-with a mean of 66.1. The duration of illness ranged from one month to 10 years. We assessed the efficacy as excellent, good, moderate and none. Four Neurotropin Tablets per day were given every day for more than 4 weeks. We assessed after 4 weeks administration. Fourteen cases (40.0%) showed excellent improvement, 5 cases (14.3%) were good, 11 cases (31.4%) were moderate, and 5 cases were none. Side-effects were seen only in 3 cases, which were nausea in one case, diarrhea in one and swelling of hand in one. In the present study, Neurotropin was very effective for tension-type headache. We recommend this drug as one of useful therapy for this headache.

P2G22

Effect of episodic tension-type headache on the health-related quality of life in employees of a Brazilian public hospital

Hilton Mariano Da Silva*[1], Roberta Garbelini[1], Carlos Bordini[1] & José Speciali[1]
[1]*Department of Neurology, Sao Paulo University, School of Medicine at Ribeirao Preto, Ribeirao Preto, Sp, Brazil*

Objectives To evaluate the impact of ETTH on the health-related quality of life in a sample of employees of a Brazilian public hospital.
Methods From March to April of 2000, 350 employees that work at the Hospital Mário Gatti, Campinas–SP, were interviewed. The SF-36 was applied and they were asked about the headache in the last 6 months (criteria of the IHS/1988). Patients suffer from diseases known to have influence on HRQL tool scores were excluded.
Results Two groups were studied 1. Episodic Tension-type headache group: 162 employees – 81 (71.6%) female and 46 (28.4%), male. The mean age was 36,4 years with a SD of 8.52. 2. Control group (without headache complaint): 124, 71 (78.9%) female and 53 (21.1%) male, with the mean age of 37,8 and a SD of 10,2.

The Mann–Whitney test was used. In the analysis of the bodily pain, the value obtained by ETT headache group was significantly smaller ($P < 0,05$) than the control group. In the dimension of vitality, the values obtained by the ETT group ($P < 0,0113$) were smaller than the control.
Conclusion Our results suggest the domain vitality evaluated by the SF-36 is affected by ETTH.

P2G23

Valdecoxib: treatment for episodic tension-type headaches

John Claude Krusz*[1]
[1]*Anodyne Headache and PainCare, Dallas, USA*

Introduction Valdecoxib is a COX-2 inhibitor that is an anti-inflammatory substance. Cox-2 inhibitors are useful in treating headaches, including migraines. Valdecoxib was tried as acute therapy for patients with tension-type headaches (TTH) and migraines.
Methods 30 patients were studied. All had episodic TTH with coexistent migraines 1–4 per month. Patients took 10–20 mg of valdecoxib at the onset of headache. In some, 30–40 mg were used.
Results 18 patients reported better than 50% reduction in headache severity (average 5.4/10–2.5/10) with fewer total hours of ETTH per month (110 h vs. 190 h). 5 patients had partial response (25–50% reductions) and 7 had minimal or no response (less than 25%). 12 patients treated the onset of a migraine successfully, and 10 delayed treatment with migraine-specific therapy. Average dose taken was 30 mg; up to 60 mg was taken for a single headache episode.

2 patients complained of dyspepsia, 2 had nausea, and one had fluid retention. No patients stopped the drug for serious side-effects; only for lack of efficacy.
Conclusion Valdecoxib has value in treatment of moderate ETTH and migraines, with an excellent safety profile. It should be studied double-blind for moderate TTH and migraines.

P2G24

The well-being and functional status of children and adolescents with tension type of headache

Bożena Galas-Zgorzalewicz*[1] & Dorota Talarska[1], Małgorzata Zgorzalewicz[1]
[1]*University of Medical Sciences in Poznan, Poland*

Objectives One of the most common children's aliments are headaches. About 75% of the youth suffers from them. The aim of the study was to evaluate the influence of headache on the health related quality of life (HRQOL) in children and adolescents.
Material and method The study group was performed in a large sample of subjects with tension type of headaches, between the age 12 and 18 both sexes, classified according to IHS. The investigation was conducted with the help of special constructed anonymous quantitative questionnaires. The questions, contained in it played a multidimensional role since, on one hand they were related to the educational, mental, physical and social problems and on the other hand they informed us about the headaches frequency, intensity and localization.

The respondents were mostly the patients of Chair and Department of Developmental Neurology at the University of Medical Sciences in Poznañ and their outpatient clinic.
Results Changes in bio-psycho-social existence in examined group were found. Negative emotional states and the feeling of diminished self – value in children and adolescents were estimated. An impairment of memory and remembering processes which influence school records were also observed. A correlation was found between the experienced stress and the frequency of headache.
Conclusion The occurrence of tension type of headaches was observed to influence HRQOL negatively and to impair the bio – psycho – social functioning in children and adolescents.

Scientific Session 3

Phenotypic migraine markers

P3H1

Cerebrospinal fluid glial cell line-derived neurotrophic factor and somatostatin levels in chronic daily headache and fybromyalgia

Paola Sarchielli*[1], Andrea Alberti[1], Beatrice Gallai[1], Antonio Candeliere & Giovanni Mazzotta[1]
[1]*Neuroscience Department, Institute of Clinical and Applied Biochemistry, University of Perugia,* [2]*Department of Internal Medicine, Institute of Clinical and Applied Biochemistry, University of Perugia*

Aim of the study The aim of the present study was to verify the CSF levels of GDNF and somatostatin levels of 20 patients affected by chronic daily headache (CDH) with a previous

history of migraine. These levels were compared with those of 20 control subjects, with no systemic or neurological diseases and 15 patients affected by primary fibromyalgia syndrome (PFMS).
Methods GDNF and somatostatin levels were determined by sensitive sandwich immunoassays (ELISA).
Results Significantly lower levels of GDNF were found in the CSF of both CDH and PFMS patients compared with control subjects ($P < 0.001$ and $p < 0.002$, respectively). Both patients groups also had reduced CSF levels of somatostatin ($P < 0.002$ and $p < 0.01$, respectively). A significant positive correlation emerged between CSF values of GDNF and those of somatostatin both in CDH ($R = 0.58$, $p < 0.01$) and PFMS patients ($R = 0.41$, $p < 0.01$).
Conclusion Altered levels of some neurotrophins has been shown in CDH (1,2).

This study suggests a down-regulation of the release of somatostatin due to low GDNF levels in central sites involved in nociceptive transmission. The decrease of both GDNF and the antinociceptive neuropeptide somatostatin in the CSF does not seem to be specific for CDH, but is common to fibromyalgia.

References

1 Sarchielli P, Gallai V et al. Neurology 2001; 57 (1): 132–4.
2 Sarchielli P, Gallai V et al. J Headache Pain 2002; 3: 129–135.

P3H2

Adhesion molecules and integrin expression on lymphocytes from internal jugular venous blood of migraine patients during attacks

Paola Sarchielli*[1], Andrea Alberti[1], Luana Vaianella[1] & Laura Pierguidi[1] Alessandro Floridi [2]
[1]*Neuroscience Department, Institute of Clinical and Applied Biochemistry, University of Perugia,* [2]*Department of Internal Medicine, Institute of Clinical and Applied Biochemistry, University of Perugia*

Aim of the study This study verified the levels of some soluble adhesion molecules and proinflammatory cytokines in serial samples of internal jugular venous blood taken from 8 migraine in-patients without aura (MwoA) during attacks.
Methods Levels of L- and E-selectins, ICAM-1, VCAM-1, TNF-α, IL-1a, IL-4 and IL-6 were measured with ELISA methods. The expression of leukocyte function antigen-4 (LFA-4) and very late activation antigen-4 (VLA-4) was also assessed on T lymphocytes obtained from internal jugular venous blood by flow cytometry.
Results A transient increase of soluble ICAM-1 in the internal jugular venous blood of MwoA patients was observed at the 1st and 2nd hours ($P < 0.03$). They were significantly correlated with TNF-α levels in jugular blood at the same times ($R = 0.65$, $p < 0.003$; $R = 0.59$ $p < 0.02$, respectively). The proportion of LFA-1 high expressing T-cells instead showed a progressive down-regulation (ANOVA: $p < 0.02$). No variation in the proportion of VLA-4 expressing cells was observed at any times of the study.
Discussion The transient increase in soluble ICAM-1 and TNF-α production can be induced by sensory neuropeptides released as a consequence of trigeminal activation (1). The subsequent reduction in ICAM-1 levels and the down-regulation of LFA-1 could contribute to antagonize lymphocyte transvascular migration, supporting the hypothesis of a sterile inflammation in the dura mater during migraine attacks.

Reference

1 Sarchielli P, Gallai V et al. Cephalalgia 2000; 20 (10): 907–18.

P3H3

Contingent negative variation (CNV) as a functional genetic marker in migraine without aura

Michael Siniatchkin*[1], Peter Sandor[2], Jean Schoenen[3] & Wolf-Dieter Gerber[1]
[1]*Institute of Medical Psychology, University of Kiel, Germany,* [2]*Department of Neurology, University of Zurich, Switzerland,* [3]*Department of Neurology, University of Liege, Belgium*

Objective Genetics contributes to a large degree to the etiopathogenesis of migraine. Migraine patients are characterized by increased amplitudes and reduced habituation of the CNV. The aim of this study was to assess similarities between related and nonrelated individuals in migraine ($n = 43$) and healthy ($n = 40$) families according to amplitudes and habituation of the CNV using a Monte-Carlo statistical method.
Methods The CNV (reaction time paradigm, filters 0.03–35 Hz, 100 Hz digitalization rate, ISI = 3 s, Cz with linked mastoids, impedance < 5 kOhm, on-line EOG control) was recorded in all family members. The means of CNV parameters for related pairs were compared to the distribution of mean values obtained for those of artificially generated samples of unrelated pairs (Sandor et al. NeuroReport 1999; 10: 1235–1238).
Results Similarities for the early CNV component amplitude and habituation were significantly more pronounced between related individuals suffering from migraine than between healthy subjects from migraine families, subjects from healthy families or individuals from constructed unrelated pairs.
Discussion The early CNV component undergo a familial influence associated with migraine. A shared genetic disposition for both CNV and migraine may be proposed.

P3H4

Urinary nitric oxide metabolites in migraineurs

Monika Empl*[1], Konrad Redjak[1], Gavin Giovannoni[1], Peter J. Goadsby[1] & Holger Kaube[1]
[1]*Headache Group & Department of Neuroinflammation, Institute of Neurology, Queen Square, London, UK*

Objective To assess the variation in nitric oxide metabolites in the urine of migraineurs in relationship to their attacks.
Methods Nitric oxide metabolites (NOx) were analysed in daily morning urine samples of 12 migraine patients and eight headache-free controls over a period of 40 days. NOx was determined spectrophotometrically, and corrected for creatinine (HPLC). Quantitative analysis was based on a percentile based estimator as threshold criterion to identify peaks.

Results Mean levels of urinary nitrate and nitrite for migraineurs (1317.8 μM/g creatinine) compared to controls (878.4 μM/g creatinine) were not significantly different (Mann–Whitney, $Z = -1.77$, $P = 0.08$). The excretion of NOx was pulsatile and migraineurs had more peaks compared to controls (Mann–Whitney, $Z = 2.23$, $P < 0.05$). In seven patients, NOx peaks coincided with headache days. This was significantly more frequent than expected by random association in four patients (Monte-Carlo odds ratio- 2.16–7.77; no. 95% CI overlap). In four patients, NOx peaks preceded or followed headache days more frequently than expected.
Conclusions The variable temporal association of NOx peaks and headaches suggests a complex role of NO in migraine. The intermittent perturbation of NO production in migraineurs may be a trait marker in this condition.

P3H5

Persistent oculomotor disturbance in migraine without aura

Thomas Wieser*[1], Roberto Wolff[2], Hans-Peter Hoffmann[2], Wilhelm Schult-Mattler[1] & Stephan Zierz[1]
[1]*Department of Neurology, Martin-Luther-Universität Halle/Wittenberg,* [2]*Fachhochschule Anhalt, Köthen, Germany*

Objectives Although clinical examination of migraine patients is normal, a slight disturbance of smooth pursuit eye movements in these patients caught our attention. The objective of this study was to demonstrate that this is a specific and unique finding in migraine patients.
Methods We examined 25 patients with migraine without aura free of any continuous medication in the headache free interval. Results were compared to an age and sex matched group of controls. Standard oculography (optokinetic nystagmus, saccades, smooth pursuit and spontaneous nystagmus) was performed.
Results Migraineurs showed repeatedly catch up saccades and continuous deviances from the target in smooth pursuit. While gain showed a tendency to be delayed, phase was significantly changed compared to controls ($P = 0.005$).
Conclusions We identified significant impairment of smooth pursuit eye movement in patients with migraine without aura. The data suggest a persistent disturbance of premotor centres of oculomotor function most likely due to cerebellar or brain-stem nuclei pathology. This is consistent with previous studies indicating subclinical cerebellar impairment and an important role of the brain-stem in generating migraine attacks.

P3H6

The contingent negative variation is influenced by duration of the individual migraine disease

Peter Kropp*[1], Thomas-Martin Wallasch[2] & Wolf-Dieter Gerber[1]
[1]*Institut für Medizinische Psychologie, Universitaet Schleswig-Holstein, Kiel, Germany,* [2]*Schmerzpraxis im ZAR, Berlin, Germany*

Objectives Migraine patients produce higher negative CNV-amplitudes compared with controls. Little is known about the dependencies of high CNV amplitudes and the duration of the disease. Aim of the study is a comparison of CNV-amplitudes in patients suffering from migraine without aura with respect to their individual duration of migraine disease (DOD).
Methods All patients ($n = 48$) suffered from migraine without aura. CNV were recorded at Cz during the pain free interval. For CNV analysis total CNV (tCNV), early component (iCNV), and late component (lCNV) was computed.
Results By median split two groups with different mean -DOD could be computed (short lasting: 78 months, SD: 36, longlasting: 320 months, SD: 136).

Only icnv differed significantly, shortlasting: –9,3 μV, longlasting: –12,8 μV, $p < 0.05$). Between DOD and iCNV a correlation of $r = 0.390$ could be calculated.
Discussion High iCNV amplitudes correlate with the individual duration of disease and may be a marker of chronicity in migraine patients. Stimulus processing as recorded by CNV may be altered with the long lasting effect of migraine disease.

P3H7

Allodynia in migraine

Ninan T. Mathew*[1], Jayasree Kailasam[1] & Lori Meadors[1]
[1]*Houston Headache Clinic, Houston, TX, USA*

Objective To report the incidence and manifestations of allodynia in migraine patients.
Methods 295 consecutive IHS migraine patients were interviewed using a semistructured questionnaire to evaluate the presence and characteristics of allodynia.
Results 157(53.5%) reported allodynia. Of those, 133(45%) had cephalic, 54(18%) had both cephalic and extracephalic, and 24(8.5%) exhibited only extracephalic allodynia. Scalp symptoms were, sensitivity to touch 61, soreness or tenderness 52, tingling 32, difficulty brushing, combing or washing the hair 30, difficulty to rest the head on allodynic side 15, and feeling hot or burning 9, paresthesias involving face, cheek, lips, neck 16, circumscribed areas of tenderness 4, itchy scalp 2.

Scalp allodynia was ipsilateral to predominant headache side in the majority and occurred at the height of headache, though persisted for hours to days in 29 patients.

Upper limb allodynia occurred in 72 (unilateral 35, bilateral 37), toes in 6. Impaired fine coordination and clumsiness of hands occurred in some. Bilateral headache caused unilateral limb allodynia in 18 out of 42, unilateral headache resulted in ipsilateral limb allodynia in 21 out of 36 and bilateral in the rest.

Allodynia was not correlated to age, duration or frequency of migraine.
Conclusion Clinically detectable allodynia is common in migraine. It should become a part of diagnostic criteria.

P3H8

Impairment of neuromuscular transmission in migraine with aura

Stefan Evers*[1], Jan Meyer[1], Alexandra Rahmann[1] & Achim Frese[1]
[1]*Department of Neurology, University of Muenster*

About 50% of patients with Familial Hemiplegic Migraine show mutations in the CACNA1A gene resulting in a impairment of a P/Q-type calcium channel with subsequent changes of the neuromuscular junction. Previous studies suggested that the neuromuscular transmission is also impaired in other types of migraine. We aimed to evaluate changes of the neuromuscular transmission in migraine patients by clinical neurophysiological testing.

We enrolled 51 patients with migraine (17 with aura and 34 without aura) and 31 age-matched healthy control subjects. Decrement and increment of the neuromuscular transmission were measured by examination of the Musculus abductor pollicis brevis and of the Musculus abductor digiti minimi, respectively.

Patients with migraine with aura showed a significantly lower increment (both when analysing the amplitude and the integral of the motor potential) as compared to patients with migraine without aura and as compared to healthy control subjects. The decrement was not different between the three examination groups.

Our data suggest that the neuromuscular transmission is impaired in migraine with aura but not in migraine without aura. This might be the consequence of decreased calcium uptake of the muscle cells caused by deficient calcium channel properties. Our data furthermore show that these impairment in migraine with aura can be evaluated by routine neurophysiological measurements.

P3H9

Equilibrium disturbances in patients with primary headache: a reality or a subjective phenomenon? Qualitative and quantitative evaluation by computerized static stabilometry

Cristiana Rossi*[1], Andrea Alberti[1], Mario Faralli[2], Costantino Simoncelli[2] & Virgilio Gallai[1]
[1]*Headache Center. Neuroscience Department, University of Perugia, Italy,*
[2]*Otorhinolaryngology Clinic, University of Perugia, Italy*

The aim of the study was to investigate the occurrence of equilibrium disturbances in patients with primary headache during the intercritical period by computerized static stabilometry.

41 patients were studied: 28 affected by migraine without aura (MwoA), 10 by migraine without aura and episodic tension-type headache (MwoA + ETTH) and 3 by chronic tension-type headache (CTTH). Patient history included recording of imbalance conditions. The following parameters of the stab-examination were considered: length (L) and area (A) of the statokinesigram obtained during eyes open (EO), and closed (EC) condition with and without occlusal bite, EC with head retroflexion (ECR), and optokinetic stimulation (OKN). Normal ranges were obtained from 20 healthy subjects. 35 headache patients had a positive history of imbalance disturbances. The stabilometric examination showed the alteration of at least one of the parameters in 30 patients (73%): of these 19 suffered from MwoA 8 from MwoA + ETTH and 3 from CTTH.

In CTTH and ETTH + MwoA patients, the stabilometric results show a marked proprioceptive alteration induced by muscular contraction in the cervico-facial area. The alterations in MwoA patients seem to be due to a destabilization of visual input especially under optokinetic stimulation. These data suggest an impairment of control in involuntary oculomotility.

P3H10

Intracellular regulation of cytokine signalling on migraine: Suppressor of Cytokine Signaling1(SOCS1) inhibits the JAK/STAT signalling pathway

Massimo Realacci*[1], Alessandra Zicari[1], Carmela Sant'Angelo[2], Paola Denora[1], Sergio De Filippis[3], Gabriella Coloprisco[3], Anna Rodio[3], Giuseppe Fiore[3], Pier Giorgio Santi[3] & Paolo Martelletti[3]
[1]*Department of Experimental Medicine and Pathology, University,*
[2]*Department of Clinical Sciences, 1st Scool of Medicine, University,*
[3]*Department of Internal Medicine, Headache Center, Sant'Andrea Hospital, 2nd School of Medicine, University*

In the last years many studies showed impaired levels of several cytokines in migraine patients without aura (MWA) and *in vitro* basic studies suggest that Suppressor Of Cytokine Signalling (SOCS) proteins negatively regulate cytokine signalling. In order to relate this new family of proteins to their potential importance in regulating cytokine actions in MWA, we investigated SOCS1 mRNA expression in PBLMs of MWA patients in the interictal period and during NOD MWA. Total RNA obtained from PBLMs of both MWA patients ($n = 8$) and healthy subjects ($n = 10$) was analysed by RT-PCR in order to evaluate SOCS1 expression. Specific oligonucleotide primers were designed to amplify SOCS-1 (110 bp) and 18S (497 bp) molecules. Densitometric analysis, after gel electrophoresis, was performed using the CCD (Charge-Coupled device) camera instrument Gel Doc 2000 (BIO-RAD Laboratories). The bands density of SOCS-1 was than plotted against the 18S density values. In MWA patients we detected a higher level of SOCS1 expression in the interictical period (70.3), whereas SOCS1 is only weakly increased during the NOD migraine (60.5) respect to healthy subjects (50.6).

P3H11

Clinical and thermographic evaluation of the trigemino-vascular system during migraine attacks in patients treated with triptans and/or ketoprophen

Giorgio Dalla Volta*[1], Simona Griffini[1], Alessandro Pezzini[2] & Patrizia Civelli[1]
[1]*U.O Neurologia Ist,* [2]*Clinica Neurologica*

Telethermography is a reliable technique for the assessment of skin microcirculatory changes due to sympathic and trigemino-vascular activity.

Methods We randomly administered triptans, ketoprophen or placebo to 20 consecutive patients (12 males, mean age 32 ± 2) during migraine attack and assessed clinical and thermographic responses. Visual Analogic Scale (VAS) before drug assumption and 5, 30, and 120 min after, served as clinical outcome measure. Optimal response was considered a VAS reduction of more than 70%. Microcirculatory skin changes detected on the forehead at the same time-points of clinical evaluation served as telethermographic outcome measures. Pathognomonic marker of migraine was considered an asimmetric distribution of the thermographic pattern.
Results Complete disappearance of the asimmetric termographic pattern was observed in all patients with an optimal response to treatment ($n = 15$ 75%) as opposed to patients without ($n = 5$ 25%). This effect turned out to be independent on the specific drug administered.
Conclusions Skin microcirculatory changes detected by the telethermographic investigation in migrainous seem to be related to the neurovascular modifications due to pain relief rather than to the specific mechanism of action of each drug on trigemino-vascular and autonomic systems.

P3H12

The autonomic response to mental stress in migraineurs

Kristian Bernhard Nilsen*[1], Rune Bang-Leistad[1], Trond Sand[1], Lars Jacob Stovner[1], Linda R. White[1] & Rolf H. Westgaard[2]
[1]*Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway,* [2]*Department of Industrial Economics and Technology Management, Norwegian University of Science and Technology, Trondheim, Norway*

Objectives To measure autonomic responses to a psychometric test in migraineurs compared to pain-free controls.
Methods Twenty-three migraine patients (21F, 2M; age 40.3 ± 13.9 y) outside attack and 34 headache-free healthy controls (32F, 2M; age 41.2 ± 12.0 y) were studied while performing a computerized stressful cognitive task. Measurements included continuous blood pressure (Portapres) and skin blood flow (measured as red blood cell flux by laser Doppler flowmetry) in addition to plasma catecholamine determination before and after the test.
Results Skin blood flow was significantly higher before, during, and after the stressor in migraine patients compared to controls ($P = 0.011$). Additionally, a lower level of noradrenaline was measured in migraine patients compared to controls after the test for both platelet-poor plasma, platelet-rich plasma and in platelets ($0.074 \geq P \geq 0.009$). There was no difference in noradrenaline content between the groups before the test.
Conclusions The results indicate that there is less sympathetic activity in migraine patients during a prolonged stressful task compared to headache-free controls.

P3H13

Aminergic tone in alexithymic migraineurs: a study using the Tridimensional Personality Questionnaire

Gianluca Bruti*[1], Laura Di Clemente[1], Costanza Rossi[1], Claudio Mostardini[1], Fabrizio Di Stani[1], Veronica Villani[1], Vittoria D'Agostino[1], Gian Luigi Lenzi[1], Rosanna Cerbo[1] & Vittorio Di Piero[1]
[1]*Department of Neurological Sciences, University of Rome La Sapienza*

An information-processing dysfunction related to high noradrenergic activity has been showed in both migraine and alexithymia.

We investigate the relationships between migraine, alexithymia, and the aminergic tone by means of the Tridimensional Personality Questionnaire (TPQ).

Two hundred migraineurs, according to IHS criteria, and 70 healthy controls were recruited. All subjects were submitted to Beck Depression Inventory (BDI), Toronto Alexithymia Scale 20 (TAS-20) and TPQ (Cloninger, 1994). TPQ describes four dimensions of personality: Novelty Seeking (NS: dopamine), Harm Avoidance (HA: serotonin), Reward Dependence (RD: noradrenaline) and Persistence (P: glutamine).

Migraineurs showed higher score in BDI ($P = 0.03$), the HA dimension of TPQ ($P = 0.0001$), and TAS-20 ($P = 0.01$) than healthy controls. A higher occurrence of alexithymia was found in migraineurs than healthy controls ($P = 0.003$). We found that alexithymic migraineurs presented higher score in the HA dimension (high serotonergic tone) ($P < 0.0001$) and in BDI scale ($P = 0.00001$) and lower score in the RD dimension (high noradrenergic tone) ($P = 0.0001$), than those without alexithymia.

Our findings are in accordance with the concept that migraine is an heterogeneous biobehavioural syndrome associated with different temperament profile. From clinical point of view a characterization of these personality trait using multiple dimensional model may be useful in the prediction of treatment outcome.

P3H14

Chemokine levels in cerebral circulation during migraine attacks

Paola Sarchielli*[1], Andrea Alberti[1], Giovanni Mazzotta[1], Beatrice Gallai[1], Luana Vaianella[1] & Ardesio Floridi[2]
[1]*Neuroscience Department, Institute of Clinical and Applied Biochemistry, University of Perugia, Italy,* [2]*Department of Internal Medicine, Institute of Clinical and Applied Biochemistry, University of Perugia, Italy*

Aim of the study The present study investigated the levels of chemokines IL-8, MCP-1 and RANTES, as well as sensory neuropeptide calcitonin gene-related peptide (CGRP) in serial samples of internal jugular venous blood of 8 migraine inpatients without aura (MwoA) during the attacks.
Methods Blood samples were taken immediately after catheter insertion, at the 1st, 2nd, and 4th hours after attack onset, and within 2 h from its cessation. Chemokines and CGRP levels were measured by ELISA method.
Results Higher CGRP levels emerged in the internal jugular venous blood of MwoA patients compared with the time of

catheter insertion (ANOVA: $p < 0.0001$) with a peak at the first hour. A transient increase in IL-8 was observed at the 2nd and 4th hours, whereas no changes in the levels of MCP-1 and RANTES were found.

Discussion The transient increase in the levels of IL-8 concurs with the results of recent research showing a CGRP-induced activation of IL-8 gene expression. Although this chemokine promotes leukocyte recruitment, an accumulation of neutrophils in meningeal tissue due to neurogenic inflammation is unlikely. Inhibition of adhesion molecules expression and proinflammatory cytokines may counteract transvascular leucocyte migration during migraine attacks.

P3H15

Estimation of time by migraine sufferers

Euaggelos Anagnostou[1] & Dimos Mitsikostas*[1]
[1]*Athens Naval Hospital, Neurology Department, Athens, Greece*

Objectives There are case reports indicating impaired time perception (TP) among migraineurs. We aimed to investigate in a matched-pairs design whether TP is altered in migraine sufferers.

Methods We compared the performance of 40 migraineurs with 40 matched controls (1) on an auditory duration discrimination task for both brief (milliseconds) and long tone intervals (seconds); (2) on a time awareness questionnaire; (3) on a sustained attention test by using a computerized procedure; and (4) on the Hamilton's Rating Scale for Depression (HRSD) score.

Results We found no differences in the duration discrimination test, neither for brief nor for longer intervals, even after excluding the depressive subjects. Sustained attention performance showed a differential effect on discrimination ability for brief and long intervals, but this effect was similar in migraineurs and controls. Depressive migraineurs (HRSD-score > 14) exhibited slowed time perception on the time awareness questionnaire compared with nondepressive migraineurs.

Conclusions The TP seems to be intact among migraineurs, indicating that there is no systematic slow-down or speed-up of neuronal timekeeping operations in the migraineur brain. The TP may occasionally be impaired in migraineurs, due to other comorbidited brain disorders, such as depression.

P3H16

Rapid elimination of Allodynia with occipital nerve block and tender point injection in a migraine patient

William Young*[1], Valentin Mateos[2] & Avi Ashkenazi[1]
[1]*Thomas Jefferson University, Philadelphia, USA,* [2]*Hospital Central de Asturias, Oviedo, Spain*

Background Seventy to 80% of persons with migraine develop allodynia during the course of a severe attack. Brush (mechanical dynamic) allodynia is a subtype of allodynia that is easily tested.

Methods Case report.

Results A 47-year-old-woman with severe left-sided menstrual migraine and chronic left more than right-sided posterior neck pain was evaluated. Her last severe menstrual migraine lasted 3 days, ending 7 days prior to presentation, and her neck pain was at its baseline. On examination she had moderate cervical paraspinal tenderness and left-sided allodynia from C2 to T5, including the arm. Brush allodynia was tested by stroking the subject repetitively with a folded gauze pad at 2 Hz until the subject experienced an unpleasant sensation or 8 brushes were completed.

A left greater occipital nerve (GON) block and bilateral tender point injections C2 and left C5 paraspinal and trapezius muscles were given. A total of 5cc of 2% lignocaine and 10 mg of triamcinolone were used. One minute after achieving GON anesthesia the allodynia was reduced in intensity and after 5 min all allodynia and neck pain had resolved.

Discussion GON block with paraspinal tender point injection can eliminate allodynia caudal to the site of injection.

P3H17

Migraine modular theory; Part I: the premonitory symptoms (PRODROME)

Leslie Kelman*[1]
[1]*Headache of Atlanta*

Objectives To investigate premonitory characteristics in a large group of migraine patients, to correlate prodrome with multiple variables, and to explore the modular theory of migraine.

Methods 893 migraine patients' (IHS 1.1–1.7) headache characteristics, medication responses, adverse effects, demographics, social, psychological, and personal characteristics, disability, sleep patterns, and women's issues were rated (from 0 to 3 or 0–10) at 1st visit. Prodrome frequency, duration and characteristics were correlated in total and IHS migraine.

Results 29.7% of patients reported prodrome symptoms, predominantly tiredness, mood change and gastrointestinal symptoms; all three present in 17%. Prodrome probability was higher when headache less frequent, pain less severe and shorter in duration, function during headache better, triggers and associated symptoms more prominent, headache worse with movement, eye location of headache present, diffuse location absent, postdrome symptoms present, time to recurrence short, sleep abnormal, and disability and severe days per month less. IHS migraine showed similar findings. Prodrome duration was up to 4 h in 75.2%, 4–12 in 11.3%, greater than 12 in 13.6%. Prodrome correlated with other variables but not with symptom severity.

Conclusions This study highlights some important prodrome correlations with the migraine attack and provides a framework for further analysis of the modular theory.

P3H18

NGF and SP in the saliva of migraine sufferers using FANs daily

Maria Nicolodi*[1,2], Maria Grazia Spillantini[2,3], Federigo Sicuteri[1,2] & E. Del Bianco[1]
[1]*Interuniversity Headache Centre, Florence, Italy,* [2]*Foundation 'Prevention and Therapy of Primary Pain and Headache', Florence, ItalyInteruniversity Headache Centre, Foundation 'Prevention and Therapy of Primary Pain and Headache', Florence, Italy,* [3]*MRC Cambridge, UK*

The protein nerve grow factor (NGF) was shown in the saliva of submandibular glands of rodents. It is a trophic substance for those primary sensory neurons containing substance P.

Following 2 days wash-out out period We sampled total saliva in 15 healthy controls (8 males, mean age 41.1 ± 5.1) and 16 chronic migraine sufferers (7 males, mean age 39.8 ± 7.5) using FANS daily as acute abortive treatment. Samples were stored at –80 °C. Bioassay for evaluating NGF levels was performed by using sensory neurons. NGF concentration ≥ 15 pg/mL could be determined by this assay system. RIA was used to evaluate SP levels in the same samples.

A lower level of NGF ($P > 0.02$) as well as of SP ($P > 0.2$) was observed in migraine sufferers when compared to controls. The outcome might depend on a different set-up distinguishing migraine sufferers from controls or may be due to a block induced by FANS on retrograde axonal transport.

P3H19

Laser Doppler Flowmetry in migraine

Milena De Marinis*[1], Isabella Matteucci[1], Linda Natale[1] & Neri Accornero[1]
[1]*Department of Neurological Sciences – 'La Sapienza' University – Rome, Italy*

Objective To assess microvascular blood flow in extracranial districts in migraine patients during and outside attacks.
Methods We studied 15 patients with migraine without aura (out and during spontaneous attacks) and 15 controls. We used Laser Doppler flowmetry and measured cutaneous responses to hyperthermic stimulation on symmetric skin areas of the face, neck and fingers of the upper limbs bilaterally.
Results No differences between patients and controls were found on the face and neck in the basal assessment. Sings of Raynaud phenomenon were observed in 9 (60%) headache-free patients and 2 controls (13%). During the attacks of migraine, 6 patients (40%) had an increase in flowmetry at the level of the face and neck, 4 patients (27%) had a decrease in flowmetry in the same areas. The remaining 5 patients (33%) had no significant changes in flowmetry in any of the studied areas.
Conclusions Our results indicate that the extracranial vascular involvement is quite dysomogeneous during migraine attacks and may be implicated in Raynaud phenomenon. Migraine patients are particularly susceptible to microvascular instability.

P3H20

Nocioceptive specific pain threshold reduced in migraine patients

Joseph O. Di Duro*[1]
[1]*Private Practice, Vicenza, Italy*

Objective Sensitisation of the trigeminal pain system has been previously reported during an active migraine and in the interictal period to stimulation of A delta fiber specific nocioception in the blink and corneal reflex, respectively. Cutaneous allodynia has also been demonstrated on the forehead in active migraine patients, which frequently extends to extracephalic forearm regions.
Methods Twenty patients with migraine without aura served as subjects with a group of 19 age and sex matched controls. Each patient was examined in the interictal period within 72 h of the last pharmacologically untreated migraine headache. Painful pinprick threshold to electric stimulus was tested with a concentric electrode which preferentially stimulate A-delta fibers in the superficial dermis. For each patient a 6 matched points right and left on the head, forearm and leg were stimulated.
Results The results of this study demonstrated that whole body hyperalgesia to punctuate stimulus is prominent in migraine patients, even at 72 h after an attack [F (1,27) = 81.843, $P < 0.0001$]. Phasic, pin- prick pain thresholds by electrical stimulation of A-delta nocioceptive specific neurons are significantly and symmetrically reduced far from the trigeminal area.

P3H21

Possible predictive factors for the chronic evolution of migraine without aura: a longitudinal clinical population-based study

Gian Camillo Manzoni*[1,2] & Paola Torelli[1,2]
[1]*Headache Center, Unit of Neurology, Department of Neuroscience, University of Parma, Parma, Italy,* [2]*University Centre For Adaptive Disorders and Headache (UCADH)*

The progressive transformation of migraine without aura (MO) – a typically ictal form of primary headache – into a chronic daily headache (CDH) is generally attributed to overuse of symptomatic drugs, arterial hypertension, surgical menopause, and concurrent psychological distress. However, no controlled longitudinal studies exist in the literature on the actual role played by these, as well as any other negative prognostic indicators.

We thought it useful to compare the clinical records of all patients first seen at the University of Parma Headache Center on a diagnosis of MO since 1978 and seen again for CDH (Group A, $n = 42$) with those of a series of MO patients presenting with an unchanged headache subtype at the follow-up visits (Group B, $n = 84$). Controls in Group B were matched 2–1 with patients in Group A by sex, age (± 2 years) and period of observation.

The major differences in Group A vs. Group B were a more frequent family history of MO, younger age at onset of MO, longer duration of perimenstrual attacks, and a higher inci-

dence of arterial hypertension. The two groups also differed for the types of symptomatic drugs taken at the time of the first observation.

P3H22

Stimulated single-fibre EMG in familial hemiplegic migraine

Esther Kors*[1], Gisela Terwindt[1], Alla Vein[1], Michel Ferrari[1] & Gert van Dijk[1]
[1]*Department of Neurology and clinical neurophysiology, Leiden University Medical Centre, the Netherlands*

Background Familial hemiplegic migraine (FHM) is an autosomal dominant subtype of migraine with aura. A mutation in the P/Q type calcium channel subunit gene CACNA1A on chromosome 19p13 has been identified in the majority of families. This channel is also present in the neuromuscular junction (NMJ), the function of which can be studied with single-fibre EMG (SFEMG). SFEMG abnormalities were shown in episodic ataxia type 2, also due to a CACNA1A mutation.
Objectives To investigate NMJ function in FHM patients with and without a mutation in the CACNA1A gene with SFEMG, and compare results with control values.
Methods In a single blind study, stimulated SFEMG of the frontalis muscle was performed in 6 FHM patients with a proven mutation, 5 without a mutation and 9 healthy controls. Mean jitter and mean blocking percentage were compared.
Results No blocking was found. Mean jitter in FHM patients (13.4 ± 3.6 ìsec) was not significant different compared to healthy controls (13.9 ± 1.5 ìsec, p = 0.7). Mean jitter in patients with a mutation (14.8 ± 4.1 ìsec) was not significantly different from that of patients without a mutation (11.6 ± 2.0 ìsec, p = 0.14).
Conclusions No abnormality of the neuromuscular junction was found in FHM patients with or without a CACNA1A mutation.

P3H23

Evaluation of trace amine receptor-1 mRNA expression in leucocytes of patients with primary headache by Real-Time reverse transcription polymerase chain reaction

Salvatore Terrazzino*[1], Alberta Leon[1] & Giovanni D'Andrea[2]
[1]*Research Innovation (R & I) Company, Padova,* [2]*Headache and Comorbidity Center, Depatment of Clinical Pathology, Este, Monselice Hospital*

The recent identification of mRNA expression of trace amine receptors (TARs) in circulating leukocytes provides a molecular approach to test whether changes of these receptors occur in primary headaches. In the present study, by using quantitative Real-Time RT-PCR, TAR-1 mRNA expression was evaluated in leucocytes obtained from control healthy subjects (n = 9), and from patients with cluster headache (CH, n = 7), migraine without aura (MO, n = 9), and migraine with aura (MA, n = 7). To correct for both mRNA quantity and reverse transcription efficiency, number copies of TAR-1 of each sample were normalized by dividing with respective number transcripts of the housekeeping gene β-2-microglobulin. A significant reduction of TAR-1 expression was observed in leucocytes of MA patients (one way-ANOVA, $p < 0.01$) compared to control subjects. In addition, although this effect was not statistically significant, decreased expression of TAR-1 was consistently found in the two other groups of patients. These preliminary findings are in line with the hypothesis that changes of trace amines and/or their receptors may be of pathophysiological significance in primary headaches and, in particular, in migraine with aura.

P3H25

The blink reflex in side-locked unilateral migraine

Alexandros Voulgaris*[1] & Theodoros Constantinidis[2]
[1]*Corfu Headache Center,* [2]*Cognition and Action Group, Neurologic Clinic, Athens National University*

Migraine is regarded as a neurovascular disorder of trigeminal sensory processing, generated probably at the level of the brainstem. The blink reflex (especially the R1 component latency) is an objective and useful method to study the trigeminal system and its role in migraine pathophysiology. In the past, electrophysiological studies in unilateral migraine headache patients, have shown no R1 latency differences in migraineurs compared with controls.

The purpose of this study was to re-examine the blink reflex in migraine patients especially in those with side-locked unilateral pain.

R1 component latencies were recorded in 18 migraine patients. They were investigated in both symptomatic and nonsymptomatic sides. The electrophysiological procedure was carried out during the pain free phase. The findings on the painfull side were compared with those on the non painfull side, using the paired t-test method.

Significantly shorter R1 latencies (t-test, p = 0035) were found on the symptomatic side (mean = 10,19 ± 0,50) than on the nonsymptomatic side (mean = 10,40 ± 0,64).

The results suggest that a state of hyperactivity may be present in the ipsilateral trigeminal nucleus in side-locked unilateral migraine during headache-free periods.

P3H26

Migraine and motion sickness

Amnon Mosek*[1] & Vladislav Yerumin[1]
[1]*The Headache Clinic, Department of Neurology, Sourasky Medical Center, Tel Aviv, Israel*

Objective To evaluate the prevalence of past and present motion sickness (MS) among adults and to assess its relationship to migraine.
Methods Employees at our Medical Center were interviewed for past and current MS and headache. MS was defined when nausea, vomiting or dizziness recurrently developed while traveling in a car, bus, train, airplane or boat. Headache was defined according the IHS criteria. This is an ongoing study.

Results We interviewed 233 participants. Four were excluded due to inability to recall data. MS was reported by 112 participants (49%; average age 35 ± 8 years; average age of onset 7 ± 3 years, range 3–16 years). The group of those who had MS included more women in comparison to the rest (67% and 54%, respectively); reported on higher frequency of migraine (19% and 12%, respectively) and of tension type headache (20% and 15%, respectively) these differences were nonsignificant. The two groups did not differ in their average age.
Discussion We found that MS was more common in women and this might have resulted in the higher prevalence of headache in this group. Our results show that MS is highly prevalent in the general population and that migraine and MS are probably unrelated.

P3H27

Acute confusional state may be associated with familial hemiplegic migraine

Dalius Jatuzis[1] & Ruta Mameniskiene*[1]
[1]*Department of Neurology, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania*

Acute confusional migraine was described as rare peculiar clinical form of migraine. Only few reports have been published on this condition, associated with familial hemiplegic migraine. We described 18-year-old male patient with recurrent attacks of migraine with hemiplegic aura from the age of 16. His father and sister also have hemiplegic migraine. Recently he experienced a prolonged confusional state that was needed for hospitalization and exclusion of other underlying conditions. Migraine attack started with hemiplegic aura (weakness and tingling of left extremities, scintillation), evolving to severe headache. After few hours patient became agitated and severely disoriented. He was hospitalized to the department of intensive care with suspicion of subarachnoid hemorrhage. Neurological examination did not reveal focal neurological signs or meningeal irritation. The EEG showed mild diffuse nonspecific abnormalities. Neuroimaging examinations (CT and MRI) were unremarkable. Blood tests showed mild leukocytosis. Patient presented with subfebrile temperature at first day of confusional state, therefore encephalitis was suspected and lumbar puncture was performed twice. CSF examination was normal. Psychomotor agitation, mental confusion was severe and gradually resolved after two days. We assume that acute confusional migraine represents a phenotypic form of migraine that might be associated with familial hemiplegic migraine.

P3H28

Comparison of serum proline concentrations between migraine patients and healthy controls

Kyoko Gotoh*[1], Yuki Katoh[1], Toshihiko Shimizu[1], Eiichirou Nagata[1] & Junichi Hamada[1]
[1]*Department of Neurology, Keio University School of Medicine, Tokyo, Japan*

Much attention has been paid on the functions of the vascular endothelial cells including nitric oxide (NO) metabolism in relation to the pathophysiology of migraine. Arginine, a substrate of NO, is converted to glutamate and proline. Proline, one of $ B&A B-amino acids, is a major constituent of collagen, which is necessary for the formation of various tissues including vascular walls. Recent studies suggest it might also play an important role in neurotransmission. In this study, we discuss the possibility of the participation of serum proline in the pathophysiology of migraine.

37 patients with migraine with aura (MwA), 16 with migraine without aura(MoA) during an attack-free period and 10 healthy controls participated in the study. They had been prohibited taking caffein, alcohol and cheese since 12 h before the examination. Blood samples were taken after 15 minutes' rest at supine position from ulnar artery. The serum proline concentrations of both MwA (133.5 nmol/mL ± 33.8 nmol/mL) and MoW (152.0 nmol/mL ± 44.2 nmol/mL) were lower than that of healthy controls (162.5 nmol/mL ± 53.8 nmol/mL). Although the difference was not statistically significant due to the lack of the number of controls, there is a possibility that proline might be somehow related to the mechanism of migraine.

P3H29

Peculiarities of clinical manifestation in migraine patients

Stanislav Groppa[1], Eremei Zota*[1], Diana Manea[1] & Larisa Moshneaga[1]
[1]*City Emergency Hospital, Clinic of Neurology, Chishinau, Moldova*[10]

Despite progress in domain of migraine study, this disorder remains underdiagnosed and the available therapies underused.

The aim of our study was evaluation of clinical polymorphism of Migraine.
Materials and methods Our study was perform on a group including 256 women. All patients were divided in groups according to age, civil status, age of onset, frequencies of headache attacks.
Results The prevalent age in patients with migraine without aura was more then 30 years (85%), 73% of them were married, 10% not married and 14% were widows or divorced. In 132 cases (52%) the onset of the disease was at age under 20, in 85 (34%) at age between 20 and 30-year-old-and only in 14% at age of 30–40 years. The frequency of attacks is 1 per month in 47%, twice per month in 37%, and 16% have weekly attacks. Duration of an attack was 24 h in 45%, in 32% was 24–48 h and in 23% more then 72 h.
Conclusions Although attacks of migraine may start at any age, the incidence peaks in early to mid-adolescence. Majority of patients are of active age, thus migraine attacks lead to temporary disability with considerable economical prejudices.

P3H30

Probable migraine in platelet disorders: a case with thrombocythaemia

Cherubino Di Lorenzo*[1], Pasquale Marchione[1], Grazia Sances[2], Fabio Blandini[2], Natascia Ghiotto[2], Patrizia Giacomini[1] & Giuseppe Nappi[1,2]
[1]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy,* [2]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH), Italy*

Numerous evidences account for an implication of platelets in pathophysiology of migraine; an hyperaggregability and/or degranulation have been suggested. Interestingly, headache has been described in thrombocythaemia despite the clinical features have not been defined (Kesler et al. Acta Neurol Scand 2000). We report the case of a 65 years old man who presented a late-onset (47-years-old) high frequency headache with clinical features of probable migraine and a typical modification of urinary colour and smell after resolution of pain. In clinical history, a previous diagnosis of uveitis (1975) treated with steroids and immunosuppressive for 10 years with residual ambliopia was reported. Idiopathic thrombocythaemia was diagnosed in 1996 with a mean platelets number of 700.000–900.000/μL. The patient underwent standard NTG test (0.9 mg sublingually) and experimented an early migraine-type response during which 5HT, 5HIAA and platelets number did not vary significantly in blood. Indeed, after a spontaneous attack, in 24 h urine sample vanilmandelic acid (19,9 mg/24 h, normal values: 1,8–6,7) and 5HIAA (10,3 mg/24 h, normal values: 0,7–8,2) was significantly high. In our opinion, abnormal piastrinic degranulation could be suggested as consequence of a possible increased aggregation and/or biochemical instability following thrombocythaemia. Headache in platelet disorders could be an attractive link between platelets and migraine.

P3H31

Migraine with aura attacks overriding dreams

Pedro Andre Kowacs*[1], Elcio Juliato Piovesan[1], Marcos Christiano Lange[1], Lineu Cesar Werneck[1] & Marcelo Rezende Young[1]
[1]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil*

A 28-years-old white female with migraine with aura described how during sleep her migraine aura, presenting as the usual fortification spectra, would override her dreams, heralding a migraine attack. This rather rare phenomenon opens some windows to the physiology of aura and of dreams. Dreams' templates are presumed to be of either an hyppocampal or a temporo-occipital origin and fortification spectra aura are presumed to be of a primary occipital cortex origin. Thus, the coincidence of both conditions during dreams suggests that aura may project to the temporo-occipital cortex even when either visual input or vigilance are lacking. A more audacious hypothesis is that the aura engram can be stored during wakefulness and rehearsed during dreams, triggering the rest of the migraine attack.

P3H32

Neuro-endoscopy of the third ventricule trigger orbital head pain

Bruno Marcello Fusco*[1,2], Giorgio Barzoi[1], Pierluigi Longatti[3] & Felice Eugenio Agrò[1]
[1]*School of Medicine, University 'Campus Biomedico', Rome, Italy,* [2]*Department of Pharmaceutical Science, University of Salerno, Salerno, Italy,* [3]*Neurosurgical Department, Regional Hospital, Treviso, Italy*

Neuro-endoscopy is used, even in awake patients, to create a stomia between the third ventricule and the prepontine cistern, to resolve tri-ventricular hydrocephalus. Due to the patients being awake, the evoked sensations could be recorded. The observation was carried out on 15 patients (9 men and 6 women, age ranged from 41 to 69) who were affected by a ventricle stenosis induced by primitive or secondary neoplasia. A flexible endoscope was guided, under local anesthesia, after a precoronal scalp and meningeal incision, in the lateral and then into the third ventricle. Trough the endoscope, a monopolar coagulator and a Fogarty's balloon were inserted, without evoking sensations. When both the coagulation and the Fogarty's balloon dilatation were performed on the floor of the third ventricle to obtain the stomia, all subjects reported bilateral orbital pain. Pain was referred to as intense, pulsating and uncomfortable. In three patients pain was so intense as to require an i.v. bolus of Fentanyl. Pain disappeared as soon as the maneuvers ended. The floor of the third ventricle is close to important centers in the control of the pain. Our study indicates that stimulation involving the areas around the acqueductal system could evoke migraine-like pain.

P3H33

Peripheral markers of serotonergic activity and neurotrophic factors in migraine patients

Roberto Fancellu*[1,2], Grazia Sances[3], Cristina Tassorelli[3], Giuseppe Nappi[3,4], Anna Mangiagalli[1], Alberta Samuele[1], Alberta Leon[5], Luciano Rinaldi[5] & Fabio Blandini[1]
[1]*Laboratory of Functional Neurochemistry, IRCCS C. Mondino Institute of Neurology,* [2]*University of Insubria, Varese,* [3]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia,* [4]*Department of Neurology and ORL, University of Rome La Sapienza, Rome,* [5]*Research & Innovation S.C.R.L., Padova*

Serotonin (5-HT) is involved in the pathophysiology of migraine and, more in general, in the central modulation of pain. A major role in central nociception is also played by neurotrophins, such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF). Given the established relationship between BDNF and serotonergic activity in the context of pain modulation, we sought to explore the existence of a functional relationship between serotonergic neurotransmission and neurotrophic factors, in migraine. For this purpose, we measured concentrations of 5-HT and its major metabolite, 5-hydroxyindoleacetic acid (5-HIAA), along with levels of NGF and BDNF in peripheral blood platelets of subjects suffering from migraine – with or without aura – and healthy controls, matched for age and gender distribution.

Our results show increased levels of platelet 5-HT and 5-HIAA, coupled with decreased levels of NGF and BDNF, in both populations of migraine patients, compared to control subjects. These findings confirm the existence of a dynamic interaction between serotonergic activity and neurotrophic factors in painful conditions. In particular, they show, for the first time, that such interaction is likely to occur in migraine patients, thus providing useful insights in migraine pathogenesis and, possibly, new hints for novel therapeutic approaches.

This work was supported by a grant from the Italian Ministry of Health (RC 2002).

P3H34

Migraine attack delays gastric emptying: an ultrasonographic study

Nadia Pallotta[1], Maurizio Inghilleri[2], Piero Barbanti*[2] & Enrico Corazziari[1]
[1]*Department of Clinical Sciences, University,* [2]*Department of Neurological Sciences, University*

Objectives To evaluate gastric emptying (GE) in migraineurs during spontaneous attacks and in headache-free period.
Methods We studied 8 migraine patients (1 M, 7 F; MO: 7, MA: 1; age 51 ± 11 year) with normal upper GI endoscopy. GE was assessed by serial ultrasonographic measurements of gastric antrum volume (AV) in fasting condition and for 5 h after ingestion of a standardized everyday 1050 kCal meal (1). Delayed GE was defined as an AV (31 mL) exceeding two SD above normal control values at 5 h from the end of meal ingestion. Each patient was assessed twice, in headache-free period and during spontaneous untreated attacks.
Results GE was normal In all patients but one in headache-free period and delayed during migraine attack (AV: 24 ± 10 mL and 49 ± 14 mL, respectively) ($P < 0.01$). During the migraine attack all patients complained of nausea, upper GI discomfort or pain, fullness and belching.
Conclusions Migraine patients with proven exclusion of organic gastric diseases present a normal GE outside the attack but reveal a relevant delaying in GE during untreated attack. Ultrasonography appears a useful technique to investigate gastric motor function during migraine attack and may be applied to assess the effects of acute migraine treatment on gastric motility.

Reference

1 Ricci R et al. Real time ultrasonography of the gastric antrum. Gut 1993; 34 : 173–6.

Experimental studies in animals

P3I1

Differential modulation of nociceptive dural input to [hypocretin] Orexin A and B receptor activation in the posterior hypothalamus

Thorsten Bartsch*[1], M. J. Levy[1], Y. E. Knight[1] & P. J. Goadsby[1]
[1]*Headache Group, Institute of Neurology, London, U.K*

Objective To study the effects of orexin A and B receptor activation in the posterior hypothalamic area (PH) of the rat on dural nociceptive input.
Methods Orexins A or B were microinjected into the PH and the effects on responses of neurones in the trigeminal nucleus to dural and facial stimulation studied with electrophysiological techniques.
Results Injection of orexin A ($n = 13$) decreased the A- and C-fibre responses to dural electrical stimulation. Spontaneous activity and responses to noxious thermal stimulation of the facial skin were decreased. Injection of orexin B into the PH ($n = 12$) elicited increased responses to stimulation in A- and C-fibre responses and resulted in increased spontaneous activity. Responses to facial thermal stimulation were also increased. Control vehicle injections had no effect.
Conclusions The results show a differential modulation of dural nociceptive input by orexin A and B receptor activation in the PH, and support the role of the PH in the nociceptive processing of meningeal input. Since both peptides are involved in hypothalamic regulation of neuroendocrine and autonomic functions orexinergic mechanisms in the PH may provide a link between endocrine and autonomic changes as well as nociceptive phenomena seen in primary headache disorders.

P3I2

Nitric oxide scavenging may explain the potential antimigraine effect of melatonin

Anan Srikiatkhachorn*[1], Supang Meneesri[1], Juntima Pattamanont[1] & Suthiluk Patumraj[1]
[1]*Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok*

Objectives To investigate the possible involvement of nitric oxide (NO) system in the protective effect of melatonin upon cerebral microvascular response evoked by cortical spreading depression (CSD).
Methods CSD was induced in rat brains by applying solid KCl on parietal cortex. Both CSD and control rats were further divided into groups receiving melatonin (40 mg/kg BW), naratriptan (0.1 mg/kg BW) or L-NAME (10 mg/kg BW). All drugs were given intraperitoneally 30 min before CSD induction. Cortical blood flow (CBF) was monitored by laser Doppler flowmetry and pial microcirculation was visualized by intravital fluorescent videomicroscopy.
Results Cortical application of KCl resulted in repeated cycles of cortical hyperaemia and pial microvascular dilation. CBF gradually rose to 180–200% of baseline value before declining to the baseline Pretreatment with melatonin signifi-

cantly minimised the peak amplitude of CSD-evoked hyperaemia. The cycle duration became lengthen and eventually abolished. The same response was observed in rats pretreated with L-NAME. In contrast, CSD-evoked cerebral hyperaemia was slightly affected by pretreatment with high dose of naratriptan. This finding reflected that vasoconstriction alone could not completely abolish the CSD-evoked hyperaemia.
Conclusion Our findings suggested that minimising NO production or scavenging of NO is a possible explanation of attenuating effect melatonin on cerebral microvascular response to CSD.

P3I3

Cyclical expression of tryptophan hydroxylase and interleukin-1-beta in the trigeminal ganglion: relevance to menstrual migraine

Nancy Berman*[1], Veena Puri[1], Christopher Liverman[1], Michael Welch[2], Robert Klein[1] & L. Cui[1]
[1]*Department of Anatomy and Cell Biology, University of Kansas Medical Center, Kansas City,* [2]*Office of the President, Chicago Medical School, Finch University of Health Sciences*

Migraine is three times as prevalent in women as in men, and is associated with natural changes in levels of ovarian steroids. The trigeminovascular system is the key to the initiation of migraine, and the trigeminal ganglion is the locus of gene activity in this system. Our goal was to analyse the link between the estrous cycle and gene expression in the trigeminal ganglia of mice. Normally cycling mice were selected at diestrus, proestrus, and estrus. RNA was isolated from trigeminal ganglia, and RT-PCR for tryptophan hydroxylase, a critical enzyme in the serotonin synthesis pathway and interleukin-1-beta (IL-1β), a key proinflammatory cytokine was performed. Immunohistochemistry was used to localize proteins. Tryptophan hydroxylase-1 mRNA expression was higher at proestrus and estrus than at diestrus. Immunohistochemistry revealed localization of tryptophan hydroylase in small and medium-sized trigeminal neurons. IL-1β expression showed a sharp peak at estrus. These data show that in trigeminal ganglia, the key enzyme involved in serotonin synthesis is regulated by ovarian steroids, and is expressed at low levels when estrogen is low. In addition, expression of IL-1β mRNA is regulated by ovarian steroids. Our findings demonstrate that critical inflammatory and pain mediators are regulated by ovarian steroids in the trigeminovascular system.

Supported by the Lied Foundation, American Heart Assn./ Heartland Affiliate and the American Headache Society.

P3I4

Anandamide shows both cannabinoid and vanilloid properties in an *in vivo* model of trigeminovascular mediated headpain

Simon Akerman*[1], Holger Kaube[1] & Peter Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square London UK*

Objectives To examine role of anandamide, the cannabinoid CB_1 and CB_2 receptor endogenous ligand, in the dural trigeminovascular system.
Methods Rats were anaesthetised and cannulated for measurement of blood pressure and intravenous administration of experimental drugs, and supplementary anaesthesia. The parietal bone was thinned to form a cranial window through which the diameter of a branch of the middle meningeal artery was measured on-line with a video dimension analyser.
Results Electrical stimulation (50–300μA) and CGRP injections reproducibly caused dural vessel dilation, 135 ± 4% and 106 ± 7%, respectively, as measured by intravital microscopy rat. Anandamide inhibited both neurogenic dural vasodilatation (3mgkg^{-1}, n = 12, $P < 0.05$) and CGRP induced dilation ($n = 6$, $P < 0.05$). It was also able to cause a dose-dependent vasodilation that was inhibited by capsazepine, a VR1 receptor antagonist ($n = 6$, $P < 0.05$), rather than a CB_1 receptor antagonist.
Conclusions Anandamide is able to block CGRP postsynaptically and block dural vessel dilation. CB receptors therefore have potential as novel therapeutic targets in migraine. Anandamide is also an agonist at the VR1 receptor and causes vasodilation, presumably by activating the release CGRP. Its action is blocked by capsazepine, the VR1 receptor antagonist.

P3I5

Stimulation of the superior sagittal sinus (SSS) in cat evokes fos activation in restricted nuclei of the hypothalamus

L. Benjamin*[1], M. Levy[1], M. Lasalandra[1], J. Classey[1] & P. Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London, UK*

Objectives This study sought to examine the distribution of fos protein-like immunoreactivity (fos) in the hypothalamus of the cat after stimulation of the SSS.
Methods Cats were anaesthetised with halothane and a-chloralose (60 mg/kg, ip) and prepared for physiological monitoring. The SSS was isolated and stimulated electrically. Fos was determined in stimulated ($n = 8$) and sham-stimulated (control, n = 4) animals, plotted onto sections and counted by a blinded observer.
Results There was little fos expression in most regions of the hypothalamus both rostral and caudal. Only the paraventricular hypothalamus had notable levels with a median of 38 fos-positive neurons (95% confidence interval: 0–90). Control expression in the supraoptic (SO) region was 3 (0–13) cells. This increased to 53 (32–76; $\chi^2 = 7.41$, $P = 0.005$) with SSS stimulation. Posterior hypothalamic (PH) fos expression increased from 4 (0 to 14) to 35 (17–45; $\chi^2 = 6.01$, $P = 0.015$) with stimulation. No significant difference in expression in stimulated animals was observed in any other hypothalamic nuclei
Conclusions Activation of trigeminovascular nociceptive pathways results in significant activation of the SO and PH regions. Defining the role of hypothalamic neurons in the pathophysiology of primary headaches will shed light on these disorders.

P3I6

Only abluminally applied CGRP induces rat pial artery dilatation *in vitro* and *in vivo*

Kenneth A. Petersen*[1], Elisabet Nilsson[2], Jes Olesen[1] & Lars Edvinsson[2,3]
[1]*Danish Headache Centre, University of Copenhagen and Department of neurology, Glostrup University, Denmark,* [2]*Department of Internal Medicine, Lund University Hospital, Lund, Sweden,* [3]*Department of Clinical Experimental Research, Copenhagen University Hospital, Glostrup, Denmark*

Calcitonin gene-related peptide (CGRP) is involved in migraine pathogenesis. To understand the vasomotor mechanisms in the cerebral circulation, we performed two studies: a pressurized arteriography of the middle cerebral artery (MCA) and a 'closed cranial-window' study.

Using pressurized arteriography, MCAs from Sprague-Dawley rats were mounted onto micropipettes, pressurized to 85 mmHg and luminally perfused. The diameter responses to luminally and abluminally applied r-αCGRP, r-βCGRP, amylin and adrenomedullin were compared to the resting diameter.

The 'closed cranial-window' model allowed video-microscopic visualization of the pial arteries in anaesthetized Sprague-Dawley rats. Changes in vessel diameter to intravenously administered r-αCGRP and r-βCGRP were compared to preinfusion baseline.

Only abluminal applied CGRP induced a dilatation of the MCA, E_{max} for r-αCGRP and r-aCGRP were 35 ± 0.5%(SEM), 10.8 ± 0.2%(SEM), respectively. Intravenous infusion of r-αCGRP and r-βCGRP, 3 μg kg^{-1}, induced a dilatation of the pial artery of 40.9 ± 5.7(SEM)% and 47.6 ± 8.8(SEM)% in the cranial-window model. However, this was most likely secondary to a drop in blood pressure, 39.1 ± 2.4%(SEM) and 41.4 ± 3.1%(SEM), respectively.

In conclusion, the used experimental models maintain the endothelial barrier in the pial arteries and prevent infused or perfused agents in reaching their receptors. Secondly, no receptors of the CGRP peptide-family seem to be present on pial endothelial cells.

P3I7

Activation of ipsilateral pia-arachnoid cells and matrix metalloproteinases by cortical spreading depression in a migraine model

Hayrunnisa Bolay*[1], Yasemin Gursoy-Ozdemir[1], Jianhua Qui[1], Daniela Bermpohl[1], Xiaoying Wang[2], Gary Rosenberg[3], Eng H. Lo[2] & Michael A. Moskowitz[1]
[1]*Stroke and Neurovascular Regulation Laboratory, Masschusetts General Hospital, Harvard Medical School, Charlestown, Massachusetts,* [2]*Neuroprotection Research Laboratory, Department of Neurology, Masschusetts General Hospital, Harvard Medical School, Charlestown, Massachusetts,* [3]*Department of Neurology, University of New Mexico, Albuquerque, New Mexico*

We demonstrated that CSD, an intrinsic brain event underlying migraine visual aura activates trigeminovascular system. We aimed to investigate how intense activity within the brain parenchyma (CSD) triggers perivascular trigeminal nerve axons in pia-arachnoid through the glia limitans and BBB. Cortical and meningeal tissues were examined at 1–48 h after CSD by immunohistochemistry, immunoblotting and: zymography.

Results Were as follows (1) CSD promoted c-fos expression strictly within ipsilateral pia-arachnoid membranes, mainly within S100B(+) cells and not in overlying dura mater. (2) Endothelial barrier antigen immunohistochemistry(a marker for BBB function) was profoundly reduced within pial and cortical penetrating vessels on the CSD side. Evans blue studies revealed perivascular leakage on the CSD side. (3) *In situ* zymography of the pia-arachnoid showed increased gelatinolytic activity around the large penetrating blood vessels and pia mater. Gelatin zymography revealed MMP-9 and MMP-2 up-regulation in the pia and dural tissues. These data show that CSD activates ipsilateral cells in the 'pain sensitive' pia-arachnoid compartment, and leads to limited BBB disruption and MMP activation which may relate to breakdown of substrate proteins within glial–pial barriers.We postulate that such a breach in basement membranes may allow substances released from brain parenchyma during CSD(K + ,ATPetc.) to access the pia-arachnoidal membranes and thereby discharge trigeminovascular axons.

P3I8

Capsaicin stimulation of the meningeal artery induces CREB Phosphorylation (P-CREB) within the rat Trigeminal Ganglion (TG)

Dimos Mitsikostas*[1] & Peter Goadsby[2]
[1]*Athens Naval Hospital, Neurology Department, Athens, Greece,* [2]*Headache Group, Institute of Neurology, Queen Square, London, U.K*

Objectives To investigate whether P-CREB would act as a marker of neuronal activation within the trigeminal ganglion after nociceptive stimulation.

Methods Trigeminal nociceptive neurons were stimulated by direct application of capsaicin (1 μmol) onto the middle meningeal artery (10 mins) in rats ($n = 4$) anaesthetized with pentobarbital ip (60 mg/kg) and 10 min later the animals were perfused. CREB and P-CREB were immunohistochemically detected within the TG and the trigeminal nucleus caudalis (Sp5C) neurons. Two nonstimulated rats were served as controls.

Results CREB and P-CREB were expressed widely in the brainstem, in all laminae, in all nuclei, as well as in the leptomeninges (about 350–400 neurons in each side of Sp5C, depending on the level). No difference could be detected between stimulated and nonstimulated animals because of the high density of the labeling. Both CREB and P-CREB were detected within TG as well. Capsaicin stimulation significantly altered the TG P-CREB immunoreactivity.

Conclusions P-CREB may serve as an early marker of neuronal activation within the trigeminal ganglion.

P3I9

Comparative effects of donitriptan, naratriptan, rizatriptan and sumatriptan on jugular venous oxygen saturation in anesthetized pigs

Robert Létienne*[1], Yvan Verscheure[1] & Gareth W. John[1]
[1]*Centre de Recherche Pierre Fabre, Castres Cedex, France*

The objective of this study was to compare the effects of donitriptan on jugular venous oxygen saturation to those of sumatriptan, rizatriptan and naratriptan.

Experiments were performed in 40 pentobarbitone-anesthetized pigs. Oxygen and carbon dioxide partial pressures in systemic arterial and jugular venous blood as well as hemoglobin oxygen saturation were determined by conventional blood gas analysis. Vehicle (either 40% PEG in saline, $n = 9$, or saline, $n = 10$), donitriptan (0.01, 0.04, 0.16, 0.63, 2.5, 10 and 40 μg/kg, $n = 7$) or naratriptan, rizatriptan, or sumatriptan (0.63, 2.5, 10, 40, 160, 630 and 2500 μg/kg, $n = 7$) were cumulatively infused over 15 min per dose.

Donitriptan and rizatriptan markedly and dose-dependently decreased jugular venous oxygen saturation [ED_{50} 0.5 (0.3–1.1) μg/kg and 18 (1–59) μg/kg, respectively,]. Naratriptan and sumatriptan also significantly decreased venous oxygen saturation (– 13.9 ± 3.5, $P < 0.05$ and – 13.4 ± 6.3%, $P < 0.05$ compared to vehicle, respectively) but in a less pronounced manner than donitriptan or rizatriptan (– 32.3 ± 7.5, $P < 0.05$ and –26.2 ± 8.5%, $P < 0.05$, respectively). Interestingly, donitriptan from 2.5 μg/kg and rizatriptan from 40 μg/kg induced marked and significant increases in carbon dioxide partial pressure in venous blood (max. increase 18.8 ± 5.7%, $P < 0.05$ and 24.9 ± 8.9%, $P < 0.05$ compared to vehicle). Naratriptan and sumatriptan failed to significantly affect carbon dioxide partial pressure in venous blood, but tended to increase values (max. increase 6.1 ± 4.0%, $P = 0.22$ and 7.6 ± 5.7%, $P = 0.09$, respectively). In parallel, donitriptan, naratriptan, rizatriptan and sumatriptan dose-dependently increased carotid vascular resistance, ED_{50} 0.9 (0.7–1.1); 7.1 (4.1–12.1); 15.6 (12.8–17.9) and 16.4 (13.3–21.5) μg/kg, respectively.

In conclusion, the triptans investigated decreased the oxygen saturation of venous blood draining the head concomitantly with cranial vasoconstriction. In addition, donitriptan and rizatriptan markedly increased carbon dioxide partial pressure in venous blood whereas sumatriptan and naratriptan tended to increase this parameter. The data suggest that triptans stimulate cerebral oxygen consumption and metabolism in addition to constriction of cranial arteriovenous anastomoses.

P3I10

Distinctive distribution of 5-HT1B receptor in trigeminovascular system in the rat – another implication for pharmacological action sites of triptans

Manami Tomita*[1], Norihiro Suzuki[1] & Fumihiko Sakai[1]
[1]*Department of Neurology, Kitasato University, Sagamihara, Japan*

To explore the precise action sites of triptan, we investigated distribution of the 5-HT_{1B} receptors in the trigeminovascular system of rats and effect of triptan on 5-HT_{1B} receptors by immunohistochemistry.

The trigeminal ganglia (TG), dorsal root ganglia (DRG), cerebral vessels, dural vessels, trigeminal caudal nucleus and thalamus were obtained from five rats.

5-HT_{1B} receptors were detected in the cell bodies of TG and DRG neurons as well as neurons in the trigeminal caudal nucleus and cerebral cortex, but were scarce in the thalamus. 5-HT_{1B} receptors were also observed in all three layers of the cerebral vessels. Among these regions, they were remarkably prominent in TG and DRG. The number of immunoreactive materials in TG was 85.5 ± 3.2 (mean ± SEM)/neuron ($n = 100$) in control group, while 65.6 ± 2.8/neuron ($n = 100$) in triptan group ($P < 0.0001$). As of DRG was 75.7 ± 2.9/neuron ($n = 100$) in control group, while 51.5 ± 2.2/neuron ($n = 100$) in triptan group ($P < 0.0001$).

Although the target of the action sites for triptans have been reported to the smooth muscle and perivascular trigeminal nerve terminals and trigeminal caudal nucleus, present study suggested that triptan is feasible to act on 5-HT_{1B} receptors in TG and DRG neurons where BBB is lacking rather than above mentioned sites with BBB.

Supported by Grants of Health and Labour Sciences Research Grants, Japan (Research on Psychiatric and Neurological Diseases and Mental Health | 14220901).

P3I11

Calcium channels may be involved in CGRP release in trigeminal neurons and modulate subsequent dural dilation

Simon Akerman*[1], David Williamson[2] & Peter Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square London UK,*
[2]*Merck, Sharp and Dohme, Terlings Park, Harlow, Essex, UK*

Objectives We examined the role of voltage-dependent calcium channels (VDCCs) in the trigeminovascular system in modulating dilation of dural blood vessels.

Methods Rats were anaesthetised and cannulated for measurement of blood pressure and intravenous administration of experimental drugs and supplementary anaesthesia. The parietal bone was thinned to form a cranial window through which the diameter of a branch of the middle meningeal artery was measured with a video dimension analyser.

Results Electrical stimulation (50–300μA) and CGRP injections produced reproducible dural vessel dilation of 135 ± 4% and 106 ± 7%, respectively. P/Q (ω-agatoxin-IVA, 3, 10 and 20 μgkg^{-1}, $n = 7$), N (ω-conotoxin-GVIA, 10 and 20 μgkg^{-1}, $n = 8$ and 40 μgkg^{-1}, $n = 7$) and L-type (calciseptine, 7 and 10 μgkg^{-1}, $n = 8$ and 20 μgkg^{-1}, $n = 7$) VDCC blockers inhibited the neurogenic dural vasodilatation, but were unable to prevent CGRP-induced dilation.

Conclusions The P/Q, N and L-type VDCCs would seem to exist presynaptically on trigeminovascular neurons, and blockade prevents CGRP release, and dural blood vessel dilation. This suggests that the P/Q, N and L-type VDCC may represent novel therapeutic targets, or be involved in the pathophysiology of migraine, or both.

P3I12

Chemical sensitization of the dura causes short-term inhibition followed by long lasting sensitization in the trigeminal nucleus caudalis

Elcio Juliato Piovesan[1], Jia Luo[1] & Michael Oshinsky*[1]
[1]*Department of Neurology, Thomas Jefferson University, Philadelphia, USA*

Objective In order to understand the electrophysiology and neurochemistry of central sensitization of the trigeminal nucleus caudalis (TNC), we used electrophysiological and microdialysis methods to monitor the changes in impulse activity and extracellular neurotransmitters in the TNC.
Methods Using electrophysiology, we isolated a single unit recording of a secondary sensory neuron in the TNC. Central sensitization of the TNC was induced by the application of the inflammatory soup on the superior and transverse sinuses of the dura. We applied mechanical stimuli over the periorbital region before and 40 min, 2, 3, 4 h after the soup. We recorded changes in impulse activity of the WDR neurons of the TNC. *In vivo* microdialysis was performed to determine the changes of the neurotransmitters in the TNC, including glutamate, glutamine and GABA.
Results The mechanical threshold increased 40 min after the soup, while glutamate decreased; at 2,3, and 4 h postsoup, the mechanical threshold decreased, while the glutamate increased to about 3 times of the basal level.
Conclusions Sensitization of the dura leads to an initial (40 min) decrease in TNC excitability and extracellular glutamate, followed by sensitization and a significant increase in glutamate at 2–4 h. These results bring new insights into the physiopathology of headaches.

P3I13

Cortical spreading depression induces cerebral hyperaemia but not perivascular inflammation

Juntima Pattamanont*[1], Supang Maneesri[2], Suthiluk Patumraj[2] & Anan Srikiatkhachorn[2]
[1]*Department of Physiology, Faculty of Medicine, Chiang Mai University, Bangkok, Thailand,* [2]*Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Objectives This study aimed at investigating the effect cortical spreading depression (CSD) on cortical blood flow (CBF) and perivascular meningeal inflammation and roles of nitric oxide (NO) in this process.
Methods CSD was induced in rat brains by applying solid KCl on parietal cortex.

Pial microcirculation and leukocyte–endothelial cell interaction were visualized by intravital fluorescent videomicroscopy. CBF was monitored by laser Doppler flowmetry (LDF). Ultrastructure of cortical microvessels was studied using electron microscopy. To determine the effect of NO, L-NAME (1–100 mg/kg BW) was given intraperitoneally 30 min before CSD induction.
Results Cortical application of KCl resulted in repeated cycles of pial microvascular dilation. However, neither leukocyte adhesion nor leakage of fluorescent dye was observed. These findings reflected that the integrity of blood–brain barrier was still intact. LDF study showed cyclic pattern of cortical hyperaemia with corresponding temporal profile. CSD also evoked substantial changes in endothelial cell ultrastructure, characterising by increased pinocytosis and microvillus formation. Pretreatment with L-NAME was able to diminish or abolish CSD-evoked cortical hyperaemia in dose-dependent manner.
Conclusion Our findings suggest that CSD can cause cortical hyperaemia via NO-dependent mechanisms. However, the lack of leukocyte–endothelial cell interaction implies that CSD does not seem to induce substantial perivascular inflammation.

P3I14

Mechanisms of the antinociceptive effect of subcutaneous BOTOX®: inhibition of peripheral and central nociceptive processing

K. Roger Aoki[1] & Minglei Cui*[1]
[1]*Allergan, Inc.; Irvine, CA, USA*

Botulinum toxin type A (BOTOX®) has been used to treat pathological pain conditions although the mechanism is not entirely understood. Subcutaneous (SC) BOTOX® also inhibits inflammatory pain in the rat formalin model, and the present study examined whether this could be due to a direct action on sensory neurons. BOTOX® (3.5–30 U/kg) was injected SC into the subplantar surface of the rat hind paw followed 1–5 days later by 50 µL of 5% formalin. Using microdialysis, we found that BOTOX® significantly inhibited formalin-induced glutamate release (peak inhibitions: 35%, 41%, and 45% with 3.5, 7 and 15 U/kg, respectively). BOTOX® also dose-dependently reduced the number of formalin-induced Fos-like immunoreactive cells in the dorsal horn of the spinal cord and significantly (15 and 30 U/kg) inhibited the excitation of wide dynamic range neurons of the dorsal horn in Phase II but not Phase I of the formalin response. Finally, we found that BOTOX® inhibited capsaicin-induced thermal hyperalgesia, suggesting an action on substance P. These results indicate that SC BOTOX® inhibits neurotransmitter release from primary sensory neurons in the rat formalin model. Through this mechanism, BOTOX® inhibits peripheral sensitization in these models, which leads to an indirect reduction in central sensitization.

P3I15

Mental stress up-regulates endothelial nitric oxide synthase expression in rat dura mater and cerebral arteries

Tina Zinck*[1], Regitze Illum[1] & Inger Jansen-Olesen[2]
[1]*The Danish University of Pharmaceutical Sciences, Copenhagen, Denmark,* [2]*Glostrup Hospital, Glostrup, Denmark*

Objectives More than half of migraine patients denote stress as the primary precipitating factor for their migraine attack. However, it still remains to be investigated how stress and migraine are related. As nitric oxide is believed to play a

central role in the patophysiology of migraine we have investigated whether endothelial nitric oxide synthase (eNOS) expression is up-regulated in the cerebral arteries and dura mater of mentally stressed rats.

Methods Rats were killed 1, 2, 3 and 4 h after the stress exposure. Dura mater and cerebral arteries were dissected out and analysed by either Western blotting or real-time PCR for the expression of eNOS.

Results Two hours after stress exposure the protein expression of eNOS was up-regulated 40 ± 0.15% (mean ± S.E.M.; n = 8) in cerebral arteries and 70 ± 0.26% in dura mater (n = 4) when compared to control rats. No significant protein up-regulation was found at the other time points. Real-time PCR did not show any up-regulation of mRNA for eNOS in the two tissues at any timepoint after stress.

Conclusion Mental stress in rat, causes an up-regulation of eNOS protein in cerebral arteries and dura mater, that might be due to a translational regulation mechanism.

P3I16

Administration of lysine acetylsalicylate but not of sumatriptan inhibits nitroglycerin-induced nNOS increase in rat trigeminal nucleus caudalis

Arpad Pardutz*[1,3], Laszlo Vecsei[1,4] & Jean Schoenen[2,3]
[1]*Department of Neurology, University of Szeged, Hungary,* [2]*Department of Neurology, Headache Research Unit. University of Liège, Belgium,* [3]*Research Center of Cellular & Molecular Neurobiology, Neuroanatomy Laboratories, University of Liège, Belgium,* [4]*Neurology Research Group of the Hungarian Academy of Sciences and University of Szeged*

We have shown earlier that the nitric oxide donor (NO) nitroglycerin (NTG. 10 mg/kg s.c) is able to increase significantly after 4 h the number of neuronal nitric oxide synthase (nNOS)-immunoreactive neurons in the cervical part of trigeminal nucleus caudalis in rats. In the present experiments, we demonstrate that the 5-HT$1_{B/D}$ agonist sumatriptan (0.6 mg/kg s.c) does not alter this phenomenon when given before NTG. By contrast, pretreatment with lysine acetylsalicylate (50 mg/kg i.m) attenuates the NTG-induced nNOS expression in the superficial laminae of trigeminal nucleus caudalis. These data contribute to the better understand the role of NO in the pathogenesis of headaches and the action of antimigraine drugs.

P3I17

Effect of nitric oxide on the nociceptive transmission in an experimental migraine model

Shengyuan Yu*[1], Hebo Wang[2] & Weidong Wang[3]
[1]*Department of Neurology, Chinese PLA General Hospital, Beijing,* [2]*Department of Neurology, Hebei Province People's Hospital, Shijiazhuang,* [3]*Medical Engineering Center, Chinese PLA General Hospital, Beijing*

Objective We reported the role of NO on the nociceptive transmission in second-order neurons of trigeminal nerve of cats in the experimental model of migraine and other vascular headaches.

Methods 40 cats were divided randomly into sham-operation, stimulation, saline, L-NAME and 7-NI groups. The same volume of saline, L-NAME (100 mg/kg) and 7-NI(10 mg/kg) was injected, respectively, in the saline, L-NAME and 7-NI groups before the dura matter near the superior sagittal sinus was electrically stimulated.

Results The neurons with expression of nNOS and c-fos immunoreactivity were concentrated in the laminae I and II of the trigeminal nucleus caudalis and the dorsal horn of the C1 segment of the cervical cord. The number of neurons with expression of nNOS and c-fos immunoreactivity was significantly increased in the stimulation group comparing with those in the sham-operation group($P < 0.01$), and was significantly decreased in the L-NAME and 7-NI groups than in the stimulation and saline groups($P < 0.01$), although there was no significant difference between the L-NAME group and the 7-NI group($P > 0.05$).

Conclusions NO could mediate nociceptive transmission from the superior sagittal sinus to second-order neurons of trigeminal nerve in the experimental model of migraine and other vascular headaches.

P3I18

The 5-HT1B/D receptor agonist naratriptan microinjected into the periaqueductal grey selectively inhibits meningeal nociception

Thorsten Bartsch*[1], Y. E. Knight[1] & P. J. Goadsby[1]
[1]*Headache Group, Institute of Neurology, London, U.K*

Objective To investigate a possible brainstem site of action of triptans in an animal model of dural nociception.

Methods The 5-HT$_{1B/1D}$ agonist naratriptan was microinjected into the ventrolateral periaqueductal grey (vlPAG) and the modulation of nociceptive dural input in the trigeminal nucleus caudalis (TNC) of rats was recorded using electrophysiological methods. Responses of nociceptive neurones to dural, facial cutaneous and corneal stimulation were studied before and after injection of naratriptan.

Results Injection of naratriptan (50–200 nL, 10 mg/mL) into the PAG decreased the excitability to electrical stimulation of the dura mater in the A- and C-fibre responses and spontaneous activity (n = 17). The mechanical von Frey thresholds of neurons with dura mater input increased. Noxious thermal stimulation of the facial skin and mechanical stimulation of the cornea were not altered by injection of naratriptan into the PAG. Control injections had no effect.

Conclusions These results suggest that 5-HT$_{1B/1D}$ receptor activation in the vlPAG activates descending pain-modulating pathways which inhibit dural, but not facial and corneal nociceptive input. These findings may have implications in understanding the action of triptans in migraine and cluster headache, offering an additional possible site of action in the brainstem.

P3I19

Leukotriene increases upon trigeminovascular activation in the rat

Norihiro Suzuki*[1], Michinari Fukuda[1], Shinnya Tsukahara[1], Fumihiko Sakai[1], Manabu Fujita[2] & Y. Yonetomi[2]
[1]*Department of Neurology, Kitasato University, Sagamihara, Japan,*
[2]*Minase Research Institute, Ono Pharmaceutical, Mishima, Osaka, Japan*

To explore the role of leukotrienes in acute migraine attacks, the change of leukotriene D4 (LTD4) was investigated utilizing the rat trigeminovascular activation model.

The internal jugular veins (IJV) were catheterized in 6 male Sprague-Dawley rats. The parietal cortical blood flow (CoBF) on the right side was continuously monitored with the Laser-Doppler flow meter system. The right nasociliary nerve (NCN) was electrically stimulated (1–5 V, 0.5 ms duration, 10Hz, 30 s stimulation). The blood sample was obtained from IJV before and after NCN stimulation. The content of LT D4 was measured with a multispecific enzyme immunoassay kit for LTD4 (1).

CoBF (Fig. 1) was significantly increased upon electrical NCN stimulation at 30 s from the initiation of stimulation (18.5 ± 7.7%). The contents of LTD4 increased from 374.04 ± 18.29 pg/mL in the control state to 395.82 ± 21.78 pg/mL just after electrical stimulation of NCN.

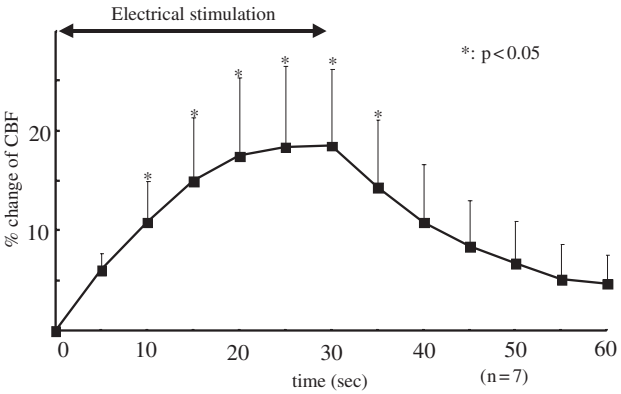


Figure 1

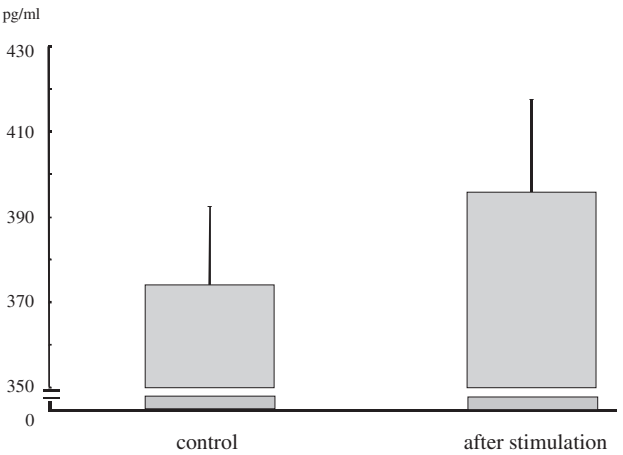


Figure 2

This study demonstrated that leukotriene was released upon activation of trigemino- vascular system in the rat migraine model. A specific D4 leukotriene receptor antagonist, montelukast, has been shown to be a well-tolerated and effective prophylactic agent for migraine in a clinical study (Fig. 2). Taken together, the leukotriene may play a crucial role in the migraine pathogenesis.

Supported by Grants of Health and Labour Sciences Research Grants, Japan (Research on Psychiatric and Neurological Diseases and Mental Health | 14220901).

References

1 Fujita M et al. Eur J Pharmacol 369 (1999) 349–356.
2 Sheftell F et al. Headache 40 (2000) 158–163.

P3I20

Role of CGRP receptors in cerebral blood flow increase upon trigeminovascular activation in rats

Shinya Tsukahara*[1], Michinari Fukuda[1], Norihiro Suzuki[1], Shigeyosi Maruyama[2] & Fumihiko Sakai[1]
[1]*Department of Neurology, Kitasato University, Sagamihara, Japan,*
[2]*Laboratory Animal Science, Kitasato University, Sagamihara, Japan*

In order to explore the role of CGRP receptor in acute migraine attacks, the cerebral blood flow change was investigated in rat trigemiovascular activation model utilizing CGRP receptor antagonist.

In 7 male Sprague-Dawley rats, both parietal cortical blood flow (CoBF) on the right side and thalamic blood flow (ThBF) on the left side were continuously monitored with the Laser-Doppler flow meter system The nasociliary nerve (NCN) was electrically stimulated (1–5 V, 0.5 ms duration, 10Hz, 30 s stimulation). CoBF and ThBF were measured before and after electrical stimulation of NCN under intravenous injection of hCGRP 8–37 (60 μg/kg) followed by 5-$HT_{1B/1D}$ receptor agonist, sumatriptan (25 μg/kg).

Both CoBF (Fig. 1) and ThBF (Fig. 2) were significantly increased upon electrical NCN stimulation at 30 s from the initiation of stimulation (18.5 ± 7.7% and 23.5 ± 9.9%, respectively) in control state. These increase were significantly suppressed after hCGRP 8–37 administration by 2.8 ± 1.4% (CoBF) and 6.3 ± 2.0% (ThBF) at 20 s. They were also suppressed after sumatriptan administration by 3.1 ± 2.1% (CoBF) and 3.8 ± 1.5% (ThBF) at 25 s. Each value of blood flow increase under hCGRP 8–37 or sumatriptan administration was significantly low compared with control.

CGRP is the most important neurotransmitter substance in the trigeminal neurogenic vasodilatation.

Supported by Grants of Health and Labour Sciences Research Grants (Research on Psychiatric and Neurological Diseases and Mental Health | 14220901).

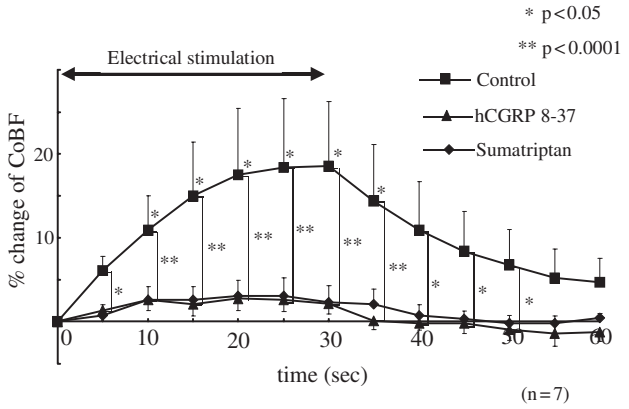


Figure 1

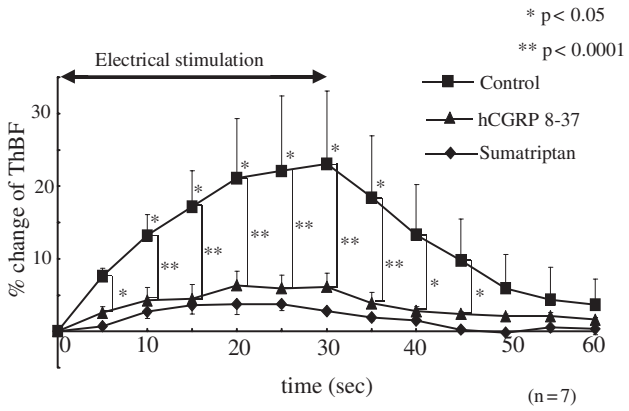


Figure 2

P3I21

Effect of IL-1b microinjection into the posterior hypothalamic area on trigeminal nociception in the rat

Miles Jonathan Levy*[1], Yolande Knight[1], Celestine O'Shaunessy[2] & Peter Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London, UK,* [2]*Centre for Excellence in Drug Discovery (Neuroscience) GlaxoSmithKline, Harlow, Essex, UK*

Objectives To determine the effect of IL-1β microinjection into the posterior hypothalamic area on trigeminal nociception in the rat.
Methods We recorded from the trigeminal nucleus caudalis of rats using extracellular electrophysiological methods from neurons responding to electrical stimulation of the peri-middle meningeal artery and having receptive fields in the ophthalmic division of the trigeminal nerve.
Results Data were collected from nine wide-dynamic range neurons with stable baseline firing responses between 97 and 101% ($n = 3$ for each unit) to stimulation. Microinjection of IL-1β into the posterior hypothalamus resulted in a modest inhibition of evoked trigeminal responses in three units, no effect in six and no overall effect for the entire cohort studied. The mean maximum effect was to reduce firing to 83 ± 7% ($n = 9$) at 30 min postinjection of IL-1β. There was some variation of effect dependent on site of injection with central posterior hypothalamus being the predominant area that resulted in inhibition.
Conclusions The hypothalamus has been implicated in the pathophysiology of migraine and cluster headache. Interleukin-1β (IL-1β) is highly expressed in the hypothalamus. If there is an important effect for IL-1β in the posterior hypothalamus it is likely to be somatotopically restricted.

P3I22

Prostaglandin E2 injected into the posterior hypothalamus has no effect on trigeminal nociception in the rat

Y. Knight*[1], M. Levy[1], C. O'Shaugnessy[1] & P. Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London, UK*

Objectives Prostaglandin E2 (PGE2) was microinjected into the posterior hypothalamus to investigate its effect on central modulation of trigeminal nociception.
Methods Rats were anaesthetised with pentobarbitone sodium (65 mg/kg i.p. induction, maintenance with α-chloralose 15 mg/kg i.v), and prepared for electrophysiological recordings using tungsten wire electrodes. Trigeminal nucleus caudalis neurons responsive to noxious middle meningeal artery stimulation and inhibited by bicuculline activation of the posterior hypothalamus were studied.
Results Data were collected from wide-dynamic range units in the trigeminal nucleus caudalis in seven animals. Injection into the posterior hypothalamus of a nonpyrogenic dose of PGE2 (2.5 μg/mL) produced no effect on nociceptive trigeminal nucleus caudalis neurons compared with saline injection ($P = 0.291$, $n = 7$). The mean response within 60 min of PGE2 injection was 97% of baseline.
Conclusions We conclude that PGE2 in the posterior hypothalamus is unlikely to play a role in trigeminal nociception or headache pathophysiology.

P3I23

Role of nitric oxide in meningeal nociception in the rat

Karl Messlinger*[1], Stanislav Koulchitsky[1], Roberto De Col[1], Phillip Schlechtweg[1], Thomas Strecker[1] & Richard Carr[1]
[1]*Institute of Physiology and Exper. Pathophysiology, University of Erlangen, Germany*

Nitric oxide (NO) has been supposed to play a causative role in the pathogenesis of primary headaches. Infusion of NO donators can trigger headache attacks in patients suffering from migraine and cluster headache, while products of the NO metabolism are increased in the cranial circulation in these patients. In some rat models of meningeal nociception we examined the effects of NO donators on meningeal blood flow and trigeminal activation.

NO donators applied to the exposed cranial dura mater increased meningeal blood flow, partly mediated by calcitonin gene-related peptide (CGRP). In an *in vitro* hemisected cranial preparation, NO donators caused CGRP release from the dura. In the isolated cranial dura, afferent activity recorded from meningeal nerves increased during NO donator super-

fusion. In the spinal trigeminal nucleus, the discharge activity of neurons with meningeal input was continuously increased and the mechanical threshold was decreased 1–3 h after NO donator infusion.

We conclude that NO released from intracranial tissues activates meningeal nociceptive processes through several mechanisms. In the meninges NO causes vasodilatation, neuropeptide release and afferent activation. In the trigeminal nucleus NO induces delayed discharge activity of second order neurons. These mechanisms may contribute to the development of primary headaches.

P3I24

Activation of the transcription factor NF-KB in the nucleus trigeminalis caudalis in an animal model of migraine

Rosaria Greco*[1], Cristina Tassorelli[1,2], Cristina Meazza[1], Fabio Blandini[2] & Giuseppe Nappi
[1]*Laboratory of Pathophysiology of Integrative Autonomic Systems, Pavia, Italy,* [2]*University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [3]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

Recent findings suggest that the transcription factor nuclear factor-kappaB (NF-KB) is implicated in the cascade of events that lead to protein plasma extravasation in the perivascular meningeal tissue. In the present study we tested whether NF-KB is also likely to play a role at the neuronal level in the determinism of migraine attacks.

Under basal conditions, NF-KB is in its cytoplasmatic form but following a variety stimuli, the phosphorylation of two serine residues, induces the translocation of subunit P65 into the nucleus. Therefore P65 immunoreactivity may be adopted as an indicator of NF-KB activation. Male Sprague-Dawley rats were systemically injected with nitroglycerin and killed 4 h later. Sections of lower brainstem and spinal cord were immunohistochemically processed for P65 subunit of NF-KB. A significant activation of NF-KB was detected in lamina I and II of nucleus trigeminalis caudalis in the rats injected with nitroglycerin when compared to the vehicle group.

This data contributes to expand the understanding of the complex mechanisms by which NO is involved in migraine and provides further sites and targets for the development of innovative migraine therapies.

This study was supported by a grant from the Italian Ministry of Health (RC 2002).

P3I25

Expression of calcitonin gene-related peptide and substance P in the nucleus trigeminalis caudalis during different models of hyperalgesia

Cristina Tassorelli*[1,2], Rosaria Greco[1], Giorgio Sandrini[2] & Giuseppe Nappi[2,3]
[1]*Laboratory of Pathophysiology of Integrative Autonomic Systems, Pavia, Italy,* [2]*University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [3]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

Systemic administration of nitroglycerin (NTG) triggers spontaneous–like migraine attacks in migraineurs. Calcitonin gene-related peptide (CGRP) and substance P (SP), key transmitters in primary nociceptive afferents, have been implicated in the pathogenesis of migraine attacks.

The aim of this study was to evaluate the expression of CGRP and SP in the nucleus trigeminalis caudalis (NTC) of the rat during hyperalgesia induced by two different models. CGRP and SP immunoreactivity was quantified in male Sprague-Dawley rats at various time points after formalin test or systemic nitroglycerin administration. Formalin injection induced a significant decrease in CGRP immunoreactivity 1 h after the test, while no change was observed in SP immunostaining. Following nitroglycerin administration, CGRP immunoreactivity steadily decreased during the 4- h observation period. Conversely, SP immunoreactivity increased, but only at 1 h after the drug administration.

CGRP plays a long-lasting role in nitroglycerin-induced hyperalgesia and may represent a better target than SP for developing new antimigraine drugs.

This work was supported by a grant from the Italian Ministry of Health (RC 2002).

P3I26

Gender and estrogen modulation of nytroglycerin-induced FOS protein in the rat brain

Rossella E. Nappi*[1], Antonella Smeraldi[2], Rosaria Greco[2], Cristina Tassorelli[3], Alfredo Costa[2] & Giuseppe Nappi[3,4]
[1]*Department Obstetric and Gynecology, IRCCS San Matteo, University of Pavia,* [2]*Laboratory of Neuroendocrinology, Department of Neurology, IRCCS C. Mondino, University of Pavia,* [3]*University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino, University of Pavia, Italy,* [4]*Department of Neurology and ORL, University of Rome La Sapienza, Rome, Italy*

Migraine is highly prevalent in women and hormonal fluctuations affect the clinical expression of the disease.

We investigated the effect of gender and estrogen treatment on nytroglicerin (NTG)-induced FOS protein expression, a marker of neuronal activation in the rat brain.

Intact and castrated male and female and estrogen-replacement female adult rats (250–300 g) were injected i.p. with NTG (Astra, Italy). Rats were anesthetized and perfused transcardially with saline and ice-cold 4% paraformaldehyde 4 h after the drug administration (10 mg/kg). Frozen brains were mounted on a microtome, cut in 50 μm slices and then processed for the detection of FOS protein by immunocytochemistry.

(a) a gender difference in the number of positive FOS-ir cells was found with a significantly higher expression in the PVN, SON, SPVC of intact females. Interestingly, ovariectomy abolished such a difference following NTG injection; (b) in estrogen-replaced female rats the number of positive FOS-ir cells was significantly higher in comparison to ovariectomized rat in all the structures activated by NTG (PVN, SON, AMI, NTS, AP, SPVC).

Our experimental model showed that there is a sexual dimorphic neuronal activation induced by NTG supporting the idea that estrogens significantly influence the rat brain structures implicated in the pathophysiology of migraine.

This work was partly supported by a grant from the Italian Ministry of Health (RC 2002).

P3I27

Nitroglycerin infusion does not cause CGRP release in the rat and attenuates capsaicin-induced c-fos expression within trigeminal nucleus caudalis

U. Reuter*[1], N. Offenhauser, T. Zink, J. Hoffmann, K. Schiemann, S. Schuh-Hofer, C. Böhnke, G. Arnold & U. Dirnagl
[1]*Charité, Department of Neurology, Humboldt University of Berlin, Germany*

Objectives Nitric oxide (NO) has been implicated in the pathophysiology of headaches. We determined the release of CGRP after GTN infusion and investigated the effects of GTN on c-fos expression within the trigeminal nucleus caudalis (TNC). In order to mimic conditions in migraineurs the trigeminal system was prestimulated with capsaicin.
Methods SD rast were used. (1) For CGRP determination GTN was infused (30 mins) into the carotid artery (GTN 2 or 50 μg/kg/min/NONOate/saline). Blood samples were collected from the jugular vein. CGRP was determined using a RIA kit.2) c-fos staining was assessed using routine histological techniques.
Results (1) GTN and NONoate did not cause CGRP release up to 35 mins after infusion, whereas infusion of capsaicin (3 μmol/kg; at the end of each experiment) led to CGRP release. (2) GTN (2 μg/kg/min for 30 mins) did not cause significant c-Fos expression within TNC. Capsaicin caused a dose dependent expression of c-fos in TNC after 2 h, which was significantly attenuated by GTN, and the NOS inhibitor L-NAME 50 mg/kg but not by L-NAME 5 mg/kg or D-NAME.
Conclusion (1) We did not find evidence that GTN activates the trigeminal nerve system as determined by CGRP release. (2) Capsaicin induced c-fos expression within TNC is mediated by NO-dependent mechanisms.

P3I28

Superior sagittal sinus dura matter stimulation enhanced fos and co-localization of 5-HT with fos in periaqueductal grey matter in the rat

Shengyuan Yu*[1], Juntang Guo[1] & Ruozhuo Liu[1]
[1]*Department of Neurology, Chinese PLA General Hospital, Beijing*

Objectives To explore the periaqueductal gray potentially involved in the transmission of nocicepitive information related to vascular headache such as migraine.
Methods The Fos expression and colocalization of 5-HT with Fos were investigated in periaqueductal grey matter following stimulation of superior sagittal sinus dura matter in rats.
Results 5-HT immunoreactive neurons were found throughout the PAG although their greatest density is in the ventrolateral and ventromedial sector. Neurons Fos-like immunoreactivity were more intense in stimulation group than sham-operated group and control group. Fos-like immunoreactivity was detected in 15% of 5-HT immunoreactive neurons and the double-labelled population mainly distributed in ventrolateral sector.
Conclusion This suggested that the activity of 5-HT-LI cells is not significant different from two other control groups statistically. Other kinds of excitability neurons were to be explored in future.

P3I29

The effect of histamine on sensory afferents supplying the cranial meninges

Richard Carr*[1], Ronny Enk[1] & Karl Messlinger[1]
[1]*Institute of Physiology and Experimental Pathophysiology, University of Erlangen-Nuernberg, Germany*

Sensory nerve terminals with Aδ and C fibre axons in the cranial meninges are thought to be the locus for some forms of headache and migraine. Histamine is considered one of several potential chemical mediators of such conditions and can induce headache in migraineurs. This effect may be mediated by activation of primary afferents in the cranial meninges. Consequently, we have examined the response of meningeal primary afferents to bath applied histamine using an *in vitro* isolated preparation of the dura.

Rats were killed by CO_2 inhalation. The skull was divided longitudinally and the meninges were isolated along with a portion of the spinosus nerve from each half. The tissue was continuously perfused with physiological solution buffered to pH 7.4 and held at 36 °C. Nerve activity was recorded from a suction pipette attached to the spinosus nerve. Units were identified by their responses to mechanical and capsaicin (10^{-6}M) stimuli. Seventeen percent of units responded to histamine in the range (10^{-9}-10^{-5}M). Histamine sensitivity was not correlated with either mechanical or capsaicin sensitivity. The high histamine sensitivity of some units suggests a possible role for these afferents in trigeminal pain states associated with mast cell de-granulation.

P3I30

Central projections of sensory innervation of the rat superior sagittal sinus

Yi Liu*[1], Jonas Broman[2] & Lars Edvinsson[1]
[1]*Department of Internal Medicine, University Hospital, Lund, Sweden,*
[2]*Department of Physiological Sciences, Lund University, Lund, Sweden*

Evidence has shown that the superior sagittal sinus (SSS) is a pain sensitive intracranial vessel, which is implicated in primary headaches. In this study the central projections of afferent nerve fibers in the SSS was examined by anterograde tract tracing techniques.

Wheat germ agglutinin conjugated horseradish peroxidase (WGA-HRP, labels primarily unmyelinated C-fibers and Aδ-fibers) or cholera toxin subunit b (CTb, labels myelinated A fibers) was applied on the wall of the SSS in anesthetised rats. After 2–5 days, the animals were re-anesthetised and fixed by perfusion. The brainstem, the upper three cervical spinal segments, the bilateral trigeminal (TG) and the C2 dorsal root

ganglia (DRG) were removed and processed for histochemistry and immunocytochemistry. The labelled afferent nerve terminations were primarily located in the most ventral part of the bilateral C1-C3 spinal dorsal horns and in the caudal part of the spinal trigeminal nucleus. In the spinal cord, WGA-HRP labelled terminations were located in laminae I and II, while CTb labelled terminations located in laminae III and IV. In the CTb cases, terminations were also found in the interpolar part of the trigeminal nucleus and in the dorsolateral part of the cuneate nucleus. Labelled cell bodies were seen in TG and DRG bilaterally regardless of side of CTb or WGA-HRP application.

P3I31

Hyperoxia reduces plasma protein extravasation in the model of electrically stimulating the rat trigeminal ganglion

Sigrid Schuh-Hofer*[1], Wiebke Siekmann[1], Carsten Boehnke[1] & Uwe Reuter[1], Ulrich Dirnagl[1], Guy Arnold [1]
[1]*Department of Neurology, Charité Hospital Berlin, Germany*

Objectives The pathophysiological mechanism by which 100% O_2 aborts cluster headache attacks is unknown. We aimed to study the effect of hyperoxia on dural plasma protein extravasation (PPE), induced by unilateral electrical stimulation of the rat trigeminal ganglion (TG).
Methods Dural PPE was assessed by a histological, fluorescence-based method, using a confocal laser microscope. The fluorescence dye Evans Blue was injected i. vs. 5 min prior to TG-stimulation (1,2 mA, 5 Hz, 500 ms). During TG-stimulation, rats were either ventilated under normoxic (pO_2 80–100 mmHg) or hyperoxic conditions (pO_2 380–400 mmHg). The fluorescence intensity (FI) of the dura mater, reflecting the respective amount of extravasated Evans Blue, was measured by a software programm. Per dura mater preparation, ~8 regions of interest in the proximity of large meningeal vessels were analysed. The FI of the ipsilateral dura mater was compared to the contralateral side (PPE-ratio).
Results The PPE-ratio was 1,74 ± 0,18 ($n = 5$) under normoxic and 1,1 ± 0,18 ($n = 6$) under hyperoxic conditions. Sumatriptan (300 µg/kg) abolished PPE (1,0 ± 0,16).
Conclusion Hyperoxia effectively reduces dural PPE in the model of electrically stimulating the rat TG. Hyperoxia may have anti-inflammatory effects on neurogenically induced dural inflammation.

P3I32

The effect of stimulation of the trigeminal ganglion on the poly (ADP – ribose) polymerase (PARP) activity of the trigeminal nucleus caudalis (TNC) in the rat

Janos Tajti*[1,2], Hedvig Varga[2], Judit Soós[1], Aurelia Ungurean[1], Laszlo Vecsei[1,2], A. Párdutz[1], Z. Chadaide[1] & J. Engelhardt[1]
[1]*Department of Neurology, University of Szeged, Szeged, Hungary,*
[2]*Neurology Research Group of the Hungarian Academy of Sciences*

The primary cause of migraine headache is still unknown. The effects of stimulation of the trigeminal ganglion or the superior sagittal sinus have been regarded as experimental equivalents of the alterations observed during migraine attacks (Goadsby et al. 1990, Zagami et al. 1990, Goadsby and Edvinsson 1993, 1994). It has been observed that stimulation of the trigeminal ganglion results in accumulation of the immediate early genes C-fos and C-jun in the TNC (Knyihár-Csillik et al. 1997, Knyihár – Csillik et al. 2000).

Breaks in the DNA strands activate PARP, which brings about poly(ADP – ribosyl)ation of the nuclear proteins.

In order to study the energy alterations during the 'migraine attack' in the TNC, we have examined the immunoreactivity of poly(ADP – ribose) after electrical stimulation of the trigeminal ganglion in the rat.

We have demonstrated an enhanced level of poly(ADP – ribosyl)ation in the TNC. The findings appear to suggest an energy failure in the migraine attack.

The results may give a clue to the development of new drugs acting on the brainstem region.

Neuroimaging

P3J1

Central neuromodulation with implanted suboccipital stimulators in patients with chronic migraine

M. Matharu*[1], T. Bartsch[1], N. Ward[2], R. Frackowiak[2], R. Weiner[3] & P. Goadsby[1]
[1]*Headache Group, Institute of Neurology, London, UK,* [2]*Imaging Neuroscience, Institute of Neurology, London, UK,* [3]*Department of Neurosurgery, Presbyterian Hospital of Dallas, Dallas, USA*

Objective To determine the brain structures modulated by suboccipital stimulation in chronic migraine using positron emission tomography (PET).
Methods Eight patients (age 32–53 years) with Chronic Migraine (IHS 2nd edition) with a marked beneficial response to subcutaneously implanted suboccipital neurostimulators (Medtronic Synergy®/Itrel®) were studied. Twelve consecutive $H_2{}^{15}O$ PET scans were done in randomised order in 3 states: (1) stimulator at optimum settings: pain free and paraesthesia; (2) stimulator off: pain and no paraesthesia; (3) stimulator partially activated; intermediate levels of pain and paraesthesia. All images were analysed using SPM99.
Results Activation was positively correlated with pain in the dorsal rostral pons ($Z = 3.65$) and anterior cingulate cortex ($Z = 4.09$) and with paraesthesia in the left pulvinar ($Z = 3.49$). In the dorsal rostral pons, activity was increased in state 1 and 2 relative to 3. Activity in the left pulvinar was increased in state 1 and decreased in state 2 relative to state 3.
Conclusions Relative activation of the dorsal rostal pons with both pain only and stimulation only, but a relative deactivation in the presence of both, is highly suggestive of a role for this region in the pathophysiology of Chronic Migraine.

P3J2

Circulating adenosine is not an effective mediator of headache

Steffen Birk*[1], Kenneth Petersen[1], Christina Kruuse[1], Regis Guieu[2], Olga Jonassen[3], Wolfgang Eisert[4] & Jes Olesen[1]
[1]*Danish headache center, Department of neurology, University of Copenhagen, Glostrup hospital, Glostrup, Denmark.,* [2]*Department of biochemistry, CHU Timone, Marseille, France,* [3]*Department of nuclear medicine and physiology, University of Copenhagen, Glostrup Hospital, Glostrup, Denmark,* [4]*Boehringer-Ingelheim, Ingelheim am Rhein, Germany*

Adenosine may be involved in migraine, because plasma levels are elevated during migraine, and adenosine infusion reportedly precipitates attacks. Furthermore, the nucleoside dilates human cerebral arteries *in vitro*, and middle cerebral artery (MCA) dilatation is often associated with migraine pain. The effect of adenosine on headache and MCA diameter changes has not previously been investigated in man.

12 healthy volunteers received adenosine 80, 120 µg/kg·min^{-1} and placebo intravenously, in a double-blind, crossover, randomised design. Headache was rated on a verbal scale (0–10). Measurement of CBF with 133 Xenon inhalation and SPECT, and MCA flow velocity (VMCA) with transcranial Doppler in close time relationship. MCA diameter changes were calculated.

Six developed headache on 80 µg/kg·min^{-1} and 6 on 120 µg/kg·min^{-1} compared to 0 on placebo ($P = 0.006$, Cochran Q-test). The headache was very mild and predominantly described as a nonpainful pressing sensation. Calculated change in MCA diameter was $0.5 \pm 6.6\%$ (SD)% during infusion of adenosine 80 µg/kg·min^{-1}, and $1.9 \pm 4.7\%$ during 120 µg/kg·min^{-1} ($P = 0.4$). CBF remained unchanged ($P = 0.15$).

These results suggest that circulating adenosine is not an important mediator of headache.

P3J3

Proton MR spectroscopy study of hypothalamus metabolism in patients with cluster headache

Raffaele Lodi*[1], Giulia Pierangeli[2], Caterina Tonon[1], Sabina Cevoli[2], Fabiola Magnifico[2], Stefano Iotti[1], Pietro Cortelli[2], Bruno Barbiroli[1] & Pasquale Montagna[2]
[1]*Dipartimento di Medicina Clinica e Biotecnologia Applicata, Policlinico S. Orsola-Malpighi,* [2]*Dipartimento di Scienze Neurologiche, University of Bologna, Bologna, Italy*

The pathophysiology of cluster headache (CH), is still poorly understood. Recent PET (May A et al. *Lancet*, 352, 275, 1998) and voxel-based morphometric MRI (May A et al. *Nat. Medical*, 5, 836, 1999) studies have found altered function and volume of the hypothalamus in CH. We studied, using *in vivo* proton MR spectroscopy (^{1}H-MRS) 22 CH patients in a headache free state. ^{1}H-MRS studies were performed in a 1.5T GE Medical Systems scanner. Spectra were obtained from the hypothalamus in 22 CH patients (8 patients with the chronic form, 7 with episodic CH within the cluster period and 7 with episodic CH outside the cluster period) and 11 sex- and age-matched controls using the PRESS single voxel localisation sequence (TE = 144 ms; TR = 1500 ms; number of acquisition = 1536). In CH patients hypothalamic NAA/Cr (1.64 ± 0.22) was significantly reduced compared to controls (1.92 ± 0.20; $p = 0.001$). Hypothalamic NAA/Cr was significantly reduced in each CH patients' subgroup (data not shown). Reduction in hypothalamic NAA content can be related to neuronal loss/dysfunction and/or changes in the relative content of glial and neural cells. This alteration may be linked to the pathophysiological mechanism underlying headache attacks in CH.

P3J4

Deep brain stimulation in cluster headache: preventing intractable pain by activating the pain network

Arne May*[1], Massimo Leone[2], Henning Boecker[3], Gennaro Bussone[2], Till Sprenger[4], Bogdan Draganski[1] & Thomas Tölle[4]
[1]*Department of Neurology, University of Regensburg,* [2]*Instituto Carlo Besta, Milano,* [3]*Department of Nuclear Medicine, University of Munich,* [4]*Department of Neurology, University of Munich*

A significant structural difference in grey matter density, coinciding with the inferior posterior hypothalamus, was found in cluster headache patients when compared to healthy volunteers[(1)]. This prompted Leone et al. to use deep brain stimulation of this area, successfully preventing cluster headache attacks in selected severe therapy-refractary cases[(2,3)].

It is not understood how stimulation of an area which is thought to act as a pace-maker for acute cluster attacks, is able to prevent these attacks to happen. We examined the first five chronic cluster patients operated so far using $H_2{}^{15}O$-PET, alternately switching the hypothalamic stimulator on and off. The stimulator induced activations in the ipsilateral hypothalamus (the site of the stimulator tip), the contralateral thalamus, parietal lobus and praecuneus, the brainstem and the ipsilateral basal ganglia. In contrast to acute cluster headache attacks, we observed additionally deactivations in the anterior cingulate cortex, the primary somatosensory cortex and bilateral insulae. Both, activations and deactivations, are situated in cerebral structures belonging to neuronal circuits usually activated in pain transmission. Our data suggest that the spontaneous bursts of activation in the inferior posterior hypothalamus result in excruciating head-pain, whilst continuous electrical stimulation of the identical area is able to prevent these attacks.

P3J5

Cutaneous allodynia in transformed migraine with medication overuse

Christelle Créac'h*[1], Françoise Radat[2], Magalie Laffitau[2], Sandrine Irachabal[2] & Patrick Henry[2]
[1]*CHU de Saint-Etienne, Saint-Etienne, France,* [2]*CHU Pellegrin, Bordeaux, France*

Comparison of heat-pain thresholds was performed in 38 patients with Transformed Migraine and medication overuse (Silberstein 1996) and in 33 migraineurs without medication overuse. The aim of our study was to determine whether

facial and/or extracranial allodynia may be evidenced in these patients and whether allodynia may be controlled by drug withdrawal.

Extracranial allodynia was more frequent in transformed migraine than in episodic migraine (39.5% vs. 12.1%; p = 0015). This difference was not found on face. ANOVA didn't reveal any significant differences of heat pain thresholds between groups. Pain thresholds were neither correlated with the duration of migrainous disease, nor with medication consumption, or with pain anxiety. Drug-withdrawal was not associated with any significant changes in pain threshold.

The greater frequency of extracranial cutaneous allodynia in transformed migraine may reflect a central sensitization of pain processing because of chronic headache. A diffuse modulation of pain system rather than trigeminal sensitization is likely to explain our results.

Allodynia is not modified by drug-withdrawal, despite improvement of headache. Thus it seems that allodynia may depend on long-term effects of medication overuse.

P3J6

Cilostazol causes headache in healthy volunteers; evidence for involvement of cAMP?

Steffen Birk*[1], Christina Kruuse[1], Kenneth Petersen[1], Olga Jonassen[2], Peer Tfelt-Hansen[1] & Jes Olesen[1]
[1]*Danish Headache Center, Department of neurology,* [2]*Department of clinical physiology and nuclear medicine, University of Copenhagen, Glostrup Hospital, Glostrup, Denmark*

We have shown that increased levels of cyclic guanosinemonophosphate (cGMP) may cause headache and migraine. However, cyclic adenosinemonophosphate (cAMP) may also be involved, since calcitonin gene-related peptide is involved in migraine pathogenesis. We therefore used cilostazol, an inhibitor of cAMP degradation in our experimental headache model.

Twelve healthy volunteers were included in a double-blind, randomised, crossover design. Placebo or cilostazol (200 mg p.o.) was administered on two separate study days. Headache was scored on a verbal rating scale (0–10), and mechanical pain thresholds were measured with von Frey hairs. Relative changes in middle cerebral artery (MCA) calibre were assessed by simultaneous measurement of MCA blood flow velocity (V_{MCA}) with transcranial Doppler, and regional CBF with 133 Xenon and SPECT.

Mean peak headache score 0–16 h postdose was 0 (range 0–2) after placebo, and 3.5 (0–7) after cilostazol ($P = 0.003$). Two volunteers fulfilled IHS criteria of migraine without aura. V_{MCA} decreased significantly ($P = 0.02$) but there was no change in regional CBF ($P = 0.82$) MCA cross-sectional area increased 35.6 ± 9.1% on cilostazol. No change in mechanical pain thresholds in the forehead was seen ($P = 0.25$).

The study shows that increased levels of cAMP may also play a role in headache and migraine pathogenesis.

P3J7

Collapsed superior ophthalmic veins in patients with spontaneous intracranial hypotension

Shuu-Jiun Wang*[1,4], Wei-Ta Chen[3], Jiing-Feng Lirng[2,4] & Jong-Ling Fuh[1,4]
[1]*The Neurological Institute, Taipei Veterans General Hospital,* [2]*Department of Radiology, Taipei Veterans General Hospital,* [3]*Taiwan, Chu-Tung Veterans Hospital, Taiwan,* [4]*National Yang-Ming University School of Medicine, Taipei, Taiwan*

Background and Purpose A positive correlation between SOV diameter and intracranial pressure (ICP) has recently been found. Patients with increased ICP have engorged SOVs. This study was to investigate if SOV diameter was decreased in patients with spontaneous intracranial hypotension (SIH).
Method We recruited SIH patients and measured their SOV diameter on postcontrast coronal T1-weighted brain MRI with fat-saturation pulse sequencing. Diameter data from bilateral SOV were averaged for each patient and further compared with those of neurology in-patients with normal CSF pressure (90–200 mmH_2O). Additional analyses focused on the SOV diameter changes after intravenous hydration therapy in the patients who had follow-up MRI.
Results Eighteen 18 SIH patients and 18 control patients with normal CSF pressure were recruited. The SOV diameters in SIH group averaged 0.98 ± 0.44 mm (range, 0.30–1.75 mm), significantly lower than the control group (1.71 ± 0.98 mm, $p < 0.001$). Ten SIH patients who were followed up with MRI at a mean interval of 174 ± 247 days (range 20–840), had an enlarging SOV diameters (0.85 ± 0.19 vs. 1.05 ± 0.17 mm, p = 0.023).
Conclusion The patients with SIH had decreased SOV diameters. This study suggests a new and additional neuroimaging finding to the MRI characteristics for SIH.

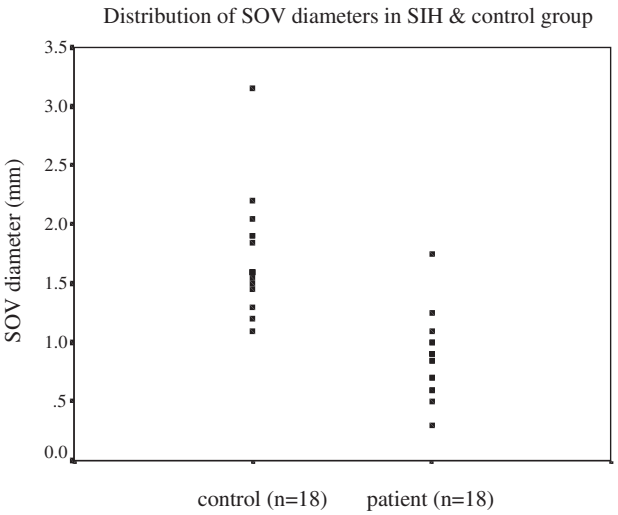


Figure 1

P3J8

Migraine with sustained visual aura: description of a new case with brain SPECT and perfusion MRI study

Giuliano Relja*[1], Antonio Granato[1], Maja Ukmar[2], Marino Zorzon[1], Rodolfo Maria Antonello[1], L. Locatelli[1], A. Bosco[1] & G. Ferretti[3]
[1]*Clinical Neurology – Headache Center, University of Trieste,* [2]*Unit of Radiology, University of Trieste,* [3]*Nuclear Medicine, Azienda Ospedaliera*

Introduction A rare form of migraine with aura, with sustained or persistent visual symptoms, lasting months or years without evidence of infarction, has been reported, at the best of our knowledge, in only 20 patients.

We report a new case who underwent brain SPECT and perfusion MRI.

Case report A 43-year-old-woman had a 31-year history of migraine with typical visual. At presentation, she experienced a visual aura in her right hemifield followed by a pulsating headache lasting for some hours. The visual symptoms became persistent. There were no abnormal findings on neurologic and ophthalmologic examinations. Routine hematologic examinations, EEG, VEPs, brain CT and MRI were all normal. Both brain SPECT with Tc99mHMPAO and brain perfusion MRI, performed one month after the onset of visual symptoms revealed decreased left fronto-parieto-occipital and right occipital blood perfusion. After 9 months the patient reported a 90% symptoms reduction. A new perfusion MRI didn't show any significant change compared to previous examination.

Discussion As previously reported, a cortical hypoperfusion has been shown by SPECT in this patient, in spite of normal MRI, VEPs and campimetry. For the first time this finding has been confirmed by perfusion MRI in a case of sustained visual aura.

P3J9

Visual suppression is impaired in migraine and is consistent with reduced cortical inhibition

Sheena Aurora*[1], Edward Chronicle[2], Wim Mulleners[3], Pat Barrodale[1] & Reda Tipton[1]
[1]*Swedish Headache Center, Seattle, USA,* [2]*Department of Psychology, Lancaster University, Lancaster, U.K.,* [3]*Department of Neurology, Atrium Medical Center, Heerlen, the Netherlands*

Objectives This study aimed to confirm a recent finding that suppression of visual perception by transcranial magnetic stimulation (TMS) over the occipital cortex is altered in migraine patients between attacks.

Methods 5 IHS migraineurs and 5 control subjects were tested. Patients were free of medications and were tested between attacks. Each subject underwent a randomized sequence of 54 trials, controlled by computer. In each trial, three letters were presented on screen for 30 ms, followed by a variable delay (0–190 ms) and then a single TMS pulse from a 90-mm round coil of a MagStim 200 stimulator. Subjects reported the letters that they were able to identify.

Results The percentages of letters correctly reported in each patient group and delay condition were submitted to analysis of variance. There was a significant difference in the pattern of suppression across groups ($F[5,40] = 6.54$; $p < 0.01$). Migraine patients were more accurate at reporting letters at 100 ms delays.

Conclusions Suppression of visual perception by TMS is a robust and objective method of assessing cortical function. This study confirms an impairment of visual suppression in migraine patients. A parsimonious interpretation of this finding is that intracortical inhibition is disordered in migraine.

P3J10

Intracranial distribution of Eletriptan visualized by [11C]-Eletriptan Positron Emission Tomography (PET)

Peter Goadsby*[1], K. Taylor[2], R. Rubens[3], B. Hilliard[2] & A. Otte[3]
[1]*Institute of Neurology & National Hospital for Neurology and Neurosurgery, London, UK,* [2]*Pfizer Inc., New York, NY,* [3]*Pfizer Gmbh, Freiburg, Germany*

Objective To examine the extent that eletriptan crosses the blood–brain barrier; to compare intracranial and regional cerebral distribution of eletriptan in migraineurs (both during migraine and headache-free) and migraine-free controls.

Methods Five migraineurs (IHS criteria) and 5 controls underwent three PET investigations: a [^{15}O]-CO scan to allow subtraction of intravascular tracer and obtain information on regional cerebral blood volume; a [^{15}O]-H_2O scan for measuring regional cerebral blood flow and mapping regions of interest; a 1- h [^{11}C]-eletriptan PET scan following 4 mg-IV eletriptan. Standardized uptake values (SUV) were adjusted for intravascular tracer. Blood was drawn for pharmacokinetic data. Migraineurs had investigations within 6 h of migraine onset and while headache-free; controls were studied once.

Results Eletriptan was visualized intracranially rapidly, but entered brain parenchyma minimally (SUV~0.1). Regional cerebral distribution was uniform. Radiolabeled eletriptan was highest in CSF (7-times greater than whole brain) and choroid plexus (10-times greater). Intracranial uptake was highest in migraineurs during an attack.

Conclusions Eletriptan achieved rapid intracranial distribution in both migraineurs and controls, with highest uptake in migraineurs during migraine. In all groups, highest uptake was in CSF and choroid plexus. Parenchymal cerebral uptake was minimal. Meningovascular neural structures may be a target for the antimigraine action of eletriptan.

P3J11

Is habituation of the VEP coupled to vascular response? Implications for neurovascular coupling in the healthy and the interictal migraine brain

Heike Israel*[1], Hellmuth Obrig[1], Arno Villringer[1] & Guy Arnold[1]
[1]*Department of Neurology, University Hospital Charité, Berlin, Germany*

Background Previous studies have shown that electrophysiological habituation is mirrored by vascular changes supporting the hypothesis of the linear aspects of neuro-vascular coupling in the healthy adult (1). We investigated neurovascular coupling under pathological conditions (lack of habitu-

ation) as thought to be an effect of lacking inhibition in migraine patients.

Objective The study compared regional concentration-changes in oxy- and deoxy-hemoglobin with simultaneously acquired VEPs during prolonged stimulation in migraine patients and healthy volunteers.

Methods 15 interictal migraine patients and 15 healthy volunteers were investigated. VEPs were elicited by an annular checkerboard, reversing at 3 Hz. Peak-to-peak amplitudes of N75P100 and P100N135 were calculated. Vascular response was acquired by a frequency-domain nearinfrared spectroscopy monitor.

Results Within the 1 min stimulation period we found a decrease in P100N135 component amplitude in the volunteers closely coupled to an attenuation in [deoxy-Hb]-response. In contrast, the patients showed no habituation of the P100N135 component amplitude which was not reflected in the vascular response.

Discussion Though, there was a reproducible lack of VEP habituation in interictal migraine patients the difference in vascular response as measured by NIRS did not reach statistical difference. This may be a hint at an altered neurovascular coupling in these patients.

Reference

1 Obrig, H et al. NeuroImage, 2002 September; 17(1): 1–18 (2) Afra J et al. Clin Neurophysiol. 2000 June; 111(6):1124–9.

P3J12

Development of a craniofacial pain map for use in neuroimaging studies

Alexandre DaSilva*[1], Elizabeth Loder[2], A. Gregory Sorensen[1] & Nouchine Hadjikhani[1]
[1]*MGH-NMR Center, Harvard Medical School, Charlestown, MA, USA,* [2]*Spaulding Rehabilitation Hospital, Boston, MA, USA*

A head and neck map was developed to objectively measure pain location in subjects prior to neuroimaging studies. This craniofacial pain map is a coordinate map of the head and neck region on which the pain area can be precisely described and measured. Its application in clinical and research settings can improve spatial localization of primary headaches, and other trigeminal and cervical pain pathologies, including trigeminal neuropathies.

The map is based on a squared grid system with vertical and horizontal coordinates using anatomical landmarks. Each quadrangle, measuring approximately 1.6 cm × 1.6 cm, frames well-detailed craniofacial and cervical areas for the patient fill up to express his/her exact pain location. In the clinical setting the grid system permits the precise identification of pain location, statistically measuring the spatial increase or decrease of the area after specific treatment and/or time period. In the research setting the pain area described can be correlated with structural and functional changes in the nervous system, detected by neuroimaging techniques, in one subject, or an averaged population.

Use of the Craniofacial Pain Map can improve the integration of clinical and research data and facilitate imaging and understanding of the pathophysiology of craniofacial pain disorders.

P3J13

Interictal SPECT and neuropsychological performance in migraine patients

Elena Pita Calandre*[3], Rafael Nieto[1], Francisco Gonzalez[1], Judith Bembibre[2] & Maria Luisa Arnedo[2]
[1]*Instituto de Neurosciencas, Universidad de Granada, Spain,* [2]*Servicio de Medicina Nuclear, Hospital Clínico San Cecilio, Granada, Spain,* [3]*Facultad de Psicología, Universidad de Granada, Spain*

Objectives In a previous work we found that neuropsychological performance in chronic migraine patients was altered and that the prevalence of interictal SPECT abnormalities was higher than in healthy subjects (1). The present study tries to evaluate, with a bigger sample of patients, the potential relationship between SPECT abnormalities and neuropsychological functioning.

Methods A neuropsychological evaluation and an interictal SPECT were performed in 73 migraine patients and in 19 healthy controls. An ANOVA was applied to compare data from patients with normal SPECT ($N = 41$), patients with abnormal SPECT ($N = 32$) and controls.

Results The scores of the Rey Auditory Verbal Learning test, visual reproduction of the Wechsler Memory Scale, and the Digit Symbol Substitution Test were significantly lower in migraineurs with SPECT abnormalities than in the other two groups ($P = 0.01$, 0.03 and 0.01, respectively). Patients of this group had also higher frequency of headache than those of the normal SPECT group. ($P = 0.048$)

Conclusions Increased prevalence SPECT abnormalities seems to be related with some degree of disturbances in verbal and visual memory, as well as in visuomotor speed processing; both data could be linked to an increase in the chronicity of migraine.

Reference

1 Calandre EP et al. Cephalalgia 2002; 22 : 291–302.

P3J14

Effect of 5HT 1a/1c Receptor agonist on cerebral vasodiameter using magnetic resonance angiography technique

Hotaek Kim*[1], Kunio Shimazu[1], Nobuo Araki[1], Misato Takahama[2] & Aya Okuma[1]
[1]*Department of Neurology, Saitama Medical School,* [2]*4th Department of Internal Medicine, Saitama Medical Center*

Purpose Few studies reported the effects of 5HT1a/1c receptor agonists (triptans) on cerebral vasodiameter of migraineurs during attack whereas it has been considered that triptans strongly constrict the cerebral arteries. Our study was designed to clarify the effect of triptan on cerebral vasodiameter during attack using magnetic resonance angiography technique.

Objects and methods Two migraineurs (with aura and without aura) and 2 healthy volunteers were studied. MRAs of migraineurs were taken at the time of attacks and post-treatment (sumatriptan i.c.) headache-free periods using time-of-flight method. Cerebral diameter images were analyzed by NIH-image technique.
Results Cerebral vasodiameters of both migraineurs and healthy controls were constricted up to about 70% from the baseline.
Conclusion 5HT 1a/1c receptor agonist really constricts human cerebral arteries *in vivo*.

P3J15

Cerebral blood flow in drug abuse headache

Taner Ozbenli*[1], Cem Ortaçbayram, Nilgün Cengýz, Taryk Baþoðlu, Fevziye Canbaz & Musa K. Onar
[1]*Ondokuz Mayis University, Medical Faculty, Departments of Neurology and Nuclear Medicine, Turkey*

Objectives To investigate regional cerebral blood flow (rCBF) in drug abuse headache (DAH).
Methods 99 m Tc HMPAO SPECT brain imaging was performed 38 patients (30 F, 8 M, average age of 36.7 ± 9.2 SD.) who diagnosed DAH. 99 m Tc HMPAO brain SPECT studies was repeated after the patients received prophylactic drug. In order to calculate the perfusion index, the average counts from the total 45 brain regions other than the cerebellum were divided by the average counts which was obtained from the whole cerebellum. 99 m Tc HMPAO brain SPECT was performed six healthy volunteers.
Results There were no asymmetry in rCBF on pretreatment phase. Post-treatment phase brain SPECT studies were revealed hypoperfusion at 12 of total 45 brain regions ($P < 0.05$). Nine of 11 patients who observed hypoperfusion also decreased headache frequency and severity. After treatment hypoperfusion rates were significant who abused ergotamin ($P < 0.05$).
Conclusions An interictal dysregulation of rCBF is possibly present interictally in migraine with aura. The results of this study indicate that brain imaging with 99 m Tc HMPAO SPECT is able to show alterations pre- and post-treatment phases in DAH patients. After stopping symptomatic medications, hypoperfusion was seen significantly in patient group. The possible neurophysiologic mechanism of DAH is central sensitization. Our results showed that cerebral hemodynamics may be related the pathophysiology of DAH.

P3J16

Cranial CT correlation in Indian migraine

Niranjan Narain Singh*[1] & Surendra Misra[1]
[1]*Institute of Medical Sciences, Banaras Hindu University,* [2]*Institute of Medical Sciences BHU Varanasi India*

Objective To know the predictive value of clinical diagnosis of migraine headaches when neurological examination is normal.
Methods Prospective study from January 1999 to January 2002 among patient who attended neurology clinic or medicine OPD for headache and who met the IHS diagnostic criteria for migraine and who demanded cranial CT scan by them selves or relatives or already came with a CT scan by their primary care physicians.
Results Among 300 CT scan performed only 21 provided positive findings. Calcification over brain parenchyma was seen in 4 (1.33%), small single ring enhancing lesion in 14(4.66%), lacunar infarctin 1, glioblastoma in 1, and AVM in 1.
Conclusion The most common finding in CT was SSECTL, which is endemic in South-east Asia including India; NCC is a probable diagnosis in all such cases. NCC can present with various nonepileptic manifestation, vascular type headache is one of the commonest. Other less common finding in CT may be a chance association. Clinician needs to recognize this clinical entity, which although presents like vascular headache treatment and prognosis is different

P3J17

Headache neuroimaging: clinical experience in children

Elisabetta Tozzi*[1], Maria Immacolata Florio[1], Rosanna Savini[1], Elena Cicconi[1], Giovanni Mazzotta[2], Elisabetta Cittadini[2], Francesca Floridi[2] & Virgilio Gallai[2]
[1]*Clinica Pediatrica Università degli Studi L'AQUILA,* [2]*Dipartimento di Neuroscienze Università degli Studi, Perugia, Italy*

Aim of this study is retrospective analysis of patients with headache observed during 1998–2002 years in L'Aquila and in Perugia University, in order to verify the utility of neuroimaging. 210 patients, with headache during from 6 months, are selected. Diagnosis of headache, according to IHS 1988 criteria: Mwa (77 children) Mwoa (13 patients), Migraine like disorder (16 pt) Stabbing headache(5 children), TTH (46 children),headache associated in 21 and headache not classifiable(HNC) in 22 children. Neuroimaging, according to flow chart of Ad hoc Committee of Juvenile headache Guide Lines of Italy Headache Study group (Gallai)., was brain MR in 120 children, TC in 50 patients.
Results Facial inflammations and dimorphisms (30.7%), cerebral malformations(16%); PV leukimalacia and cerebral calcifications(8%), cortical displasia and neoplasms (3.7%). These anomalies were in this way: 30% of Migraines, 33% of stabbing headaches, 21% in TTH, 100% of HNC, 14% of headaches with endocrinological diseases associated, 45% of headaches with neurological diseases and 55% of patients with EEG and/or neurological examination abnormal. Only TC alterations as sphenoid sinusitis in 3 children have modified the headache diagnosis. In patient with normal neurological examen not neuroimaging, but clinical follow up, represent the useful investigation.

P3J18

The value of magnetic resonance imaging (MRI) in patients with migraine

Ljubo Markovic*[2], Ranko Raicevic[1], Aleksandar Radosavljevic[2] & Toplica Lepic[1]
[1]*VMA Clinic of Neurology, Belgrade,* [2]*Institute of Radiology, VMA, Belgrade*

Introduction Migraine is an episodic, paroxysmal disorder accompanied with different neurological, gastrointestinal and vegetative changes. Results of the recent studies have shown certain correlation between transitory clinical manifestation with focal reduction of cerebral circulation and possible ischemic lesions in patients with migraine.
Methods and Results The purpose of this study was to evaluate the possible presence of the structural lesions of brain parenchyma in patients with migraine with MRI. This study included patients which according to known criteria had migraine preceded or not by an aura. All patients underwent MRI examination without and with contrast media (Gadolinium dimeglumine Gd-DTPA). Examination was performed in 30 patients with common migraine and in 20 patients with migraine preceded by an aura and focal neurological manifestations. Patients with serious risk factors for ischemic brain disease were excluded.

In 6 (20%) patients with classic form migraine MRI was recorded T2-weighted enhancement of signal intensity of white matter, and only in 2 (6.5%) patient focal change of signal intensity what is characteristics for ischemic lesions of brain parenchyma. In patients with migraine preceded by an aura and focal neurological manifestations (deficits) MRI showed T2-weighted change of signal intensity of white matter in 12 (60%) patients, and focal ischemic brain lesions in 4 (20%) patients.
Conclusion Our results showed that MRI necessary examination in complicated migraine patients and in patients with frequent and serious attacks.

P3J19

Transcranial Doppler evaluation in headache sufferers of the Headache Clinic in Athens General Hospital 'G. Gennimatas'

Angeliki Tsikkine[2], Georgia Hatzidaki[1], A. Drakotos[2], P. Brestas[2], Vassiliki Sakkou[1], Vassilios Grinias[1], Marinos Tsouroulas[2], Climentini Karageorgiou* [1]
[1]*Neurology Department, Athens General Hospital,* [2]*Neuroimaging Department, Athens General Hospital*

Objective The aim of this study is to compare the blood flow velocity in the middle cerebral artery by Transcranial Doppler ultrasonography, through different types of primary headaches, during the headache attack and the interictal period.
Patients and Methods Sufferers, from the Outpatient Headache Clinic with different types of Headache, have been studied with Transcranial Doppler examination (TCD). All sufferers were investigated during the Headache attack at 3 different moments according to the severity of pain, as well as during the Headache free period.

The Mean Flow Velocity was examined in basal conditions, in hypocapnia, and in hypercapnia.
Results The Migraineurs had increased Mean Flow Velocity (MFV) values. The RI to hypocapnia was increased in Migraine without aura. The TTH and CDH sufferers had no significant increase in MFV values. The MFV has a positive correlation to the intensity of pain.

Scientific Session 4

Genetics

P4K1

The insertion/deletion polymorphism of angiotensin-converting enzyme gene in patients with migraine

Hisanori Kowa*[1], Kenichi Yasui[1], Masayoshi Kusumi[1], Takao Takeshima[1], Kenji Nakashima[1], T. Ijiri[1], K. Ishizaki[1] & K. Nakaso[1]
[1]*Department of Neurology, Institute of Neurological Sciences, Faculty of Medicine, Tottori University, Yonago, Japan*

Objectives The pathophysiology of migraine is not yet fully understood but may involve painful vasodilatation of cerebral blood vessels. Angiotensin-converting enzyme (ACE) is one of the key enzymes in the renin-angiotensin-aldosterone system, which modulates vascular tension and blood pressure. It has been reported that insertion(I)/deletion(D) polymorphism in the ACE gene was related to serum ACE levels. Individuals who were homozygous for the D allele showed increased ACE activity levels. This study was designed to determine the prevalence of the ACE polymorphism in Japanese patients with migraine and tension-type headache (TH).
Methods This study consisted of 54 patients suffering from migraine with aura (MwA), 122 from migraine without aura (MoA), 78 from TH, and 248 normal controls. Genotyping of ACE I/D polymorphism was performed by polymerase chain reaction.
Results We detected that the incidence of the homozygous genotype (D/D) in migraine sufferers (18.8%) was higher than that in controls (12.5%). Moreover, the frequency of the D/D genotype in individuals of MwA was significantly high (25.9%).
Conclusions Our results support the conclusion that the ACE gene may be a genetic risk factor for migraine.

P4K2

Involvement of a low density lipoprotein receptor (LDLR) gene polymorphism in susceptibility to migraine

Giulia Pierangeli*[1], Sabina Cevoli[1], Mirella Mochi[1], Pietro Cortelli[2], Grazia Sances[3], R. E. Nappi[4], Giuseppe Nappi[3,5], Pasquale Montagna[1] & C. Canali[1]
[1]*Department of Neurological Science, University of Bologna, Bologna, Italy,* [2]*Department of Neurology, University of Modena and ReggioEmilia, Modena, Italy,* [3]*Headache Centre, University Centre for Adaptive Disorders and Headache (UCADH), IRCCS Mondino Institute of Neurology, Pavia. Italy,* [4]*Department of Obstetrics and Gynaecology, IRCCS S. Matteo, University of Pavia, Italy,* [5]*Department of Neurology and ORL, University 'La Sapienza', Rome, Italy*

Background The LDLR is the major gene involved in the binding and internalisation of cholesterol. LDLR exons share homology with clotting and coagulation proteins.

Objective To asses of the role of LDLR gene in the genetic liability to migraine.
Methods We performed an association study using a polymorphism in the LDLR gene (a triallelic (TA)n repeat in the 3′ UTR in exon 18). The genotypic and allelic frequencies were assayed on 140 individuals with migraine with aura (MA), 220 with migraine without aura (MO), on an heterogeneous group of 34 individuals with hemiplegic migraine (HM), both sporadic or familial, or with complicated migraine, along with 200 controls.
Results The allelic distribution of the polymorphism investigated was significantly different between MO and both controls and MA. As a corollary we found a long polymorphism (11 repeats) in three patients only: a woman with sporadic HM and celiac disease, and two related males with familial HM. The 11 repeats allele has never been described in literature and it was not found in any other person in our sample.
Conclusions Genetic predisposition to MO and possibly HM is associated with the LDLR polymorphism or another polymorphism in linkage disequilibrium with (TA)n.

P4K3

Stroke-related genes increase susceptibility to migraine

Rod Lea*[1,2], James Sundholm[2], Micky Ovcaric[2], Leah Solyom[2] & Lyn Griffiths[2]
[1]*Genomics Research Centre, Griffith University, Queensland, Australia,* [2]*Institute for Molecular Systematics, School of Biological Sciences, Victoria University of Wellington, New Zealand*

Migraine is a debilitating neurovascular disorder that affects at least 12% of the Caucasian population. The aetiology of migraine is likely to be comprised of a number of susceptibility genes acting synergistically to confer a moderate effect on the disease. The comorbidity of migraine and stroke, coupled with the pathophysiological similarities of these diseases, suggests that the genes implicated in risk of stroke may also influence migraine susceptibility. The objectives of our study were to investigate two well-known genetic risk variants for stroke (MTHFR-C667T and ACE-I/D) (1,2) for involvement in migraine susceptibility using a balanced case-control sample ($n = 275$ cases). Logistic regression (LR) analysis showed that the MTHFR TT genotype substantially increased risk of disease after adjusting for the effect of the ACE D alleles (OR = 2.405, 95% CI:1.296–4.464, $P = 0.005$). Interaction analysis provided good evidence that the MTHFR (TT) and ACE (ID/DD) genotypes act *synergistically* to further increase migraine susceptibility, particularly risk of MA (OR = 2.893, 95% CI:1.464–5.716, $P = 0.002$). We conclude that the MTHFR and ACE gene variants combine to contribute to migraine susceptibility and suggest that these genetic variants may represent an underlying genetic link between migraine and stroke.

References

1 Wald DS, Law M, Morris JK. Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. BMJ 2002 November 23; 325(7374):1202.
2 Sharma P. Meta-analysis of the ACE gene in ischaemic stroke. J Neurol Neurosurg Psychiatry 1998 February; 64(2):227–30.

P4K4

CACNA1A or INSR are not major susceptibility loci in Finnish MA families

Päivi J. Tikka*[1], Mari A. Kaunisto[1], Mikko Kallela[2], Arja Korhonen[3], Eija Hämäläinen[1], Markus Färkkilä[2], Roel Ophoff[3], Aarno Palotie[1,4] & Maija Wessman[1]
[1]*Department of Clinical Chemistry, University of Helsinki, Helsinki, Finland,* [2]*Department of Neurology, University of Helsinki, Helsinki, Finland,* [3]*Center for Neurobehavioral Genetics and Department of Human Genetics, University of Los Angeles, Los Angeles, USA,* [4]*Finnish Genome Center, University of Helsinki, Helsinki, Finland*

Missense mutations in the *CACNA1A* gene are associated with familial hemiplegic migraine (FHM1), a rare autosomal dominant subtype of migraine with aura (MA), on chromosome 19p13. Its contribution to more common forms of migraine has been debated. The contradictory results may be caused by limited sample size or explained by clinical heterogeneity. Recently, an association was reported between the *INSR* locus (in the proximity of *CACNA1A*) and migraine with and without aura.

To test the possible involvement of these two loci, we studied this 33 cM region on 19p13 genotyping 72 Finnish, multigenerational MA families with eight polymorphic microsatellite markers. Fifty of these 72 families were previously included in our genome-wide scan. Using parametric and nonparametric statistical analyses, we found no significant evidence of linkage to these markers. However, locus heterogeneity could not be excluded completely because some nominal linkage was observed in three families.

P4K5

Systematic analysis of the familial hemiplegic migraine gene ATP1A2 in migraine with aura

Unda Todt*[1], Axel Heinze[2], Vera Zumbroich[2], Alfredo Ramirez[1], Anne Stiller[1], Ingrid Goebel[1], Christian Kubisch[1], Hartmut Göbel [2]
[1]*Institut für Humangenetik, Universitätsklinikum Bonn, Germany,* [2]*Schmerzklinik Kiel und Neurologische Klinik der Universität Kiel, Germany*

Migraine with aura (MA) shows complex inheritance, yet, the causative genetic susceptibility factors remain elusive. Very recently it has been shown that mutations in the ATP1A2 gene that encodes the alpha 2 subunit of the sodium/potassium pump on chromosome 1q23 cause familial hemiplegic migraine type 2 (FHM2). To investigate whether ATP1A2 is also involved in the pathogenesis of complex MA, we pursued a systematic mutation screening of all coding exons and adjacent splice sites of ATP1A2 in index patients from 45 multiplex families with MA. Direct sequencing of PCR products revealed no obvious causal alterations, yet, several polymorphisms were identified. We performed association studies with a four base pair insertion upstream of exon 2 and a polymorphism in intron 9 in a case-control sample consisting of nearly 200 probands and 200 controls. No significant associa-

tion could be found. We are currently performing further association studies with additional single nucleotide polymorphisms (SNPs) we identified in ATP1A2. In summary, neither a direct mutation screening in familial MA nor an association study in a case-control sample gave evidence for a common role of the ATP1A2 gene in migraine with aura.

P4K6

Lack of association of CTLA-4 polymorphism 49 (A → G) with migraine

Simonetta Trabace[1], Marina Morellini[1], Patrizia Lulli[1], Germana Cicciarelli[1], Gabriella Coloprisco[2], Sergio De Filippis[2], Pier Giorgio Santi[2], Anna Rodio[2], Giuseppe Fiore[2] & Paolo Martelletti*[2]
[1]*Department of Experimental Medicine and Pathology, Section of Medical Genetics, 1st School of Medicine, San Camillo Hospital, Rome University 'La Sapienza', Rome, Italy,* [2]*Department of Internal Medicine, Service of Internal Medicine and Headache Centre, 2nd School of Medicine, Sant'Andrea Hospital, Rome University 'La Sapienza', Rome, Italy*

Migraine without aura and migraine with aura are disorders involving multiple environmental and genetic factors. In two previous studies, we hypothesized both a protective role for the HLA-DR2 antigen, providing additional basis for the proposed genetic heterogeneity between migraine without aura and migraine with aura and involvement of lymphotoxin α (TNF-α) as a susceptibility gene in migraine without aura.

The A/G polymorphism located within exon 1 of the gene encoding the cytotoxic T lymphocyte antigen 4 (CTLA-4) is associated with several multifactorial diseases HLA-associated, such as type 1 diabetes, inflammatory bowel diseases, etc.

CTLA-4 family shows a negative control on T cell proliferation and cytokine production (TNF-α and IL-10).

The aim of this study was to investigate the contribution of the candidate gene CTLA-4 in migraine pathophysiology.

In the present study we searched for an association between migraine and the gene encoding the cytotoxic T lymphocyte antigen 4 (CTLA-4).

Our experimental approach involved amplification of a 152-bp DNA fragment of exon 1 of this gene containing the position 49, followed by digestion with BstEII restriction enzyme for allele determination. Included in the study were 46 patients with migraine without aura, 28 patients with migraine with aura, and 108 migraine-free controls.

No association was observed between both migraine with and without aura and CTLA-4, lacking its potential role in the genetic architecture of inflammation-derived pain in migraine.

P4K7

Proinflammatory cytokines and migraine: a case-control study

Innocenzo Rainero[1], Luigi Grimaldi[2], Walter Valfrè[1], Rossana Lo Giudice[1], Chiara Rivoiro[1], Elisa Rubino[1], Lorenzo Pinessi[1]
[1]*Neurology III – Headache Center, Department of Neuroscience, University of Torino, Torino, Italy,* [2]*Neuroimmunology Unit, Department of Neuroscience, IRCCS San Raffaele, Milano, Italy*

Several studies suggested that immunological mechanism may be involved in migraine. However, available experimental data are scarce. The purpose of this study was to evaluate whether particular alleles or genotypes of the genes coding for the proinflammatory cytokines would modify the occurrence and the clinical features of migraine. In a group of 299 migraine patients and 313 healthy subjects, we tested the association of several polymorphisms in the interleukin-1 A (IL-1 A), interleukin-1B (IL-1B), interleukin 1 receptor antagonist (ILRN), interleukin-10 (IL-10) and Tumor Necrosis Factor-alpha (TNF-alpha) genes with the occurrence, the age at onset and several clinical features of migraine. We found a significant ($P < 0.001$) association between the TNF-alpha gene and the occurrence of migraine without aura. Polymorphisms within the IL1 gene cluster significantly modifies the age at onset of migraine attacks. Our data suggest that the TNF-α gene, or a linked locus within the HLA system, significantly modulates the risk for migraine without aura. In addition, IL-1 gene cluster polymorphisms may modify the clinical features of migraine.

P4K8

Genetic modifications in the Hermansky–Pudlak Syndrome gene: association with familial migraine

Iniesta Juan*[3], Corral Javier[1], González-Conejero Rocío[1], Hernández María José[4], Miñano Antonia[1], Pujol-Moix Nuria[2] & Vicente Vicente[1]
[1]*Centro Regional De Hemodonación,* [2]*Hematology Division, Hospital Santa Creu i Sant Pau. Barcelona, Spain,* [3]*Neurology Section, Hospital General Universitario, Murcia, Spain,* [4]*Family Medicine Unit, Hospital Psiquiátrico, Murcia, Spain*

Objective To investigate the association between genetic changes affecting the HPS-1 gene, deficit of platelet dense-bodies, and migraine.

Methods We analysed 16 patients with mild to severe deficit of platelet dense-bodies quantified by electron microscopy. The HPS-1 gene was sequenced in these patients. Seven HPS-1 genetic variations were analysed in 92 consecutive patients with migraine, 109 nonrelated controls, and 37 subjects belonging to six families with history of migraine.

Results Two modifications of the HPS-1 gene could play a role in migraine. The exon 3 Val4Ala polymorphism slightly increases the risk to suffer migraine (RR: 1.58, 95% CI: 0.96–2.58), specially with aura (RR: 2.37, 95% CI: 1.27–4.42), or with familial history (RR: 2.46, 95% CI: 1.44–4.18). Morover, the point mutation C2115T located in the 3'UTR was detected in three patients with migraine with visual aura and familial history but not in 109 controls. Familial studies support com-

plete linkage between this mutation and migraine with visual aura. However, these mutations did not correlate with deficit of platelet dense-bodies.

Conclusions The results of this study support a significant role of genetic modifications affecting the HPS-1 gene in common types of migraine, by an independent mechanism of the platelet dense-bodies content.

P4K9

Molecular analysis of Japanese familial migraine with aura

Miho Iigaya*[1], Naomi Kanazawa[2], Fumihiko Sakai[1] & Hisaka Igarashi[1]
[1]*Department of Neurology, Kitasato University, Sagamihara city, Kanagawa, Japan*, [2]*School of Medicine, Kitasato University, Sagamihara city, Kanagawa, Japan*

Background Several reports suggest the possible involvement of CACNA1A in nonhemiplegic migraine, but the other studies show contradictory results. While a widespread role of the CACNA1A in the causation of common migraine is known, no family with nonhemiplegic migraine has been reported to harbor the CACNA1A. Migraine, however, may genetically heterogeneous, and more studies in different families and populations are required for a definite conclusion.

Objectives We surveyed leukocyte genomic DNA mutation of CACNA1A in Japanese migraine patients with aura who have family history.

Materials and methods Thirty suffered from migraine with aura(male:female = 3 : 27, mean age = 42.1 ± 15.2). All participants gave written informed consent. The diagnosis of migraine was established in accordance with the criteria of IHS. Genomic DNA was extracted from peripheral blood leukocytes of the patients. Mutation analyses of the CACNA1A gene were performed by direct nucleotide sequence analysis of 12 exons which were reported to be affected in familial hemiplegic migraine.

Results SNIP was found in 15/30 patients in exon 16 (nt 2369, Thr 698) but no mutations identified in any of the 12 exons among 30 patients.

Conclusions Mutations in CACNA1A are not found in Japanese families with migraine with aura.

P4K10

First and second degree consanguineous in migraine 'heredity'

Maria Nicolodi*[1], Federigo Sicuteri [1]
[1]*Interuniversity Headache Centre, Foundation 'Prevention and Therapy of Primary Pain and Headache', Florence, Italy*

Our aim was to evaluate the impact of different variables of migraine heredity. Possible impact of depression and anxiety diagnosed when children-adolescents were also evaluated.

Three-hundred families with a proband (age range 33–57)suffering from migraine without aura (Group A) were examined regarding headache history of living first and second and third degree ascendants and descendants. Data were compared –McNemar X2 and MANOVA test- to the ones obtained in 309 families with a proband (age range 35–55 years) who never experienced headache during his/her life (Group B). Probands included in Group A were characterized by having more than 1 consanguineous ailed by headache with the exception of 11 subjects. A positive relation linked the number of second degree headache-suffering consanguineous and the severity of migraine of probands.

Statistics evidenced a positive relationship ($P > 0.0001$) between migraine-proneness and the presence of headache-suffering second degree consanguineous ascendants; lower impact ($P > 0.02$) is related to having a migraine suffering mother. MANOVA indicated that these parameters are largely more relevant (0.0001) than depression and anxiety suffered during juvenile age.

P4K11

The association of the T102C polymorphism of 5-HT2A-receptor gene with migraine

Po-Jen Wang*[1], Chih-Hung Chen[2], Po-Chang Huang[3], Ying-Fan Chen[3], H. Sunny Sun[4] & How-Ran Guo[5]
[1]*Department of Neurology, Sin-Lau Christian Hospital, Tainan, Taiwan,* [2]*Department of Neurology, National Cheng Kung University Hospital, Tainan, Taiwan,* [3]*Molecular Laboratory, Sin-Lau Christian Hospital, Tainan, Taiwan,* [4]*Institute of Molecular Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan,* [5]*Graduate Institute of Environmental and Occupational Health, College of Medicine, National Cheng Kung University, Tainan, Taiwan*

Objectives To investigate the association between the T102C polymorphism of 5-HT2A-receptor gene and migraine.

Background The serotonergic system has long been implicated in the pathophysiology of migraine. Several studies focused on the genes encoding serotonin and its receptors have suggested their possible involvement in migraine. Some 5-HT2 receptor antagonists are effective in decreasing the frequency of migraine. Activation of 5-HT2A-receptor can enhance NO transmission in the trigerminovascular system with resulting vasodilatation and nociceptive facilitation. There is a T to C transition at position 102 in 5HT2A-receptor gene. Its association with migraine was studied.

Materials and methods 193 migraineurs and 32 healthy controls were genotyped with restriction fragment length polymorphism in the 5-HT2A-receptor gene. Allele 1 (T102 allele) was represented by the uncut 342-bp PCR product and allele 2 (C102 allele) consisted of two fragments at 215 and 126 bp. The frequencies of each genotype were compared by Chi-square Tests.

Results The representations of the 5-HT2A-receptor genotypes were similar in the migraineurs and health controls ($P = 0.305$). The same result was also found between the frequent migraine and the episodic migraine ($P = 0.452$).

Conclusion There is no significant association between the T102C polymorphism of 5-HT2A-receptor gene and migraine. Neither the frequency of migraine is related.

P4K12

Mitochondrial homoplasmic G3316A mutation in Japanese patients with migraine

Yoshiki Adachi*[1], Haruko Araki[1], Saiko Kurihara[1], Hisanori Kowa[1], Takao Takeshima[1] & Kenji Nakashima[1]
[1]*Department of Neurology, Tottori University, Yonago, Japan*

Homoplasmic mutation from G to A at 3316th mitochondrial nucleotide has been reported to cause or raise the risk of some diseases, for example Leber's disease and diabetes mellitus. We examined this mutation in Japanese migraineous patients and normal population.

Objectives Fifty-five patients with migraine with aura (MWA), 110 patients with migraine without aura (MWOA) and 194 healthy control subjects were examined for blood test after informed consent.

Methods Mitochondrial DNAs were extracted from peripheral blood leukocytes by phenol/chloroform method. We amplified MTTL1 gene by PCR, and digested the products with NcoI. Mutant DNAs loose NcoI site and are easily checked by agar electrophoresis.

Results Two patients with MWOA and two normal controls had G3316A homoplasmic mutation and no other subjects had this mutation. The prevalence of this mutation was 0.0% in MWA, 1.8% in MWOA, 1.2% in both migraines and 1.0% in normal control subjects.

Conclusions Two patients with MWOA were revealed to have homoplasmic A3316G mutation. This mutation had been reported responsible for some mitochondrial diseases. But, the prevalence of this mutation in normal control Japanese was revealed about 1% at this study. We concluded this mutation might to be polymorphism in Japanese and not responsible for migraine.

P4K13

CADASIL: Clinical and genetic features in a patient with migraine

Joseph O. Di Duro*[1] & Gugliemo Faccin[1]
[1]*Private Practice, Vicenza, Italy*

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a rare hereditary disease characterized by recurrent transient ischemic attacks, strokes, and vascular dementia. We report a 53-year-old-female patient that presented with unresolved migraine, vertigo, neck pain and depression. Her migraine began at age 39 and had worsened after a car accident one year previous. Her father suffered headaches and her mother of 86 years of age was diagnosed with Alzheimers. The patient was treated with indicated migraine medications with no improvement of her condition. Manipulation and acupuncture also produced no beneficial results. MRI exam with T1 and T2 weighted images revealed multiple areas of hyperintense signals on T2 in the white matter subcortically in both frontal lobes. Neuropsychological testing by MMSE documented mild frontal lobe features and genetic testing is in place to confirm a Notch3 mutation. In patients who present with late onset migraine and family history of dementia who do not respond to the indicated therapies, further investigation with imaging, neuropsychological testing and genetic mapping my elucidate the proper diagnosis.

P4K14

Thymidylate synthase tandem repeat polymorphism does not affect the risk for migraine

Yolanda Bravo*[1], Natalia Valle[1], Agustín Oterino[1], Jesús Castillo[3], Julio Pascual[1], Carlos Ruiz-Alegría[2], Pablo Sánchez-Velasco[2], Francisco Leyva-Cobián[2], Pedro Muñoz[4] & Carmen Cid[1]
[1]*Service of Neurology, Hospital 'Marqués de Valdecilla', Santander,* [2]*Service of Immunology, Hospital 'Marqués De Valdecilla', Santander,* [3]*Health Center of Camargo,* [4]*Primary Care Management, Spain*

Hyperhomocysteinemia has been found to modify the relative risk for migraine with aura (MA). MTHFR T677 allele, associated with higher plasma homocysteine levels, increased the relative risk for migraine in a Japanese study. Other enzymes implicated in the folate route could modify the risk for migraine as well.

Objective To assess the role in migraine of the thymidylate synthase (TS) promoter tandem repeat 3R/3R genotype in a case-control study.

Methodology We recruited 230 migraine (78 MA; 152 MO) patients (aged 40.8 ± 15.3 years) and 204 healthy controls (39.9 ± 13.8 years) in our clinic. Genotyping of TS-2R/3R polymorphism was performed by PCR amplification of leukocyte DNA samples and identified directly after electrophoresis. Genotypic and allelic distribution was calculated by χ^2 method (Yate's correction; alfa = 0.05).

Results To date, 72 controls, 84 MO and 44 MA patients have been genotyped. In this subset of samples, both genotypic and allelic frequencies fit the Hardy–Weinberg equilibrium. There were no significant differences in the frequencies of TS-3R/3R homozygosis of controls (0.26) vs. migraine in general (0.26) or MO (0.25), or in MO vs. MA (0,29).

Conclusion From these preliminary results, TS-3R/3R homozygosis does not seem to modify the risk for migraine in our sample.

P4K15

A gene for cluster headache? Report of cluster headache on a pair of monozygous twins

Pedro André Kowacs*[1], Elcio Juliato Piovesan[1], Lineu Cesar Werneck[1], Hudson Fameli[1], Marcos Christiano Lange[1] & Salmo Raskin[2]
[1]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil,* [2]*Laboratório Genetika, Curitiba, Brazil*

A pair of identical twins with cluster headache is described. Monozygosis was confirmed by the identification of 14 DNA markers. In spite of harboring the same genes, the clinical picture presented by both twins was not exactly the same, regarding age of first bout, attack duration, laterality, and associated autonomic features. Among the so-called trigeminal-autonomic cephalalgias, cluster headache is probably the

best known one, but several issues regarding its pathophysiology remain to be answered. The cases described herein reinforce the role of genetic aspects in cluster headache pathogenesis.

P4K16

Thrombophilic derangements associated with migraine with aura. A rare report of monozygous twins

Vincenzo Pizza*[1], Domenico De Lucia[2], Umberto Ruggiero[3], Giampiero Volpe[1], Anella Agresta[1], Alfredo Bianchi[4] & Cesare Colucci d'Amato[3]
[1]*Neurophysiopatoly Service, S. Luca Hospital, Vallo della Lucania (SA),* [2]*Laboratory of Haemostasis and Thrombosis, 2nd University, Naples,* [3]*Department of Neurological Sciences, 2nd University, Naples,* [4]*Pharmacology Department, Faculty of Medicine, Catania University*

Introduction Cerebral ischaemia in young women may be associated at migraine. The nature of this connection remains essentially unknown. Several studies have been devoted to the detection of markers of a prothrombotic tendency in migrainous subjects.
Case report M.N. and M.M. (males, 52 years) are monozygous twins suffered by migraine with aura (HIS '88 criteria) from 15 years age and with a familial history of cardio-cerebral vascular disease. M.N. is affected from angina pectoris and M.M. from myocardial infarction and transient ischemic accident. Data of laboratory examinations for screening of the prothrombotic state revealed: M.N. F xi 128.2% (range 70–120), FXII:c 150.4% (range 70–120), APC-resistance 0.6 (range > 0.7), Plasma Homocysteine 29 μmol/L (range 5–15), MTHFR gene (TT/CC).

M.M. F xii 138.6% (range 70–120), APC resistance 0.6 (range > 0.7), Plasma Homocysteine 40.2 μmol/L (range 5–15), MTHFR gene (TT/CC).
Conclusion In the literature no definite **conclusions** can be drawn from the studies on prothrombotic genetic risk factors in patient suffering from migraine. Therefore, our data have been demonstrated a strict association between migraine with aura history, cardio-cerebral vascular disease and prothrombotic genetic risk factors, suggesting that haemostatic risk factors for arterial thrombosis may be carried out for studying these patients.

Secondary headaches

P4L1

Cervicogenic headache (CEH) still improving 6 years after whiplash injury

Monica Drottning*[1], Gry Tjønneland Frang[1], Trine Haug Popperud[1], Peer H. Staff[1] & Ottar Sjaastad[2]
[1]*Ulleval University Hospital, Oslo, Norway,* [2]*St. Olavs. Hospital, Trondheim, Norway*

Objectives To search for the natural course of chronic unilateral cervicogenic headache (CEH) after whiplash injury.
Methods Whiplash patients, $n = 587$, were initially followed for a year after their Emergency Service consultation. *De novo* CEH was found in 8% at 6 weeks and in 3% at one year. All patients with chronic de novo CEH at one year, $n = 20$, were called in for interviews and examinations 6 years after the accident. Four persons were lost to follow up, two persons with headache were excluded because of new neck traumas.
Results 35% ($n = 7$) still had CEH at 6 years. 10% ($n = 2$) had a bilateral daily tension type headache. Head pain could still be precipitated from the neck in 4 of the 6 headache free patients.
Conclusions CEH seems to be improving years after whiplash injury. Previous accident with neck trauma was prognostic for chronic CEH at one year in this material. Persons with chronic CEH at one year who were headache free at 6 years still have a neck vulnerability at examination at 6 years. The continuous improvement of CEH years after neck injury calls for considerable caution before making a destructive lesion.

P4L2

Headache in sleep apnea syndrome

Andrea Alberti*[1], Elisabetta Gallinella[1], Paola Sarchielli[1], Sara Micheli[1] & Virgilio Gallai[1]
[1]*Headache Centre- Sleep Medicine Centre, Neuroscience Department, University of Perugia, Italy*

Introduction Patients affected by Obstructive Sleep Apnea Syndrome (OSAS) frequently refer headache at awakening, but in literature the association between OSAS and headache at awakening is still controversial.
Patients and methods- 56 patients (7 F and 49 M, mean age: 52.38 ± 12.70 SD), affected by OSAS, who consecutively attended the Sleep Medicine Centre of our Department were examined.

They underwent a Video-Polisomnographic EEG and an accurate history for the occurrence of headache (according to the IHS 1988 criteria). Headache characteristics were compared with those of a group of 50 patients affected by insomnia.
Results Headache in the last year was referred by 48.67% (27/56) of the patients affected by OSAS, in the majority of cases with the characteristics of the tension type headache (72%); in 62.96% (17/27) headache occurred at awakening. Headache at awakening was therefore significantly more frequent in OSAS compared to insomniac patients ($P < 0.01$) and was significantly correlated with severity of OSAS. In particular a significant correlation with Apnea Index and digital oxygen de-saturation emerged.
Discussion The need for an accurate evaluation of headache at awakening is pivotal because its occurrence prompts the clinician to begin an accurate diagnostic examination to investigate the presence of OSAS in its earliest phase.

P4L3

Cough headache due to cerebrospinal fluid orthostatic hypotension

Francesco Bono*[1], Maria Rosaria Lupo[2], Luigina Mangone[1], Iris Garreffa[1], Giovanni Broussard[1] & Aldo Quattrone[1,2]
[1]*Institute of Neurology, University Magna Grœcia, Catanzaro, Italy,* [2]*Institute of Neurological Sciences, National Research Council, Piano Lago di Mangone_ Cosenza, Italy*

Headache provoked by cough is known to occur as a symptomatic or as benign condition. We report three patients with cough headache (CH) in whom we studied the lumbar CSF opening pressure and its changes in response to coughing in lateral decubitus, sitting, and upright positions.

We recorded the lumbar CSF opening pressure in the patients, and in 35 control subjects. In our patients, CSF opening pressure recorded in lateral decubitus and sitting positions was within normal values, and a bouts of coughing did not induce headache. Surprisingly, when the patients were upright, the lumbar CSF opening pressure dropped (relative to the value recorded in the sitting position), and a few bouts of coughing then induced bursting bilateral pain in the occipital region radiating to the vertex area. In the control group, postural changes (sitting and upright positions) always increased CSF opening pressure.

The present results suggest that, in our cases, cough headache was closely related to orthostatic hypotension in the lumbar CSF. We hypothesize that a sudden increase in intracranial pressure in addition to lumbar CSF orthostatic hypotension may play a role in the pathogenesis of CH.

P4L4

Migraine with prolonged aura and Sturge Weber syndrome

Carlo Lisotto*[1], Federico Mainardi[2], Ferdinando Maggioni[2] & Giorgio Zanchin[2]
[1]*Headache Unit, San Vito al Tagliamento Hospital, Italy,* [2]*Headache Centre, Department of Neurosciences, Padua University, Italy*

A 59-year-old-man with the diagnosis of Sturge Weber Syndrome (SWS) presented with a 20-year history of infrequent migraine headaches, recurring every 4–6 months, preceded by visual auras. The neurological examination revealed a facial nevus on the left forehead and a left optic nerve atrophy due to choroid angioma, with secondary severe loss of vision. No history of seizures was reported. Cranial MRI revealed a leptomeningeal angiomatosis and cortical calcifications in the left parieto-occipital lobe. Cerebral angiography showed a slightly increased blood flow in the left vertebral artery, when compared with the contralateral side. The migraine auras were characterized by scintillating scotoma that lasted for 30 min and subsequent prolonged visual loss in the right eye, lasting for about 24 h. This symptom was extremely disabling for the patient, taking into account the permanent poor vision in the left eye. The headache was bilateral, throbbing, lasting for 2–3 days and accompanied by nausea and vomiting. In summary our patient's headache can be clinically diagnosed as migraine with prolonged aura. Other similar isolated reports suggest that SWS might be a cause of symptomatic migraine, particularly with prolonged aura, possibly related to chronic focal oligemia.

P4L5

Persistent headache due to chronic cerebrospinal fluid leakage after minor head trauma

Masayuki Mizobuchi*[1], Fumitaka Murakami[2] & Chiaki Tsuji[2]
[1]*Department of Neurological Surgery, Okayama Kyokuto Hospital, Okayama, Japan,* [2]*Department of Anesthesiology, Okayama Kyokuto Hospital, Okayama, Japan*

Objectives We evaluated cerebrospinal fluid (CSF) leakage and the efficacy of epidural blood patches (EBPs) in patients previously diagnosed as cervical sprain.
Methods We examined 33 patients complaining of persistent headache between October 2002 and March 2003 (18 male and 15 female patients, age range, 22–68 years mean age; 40.5 years). Main causes were 20 traffic accidents, 3 chiroplactics, 3 sports injuries, 2 deliveries. Indium cisternography was performed. CSF leakage was recognized as findings rapid appearance of isotope in the urinary bladder or dural sleeves staining. After confirmed diagnosis, large volume EBPs were performed.
Results CSF leakage was recognized in the 32 of 33 patients, especially all of patients after traffic accidents. All patients except one showed normal lumbar pressure (pressure range, 5.5–17.5 cm H_2O mean pressure 12.7 cmH_2O). EBPs were performed in 29 patients up to three times to different spinal levels. Twenty-two of 29 patients (75.8%) improved their symptoms.
Conclusions Chronic CSF minor leakage is one of main cause inducing chronic headache after minor trauma. CSF leaks probably in the endpoint of dural sleeves. Chronic CSF leakage with compensation of intracranial pressure is a different entity from cervical sprain or acute spontaneous intracranial hypotension.

P4L6

Reversible cerebral angiopathy: efficacy of intravenous nimodipine

Valerie Domigo*[1], Mathieu Zuber[1], Catherine Lamy[1] & Emmanuel Touzé[1] Jean-Louis Mas [1]
[1]*Department of Neurology, Hôpital Sainte-Anne, Paris, France*

Background Reversible cerebral angiopathy (RCA) is characterized by sudden-onset severe headaches and reversible segmental narrowings of the medium-sized cerebral arteries. Although prognosis is usually good, intracranial vasoconstriction can occasionally be severe enough to precipitate stroke.
Methods We report three cases of RCA successfully treated by intravenous nimodipine.
Results Three patients were admitted because of thunderclap headaches. Headaches occurred during coïtus in one case and were associated with acute elevation of blood pressure in another case. No precipitating factor was identified in the last

patient. Cerebrospinal fluid and CT scan were normal in all cases. MR angiography demonstrated diffuse intracerebral stenosis of the medium-sized cerebral arteries. Transcranial Doppler (TCD) ultrasounds showed markedly elevated blood flow velocities. A left occipital intracerebral haemorrhage occurred three days after onset in one case. Headaches were not improved by usual analgesics whereas intravenous nimodipine led to a complete relief of headache over a few hours. Serial TCD showed gradual normalization of flow velocities over a few days. Control MR angiographies performed one months later were normal.

Conclusion A dramatic improvement of headaches associated with RCA may be achieved with intravenous nimodipine. Our findings also add support to the role of vasospasm in the pathogenesis of RCA.

P4L7

Headache in hemorrhagic stroke

Stojan Sarenac*[1], Dragana Sarenac[1] & Budimka Sarenac[1]
[1]*Hospital 'Vaso Cukovic' Risan, Department of Neurology*

Background and objectives Headache can be one of prominent symptoms in hemorrhagic stroke. It is seen more often and is more severe in subarachnoid than in intracerebral (intracerebelar) hemorrhage. It belongs to symptomatic headaches and is classified as the 6th group (IHS classification).

Methods Study included 479 patients with cerebrovascular disease (CVD), treated during 2-year period (1997 and 1998) in our hospital. Out of them 68 patients (14.2%) had hemorrhagic CVD. Clinical approach to each patient included computed tomografy of the brain and also the presence of any of the following symptoms and signs: headache, vomiting, fever, syncope, focal neurological disorders, meningeal signs, epileptic seizures and hypertension.

Results Out of 68 patients with hemorrhagic CVD 38 were male and 30 female, mean age 61 years. Intracerebral (ICH) hemorrhage was found in 49 patients (72%) mean age 64 years and subarachoid hemorrhage in 19 (28%) mean age 52 years. Out of 68 patients having hemorrhagic CVD headache was present in 29 (42,65%). Headache had 16 (32.6%) patients out of 49 with ICH and 13 (68,42%) out of 19 patients with subarachoid hemorrhage ($P < 0,05$).

Conclusion Headache is much more often, as a rule found in patients with subarachoid hemorrhage but often absent in those suffering from intracerebral hemorrhage.

P4L8

SUNCT–like syndrome caused by neurofibromatosis type 2: a case report

Fidel Ernesto Sobrino*[1]
[1]*Clinical Neurologist, Colsubsidio Headache Clinic, Bogotá, Colombia*

Objective A patient with SUNCT–like syndrome caused by Neurofibromatosis type 2 is described.

Background and methods The syndrome of short-lasting, unilateral, neuralgiform attacks of pain in the periorbital area associated with conjuntival injection, tearing, sweating and rhinorrhea (SUNCT) is an unusual form of primary headache. There are few reported cases of symptomatic SUNCT which have in common a posterior fossa lesion. A 28-year –old woman with a 7-years history of the bilateral hearing loss, tinnitus, central vertigo and right facial weakness. At the age of 27, the patient presented a dull intense bifrontal constant headache that was worse with valsalva maneuvers and attacks short-lasting periods of frequent attacks of the left intense orbital pain with duration of about 30 s (10/one hour), associated with ipsilateral conjunctival injection, lacrimation and rhinorrhea. Cranial MRI demonstrated a bilateral acoustic schawnnoma and frontal meningioma. (Diagnostic criteria for Neurofibromatosis type 2)

Conclusions In this report we present a new symptomatic case with clinical features resembling SUNCT associated with bilateral acoustic schawnnomas and pontomedular compression. (Neurofibromatosis type 2). The posterior fossa signs emphasize absolute need for MRI in any suspected case of SUNCT.

P4L9

Headache associated with high-dose intravenous immunoglobulin therapy

Yukiko Tada[1], Kiyoshi Negoro*[1], Motoharu Kawai[1], Junichi Ogasawara[1] & Mitsunori Morimatsu[1]
[1]*Department of Neurology and clinical Neuroscience, Yamaguchi University School, Ube, Japan*

One of the most common adverse effects from high-dose intravenous immunoglobulin (IVIg) therapy is headache. We reviewed medical records of 30 patients given IVIg therapy. Headaches were observed in 8 patients (27%): multifocal motor neuropathy 3, chronic inflammatory demyelinating polyneuropathy 2, Guillain–Barré syndrome 1, Miller Fisher syndrome 1, brainstem encephalitis 1. Most headaches occurred 3–4 days after initiation of the injection. The headaches were generally mild, but two patients had severe headache with fever, nausea and nuchal rigidity. Cerebrospinal fluid studies revealed aseptic meningitis. In many of them, the peripheral eosinocyte count and serum IgG level increased after IVIg. Headaches were rapidly improved by anti-inflammatory drugs in all patients. Although the exact mechanisms of IVIg-associated headache are unclear, an allergic meningeal reaction and serum hyperviscosity induced by the high-dose allogeneic immunoglobulin seem most likely.

P4L10

Acute blood pressure rise as a consequence of treadmill test as a cause of headache

Thomas Thomaides*[1], Anastasios Spandideas[1], Anastasios Andricos[2], Neofitos Theodorides[1], John Thomopoulos[1] & E. Manaos[1]
[1]*Neurology Department Pammakaristos General Hospital Athens,*
[2]*Cardiology Department of Agia Olga General Hospital Athens*

Aim of our study was to investigate whether the acute rise of arterial blood pressure provoked by a treadmill test could act as an exogenous stimulus causing headache.

Fifty subjects (36 men, 14 women), mean age 52 years, with no headache history, subjected to a treadmill test, for possible of coronary heart disease (CHD).

Treadmill test was negative for CHD in 34 subjects, positive for CHD in 13 and borderline in 3. The average arterial blood pressure before the treadmill test was 129/81 mmHg. During the test the achieved average rise was 181/96 mmHg. The achieved mean diastolic blood pressure (DBP) rise by the end of the test was 18.5% of the baseline DBP. Seven patients(3 men and 4 women) or 14% presented headache during the treadmill test. The mean DBP rise in this group was 18% of the baseline DBP.

In conclusion an acute DBP rise by 18.5% seems not to be related to provoke headache. Due to the applied Bruce protocol for the investigation of possible CHD patients it was impossible to reach the set by IHS rise level of DBPcriterion (> 25%). Further investigation in different groups of subjects with higher DBP rise is needed to see whether in these circumstances acute DBP rise can act as a cephalalgogenic factor

P4L11

Obstructive sleep apnoea syndrome (OSAS) associated with chronic headache

Dimos Mitsikostas*[1]
[1]*Athens Naval Hospital, Neurology Department, Athens, Greece*

Objectives To investigate the influence of OSAS in the outcome of patients suffering from chronic headache (CH, at least 15 days with headache per month, for = 6 months) not responsive to common pharmaceutical treatment.
Methods Seventeen cases of untreatable CH (prophylactic treatment with at least three drugs one after another, lasting for at least two months each one) associated with OSAS (total apnea index = 15) are presented with follow-up (= 6 months).
Results Continuous positive airway pressure treatment improved both OSAS and untreatable CH (decrease = 50% in total apnea index, or in days with headache, respectively).
Conclusions Screening questions targeting to uncover polysomnography indications should be applied to all patients with untreatable CH. In case of comorbidity with OSAS, treatment with positive airway pressure may improve CH.

P4L12

Cluster headache (CH) associated with pituitary prolactinoma

Elena Minguzzi*[1], Sabina Cevoli[1], Giulia Pierangeli[1], Pietro Cortelli[2] Pasquale Montagna[1] & C. Canali[1]
[1]*Department of Neurological Science, University of Bologna, Bologna, Italy,* [2]*Department of Neurology, University of Modena and ReggioEmilia, Modena, Italy*

Objective To describe CH-type attacks in a patient with pituitary prolactinoma.
Background CH-type symptoms have been described in association with cervical, midline, intracranial lesions and with AVM of the carotid territory. Four cases of pituitary tumors have been described associated with CH.
Results A 49-years-old woman had been suffering since age 35 years from recurrent episodes of blurred vision and sparkling scotomas in her left visual field, lasting 60 min. A mild ipsilateral parieto-temporal throbbing pain with phono-photophobia developed immediately after the end of aura symptoms, lasting up to 2 h.

Since age 46 she complained of recurrent severe and sharp left temporo-orbital pain lasting 30–90 min, associated with ipsilateral lacrimation, injection of conjuctiva, and rhinorrhea.

Attacks occurred twice a day invariably before lunch and dinner and the pain sometimes awakened the patient at the same hour in the night. Neurological examination was normal. A brain MRI showed a noninfiltrating hypophyseal tumor surrounding the left cavernous sinus, which was surgically removed. Microscopic examination revealed a benign prolactinoma. One year and six months after surgery the patient has remained totally free from cluster-like attacks. She has had rare mild migraine attacks without aura.
Conclusions Our patient had cluster-like headache and pituitary adenoma surrounding the ipsilateral cavernous sinus. Resolution of the pain after surgical treatment suggests a pathogenetic correlation between CH attacks and the adenoma.

P4L13

Cluster headache (CH) with aura associated with parieto-occipital arteriovenous malformation (AVM)

Sabina Cevoli*[1], Fabiola Magnifico[1], Giulia Pierangeli[1], Elena Minguzzi[1], Pietro Cortelli[2], Pasquale Montagna[1], Pietro Querzani[3] & C. Canali[1]
[1]*Department of Neurological Science, University of Bologna, Bologna, Italy,* [2]*Department of Neurology, University of Modena and Reggio Emilia, Modena, Italy,* [3]*Pierantoni Hospital, Neurological Unit, AUSL Forlì, Italy*

Objective To describe CH-type attacks with visual aura in a patient with parieto-occipital AVM.
Background The relationships between migraine and AVM is still controversial. Occipital AVMs may cause visual disturbances and headaches resembling migraine with aura. CH-type symptoms have been described in association with AVM in the carotid territory.
Results A 32-year-old woman had been suffering since age 14 from recurrent episodes of blurred vision and sparkling scotomas in her left visual field, lasting 15–20 min. A unilateral periorbital throbbing pain with lacrimation, nasal congestion, and conjunctival injection developed suddenly after the end of aura symptoms, lasting up to 2.5 h. Attacks occurred in a short cluster of few days, up to 15 days, with a 1–2 month free interval. The attacks occurred at the same hour every night. During the last cluster there was no visual aura. Neurological examination was normal. A brain MRI showed a large left parieto-occipital AVM.
Conclusions Our patient had cluster-like headaches preceded by visual auras, and a parieto-occipital AVM. Visual auras due to brain AVM are well recognized, but CH is not. Our case postulates a pathogenetic correlation between visual

aura/CH attacks and the AVM, but the actual mechanisms responsible remain unclear.

MURST(R.F.O) ex-60% 2000-2001-2002 grants.

P4L14

Exertional headache associated with Paget's disease: two cases

Luiz Paulo Queiroz*[1], Fabiola Dach[1] & Fabricio Molon Silva[1]
[1]*Hospital Governador Celso Ramos, Florianopolis, Brazil*

Objective To present two cases of exertional headache associated with Paget's disease of the skull, and with postural modification of the pain.

Patients *Case I*: Female, 53 years old, with a left unilateral headache, for 18 months, precipitated by short and abrupt physical exertion, like coughing and sneezing. The pain was only relieved if the patient bended forward; if she stayed in the upright position or laid down, the headache would persist and aggravate. The skull radiology was typical of Paget's disease; the brain MRI showed a basilar invagination. Headaches were prevented with the use of indomethacin. *Case II:* Female, 56 years old, with headaches for only one month. The pain was mild, daily, continuous, and relieved with the use of simple analgesics. When she coughed, sneezed or bended forward, she had an abrupt severe pain, which lasted for a few minutes. The headache was relieved with recumbency. Skull X-ray showed a 'cotton wool appearance'. Cranial CT and MRI showed a hydrocephalus, platybasia and basilar invagination. The patient had no more headaches after ventriculoperitoneal shunting.

Comments Paget's disease is an uncommon cause of symptomatic exertional headache. Interestingly, posture had an opposite influence in the pain of these two patients.

P4L15

Postural manoeuvres in the prevention of postlumbar headache

Francesco Bono*[1], Maria Rosaria Lupo[2], Luigia Mangone[1], Iris Garreffa[1], Giovanni Broussard[1], Aldo Quattrone[1,2]
[1]*Institute of Neurology, University Magna Græcia, Catanzaro, Italy,* [2]*Institute of Neurological Sciences, National Research Council, Piano Lago di Mangone, Cosenza, Italy,* [3]*Institute of Neurology, University Magna Græcia, Catanzaro, Italy,* [4]*Institute of Neurology, University Magna Græcia, Catanzaro, Italy,* [5]*Institute of Neurology, University Magna Græcia, Catanzaro, Italy,* [6]*Institute of Neurology, University Magna Græcia, Catanzaro; Institute of Neurological Sciences, National Research Council, Piano Lago di Mangone, Cosenza, Italy*

Objective To determine the effect of two postural manoeuvres in the prevention of postlumbar puncture headache (PLPH).

Methods A total of 92 subjects (19 men and 63 women, aged 16–76 years, mean 42.9 years) underwent diagnostic lumbar puncture. They were randomly allocated to one of two bed rest positions for four hours following the spinal tap (supine-horizontal, supine with head-down tilt) after which they were allowed to get up.

Results There was significant difference in the occurrence of PLPH between the two groups. Forty-five per cent of patients in the supine and horizontal group developed PLPH, whereas only 22% of patients in the supine with head-down tilt group had PLPH ($P < 0.05$).

Conclusions Evidence suggests that the spinal fluid leakage due to delayed closure of a dural defect causes PLPH. In the current study, we demonstrate that supine with head-down tilt position had a protective effect against PLPH, suggesting that this position may prevent PLPH by favouring the closure of meningeal hole.

We believe that supine with head-down tilt position may represent the optimal postural manoeuvre after lumbar puncture in reducing the occurrence of PLPH.

P4L16

Unusual causes of thunderclap headache

Christian Lucas*[1], Charlotte Cordonnier[1], Marie-Anne Mackowiak[1] & Didier Leys[1]
[1]*Department of Neurology, Lille University, Lille, France*

Case 1: a 17-year-old-man presented a thunderclap headache when coughing. He had taken before pseudo-ephedrin intranasaly for a cold a few days before. CT scan, cerebrospinal fluid (CSF) analysis and cerebral MRI were normal. Cerebral angiography showed multiple stenosis of intracerebral arteries. A second angiography performed 3 months later was normal. Pseudo-ephedrin was accidentally reintroduced 10 months later. He presented headaches, neck-pain and left facial hypoestesia 2 days after pseudo-ephedrin administration with recovering in 3 days. CT scan, cerebral MRI, MR angiography and *trans*-cranial Doppler were normal. Our final diagnosis was cerebral angiopathy due to pseudo-ephedrin.

Case 2: A 35-years-old-woman presented a right severe temporal thunderclap headache with phono-photophobia during 2 days. Cerebral MRI showed a right temporal hyperintensity in T1 and T2 weighted-sequences near the cavernous sinus and a right peri-mesencephalic thickening. Neuroradiological diagnosis was in favour of a rupture of a dermoïd cyst.

Case 3: a 65-years-old-woman presented a frontal bilateral thunderclap headache without nausea nor phono-photophobia. CT scan, EEG, cervical ultrasounds and biological examinations were normal. Cerebral MRI, performed one year later, showed a dural fistula type II in the right lateral sinus, which was a sequel of a cerebral venous thrombosis and showed also sequel of the left side due to old lateral cerebral sinus thrombosis. An endovascular treatment was performed. The patient totally recovered.

P4L17

Subsequent migraine attacks efficiently treated with Zolmitriptan revealing a carotid artery dissection

Christian Lucas*[1], Charlotte Cordonnier[1], Marie-Anne Mackowiak[1] & Didier Leys[1]
[1]*Department of Neurology., Lille University Hospital, Lille, France*

A 50-years-old-woman, with usually rare and mild/moderate attack migraine, presented, for the first time, a severe

migraine attack, without cervicalgia, and took zolmitriptan with a good efficacy in one hour. She had recurrences during 4 days with good efficacy and good tolerance of zolmitriptan at each time. However, she suffered from a transient aphasia during 10 min after the second recurrence but did not consult at this time. On the fifth day, she presented a sudden right hemiplegia with aphasia. CT scan showed a left superficial infarct in the middle cerebral artery territory. Ultrasounds examination and MR angiography showed a severe left internal carotid artery stenosis with mural hematoma, which was in favor of carotid artery dissection. The patient partially recovered with a persistent mild aphasia. MR angiography follow-up showed recanalization of the left carotid artery.

Physicians should bear in mind that an unusual course of migraine may always be a symptom of organic lesion even in migraineurs. Therefore, triptan efficacy should not be considered as a 'diagnostic test'.

P4L18

Migraine-like symptoms in phaechromocytoma. A case report

Francesco De Cesaris*[1], Alberto Moggi Pignone[1], Massimo De Luca[1], Umberto Pietrini[1] & Enrico Del Bene[1]
[1]*Headache Center, Department of Internal Medicine, University of Florence*

A female patient, aged 28, had a three years history of headache attacks, precipitated by exercise or emotions, with severe, throbbing pain associated with palpitations, sweating, photo- and phonophobia, nausea and vomiting. Attacks lasted for 15–60 min, with a poor response to analgesic medications, and occurred once per month initially, with a subsequent increase in frequency. Propanolol prophylaxis had been interrupted for aggravation of the symptoms. A few months before a severe attack had been treated in the emergency room. EEG, CT and echoDoppler of cranial and extra-cranial vessels were normal. On hospital admission she suffered from 1 to 5 daily attacks. The clinical examination was normal, with a blood pressure of 126/70. Routine blood chemistry, ECG, fundoscopic examination, and chest X-ray were normal. The blood pressure during an headache attack was subsequently found equal to 160/105. VMA in the 24-h urine was 38.9 mg (normal: 1.8–6.7), plasma levels of noradreanaline were 1852.7 pg/mL (normal: 65–400) and of adrenaline 217.3 pg/mL (normal: 5–127). Abdominal echography, adrenal CT scan and scintigraphy confirmed the diagnosis of pheochromocytoma in the right adrenal medulla. The symptoms resolved after surgical ablation of the tumour. An history of headache attacks associated with hypertension, sweating and palpitations, should pose the suspect of pheocromocytoma and encourage specific diagnostic tests.

P4L19

Headache in cerebral artery dissection with ischemic stroke

Kentaro Yamada*[1], Takemori Yamawaki[1], Kotaro Miyashita[1], Kazuyuki Nagatsuka[1] & Hiroaki Naritomi[1]
[1]*National Cardiovascular Center, Cerebrovasucular Division*

While headache is commonly observed in cerebral artery dissection (CAD) with hemorrhagic stroke, its frequency in CAD with ischemic stroke has been poorly elucidated. We studied the presence or absence of headache in 19 consecutive cases of CAD with ischemic stroke. There were 7 young patients (49 years or less), and 12 old patients (50 years or more). The dissection was found in the vertebral artery ($n = 11$), basilar artery ($n = 5$), internal carotid artery ($n = 2$), and others ($n = 1$). Headache was found only in 8 patients (42%). The incidence of headache was lower in the old patients (3/11, 27%) than in the young patients (5/8, 63%). Headache was most common in vertebral artery dissection (7/11, 63%), and most infrequent in basilar artery dissection (1/5, 20%). Headache appears to be not so common in ischemic type CAD as compared with hemorrhagic type CAD.

P4L20

The prevalence of migraine in embolic stroke patients with patent foramen ovale

Takemori Yamawaki*[1], Kentaro Yamada[1], Keiko Nagano[1], Kozue Saito[1], Kotaro Miyashita[1], Kazuyuki Nagatsuka[1] & Hiroaki Naritomi[1]
[1]*National Cardiovascular Center, Department of cerebrovasucular medicine*

The increasing risk of cerebral infarction in patients with migraine is occasionally explained by the patency of the foramen ovale and increased propensity to paradoxical cerebral embolism. However, there have been few report studying the frequency and characteristics of headache in paradoxical cerebral embolism. We therefore investigated the prevalence of headache in embolic stroke patients with patent foramen ovale (PFO). A total of 63 patients were selected from the stroke database. Five patients had a previous history of headache. Migraine was, however, found only in 3 patients (4.8%). Two remainder had a tension-type headache. The prevalence of migraine in embolic stroke with PFO appears to be rather low. The prevalence of migraine in Japanese population is known to be lower than that in Caucasian population. The results, however, suspect that PFO may not play an important role in mechanisms of migraine-related stroke.

P4L21

Headache characteristics in patients with pituitary tumours

Judit Áfra*[1] & Sándor Czirják[1]
[1]*National Institute of Neurosurgery, Budapest, Hungary*

Sellar region is of interest in primary headache pathomechanism that was the reason to assessed headache in 86 patients

who underwent surgery because of a pituitary tumour. We used a self-administered questionnaire.

Fifty-six out of 86 patients had a headache prior to the operation without correlation to the tumour size or parasellar invasion. In patients with headache familiarity was more frequent (46% vs. 17%) and tumours were hormonally more active (75% vs. 50%).

Ten headache-patients met IHS criteria for migraine without aura (MO), 12 for chronic (CTH) and 10 for episodic (ETH) tension-type headache whereas 24 had 'non-IHS' headaches. IHS-headaches were typical except for a higher age in ETH (52 year). IHS-headaches did not disappear after the operation but they became less frequent in 90% of MO, 42% of CTH and 60% of ETH pts.

In non-IHS headache patients there was a strong family history of headache (63%), pain was aggravated by physical activity (71%), frequently accompanied by photophobia (54%) and nausea (50%). After the operation headaches disappeared (50%) or became less frequent (46%).

IHS-headache was the only complaint in 1/3 of patients with pituitary tumours. Characteristics of non-IHS headaches were in our study as described by Levy et al.

P4L22

Cognitive and psychological patterns in post-traumatic headache following severe traumatic brain injury

M. Gabriella Buzzi*[1], Umberto Bivona[2], Maria Matteis[1], Francesca Spanedda[1] & Rita Formisano[1]
[1]*IRCCS Fondazione Santa Lucia, Rome, Italy,* [2]*Istituto Superiore di Sanita, Rome, Italy*

Post-traumatic headache (PTH) occurs more frequently after minor traumatic brain injury (TBI) and is related to the duration of coma, amnesia and cognitive functions recovery. We assessed cognitive and psychological patterns and association with EEG abnormalities after severe TBI. PTH was sought in 300 patients (GCS < 8; coma duration: > 15 days). EEG, brain MR, neuropsychological testing (after 12 months from TBI), and anxiety and depression measurements, were obtained in all patients. 13 patients (4.3%) complained of PTH. MR showed focal cerebral lesions in 10/13 patients despite of the long duration of unconsciousness (associated with diffuse axonal injury). Nine patients had skull fracture or surgical craniotomy. EEG paroxysmal activity was found in 11 patients. PTHs were classified as MoA (31%) or CTTH (69%) (IHS criteria). Neuropsychological testing showed mild or no impairment. Anxiety + depression were present in 57% of patients; anxiety alone in 14% and depression in 29%. PTH patients after severe TBI are those who better recover their cognitive functions. Anxiety and depression, possible pathogenetic factors for TTH, are reactions to post-traumatic conditions. MoA attacks may first occur after trauma in prone subjects. Headache and epilepsy secondary to severe and penetrating TBI may share either dural and neuronal mechanisms.

P4L23

Prednisolone alleviates withdrawal phase in drug-induced headache developed from migraine but not from tension-type headache

Hartmut Göbel*[1], Axel Heinze[1], Katja Heinze-Kuhn[1], Agnes Grohnfeldt[1], Susanne Helm[1] & Corinna Ufer[1]
[1]*Kiel Pain Clinic, Kiel, Germany*

Objectives This study investigated the efficacy of a 10-day-course of prednisolone compared to melperone in the withdrawal phase of drug-induced headache developed from migraine vs. tension-type headache.
Methods 64 patients with drug-induced headache developed from tension-type headache and 76 patients with drug-induced headache developed from migraine according to IHS-criteria were treated with prednisolone after discontinuation of headache acute medication. The prednisolone dose started with 100 mg and was reduced by 20 mg every other day. In the control group 72 patients with drug-induced headache developed from tension-type headache and 76 from migraine received the neuroleptic drug melperone 50 mg.
Results In patients suffering from migraine prednisolone led to a significant reduction of withdrawal headache and accompanying symptoms such as nausea and vomiting compared to melperone. In patients were drug-induced headache had developed from tension-type headache, however, no difference was seen between prednisolone and melperone.
Conclusions Prednisolone alleviates withdrawal symptoms in migraine patients effectively. The development of drug-induced headache in patients with migraine and tension-type headache obviously relies on different mechanisms. An inflammatory mechanisms seems to be relevant in migraine explaining the efficacy of prednisolone.

P4L24

Headache in snorers: association with apnea, desaturation and sleep quality

Trond Sand*[1] & Knut Hagen[1]
[1]*Department of Neurology and Clinical Neurophysiology, Trondheim University Hospital, Norwegian University of Technology and Science, Norway*

Objective To study possible causative factors for chronic headache and morning headache in snorers.
Methods 324 consecutive snoring patients (254 men) underwent successful ambulatory polysomnography and answered a self administered questionnaire. Headache occurring more than 14 days per month was defined as chronic headache. Headache onset during night or upon awakening was defined as morning headache.
Results Chronic headache occurred more often in female than in male snorers (29% vs. 15%, p = 0.06). Subjects with chronic headache were more obese than those without chronic headache ($P = 0.03$) and they tended to spend less time in REM sleep ($P = 0.10$).

Morning headache also occurred more often in women than in men (24% vs. 15%, p = 0.05). Patients with morning headache had lower minimal O2 saturation than those

without morning headache ($P = 0.03$). Morning headache was associated with apnea index ≥ 5 ($P = 0.04$).
Conclusion Female sex is the most significant risk factor for chronic headache and morning headache in snorers. Sleep quality parameters were in general not strongly associated with either headache type.

P4L25

Headache by spontaneous intracranial hypotension

Enrico Ferrante*[1] & Anna Savino[1]
[1]*Departments of Neuroscience and Internal Medicine Ospedale Niguarda, Milan, Italy*

We report 12 cases of headache related to the syndrome of spontaneous intracranial hypotension (SIH). They were seen in a routine clinical practice over the past 10 years. The clinical features, MRI findings, radioisotope results, therapeutic outcome and follow up of these patients are described.
Eleven patients presented orthostatic headache, 1 patient had continuous nonpostural headache. Additional clinical symptoms included nausea, vomiting, tinnitus, diplopia, and rachialgia. All the patients had low CSF opening pressure, 7 had increased CSF albumin and 4 had pleocytosis. Brain MRI showed diffuse pachymeningeal gadolinium enhancement. Other features included subdural fluid collections (haematoma/hygroma) in 4 patients, downward displacement of the brain in 4 patients and enlargement of the pituitary gland in 1 patient. Radioisotope cisternography results indicated, in 2 patients, a CSF leakage site in the cervicodorsal region, and in 1 patient showed limited ascent of the tracer to the cerebral convexity and early appearance of radioisotope in the bladder. All the patients experienced complete resolution of headache with conservative treatment.

Patients with SIH have distinct MRI and sometimes radioisotope cisternographic abnormalities and respond favourably to conservative management.

P4L26

Familiar orthostatic headache by spontaneous CSF leak

Enrico Ferrante*[1] & Anna Savino[1]
[1]*Department of Neuroscience and Internal Medicine Niguarda Hospital, Milan, Italy*

Spontaneous CSF leakage (SCSFL) from a spinal dural tear has been suggested as the underlying pathogenic mechanism of spontaneous intracranial hypotension (SIH). SIH is characterized by orthostatic headache (OH), low CSF pressure, and diffuse pachymeningeal gadolinium enhancement (DPGE) on brain MRI. Atypical pts also have been reported without headache, with normal CSF pressure or absence of DPGE. A 33-year-old woman was admitted for severe, gravative, occipital OH with nausea, tinnitus recurring over 20 days. OH disappeared on recumbency. Gadolinium brain MRI and MRI myelography were normal. Radionuclide cisternography revealed CSF leak at the lumbar region. Lumbar epidural blood patch was performed with OH disappearance after 7 days. The father (a 58-year-old man) of reported pt had suffered by gravative, occipital OH in absence of head trauma or blood diseases. Brain CT after 20 days of onset OH showed bilateral chronic subdural hematomas (CSE) with mass effect. Bilateral CSE were drained with disappearance of OH. Six months later the pt was asymptomatic and brain MRI showed DPGE suggesting a SCSFL.

These familiar cases of OH by SCSFL, never previously reported in literature, suggest familiar structural spinal dural abnormalities (probably abnormal or deficient of fibrillin and elastin) predisposing to the SCSFL.

P4L27

Headache as an isolated symptom of cervical artery dissection: a series of 19 patients

Isabelle Malissin*[1], Anne Ducros[1], Richard Djomby[1], Caroline Roos[1], Mirella Gizzi[1], Mariana Sarov[1], Marie-Germaine Bousser[2] & Dominique Valade[1]
[1]*Emergency Headache Center Lariboisiere Hospital, Paris, France,*
[2]*Department of Neurology, Lariboisiere Hospital, Paris, France*

Aim of investigation How to identify a cervical artery dissection when the patient complains of an isolated headache.
Methods A two years experiences in the emergency headache center: retrospective analyses of clinical and X-ray characteristics of 19 patients with identified cervical artery dissection.
Results 19 cervical artery dissections for 20 000 patients i.e. 1‰. 14 women (73.6%) and 5 men (26.4%). Mean age 38.5 years (23–56).

Characteristics 3/19 (15.7%) with trauma, 3/19 (15.7) with infection, 13/19 (68.6%) spontaneous. Onset: gradual 68%, acute 32%. Type: severe 33%, mild 67%. Location of pain: homolateral hemicrania: 42%, homolateral cervical pain: 32%, others: 26%. Location of dissection: 50% vertebral artery, 50% internal carotid artery of which 79% extracranial. Migraine was found in 30% patients.
Discussion In our series, we have 3 women/1 man, contrary to what is observed with classical data. 66% cases present with a misleading gradual onset and mild pain, similar to a primary headache.
Conclusion To systematically suspect this particular diagnosis and if in doubt, never hesitate to carry out an arteriography.

P4L28

Hypnic headache syndrome: report of a symptomatic case

Heui-Soo Moon*[1], Chin-Sang Chung[2], Han-Young Kim[2] & Dae-Hyun Kim[2]
[1]*Department of Neurology, Kangbuk Samsung Medical Center,*
[2]*Department of Neurology, Samsung Medical Center*

Background Hypnic headache is a rare disorder, which affects the elderly mainly. It presents as recurrent nocturnal attacks at a constant time that awaken the patient from sleep. Despite the relationship between the headache and sleep, the pathogenesis is not been documented. We describe a patient with nocturnal headache compatible with a hypnic headache syndrome that developed after stroke in the brainstem.

Case descriptions A 72-year-old man with severe nocturnal headaches that were clinically consistent with hypnic headache developed after ischemic stroke in the ventrolateral portion of the midrostral upper pons, corresponding to the pontine reticular formation. A polysomnographic study showed arousal at first rapid eye movement (REM) sleep because of a headache episode and sleep apnea with heavy snoring. We prescribed caffeine (a cup of coffee before retiring) and indomethacin without significant benefits.
Comments The patient had a direct evidence that the pontine oral reticular formation, where the neural network generating REM sleep is located, might have caused the hypnic headache. The hypnic headache syndrome developed after pontine infarction corresponded to ascending reticular formation. This is the first report of symptomatic hypnic headache with a causal relationship between the disease and the central pontine lesions.

P4L29

Unusual association: postpartum cerebral angiopathy and cervical artery dissection

Marianna Sarov*[1], Anne Ducros[1], Richard Djomby[1], Caroline Roos[1], Mirella Gizzi[1], Marie Germaine Bousser[2] & Dominique Valade[1]
[1]*Emergency Headache Center, Lariboisiere Hospital,* [2]*Service de Neurologie, Lariboisiere Hospital*

Objective Cervical artery dissection and cerebral angiopathy are common conditions in women in the postpartum period. We report two case of postpartum cerebral angiopathy associated with cervical artery dissections in migrainous patients treated by triptans and caffeine in association with bromocriptine to suppress lactation.
Methods We analyse the case of a patient, who present thunderclap headache after a normal delivery. Both have a history of migraine without aura and are on bromocriptine to suppress lactation after delivery. MRI angiography for the first show segmental narrowing of the intracranial arteries, dissection of the left internal carotid artery and right vertebral artery. The second angiography show segmentary narrowing of cerebral arteries suggesting postpartum angiopathy.
Discussion Bromocriptine is widely implicated in the pathogenesis of postpartum cerebral angiopathy and myocardial infarction as a result of coronary artery dissection during puerperium. The occurrence of bromocriptine related side-effects may depend on some constellation of factors which potentiate the vasoconstrictive side-effect of the drug. Concomitent administration of other sympathomymetic drugs can aggravate their evolution. Past history of migraine can also be a predisposing condition. The arterial wall and its extracellular matrix component may play a role in the occurrence of these pathologies, in association with pregnancy-induced degeneration of collagen.

P4L30

Headache in idiopathic intracranial hypertension (IIH) without papilledema

Beau Nakamoto[1], Kathleen Digre*[1], Judith Warner, Bradley Katz & Susan Baggaley
[1]*University of Utah*

Background IIH occurs with (IIHWP) or without papilledema (IIHWOP). Previous studies of IIHWOP described the headache and compared it with chronic daily headache; the clinical characteristics of IIHWOP, however, have not been directly compared to IIHWP.
Objective To compare the headaches associated with IIHWOP to IIHWP.
Methods All charts of patients with the diagnosis of IIH by the modified Dandy criteria were reviewed. All patients with IIHWOP were diagnosed by a neuro-ophthalmologist. The characteristics were compared with age-matched IIHWP controls.
Results There were 21 patients with IIHWOP out of a total of 353 patients with IIH. Nineteen patients were women, 84% were overweight or obese. Headaches were present in (90%) and were bilateral and daily in the majority similar to controls. Migrainous qualities were present in three-quarters of both IIHWOP and IIHWP. Transient visual obscurations, intracranial noises, and diplopia were more common in the IIHWP than IIHWOP. Five of 6 IIHWOP responded to diuretics alone (vs. controls 10/11) and 11/15 responded to a diuretic combined with migraine preventatives (10/10 controls). Lumbar/ventricular peritoneal shunting helped the headache in 3 of 4 patients (1/1 control).
Conclusion IIHWOP comprised 6% of patients with IIH in a neuro-ophthalmic practice. Headache in IIHWOP is similar to IIHWP; however, IIHWP had more associated transient visual obscurations, intracranial noises, and diplopia than IIHWOP. Treatment appears to be similar in both groups.

P4L31

Intracranial hypotension (cerebrospinal fluid volume depletion) as a cause of chronic post-traumatic headache

Masamichi Shinonaga*[1]
[1]*Hiratsuka Kyousai Hospital*

There are many patients who complain post-traumatic headache after cerebral concussion or whiplash injury. Other than headache patients have symptoms such as neck pain, nausea, dizziness, visual disturbance, impairment of memory and fatigue et al. These symptoms are considered psychogenic problem or autonomic nerve dysfunction. We noticed that symptoms of post-traumatic syndrome is similar to spontaneous intracranial hypotension. We investigated 175 cases of post-traumatic syndrome and 141 cases were diagnosed as intracranial hypotension. Cause of the trauma was automobile accident (120 cases) and sports injury (21 cases). Radioisotope cisternography was performed in 67 cases and lumbar leak revealed in 61 cases. In most cases gadorimium enhanced brain MRI showed any positive findings like sub-

dural accumulation of CSF, dural enhancement and dilatation of intracranial vein. The patients were treated with epidural blood patch. The outcome of the patients was 21 cases excellent, 74 cases good, 28 cases fair, 4 cases no change and 20 cases under observation. CSF volume depletion is suspected as a cause of post-traumatic headache The mechanism of CSF volume depletion is suspected continuous leak of CSF at nerve roots.

P4L32

Unrefreshed sleep and subjective daytime sleepiness contributing to complaints of morning headaches in severe sleep apnea syndrome

Masayuki Miyamoto*[1], Koichi Hirata[1], Tomoyuki Miyamoto[1], Hidehiro Takekawa[1], Keisuke Suzuki[1] & Shiho Yamamoto[1]
[1]*Dokkyo University School of Medicine*

Introduction It is not well known about the headache in sleep apnea syndrome (SAS). We investigated the factors associated with headaches in severe SAS.
Methods The subjects were 27 severe SAS in-patients. All the subjects were asked about sleep habits and headache by questionnaire and their daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS). Additional studies were performed, including neurological examination, analysis of the arterial blood gas upon waking, magnetic resonance imaging of the brain and polysomnography.
Results Ten of the patients (37.0%) complained of headache, all of them in the morning. We studied the factors associated with morning headache by dividing the patients into 2 groups, patients with headaches and those without headaches. No significant differences between the 2 groups were found for age, BMI, AHI, mean SpO_2, CT90% or $PaCO_2$.

These 10 patients complained of unrefreshed sleep more than the patients without headache, and their Epworth Sleepiness Scale scores were significantly higher ($P < 0.05$).
Conclusion In patients who complained of morning headaches there was a significantly high ratio of patients who complained of unrefreshed sleep and daytime sleepiness. Unrefreshed sleep and subjective daytime sleepiness especially seem to be associated with morning headache in severe SAS.

P4L33

A prospective trial of local injection in the treatment of giant cell arteritis

Shengyuan Yu*[1]
[1]*Department of Neurology, Chinese PLA General Hospital, Beijing, China*

Objective To investigate the clinic features of GCA and report the results of a prospective trial assessing whether local injection therapy has disease-controlling and steroid-sparing benefits.
Methods The clinical features of GCA of 19 patients was analyzed. They were randomly divided to local injection group (A) and traditional corticosteroid group (B). In group A, 1 mL of lidocaine (1%) and 1 mL of dexamethasone (5 mg) was injected beside temporal arteries. In group B, 60–80 mg deltacortone was taken orally at first 1–2 weeks, and then the dose was gradually decreased. The difference of VAS values and dose of steroid between the both groups were evaluated.
Results The mean age of patients with GCA was 50.62 years and 47.37% patient were under 50 years. The common clinical manifestations were newly occurring headache on temporal regions, temporal artery abnormality and raised erythrocyte sedimentation. The headache was significantly relieved and the dose of corticosteroid used was significantly lower in local injection group than traditional corticosteroid group.
Conclusion The Chinese GCA patients suffered with disease at the earlier age compared with the cases abroad. The local injection therapy is an effective method on GCA and can decrease the dose of steroid.

P4L34

Sudden onset of Cephalalgia as presenting feature of Myasthenia Gravis

Maria José Rosas*[1], J. Miguel Bernardes[1], Graça Sousa[1], Fernando Silveira[1], Clara Sambade[2] & Castro Neves[1]
[1]*Department of Neurology, Hospital de S. João, Porto, Portugal,*
[2]*Department of Pathology, Hospital de S. João, Porto, Portugal*

Background Strong association between Myasthenia Gravis (MG) and thymic follicular hyperplasia or thymoma, has long been established. One atypical clinical case is presented.

A 51–year-old woman complained of sudden onset of left hemicrania cephalalgia, left eyelid ptosis (meliorating during the day), dysphagia, dysarthria and urinary incontinence.

Initial work up oriented to cerebral vascular, neoplastic or infectious diseases was negative. Brain MRI, CSF examination and thyroid function test were normal. Repetitive nerve-stimulation test revealed decrement responses in nasalis and frontalis muscles and single–fiber electromyography of right orbicularis showed increasing 'jitter' with block. There were high acetylcholine receptor antibody titles. MG was diagnosed and pyridostigmine prescribed, achieving clinical improvement. Chest CT scan revealed anterior mediastinal mass suggesting thymoma. At surgery, the thymic mass was adherent to pericardium and tumor ressection was performed. At pathological examination a 'minimally invasive' tumor was diagnosed as 'predominantly epithelial thymoma' or 'well-differentiated thymic carcinoma' (Lattes or Muller-Hermelink classification), invading the capsule, with no lymph node involvement. Postoperative radiation was performed.
Conclusions Unusual clinical aspects include hemicranea cephalalgia and eyelid ptosis which improved over the day. These features prompted the search for vascular or neoplastic diseases but electomyographic results re-oriented the approach leading the diagnosis.

P4L35

Headaches and pineal cyst: a (more than) coincidental relationship?

Mario Peres*[1,2], Reynaldo Brandt[2], Pedro Paulo Porto[2] & Eliova Zukerman[2]
[1]*Sao Paulo Headache Center,* [2]*Albert Einstein Hospital*

Introduction Pineal cysts are common findings in neuroimaging studies, found in 2.6% of brain MRIs. The cysts are more frequent in women in their third decade of life. Pineal cysts can be symptomatic, headache is the most common symptom. The pineal gland has important physiological implications in humans, but little is known about the impact of pineal cysts in human physiology.
Objective To describe headache features in patients with pineal cyst and discuss their possible relationship.
Patients We report 5 headache patients with pineal cyst, 4 women 1 man, mean age 37,6, mean cyst diameter 10,1 mm, 2 patients had migraine without aura, 1 migraine with aura, 1 chronic migraine, and 1 hemicrania continua. Three patients had strictly unilateral headaches.
Discussion/conclusion Melatonin has many relevant mechanisms to headache pathophysiology. It modulates serotonin, potentiates GABA, and decreases dopamine neurotransmission, regulates opioid analgesia, and scavenges NO. Melatonin has been reported to be decreased in chronic, menstrual and episodic migraine patients. Headaches and pineal cysts may have a more than coincidental relationship. Patients may have an abnormal melatonin secretion. Further studies are necessary to understand melatonin secretion in patients with pineal cysts and their relationship to headaches.

P4L36

Headache for the prediction of brain metastases in cancer patients

Panagiotis Heras[1], Andreas Argyriou*[2], Mihail Corcondilas[1], George Katsoulas[2], Konstantinos Argyriou[1] & Panagiotis Polychronopoulos[2]
[1]*General Hospital of Patras-Department of Clinical Oncology,* [2]*Regional University Hospital of Patras-Neurology Department*

Aim To evaluate headache and other neurological symptoms and signs as predictors for the appearance of brain metastases in cancer patients.
Patients and method We studied 54 cancer patients with new appeared or changed headache during the last interval. To the patients were submitted questions regarding headache's onset, its character, localization, severity and the existence of accompanying symptoms. Patients were undertaken in neurological examination, foundoscopy and neuroimaging investigation. Additional information about patients' medical and psychosocial history was gathered from them and their medical files.
Results Brain metastases were found in 29 patients (53.7%). Univariate regression analysis showed an association between nine variables and occurrence of brain metastases, while multivariate regression analysis defined only four of them as significant independent predictors. The bilateral frontal-temporal headache not of tension type, with onset time = 8 weeks(OR of 11.9; 95% CI. 2.52–56.1), the daily emesis(OR of 10.2; 95% CI. 2.1–55.8), the gait instability(OR of 7.4; 95% CI. 1.75–33.9) and the Babinski sign(OR of 12.1; 95% CI. 2.2–120.7) were the four related variables with occurrence of brain metastases.
Conclusion All cancer patients manifesting new or changed headache of the above-described characteristics, with/or session existence of emesis, nausea, instability and abnormal neurological findings must be investigated for exclusion of brain metastases.

P4L37

The use of laser discectomy in the treatment of cervicogenic headaches

Leonel Limonte*[1], Bonati Alfred[1], Wolff Craig[1], Perry Michael[1] & Hirschauer David[1]
[1]*Bonati Institute, Hudson, USA*

Purpose The effectiveness of laser discectomy in the treatment of cervicogenic headaches.
Materials and methods 25 patients who presented with cervical disc pathology as verified by MRI, were studied. Headaches were characterized by the International Headache Association Assessment Protocol. Patients underwent endoscopic laser cervical discectomies for treatment of the well-documented disc disease.
Results Patients underwent 45 endoscopic laser cervical discectomies at the C5/C6 levels. Visual analog scale demonstrated that 24 of the 25 patients characterized their preoperative head pain as 10 out of 10. Post operatively 23 patients characterized their head pain as 0 of 10. Follow up was 13 months. There were no complications.
Conclusions When evaluating patients with cervicogenic headaches meeting Sjastaad criteria, the possibility of lower cervical disc disease as an etiology should also be entertained. In our patients, the headaches completely resolved after laser cervical discectomies at the C5/C6 and/or C6/C7 level. The chronicity of the headaches preoperatively, and the immediate and lasting relief after the operations make it very probable the cause was eliminated. In our view, these cases strongly support a casual relationship between pathology of the lower cervical spine and cervicogenic headache.

P4L38

The extent of headache and level of psychical desadaptation of patients with arterial hypertension

Gueorgy I. Sidorenko*[1], Natalya Arinchina[1] & Andrey Pushkarev[1]
[1]*Research Institute for Medical and Social Evaluation and Rehabilitation, Minsk, Republic of Belarus*

40 arterial hypertension patients were examined for comparison of quantitative headache evaluation criteria and factors of psychical adaptation.

For independent assessment of tactile and pain threshold a special instrument called 'Estesimetr', built by Cardiological

Centre and Visual Analogue Scale (VAS) were used. Psychical desadaptation was estimated by P. Cattell.

Patients with insignificant headache showed a level of 25 ± 2.5 mm on VAS, tactile 0.27 ± 0.06 mV and pain threshold 0.58 ± 0.08 mV (like normal). Patients with clearly defined headache showed the extent of headache 42.4 ± 4.9 mm ($P < 0.001$), tactile threshold was 0.36 ± 0.06 mV, pain threshold was 0.66 ± 0.05 mV ($P > 0.05$).

The following personality factors were typical: good self-control, caution, pessimism, conservatism, sensitivity to stress factors (F^-, G^+, M^-, N^+, Q_1^-, Q_3^+, Q_I^-, Q_{IV}^-). Increasing headache leads to increased passiveness, sensitivity, feeling of dependency, anxiety and depression. The 2nd group the extent of instability of psychical adaptation (Q_{III}), Psychical desadaptation (O, Q_4, C) the anxiety and internal disturbance (Q_{II}) were higher ($P < 0.001$).

The extent of headache (both measured and judged) is related with psychical adaptation and working abilities. In the 1st group all patients were able to work, in the 2nd group 60% could work with restriction.

P4L39

Influence of anxiety and depression on working abilities of headache syndrome patients

Natalya Arinchina*[1], Elena Katko[1] & Alina Osipova[1]
[1]*Research Institute for Medical and Social Evaluation and Rehabilitation, Minsk, Republic of Belarus*

51 patients with headache caused by arterial hypertension were examined with the help of Visual Analogue Scale (VAS). General Health Questionnaire (1991) was used. Group 1 – patients with insignificant headache, group 2 – patients with clearly defined headache.

The 1st group showed blood pressure: 158.7 ± 3.2 mmHg systolic and 95.7 ± 1.6 mmHg diastolic. Their level of headache on VAS was 34.2 ± 6.3 mm. The level of social dysfunction made 8.1 ± 0.5 points, somatic symptoms – 9.9 ± 1.2 points, anxiety and depression: 7.6 ± 1.2 and 2.5 ± 1.0 points, respectively.

The 2nd group showed authentically higher blood pressure 178.3 ± 4.4 mmHg systolic and 105.2 ± 2.6 mmHg diastolic. Their level of headache on VAS was authentically higher: 61.4 ± 3.6 mm. The level of social dysfunction made 11.4 ± 1.4 points, somatic symptoms –13.3 ± 1.2 points ($P < 0.05$). The anxiety and depression factors were higher –8.6 ± 0.2 and 4.4 ± 1.5 points, respectively.

The 1st group showed 40% were fully able to work, 50% could work with restriction, 10% could not work. In the 2nd group only 9% could work as normal, 43% could work with restrictions, 48% could not work.

The extent of headache experienced by arterial hypertension patients results in increased level of depression and anxiety and affects their ability to work.

P4L40

New-onset, prednisolone responsive headache in Indian patients with single enhancing computed tomographic lesions (SSECTL) and seizures

R. K. Garg*[1], A. M. Kar[1] & M. K. Singh[1]
[1]*Department of Neurology, Chhatrapati Shahuji Maharaj Medical University, Lucknow, India*

Objective SSECTLs are the commonest imaging abnormality in Indian patients with new-onset seizures. Sometimes patients complain of headache. SSECTLs represent inflammatory stage of cysticercosis. Usually patients require antiepileptic drugs. We are reporting 15 such patients with disabling headache.
Methods Fifteen consecutive patients with moderate to severe new-onset headache who fulfilled the following criteria were included: new-onset seizures, minimal or no neurological deficit, and no papilloedema. CT lesions were of < 20 mm diameter. Patients received antiepileptic monotherapy, analgesics and prednisolone (1.5 mg/kg/day for 7 days). Prednisolone was tapered-off in next 7 days. Patients were followed-up monthly for six months. Follow-up CT Scans were performed after 3 months.
Results Three hundred patients with SSECTL with seizures were seen during study period. Fifteen patients (male-12, female-3) had headache. Mean age was 16 ± 10.24 (range 9–33) year. All patients reported significant improvement (no headache, or mild headache) at first follow-up. After 3 months all patients were headache-free. No headache recurrence was noted. Follow-up CT showed disappearance of lesions in 13 patients; in two patients lesions calcified. There were no recurrences of seizures. No side-effect of prednisolone or antiepileptic drugs was noted.
Conclusion Short-term prednisolone is an effective treatment for headache in patients with SSECTL and seizures.

P4L41

Headache subtypes following flexion/extension (whiplash) injuries of the cervical spine

Donald Todman*[1]
[1]*Brisbane Clinic, Queensland, Australia*

Headache is a well known feature of the chronic post whiplash syndrome but there have been few studies of the overall incidence and relative subtypes of headaches in this condition. This study represents a consecutive series of 176 patients with chronic post whiplash symptoms following motor vehicle accidents who were referred to a single headache specialist over a period of 16 months. A detailed headache evaluation was made and headaches categorized according to IHS criteria. The cohort comprised patients who had suffered flexion/extension cervical injuries in motor vehicle accidents with persisting symptoms longer than 12 months (average 22 months). Demographics included 70 males and 106 females with an average age of 35 years (10–84 years). The incidence of headache overall was 86% with the most frequent headache diagnosis being chronic tension type.

Headache subtypes in this group were:
Chronic tension type 49% (87 patients)
Episodic tension type 26% (46 patients)
Migraine without aura 12% (21 patients)
Migraine with aura 1% (2 patients)
Cluster headache 0.5% (1 patient)

The recognition of headaches and accurate diagnosis is important in this condition for appropriate therapeutic intervention.

P4L42

The diagnostic validity of the Cervical-Flexion-rotation test in cervicogenic headache

Mark Ogince*[1], Toby Hall[1] & Kim Robinson[1]
[1]*School of Physiotherapy. Curtin University of Technology, Perth, Australia*

Objective Cervicogenic headache and migraine presents a differential diagnostic challenge for physiotherapists due to similarities of signs and symptoms among the different forms. Accurate diagnosis of cervicogenic headache facilitates effective treatment. This study investigated the specificity and sensitivity of the cervical flexion-rotation test in diagnosing cervicogenic headache. It was hypothesized that the cervical flexion-rotation test will enable accurate detection of subjects with cervicogenic headache from healthy controls and subjects with migraine with aura.
Methods This study tested 23 cervicogenic headache, 23 normal controls and 12 migraine with aura subjects, aged 18–66 years. In phase 1, an experienced manipulative physiotherapist identified C1/2 dysfunction using passive segmental mobility tests in the cervicogenic headache group. Those with C1/2 dysfunction participated in phase 2. In phase 2, using the flexion-rotation test, subjects were tested by two experienced manipulative physiotherapists blinded to the subjects' group allocation. Each therapist stated whether the test was positive or not based on the therapist's interpretation of range of motion.
Results The sensitivity and specificity of the flexion-rotation test was 91% and 90%, respectively. Furthermore, a receiver operating curve revealed the test to be 90% accurate.
Conclusion The cervical flexion-rotation test significantly assists in C1/2 cervicogenic headache diagnosis.

P4L43

Headache in stroke

Dragana Kuljic-Obradovic*[1], Sanja Medic[1], Sanja Atic[1] & Milan Savic[2]
[1]*'Sveti Sava' Hospital, Belgrade,* [2]*'Dr Dragiša Mišovic' Hospital, Belgrade*

Objective The objective was to compare the frequency of the headache in stroke patients depending on sex, type of stroke, the location and size of the cerebral lesion.
Methods We studied the stroke patients admitted to 'Sveti Sava' Hospital from December 2002 to March 2003. The patients were studied using a standard protocol including CT scan. The presence of headache was established by taking the history from the patients or relatives.
Results 735 patients with stroke were attended, female 343, male 392, mean age 66,5. Among these patients 48.9% had experienced headache, with higher frequency in female (62.3%). Frequency rates of headache were established for different types of stroke as follows: in patients with ischemia 39.6%, with SAH 88.1%, with hemorrhage 53.1%. The headache was the most common in patients with cortical lesions (58.3%) and with lesions located in the territory of the basilar artery (40.6%). Large lesions (>2 cm) were more frequently followed with headache (62.3% vs. 28%).
Conclusions Among the patients with stroke the frequency of the headache was higher in female ($P < 0,01$), in patients with hemorrhages ($P < 0,05$), large ischemic lesions ($P < 0,01$), located in the territory of the basilar artery ($P < 0,05$) and with cortical located lesion ($P < 0,05$).

P4L44

Closed head injury-frequency and character lesion of brain

Ranko Raicevic*[1], Ljubo Markovic[2], Aleksandar Radosavljevic[2], Toplica Lepic[1], Stevan Petkovic[1] & Nenad Rajsic[1]
[1]*VMA, Clinic of neurology, Belgrade,* [2]*Institute of radiologz, VMA, Belgrade*

Introduction Neurotrauma syndrome by its complexity but also by its frequency represent one of the leading problems of modern medicine. In closed head injuries syndrome usually is lacking connection between clinical phenomenology and objective conferment of brain tissue lesions.
Objective and methods According to that, the major outcome or goal of those studies was to determinate frequency and characteristics of brain tissue lesions using MRI and CT. As well as confirming connections between those damages with clinical parameters such as neurologic deficit and consciousness deficit disorders evaluating sensitivity and specificity of neororadiologic procedures. 40 patients with closed head injuries were investigated by the same neurologist. Grade of neurological deficit (Canadian neurological scale) and consciousness deficit disorders (Glasgow coma scale) were determined to all patients. All patients were investigated by MRI and CT.
Results In this study the MRI presented significantly higher specificity and sensitivity especially determing smaller ishemic and contusion lesions with significant correlation related to C. A technique called MRI has helped improve diagnosis and treatment of closed head injuries patients.
Conclusion This is method that might be useful to plan further evaluation and possible treatment in significant number of cases.

P4L45

Treatment of unilateral post traumatic headache of cervical origin by C2 sensory root decompression – a retrospective study

Guy Pierre Boudreau*[1], Denis Ladouceur[2], Yves Veilette[3], Luc Marchand[4] Claude Bouthillier[5], Eric Maignoux[6] & Marie-Eve Levasseur[7]
[1]*Clinique de la Migraine Val des Arbres, Laval, Quebec, Canada,* [2]*Hôpital du Sacre-Coeur, Montreal, Quebec, Canada,* [3]*Hôpital Maisonneuve, Montreal, Quebec, Canada,* [4]*CHUM Hôpital Hotel-Dieu, Montreal, Quebec, Canada,* [5]*CHUM Hôpital Notre-Dame, Montreal, Quebec, Canada,* [6]*Clinique de la Migraine, Montreal, Quebec, Canada*

Objectives To verify if C2-C3 sensory root decompression brings significant relief to patients that suffer chronic daily headache of moderate to severe intensity and that are refractory to standard medical treatments.
Method Patients were 18–65 years old, had a history of cranio-cervical trauma responsible for the onset of their headaches.

The headache was dominant on one side, daily, of moderate to severe intensity and was refractory to standard medical treatment since the accident.

They had obtained relief, from a diagnostic anesthetic block of the C2 sensory ganglion, underwent unilateral neurosurgical decompression of the C2-C3 sensory root and had been followed 6 months post operatively with headache diaries.
Results Twenty-one patients were studied retrospectively (10 women, 11 males).

Number of patients improving headache more than 50% post operatively was at: 1,3,6,12,36,60, respectively: 16/21, 4/21, 9/21, 11/21, 10/16, 8/12, and 2 of 4 patients 60 months post surgery.
Conclusions Improvement is within the first month post operatively but the benefit is most appreciable within the first six months. The surgical procedure relieves the headache, and daily prophylactic medication is not necessary for most responders.

P4L46

Headache in late period of cranio-cerebral trauma

Stanislav Groppa[1], Mihai Ganea*[1], Victoria Duca[1], Gabriela Lishinsky[1] & Liliana Iuhtimovsky[1]
[1]*Department of Neurology, State Medical and Pharmaceutical University 'Nicolae Testimitsanu', Chisinau, Republic of Moldova*

Purpose The purpose of this research is to establish the role of opened and closed cranio-cerebral trauma in appearance and development of headache.
Methods 2544 patients with different degree of disability caused by severe cranio-cerebral trauma were examined. The age was between 40 and 69 years, the time from the onset of the trauma was between 5 and 25 years. In 407 patients' motor deficits as: amputations, contractures and others were observed. 2043 (80.3%) patients presented with closed cranio-cerebral trauma and 501 patients (19.7%)-opened trauma, including of frontal region-80, temporal-51, parietal-180, occipital-43 patients, and several regions-148.
Results The number with patients with headache according to syndromes was as following: In the big majority of the patients headache was severe, occurred at physical, emotional or intellectual efforts, exposure to sun, alcohol consumption atmospheric changes, insufficient sleeping. Headache was associated with tingling, vertigo, visual and posture disturbances. As they were farmacoresistant, they influenced negatively working capacity.
Conclusions during the late period of cranio-cerebral trauma headache is seen in more than 70% cases, varying depending on neurological signs.

P4L47

Cluster-like headache: an overview

Federico Mainardi*[1], Filippo Dainese[1], Ferdinando Maggioni[1], Marco Trucco[2], Claudia Palestini[1] & Giorgio Zanchin[1]
[1]*Headache Center, Department of Neurosciences, Padua University, Pietra Ligure, Italy,* [2]*Santa Corona Hospital, Pietra Ligure, Italy*

Among the primary headaches, cluster headache (CH) presents very peculiar features. In some cases, however, symptoms may be secondary, defining the clinical picture of cluster-like headache (CLH). A careful revision of the literature from 1975 to 2002 yielded 114 reported cases of CLH. We pinpointed those ($n = 57$) giving the information allowing a diagnosis in accordance to the IHS criteria (1988). Among the aims, was the possible identification of clinical features leading to suspect a symptomatic origin. In order of frequency, the causes of CLH resulted vascular (35%), neoplastic (25%) and inflammatory (16%). At the first observation, in 31 cases all the IHS criteria for a CH diagnosis were satisfied (fulfilling group, FG), while in 26 there was at least one atypical feature (non fulfilling group, NFG). In comparison to CH, the red flags resulted, both for FG and NFG, older age of onset (CLH 43.5 ± 15.4; CH 28 ± 3); for NFG, abnormal general or neurological examination (73%), duration (35%), frequency (19%) and location (15%) of the attacks. We stress the fact that, at the first observation, more than 50% of CLH perfectly mimicked CH. Therefore, the importance of neuroimaging cannot be underestimated.

P4L48

Combination analgesics are by far the most common cause of drug-induced headache and lead to worse withdrawal symptoms than other acute headache medication

Hartmut Göbel*[1], Axel Heinze[1], Katja Heinze-Kuhn[1], Agnes Grohnfeldt[1], Susanne Helm[1] & Corinna Ufer[1]
[1]*Kiel Pain Clinic, Kiel, Germany*

Objectives (A) Analysis of the frequency of different headache acute medication causing drug-induced headache according to IHS-criteria in migraine patients. (B) Analysis of the extent of withdrawal symptoms depending on the substances overused.
Methods 160 consecutive migraine patients who were admitted in the Kiel Pain Clinic because of development of drug-induced headache according to IHS-criteria were analysed according to substance use and the intensity of withdrawal

headache was prospectively assessed with a rating scale (0 = no pain, 1 = weak; 2 = moderate; 3 = severe) every hour.

Results The following substances/drugs were overused: paracetamol $N = 1$; ibuprofen $N = 1$; combination analgesics $N = 110$; triptans $N = 37$; opioids $N = 11$. The maximum intensity of withdrawal headache was usually seen on day 2. The mean headache intensity on this day was: paracetamol plus ibuprofen 2.18; combination analgesics 2.48; triptans 2.22; opioids 2.58.

Conclusions The overuse of combination analgesics is the by far most common cause leading to development of drug-induced headache. Mono preparations are only responsible in exceptional cases. Withdrawal headache is especially severe after withdrawal from combination analgesics and from opioids. This may at least partially explain their higher potency in inducing and especially maintaining drug-induced headache.

P4L49

Orthostatic headache in a patient with Marfan's Syndrome

Enrico Ferrante*[1] & Anna Savino[2]
[1]*Department of Neurosciences, Niguarda Cà Granda Hospital, Milano, Italy,* [2]*Department of Internal Medicine, Niguarda Cà Granda Hospital, Milano, Italy*

A 26- years-old man with Marfan's syndrome had postural headache. Brain MRI with gadolinium showed diffuse pachymeningeal enhancement. MRI myelography revealed bilateral multiple large meningeal diverticula at sacral nerve roots level. He was suspected to have spontaneous intracranial hypotension syndrome. Eight days later headache improved with bed rest and hydration. One month after the onset he was asymptomatic and 2 months later brain MRI showed no evidence of diffuse pachymeningeal enhancement. The 1-year follow-up revealed no neurological abnormalities.

The intracranial hypotension syndrome likely resulted from a CSF leak from one of the meningeal diverticula.

In conclusion patients with spinal meningeal diverticula (frequently seen in Marfan's syndrome) might be at increased risk of developing CSF leaks, possibly secondary to Valsalva maneuver or minor unrecognized trauma.

P4L50

Chronic daily headache by spontaneous intracranial hypotension

Enrico Ferrante*[1] & Anna Savino[2]
[1]*Department of Neuroscience, Niguarda Cà Granda Hospital, Milano, Italy,* [2]*Department of Internal Medicine, Niguarda Cà Granda Hospital, Milano, Italy*

Silberstein used chronic daily headaches (CDH) term to refer to the broad group of headache disorders the occur more frequently than 15 days a month. We report the case of 44-year-old woman that was admitted for severe continuous gravative diffuse headache recurring over 6 weeks, without trauma history. Neurological examination was normal. CT scan showed small size frontoparietal bilateral chronic subdural hematomas (CSE). MRI revealed CSE and diffuse pachymeningeal enhancement (DPE). Coagulation studies, were normal. Suspecting an spontaneous intracranial hypotension (SIH) we performed a radionuclide cisternography that revealed a focal CSF leak at the right thoracic region (T4-T5), at that time CSF opening pressure was low. There was increased CSF albumin. With bed rest headache improved and disappeared after 3 months. Six months after onset brain MRI was normal. This pt had a SIH, however, unlike most reported pts with SIH, her headache had no orthostatic feature. CSE may be caused by the loss of buoyancy and downward displacement of the brain resulting intearing of bridging veins. CDH in this case was probably caused by continuous traction, also in recumbent position, on sensitive structures (blood vessels and dural sinuses). In conclusion SIH should be considered as a cause of CDH.

P4L51

Ventricular arteriovenous malformation bleeding in a 10-year-old girl

Hilton Mariano Da Silva*[1], Luciano Ricardo Luciano França da Silva[2], Eric Homero Albuquerque Paschoal[2], Feres Eduardo Aparecido Chaddad Neto[2], Carlos Alberto Bordini[1] & José Geraldo Speciali[1]
[1]*Department of Neurology, Sao Paulo University, School of Medicine at Ribeirao Preto, SP, Brazil,* [2]*Department of Neurology and Neurosurgery, Hospital Municipal Mário Gatti, Campinas, Brazil*

Objective Report a child with a history of sudden headache secondary to a bleeding of a ventricular arteriovenous malformation.

Case history A 10-year-old girl previously healthy was admitted to the Emergency Room with an eight- hour history of sudden onset of severe headache. On the neurologic examination, the patient was alert and well oriented with no other abnormalities but a nuchal rigidity (++/4 +). A CT of the brain revealed hemorrhage in the right lateral ventricle (Fig. 1). A MRI study of the brain disclosed a heterogeneous lesion in the mesial portion of the right temporal lobe, above and inside the temporal horn of the lateral ventricle. The lesion was hypointense on T1 and T2-weighted images and enhanced with the contrast. Another hyperintense T1 and T2-weighted images lesions were seen in the right lateral ventricle suggesting bleeding. A MR angiography and a cerebral angiography disclosed an arteriovenous malformation in part of the choroid plexus, supplied by the anterior choroidal artery(Figs 2, 3, and 4). A surgical procedure was done resulting in an almost complete excision of the AVM. The patient remains asymptomatic after one year of follow-up.

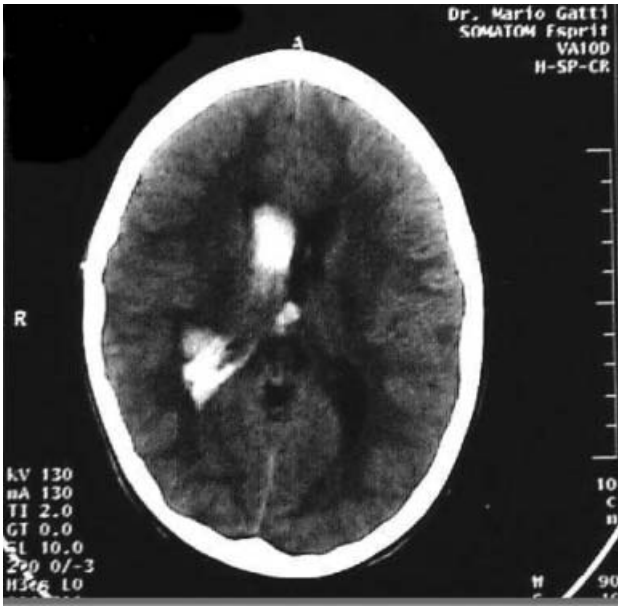


Figure 1

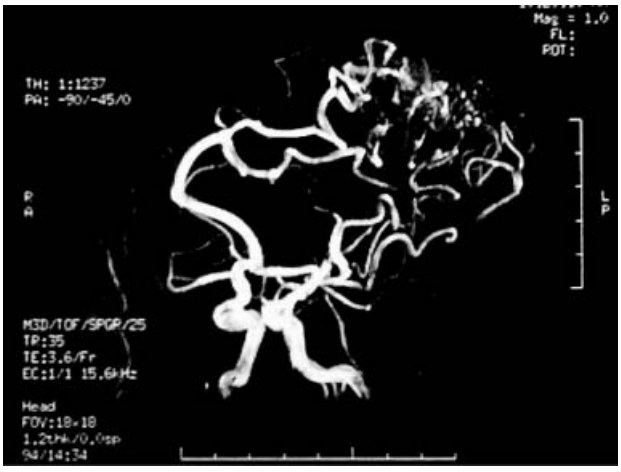


Figure 2

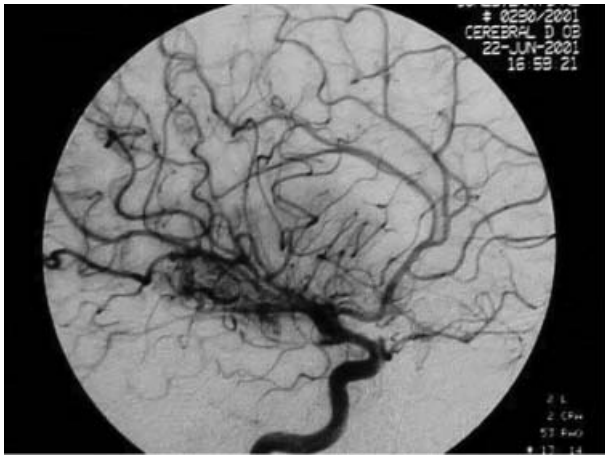


Figure 3

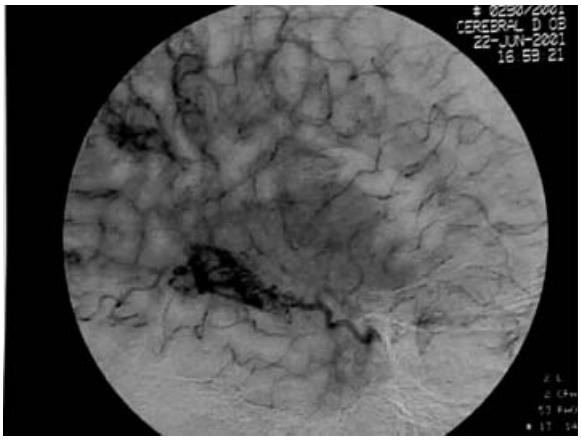


Figure 4

P4L52

Daily migraine with visual aura associated with an occipital arteriovenous malformation

Anne Donnet*[1], Henry Dufour[1] & François Grisoli[1]
[1]*Neurosurgery Department, CHU Timone, Marseille, France*

Objective Occipital arteriovenous malformations may cause headaches that satisfy the current IHS criteria for migraine. A 29-years-old woman with status migrainousus with visual aura and occipital arteriovenous malformation is described.
Background The first case of daily attacks of migraine with aura associated with an occipital arteriovenous malformations was described by Spierings in 2001.
Case report A 29-year-old woman with previous migraine with visual aura developed daily attacks of migraine with visual aura. The aura always occurred on the left and the headache always on the right side of the head. The lesion appeared to be a right occipital arteriovenous malformation.
Conclusion The migrainous visual phenomena and the headaches were responsive to lamotrigine. This case is discussed in the light of our understanding of the pathogenesis of the migraine attacks.

P4L53

Secondary headache in elderly outpatients

Jano Souza[1], Pedro Moreira Filho[1], Carlos Bordini*[2], Carla Jevoux[1], Elder Sarmento[1] & Claudio M. Brito[1]
[1]*Universidade Federal Fluminense, Brazil,* [2]*Universidade de Sao Paulo Ribeirao Preto, Brazil*

Objectives Find out whether age is an independent risk factor for secondary headaches (SH) and severe secondary headaches (SSH).
Methods We evaluated 1131 sequential outpatients (≥ 18 years), complaining headache. They were divided into young (18–59 years; n = 892) and elderly (60 + years; n = 239) and, according to age at onset of headache, into before 60 years (n = 983) and after 60 years (n = 148). Young and elderly patients

were also subdivided, according to the time elapsed since the onset of the symptoms, into more than one year and less than one year. SH/SSH were assessed in all subgroups.
Results The elderly as a whole presented more SH/SSH than the young ($P < 0{,}0001$; OR = 5,4; CI95% 3,6–8,2). Patients with symptoms starting after 60 years also presented more SH/SSH than the group with onset before this age ($P < 0.0001$; OR = 10,0; CI95% 6,5–15,5). Elderly patients with less than one year since the onset of the symptoms presented more SH/SSH than young patients with the same time of symptoms ($P < 0{,}0001$; OR = 4,6; CI95% 2,6–8,1).
Conclusion Age more than 60 years and time elapsed since onset of headache less than a year are independent risk factors for SH/SSH.

P4L54

Severe headache secondary to Autonomic Dysreflexia (AD) associated with hemibody sweating and diaphoresis. Case report

Ion Moldovanu[1], Stela Odobescu*[1] & David Dodick[2]
[1]*Neurology Department of the State Medical University of Moldova, Chisinau, Moldova,* [2]*Mayo Clinic Scottsdale, Arizona, USA*

Background Thunderclap headache associated with autonomic dysreflexia has not been previously described.
Objectives To describe and illustrate the association between autonomic dysreflexia associated with paroxysmal hypertension and thunderclap headache.
Methods A 27-year-old-patient with traumatic C-5 quadriparesis underwent a comprehensive autonomic evaluation and 24- h BP monitoring as well as a complete neurological evaluation.
Results After having a urostomy placed 1 years ago, this patient began to experience 1–2 episodes of sudden and severe occipital headache daily each lasting 1–5 h. Commensurate with her headaches, she developed hemibody heat, flushing, and diaphoresis. During these episodes, systolic blood pressure (BP) elevated from 70 to 90 mmHg to 150–170 mmHg. Diastolic blood pressure increased from 60 to 70 mmHg baseline to over 120 mmHg. Headache relief occurred coincident with BP normalization. Three weeks ago her headaches disappeared spontaneously. She still experiences episodes of AD without elevated BP manifested as heat and hemibody sweating associated with increased bilateral lower extremity muscle spasms.
Conclusions Headache in patients with spinal cord injuries may occur in association with autonomic dysreflexia and paroxysmal hypertension. While the mechanism between paroxysmal hypertension and occipital headache remains unclear, the reduced capacity for autoregulation in the posterior circulation may be relevant.

P4L55

Status migrainosus in recurrent pheochromocytoma

Hyung In Cho*[1], Chin-Sang Chung[1], Kyungmi Oh[1] & Hui-Soo Moon[2]
[1]*Department of Neurology, Samsung Medical Center,* [2]*Department of Neurology, Kangbuk Samsung Medical Center*

Status migrainosus is well known as a migraine varient persisting beyond three days and the attacks interrupted by headache free intervals lasting less than 4 h. The fact that status migrainosus like episodes suggest the recurrence of pheochromocytoma has rarely been previously reported. Here we report a 23-years-old woman, with family history of migraine and Multiple Endocrine Neoplasia 2 A and prior pheochomocytoma resection, had status migrainosus like symptoms accompanying nausea, pallor, profuse sweating and palpitation. She reported severe throbbing pain over the bilateral frontal and occipital area. Attacks lasted half an hour to several hours. The frequency was about three to four times a day. So far from relieving, the headache was slightly aggravated after initial antimigrainous medication such as cafergot, NSAID. Afterward, we found that her blood pressure rose up to 200/115 mmHg whenever she complained of headache. So we suspected that her headache could be the symptom associated with recurrent pheochromocytoma. The brain MRI showed patchy bilateral cerebral lesions in fluid attenuated inversion recovery with normal diffusion weighted images, consistent with hypertensive encephalopathy. Abdominal CT demonstrated a recurrence of pheochromocytoma at the site of previous right adrenalectomy. Her symptoms completely resolved only after control of hypertension and surgical resection.

P4L56

Clinical presentation of a case of bilateral spontaneous carotido-cavernous fistula

Marianna Sarov*[1], Anne Ducros[1], Richard Djomby[1], Caroline Roos[1], Mirella Gizzi[1], Marie Germaine Bousser[2] & Dominique Valade[1]
[1]*Emergency Headache Center, Lariboisiere Hospital,* [2]*Service de Neurologie, Lariboisiere Hospital*

Objective To analyse and update the clinical symptomatology, evolution and therapeutics outcomes of patient with bilateral carotido-cavernous fistula.
Background Studies of bilateral spontaneous carotido-cavernous fistula seldom appeared in neurological literature.
Results A case report of a 61-years-old woman with bilateral carotido-cavernous fistula is reported. The clinical picture is manifested by progressive diffuse headache with nausea and vomiting. No other neurological signs are present. The clinical examination 4 months after the beginning of the headache show horizontal diplopia, conjunctival injection, chemosis, bilateral VI-th nerve palsy, elevated intraocular pressure and decreased visual acuity.

MRI is normal, but evolution is in progression with terrible, bilateral retro-orbital pain, extremely resistant of all medication, even opioides. We decide to realise the angiography and show bilateral carotido-cavernous fistula supplied by

dural branches of the both internal carotid arteries through the meningo-hypophysal trunck. The evolution is spontaneously favorable with improvement of the headache, resolution of the diplopia and conjunctival injection. The intraocular pressure and visual acuity are also improved.

Discussion The clinical features of carotido-cavernous fistulas are quite variable. In our case the symptoms were primarily related to venous hypertension (pseudotumor pattern) and association of typical signs of a carotido-cavernous fistula several months later.

P4L57

Chronic paroxysmal hemicrania, hemicrania continua and SUNCT syndrome associated with organic pathologies: a systematic review

Marco Trucco*[1], Federico Mainardi[2], Ferdinando Maggioni[2], Romualdo Badino[3] & Giorgio Zanchin[2]
[1]*Department of Neurology, Headache Center, Azienda Ospedaliera Santa Corona, Pietra Ligure (SV), Italy,* [2]*Department of Neurosciences, Headache Center, Padua University, Padua, Italy,* [3]*Department of Neurology, Azienda Ospedaliera Santa Corona, Pietra Ligure (SV), Italy*

We reviewed the literature since 1975 to June 2001 to identify all the relevant case reports presented by Authors as Chronic Paroxysmal Hemicrania (CPH), Hemicrania Continua (HC) and SUNCT syndrome, in association with organic pathologies. We critically reviewed the diagnoses according to the IHS criteria for CPH and clinical criteria by Goadsby and Lipton for HC and SUNCT syndrome.

The review includes 22 cases presented as CPH-like [17 females (77.3%) and 5 males (22.7%); mean age at onset of symptoms: 41.04 ± 17.88 ys;]; in only 6 patients the symptoms definitely fulfilled IHS criteria.

Nine cases were presented as HC-like [7 females (77.8%) and 2 males (22.2%); mean age at onset: 32.78 ± 10.87].

We detected seven 'symptomatic' cases of SUNCT syndrome [5 males (71.4%) and 2 females (28.6%); mean age at onset: 43.71 ± 18.61].

Mean age and gender ratio in 'secondary' cases approximately reproduces the ratio seen in idiopathic cases, even if the sex preponderance in SUNCT syndrome is still debated.

The most commonly associated pathology with CPH-like is the neoplastic one, but also inflammatory/infectious diseases are well represented. In HC-like, post-traumatic cases are predominant. In SUNCT-like cases vascular and bone malformations in the posterior fossa are most commonly observed. These data are somewhat different from those seen in cluster-like cases, where the most frequently observed pathology in association with the headache was the vascular one.

P4L58

Spontaneous intracranial hypotension: report of unusual cases and pathogenic hypotheses

Enrico Marchioni*[1], Anna Pichiecchio[2], Luisa Chiapparini[3], Dario Alimonti[1] & Maria Rita Schifino[2]
[1]*IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [2]*Department of Neuroradiology, IRCCS C.Mondino Institute of Neurology, Pavia,* [3]*Department of Neuroradiology, IRCCS C. Besta, Milano, Italy*

Lumbar puncture headache represents the more frequent condition of symptomatic intracranial hypotension. There is a less well known syndrome, named Spontaneous Intracranial Hypotension, in which the same clinical pattern occurs, with or without a clear evidence of cerebrospinal fluid leakage. Orthostatic headache and vomiting are the more frequently observed symptoms, while pachimeningeal enhancement, subdural effusions and caudal dislocation of the cerebellar tonsils represent the main radiological features of the disease.

We report here three cases (2 females and 1 male) of Spontaneous Intracranial Hypotension characterized by heterogeneous and atypical clinical patterns. In the 1st patient the syndrome was announced by generalized seizures, prolonged stupor and cerebrospinal fluid (CSF) hypotension, while in the 2nd one a mild cervical radicular pain, with normal CSF pressure, was the unique clinical manifestation. The 3rd patient presented with a full syndrome, characterized by orthostatic headache, vomiting and radicular pain. Such heterogeneous clinical evidence was related to different cranial and spinal MRI scan patterns. The dissociation between clinical and neuroradiological findings, which was observed in our cases, allowed us to provide some hypotheses about the pathogenetic mechanisms variably involved in this syndrome.

P4L59

Characteristics of headache in Behçet's disease

S. Saip*[1], A. Siva[1], A. Altintas[1], A. Kiyat[1], E. Seyahi[2] & V. Hamuryudan[2]
[1]*Department of Neurology, Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey,* [2]*Department of Internal medicine, Division of Rheumatology, Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey*

Objective Headache is one of the most common neurological symptom seen in Behçet's Disease (BD). The objectives of this study is to determine the types of headaches seen in BD and especially to define the characteristics of nonstructural migraine-like headache which may be specific to BD.

Methods One hundred and eleven patients (68-male) from our outpatient BD clinic, who fulfilled the diagnostic criteria of the International Group for BD, were randomly recruited in the study. Demographic features and characteristics of their headache according to the criteria of the International Headache Society (IHS) and the neurologic examination were recorded.

Results Headache was reported in 59.4% (66/111) of the patients. In 7, headache was the result of neurologic involvement (5 venous sinus thrombosis, 2 parenchymal CNS involvement). According to the criteria of the IHS 19 patients had tension type and 9 had migraine without aura. Headache

of the remaining 31(46.9%) patients started right after or concomittant with BD. It was recurrent, localised, bilateral, frontal and throbbing. This type of headache, different from migraine has shorter duration, less severe intensity, less nausea and vomiting and can be triggered by oral ulcerations and uveitis.
Conclusion Independent from neurologic involvement, headache is a common symptom in BD. Other than primary headaches (migraine and tension type); nonstructural migraine – like headache is the most frequent.

Hormones and headaches

P4M1

Cortical excitability changes during the ovarian cycle: a comparative study between healthy volunteers and migraine patients

Valentin Bohotin*[1], Catalina Bohotin[1], Arnaud Fumal[2] & Jean Schoenen[2]
[1]*Neuroscience Research Center, University of Montreal, Montreal, Canada,* [2]*Departments of Neuroanatomy and Neurology, Headache Research Unit, University of Liège, Belgium*

Background Migraine patients are characterized interictally by abnormal cortical excitability. Sex hormones are able to modulate neuronal excitability: progesterone tends to decrease it via GABAergic mechanisms, whereas estrogen enhances excitability, partly through the glutamate system.
Objective To determine if there are measurable changes of cortical excitability during the ovarian cycle using transcranial magnetic stimulation (TMS) and comparing migraineurs between attacks and healthy controls.
Methods We determined thresholds for TMS activation of motor (motor evoked potential) and visual (phosphenes) cortices in 10 female migraineurs and 9 healthy volunteers during 8 equally spaced sessions over the menstrual cycle.
Results *Motor thresholds* were stable in migraineurs and healthy volunteers over the menstrual cycle, having a variability inferior to 10%. By contrast, *phosphene threshold* increased markedly between days 1 and 12 of the cycle, more so in migraine patients (41.17% ± 26.43) than in healthy volunteers (21.67% ± 20.02).
Conclusions The occipital cortex seems to have increased sensitivity in the peri-menstrual period. This could be related to the high incidence of perimenstrual attacks in most female migraineurs. Moreover, our study indicates that stage within the ovarian cycle has to be taken into account in studies of magnetophosphenes.

P4M2

Estrogen 'withdrawal': a trigger for migraine? A double-blind placebo-controlled study of estrogen supplements in the late luteal phase in women with migraine

E. Anne MacGregor*[1], Alison Frith[1], Jayne Ellis[2] & Laurence Aspinall[3]
[1]*The City of London Migraine Clinic, London, United Kingdom,* [2]*Unipath Limited, Bedford, United Kingdom,* [3]*Unilever Research, Sharnbrook, United Kingdom*

Objectives The study tested the hypotheses that migraine is associated with estrogen withdrawal in the late luteal phase of the menstrual cycle and can be prevented with optimally timed estrogen supplementation.
Methods Urine was collected daily over three menstrual cycles in 40 women with pure menstrual migraine or menstrually related migraine. Samples were analysed for E_1G, PdG, FSH and LH. Women also used the Clearplan Fertility Monitor, conducting a test daily on at least 10 days per cycle. All women kept a daily migraine diary and treated migraine with their usual acute treatment. Women subsequently entered a six-month double-blind randomised placebo-controlled study using estradiol supplements (three cycles estradiol, three cycles placebo) from nine days post LH surge, as identified by the monitor, until day 2 of menstruation.
Results Mean age was 43 (range 29–49) years. The final analysis was undertaken on cycle data from 27 women. The late luteal phase was associated with the highest proportion of migraine ($P < 0.001$). There was no significant association between ovulation and migraine. Estradiol treatment targeted at the late luteal phase was associated with a significant reduction in migraine days and migraine severity, but not migraine events, vs. placebo.
Conclusions These results support the study hypotheses.

P4M3

Abnormal degradation of endocannabinoids in migrainous women

Letizia Maria Cupini*[1], Monica Bari[2], Natalia Battista[2], Giovanni Argirò[3], Alessandro Finazzi Agrò[2], Paolo Calabresi[1] & Mauro Maccarrone[4]
[1]*Clinica Neurologica, Ospedale S. Eugenio, Università degli Studi di Roma 'Tor Vergata', Roma, Italy,* [2]*Dipartimento di Medicina Sperimentale e Scienze Biochimiche, Università degli Studi di Roma 'Tor Vergata', Roma, Italy,* [3]*Medicina Nucleare, Ospedale S. Eugenio, Roma Italy,* [4]*Dipartimento di Scienze Biomediche, Università degli Studi di Teramo, Teramo, Italy*

The endogenous cannabinoid anandamide (AEA) plays important roles in modulating pain. Head pain is an almost universal human experience, yet primary headache disorders, such as migraine without aura (MWoA) or tension-type headache (TTH), can determine a serious life impact when frequent and disabling. We assessed the activity of AEA hydrolase and AEA transporter, the agents controlling AEA levels, and the cannabinoid receptors in peripheral platelets from 21 MwoA, 20 episodic TTH and 21 healthy controls. Blood samples were collected from all subjects during the same menstrual phase. In fact, it has been shown that physiological concentrations of progesterone stimulate the activity of the endocannabinoid-degrading enzyme FAAH in human lymphocytes. An increase in the activity of AEA hydrolase and AEA transporter was found in MWoA patients compared to both TTH and control subjects, whereas cannabinoid receptors were the same in all groups. Even after adjustment for hormonal levels, FAAH and AMT activities were variables independently associated with migraine. Our results suggest that in migraineurs an increased AEA degradation by platelets, and hence a reduced concentration of AEA in blood, might reduce the pain threshold. The involvement of the endocannabinoid system in migraine is new and broadens our knowledge on this widespread and multifactorial disease.

P4M4

Predicting and preventing menstrual migraine: use of the Clearplan Fertility Monitor

E. Anne MacGregor*[1], Alison Frith[1], Jayne Ellis[2] & Laurence Aspinall[3]
[1]*The City of London Migraine Clinic, London, United Kingdom,* [2]*Unipath Limited, Bedford, United Kingdom,* [3]*Unilever research, Sharnbrook, United Kingdom*

This study aimed to assess the Clearplan Fertility Monitor, used to predict optimal timing of estradiol supplements for prevention of menstrual attacks of migraine.

Urine was collected daily for assay of E_1G, PdG, FSH and LH over 3 menstrual cycles in 40 women with menstrual or menstrually related migraine. Clearplan Fertility Monitor tests were performed at least 10 days/cycle. All women kept a migraine diary and used their usual acute treatment for migraine.

Women were instructed to use estradiol supplements perimenstrually for 6 further cycles (3 estradiol, 3 placebo) from nine days after the LH surge, as identified by the monitor, until day 2 of menstruation.

Mean age was 43 (range 29–49) years. The final analysis was on data from 27 women. Use of the monitor to identify LH surge enabled correct timing of estrogen supplements in the late luteal phase. Women were instructed not to use supplements if the monitor did not show ovulation.

97% of women reported that the monitor helped them to predict and prepare for attacks.

The Clearplan Fertility Monitor is useful for managing menstrual attacks of migraine. By identifying the LH surge, it can predict optimal perimenstrual prophylaxis timing and help to ensure endometrial protection.

P4M5

Increased migraine prevalence in women with history of PreEclampsia (PE)

Alessandra Tirelli*[1], Gianbattista Allais[2], Immacolata Blasi[1], Annibale Volpe[1], Chiara Benedetto[2] & Fabio Facchinetti[1]
[1]*Mother-Infant Department, 'Psychobiology of Reproduction' Unit, University Centre for Adaptive Disorders and Headache (UCADH) University of Modena and Reggio Emilia,* [2]*Department of Obstetric and Gynecology, University of Torino, Italy*

The pathophysiology of pregnancy-induced hypertension with proteinuria (PE) is linked to increased vascular reactivity, which is also typical of migraine. In a case-control study we evaluated the prevalence of headache forms in 51 women with PE.

Gestational age at delivery was 33.9 ± 4.1 weeks; birthweight was 2345 ± 680 g. Controls were randomly selected among women having uneventful pregnancy, matched for age and parity.

Thirty-four PE patients (66.7%) and only 11 controls (24.4%) met an IHS diagnosis ($P < 0.001$). Among patients, migraine without aura (20 cases, 58.8%) and headache with migraine features (12 cases, 35.3%) were the main forms of headache; only 2 women suffered from episodic tension-type headache (TTH). Among controls, the prevalence of TTH (18.2%) was higher. Age at onset was similar. During pregnancy more PE patients (84.4%) than controls 27.8%, P = 0.004) experienced an improvement of headache.

A comorbidity between migraine and PE has been demonstrated. Migraine sufferers should be advised they are at high risk of developing Preeclampsia.

P4M6

Hypothalamic dysfunction is associated with poor outcome in migraine without aura

Alfredo Costa*[1], Grazia Sances[1], Rossella E. Nappi[2], Natascia Ghiotto[1], Marianna Loi[1] & Giuseppe Nappi[1,3]
[1]*Headache Treatment and Diagnosis Centre, University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [2]*Department of Obstetrics and Gynecology, IRCCS San Matteo, University of Pavia, Italy,* [3]*Department of Neurology and ORL, University of Rome, Italy*

Hypothalamic changes have been involved in the mechanisms leading to chronic migraine. We tested the response of HPA and gonadal axes in 63 patients with migraine without aura (40 F, 23 M), with disease duration > 10 years; outcome was considered negative if the attack frequency during the previous year was higher, and positive if it was equal or lower, than that observed over the 3 years following disease onset. According to a case-control design, 44 patients had a negative (O-), and 19 a positive outcome (O +). Following naloxone (10 mg i.v.) to evaluate central opiod function, a blunted cortisol response and a slight reduction in LH increase were found in the O- group. This suggests an impaired opiate receptor activity most likely involving the hypothalamus, as pituitary sensitivity is preserved in evolutive migraine. Unchallenged cortisol concentrations were normal: thus, the hypercortisolism described by others may become evident only once the chronic condition is established. Central opioid inhibition of gonadal axis is maintained in evolutive migraine. Thus, chronic migraine is associated with deranged hypothalamic opioid function operating on HPA axis; this may play an important role in the mechanisms of evolution and represent a predictive factor of long-term outcome.

P4M7

Tibolone reduced analgesics consumption in postmenopausal women with primary headaches

Silvia Detaddei*[1], Rossella E. Nappi[1], Grazia Sances[2], Fabio Facchinetti[3], Benedetta Brundu[1], Natascia Ghiotto[2], Franco Polatti[1] & Giuseppe Nappi[2,4]
[1]*Department Obstetric and Gynecology, IRCCS San Matteo, University of Pavia, Italy,* [2]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [3]*Department of Gynecologic, Obstetric and Pediatric Sciences, University of Modena & Reggio Emilia,* [4]*Department of Neurology and ORL, University of Rome La Sapienza, Rome, Italy*

The course of primary headaches may be significantly affected by hormonal replacement therapy (HRT) in postmenopausal women.

Forty patients (age: 53.9 ± 3 year; age at menopause 50.2 ± 1.5 year) suffering from migraine without aura (MwA) and episodic tension-type headache (ETTH) were followed for 6 months by the use of a daily diary with the clinical features of headache attacks and analgesic use under 2 randomly assigned HRT regimens: tibolone 2.5 mg or E_2 1 mg + 0.5 mg NETA. Moreover, we evaluated climacteric symptoms and both anxiety and depression.

(a) the number of analgesics used for MwA and ETTH attacks were significantly reduced ($P < 0.01$) in women on tibolone, while a significant increase ($P < 0.02$) was found for E_2 + NETA; (b) the number of days with MwA was unchanged throughout tibolone treatment, while it was significantly increased by E_2 + NETA ($P < 0.03$); (c) the number of days with ETTH and the severity of head pain ($P < 0.01$) were significantly reduced ($P < 0.03$) on tibolone; (d) both treatments improved climacteric symptoms, but tibolone was more effective on depression ($P < 0.01$).

Tibolone is effective in managing postmenopausal women suffering from ETTH, without worsening MwA attacks. Such a positive effect may be due to the improvement of mood and well-being exerted by this tissue-specific treatment.

This work was partly supported by a grant from the Italian Ministry of Health (RC 2002).

P4M8

Neuroendocrine correlates of migraine induced by oral contraception (OC): effect of E2 supplementation during the pill-free week

Grazia Sances*[1], Rossella E. Nappi[2], Silvia Detaddei[2], Antonella Smeraldi[3], Arianna Sommacal[2], Marianna Loi[1], Franco Polatti[2] & Giuseppe Nappi[1,4]
[1]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH) IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [2]*Department Obstetric and Gynecology, IRCCS San Matteo, University of Pavia, Italy,* [3]*Laboratory of Neuroendocrinology IRCCS Mondino, University of Pavia, Italy,* [4]*Department of Neurology and ORL, University of Rome La Sapienza, Rome, Italy*

We assessed neuroendocrine correlates of migraine (M) induced by oral contraception (OC). Ten women (duration: 4.6 ± 0.5 days on 0.03 mg EE2 + 0.15 mg DSG) received the direct central serotoninergic agonist m-chlorophenylpiperazine (m-CPP) (0.5 mg/kg) orally at 8.30 AM, 48 h after stopping the pill. Six women with menstrual migraine (MM) (duration: 1.7 ± 0.7 days) served as controls. In a consecutive menstrual cycle, 5 OCM were supplemented with 2 g of percutaneous E2 gel (Sandrena, Organon) during the pill-free week and 5 OCM were treated with placebo (PL). m-CPP was repeated and blood samples were taken every 30 min over 4 h for determining plasma F and PRL levels.

(a) PRL response to m-CPP was significantly blunted in OCM in comparison with MM ($f = 4.8$, $p < 0.001$), while F response to m-CPP was absent in OCM in comparison with MM ($f = 5.8$, $p < 0.001$); (b) E2 treatment significantly augmented PRL response in OCM ($f = 2.8$, $p < 0.01$), while F response was completely restored by E2 ($f = 18.9$, $p < 0.001$). When OCM were treated with E2 basal plasma F levels were significantly lower ($P < 0.001$), probably as a consequence of a positive effect of E2 supplementation on the course of M (duration: 1.8 ± 0.4 days; $p < 0.001$).

This work was supported by a grant from the Italian Ministry of Health (RC 2002).

P4M9

Phytoestrogens in menstrual migraine prophylaxis

Letizia Maria Cupini*[1], Federica Ferrante[2] & Eugenia Fusco[3]
[1]*Clinica Neurologica Ospedale S Eugenio, Universita' Di Roma Tor Vergata, Roma, Italy,* [2]*Clinica Endocrinologica Ospedale S Eugenio, Roma, Italy,* [3]*Clinica Neurologica Ospedale S Eugenio, Roma, Italy*

Fluctuation in estrogen levels is the major provocative factor in migraine associated with menstruation. The objective was to assess the efficacy of phytoestrogens, as perimenstrual, prophylactic treatment for menstrual migraine. Consenting women with a history of menstrual migraine, defined as attacks occurring exclusively within day 1 ± 2 days of menstruation and at no other time of the cycle were included in the study. They were asked to keep a daily diary during the study period recording menstruation, and providing information on headache attacks: frequency, intensity, duration, nausea and vomiting, symptomatic medication intake and side-effects. After a 3-months run-in period, the inclusion criteria reexamined at the end of run-in period, 10 women fulfilling the inclusion criteria underwent to a three months cyclic treatment with 56 mg of genisteine and 20 mg of diadzeine per day (10 days per month starting seven days before the predicted onset of menses). The average number of days with migraine during the baseline period decreased significantly after 3 months of therapy ($P < 0.005$). There were no side-effects noted. Phytoestrogens, substances with estrogenic activity in a limited number of estrogen-target tissues, appears to be an effective treatment in menstrual migraine prophylaxis. Placebo-controlled trials on larger number of patients are necessary to confirm our findings.

P4M10

Do pharmacologically induced menstrual periods increase the severity and disability of migraine headache?

Vincent Martin*[1], Suzanne Wernke[1], Karen Mandell[1], James Liu[2], Judy Bean[4] & Robert Rebar[3]
[1]*University of Cincinnati College of Medicine, Cincinnati, Ohio,* [2]*Case Western University, Cleveland, Ohio,* [3]*American Society for Reproductive Medicine, Birmingham, Alabama,* [4]*Childrens Hospital Medical Center, Cincinnati, Ohio*

Objectives To determine if pharmacologically induced vaginal bleeding increases the severity and disability of headache in female migraineurs.

Methods After induction of a medical menopause with gonadotropin-releasing hormone agonists, female migraineurs were randomized to 50 µg (estradiol-50 group, $n = 6$) or 100 µg (estradiol-100 group, $n = 5$) transdermal estradiol patches administered every 6 days for 6 months. 4% vaginal progesterone was administered daily for the first 10 days of each month. All women recorded headache severity (0–10 scale) and disability (0–5 scale) three times per day in a

diary. Each month was divided into the following intervals: progesterone (days that progesterone and estradiol were coadministered), vaginal bleeding (days of vaginal bleeding while receiving estradiol) and estradiol (days that estradiol was administered, but no vaginal bleeding). The primary outcome measure was the headache index defined as the mean of the severity ratings, while the disability index was a secondary outcome measure.

Results No significant differences were noted between the 3 intervals for the headache or disability indices within either of the treatment groups. (*P*-values of 0.619 and 0.406, respectively).

Conclusions Pharmacologically induced vaginal bleeding in the setting of constant serum estradiol levels does not increase the severity or disability of migraine headache.

P4M11

Prevalence of migraine on each day of the menstrual cycle in women not using hormonal treatments

E. Anne MacGregor*[1] & Allan Hackshaw[2]
[1]*The City of London Migraine Clinic, London,* [2]*Wolfson Institute of Preventive Medicine, London*

This study aimed to determine the frequency and characteristics of menstrual attacks compared to nonmenstrual attacks.

155 women (median age 44 years).

17% provided data for 2 cycles, 37% for 3 cycles, 16% for 4 cycles and 30% for = 5 cycles.

A within-woman analysis allowed for each woman's own pattern of migraine during her cycle.

Women were 1.7 times (95% CI 1.45–2.01) more likely to have migraine during the 2 days before menstruation and 2.5 times (95%CI 2.24–2.77) more likely during days +1 to +3, both compared to all other times of the cycle.

Severe migraine was 2.1 times (95% CI 1.29–3.13) more likely during days –1 and –2, and 3.4 times (95% CI 2.58–4.47) more likely during days +1 to +3 compared to all other times of the cycle.

Migraine with nausea was more likely during days –2 to +3.

Few women had migraine with vomiting; such migraines were more common during days –2 to +3.

There is a clear association between migraine and menstruation. These migraines tend to be more severe and associated with nausea and vomiting. The greatest effect is seen on the first three days of menstruation.

P4M12

Comparative expression of neuropeptide Y (NPY) and orexin B (Orx B) in the anterior pituitary (AP) tumours of patients suffering from migraine-like headache

John Classey*[1], Miles Levy[1], Mike Powell[2], Eric Grouzmann[3], Karim Meeran[4] & Peter Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London, UK,* [2]*National Hospital for Neurology and Neurosurgery, Queen Square, London, UK,* [3]*Division of Clinical Pharmacology, University Hospital (CHUV), Lausanne, Switzerland,* [4]*Department of Endocrinology, Charing Cross Hospital, London, UK*

Objectives We wished to investigate whether there was a relationship between migraine-like headache and two functionally and anatomically closely associated neuropeptides in patients with anterior pituitary (AP) tumours.

Methods An immunoperoxidase method utilised paraformaldehyde-fixed, paraffin-embedded AP tumour tissue from 27 neurosurgical biopsies (M.P.) and 1 control normal post mortem AP. Tissue was cut and reacted on slides with primary antibodies specific for human NPY and Orx B. Observers, blinded to the headache status of each patient, made light microscopic observations of NPY immunoreactive (IR) and Orx B-IR tumour cells.

Results Overall, there was no relationship between headache and NPY-IR ($\chi^2 = 0.454$, $P = 0.5$). Specifically, 31% of patients had headache and NPY-IR cells, while 35% had no headache but still had NPY-IR cells. For Orx B, no patients had headache and Orx B-IR cells, while 19% had no headache and Orx B-IR cells. Overall, 100% of patients who had headache had no Orx B-IR cells in their AP tumours ($\chi^2 = 4.54$, $P = 0.033$).

Conclusions There was no relationship between NPY-IR and headache. For this cohort, all patients who had headache did not have Orx B-IR cells in their AP tumours.

P4M13

Differential expression of calcitonin gene-related peptide (CGRP) and substance P in pituitary adenomas: in search of a nociceptive peptide

Miles Jonathan Levy*[1], John Classey[1], Supang Maneersri[1], Michael Powell[2], Karim Meeran[3] & Peter J. Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square London UK,* [2]*The National Hospital for Neurology and Neurosurgery, Queen Square London UK,* [3]*Department of Endocrinology, Charing Cross Hospital, London UK*

Objectives To determine if the differential expression of CGRP or substance P in a range of pituitary tumours was related to the presence or absence of headache.

Methods Using recognised immunohistochemical techniques we examined 27 consecutive pituitary adenoma specimens for the presence of CGRP and substance P. We included one normal post mortem pituitary specimen for comparison. A separate observer divided the patients into two groups: headache and non–headache. The association between the presence of CGRP/substance P and headache was observed.

Results We observed CGRP and substance P positive immunoreactivity in eight tumour specimens (30%), with cytoplasmic staining being the predominant morphological picture. CGRP and substance P were coexpressed in the same tumour specimen in five cases. There was no significant association between the presence of CGRP and headache (χ^2 1.8; $P = 0.18$). We did not observe CGRP or SP in the control specimen. There was no correlation between tumour subtype and the presence of CGRP or substance P.

Conclusions The mechanism of many pituitary tumour-associated headaches remains undetermined. The significance of CGRP and SP positivity in pituitary tumours is unknown but does not appear to be related to headache or endocrine activity of the tumour.

P4M14

Efficacy, tolerability, and pharmacokinetics of Eletriptan in women

Anne MacGregor*[1], Jeffrey Alderman[2], Carolyn Sikes[2] & Jayasena Hettiarachchi[2]
[1]*The City of London Migraine Clinic, London, United Kingdom,* [2]*Pfizer Inc. New York NY, USA*

Objective Since migraine is common in women of reproductive age, this study was undertaken to assess efficacy, tolerability, and pharmacokinetic parameters important specifically in treating women with eletriptan.
Methods Data from two pharmacokinetic studies of eletriptan 80 mg and pooled data from women in seven double-blind, placebo-controlled clinical trials of eletriptan 40 mg (n = 2462) were analyzed.
Results Pharmacokinetic studies in menstruating women showed no clinically important changes in pharmacokinetics between the four menstrual cycle phases. Pharmacokinetic studies in lactating women demonstrated that very small quantities (0.02% of an 80-mg dose) were excreted into the breast milk, most likely by passive diffusion. In clinical studies, 2- h headache response with eletriptan 40 mg was similar between men (n = 284, 58%) and women (n = 1586, 61%). Headache response was also similar in women treated during menses (n = 274, 64%). There was no significant difference in headache response in women taking hormone replacement therapy (HRT) or oral contraceptives (OC) (HRT/OC: n = 494, 65%; No HRT/OC: n = 1376, 58%). Adverse events associated with eletriptan were similar in women who were taking concomitant hormone replacement therapy, oral contraceptives or eletriptan alone.
Conclusion Eletriptan is efficacious and well tolerated in women, with no significant differences during the menstrual cycle or with HRT/OC use.

P4M15

Migraine in a contraception clinic

E Anne MacGregor*[1] & Alison Frith[1]
[1]*The City of London Migraine Clinic, London, UK*

Objectives To assess the prevalence of migraine in women seeking contraception.
Methods We reviewed 276 notes of clients attending a dedicated family planning clinic during one week.
Results 213 clients had no migraine or significant headache recorded at any clinic visit.

63 (23%) had migraine or significant headache: 10 reported migraine in the pill-free interval of combined oral contraceptives (COC); 19 (9% of total, 30% of those with migraine) were recorded as having 'focal symptoms' of which 12 descriptions suggested migraine aura.

16 were new clients of which 13 (75%) reported migraine. 1 reported that she could not take COCs because of migraine (reason not specified). 1 reported stopping COCs after two weeks because of severe headache and nausea.

5 (31%) new clients were recorded as having 'focal symptoms': 3 symptoms suggested migraine aura (in 2 aura was associated with COC use); 2 no description (1 attended for EC only; 1 took POP).
Conclusions Migraine was common in women attending for contraception. The greater pick-up of migraine in recent consultations probably reflects better recognition of migraine as a risk factor for COC use. Despite this, the high level of migraine identified in this group was surprising and warrants further study.

P4M16

Severity and disability of menstrual and nonmenstrual attacks in outpatient women with migraine

Virginie Dousset*[1], Sandrine Irachabal[1], Nelly Fabre[2], Françoise Radat[1], Bruno Brochet[1], Patrick Henry[1] & Gilles Géraud[2]
[1]*Unité de Traitement de la Douleur Chronique,* [2]*Département de Neurologie, Université de Toulouse, Hôpital Rangueil, France*

Objectives There is a clinical impression that migraines around the time of menses are more severe, more longer and harder to treat. This study was carried out to determine the severity and disability of menstrual attacks compared to non-menstrual attacks.
Methods 140 outpatient menstruating migraineurs women completed a diary over 2 menstrual periods. 7192 diary days were recorded. The diary recorded the occurrence of menses, the migraine days, their severity (intensity, duration, intensity of associated headache features, disability), and the medications used (name, number, relief and recurrence). We compared the severity and the disability of menstrual and non menstrual attacks. More over, we compared the response to attacks treatment.
Results Among the 140 participants, 24 women were subsequently excluded because of miscompleted diaries. Among the 116 analysed diaries, 85 (73.3%) women had a menstrual-associated migraine. 24 (20.7%) had a migraine without menstrual association and 7 (6%) women had a true menstrual migraine. A total of 490 menstrual attacks and a total of 778 nonmenstrual attacks were recorded.
Conclusion The analysis of diaries should make possible to determine if menstrual and non menstrual attacks are different in term of severity. The statistical analysis is in progress.

P4M17

Menstrual migraine among headache sufferers at the headache clinic of Athens General Hospital 'G. Gennimatas'

Georgia Hatzidaki*[1], A. Kazantza[1], A. Robotis[1], V. Papadopoulou[1], M. Terzoudi[1], A. Sarafianos[1], Ch. Giannoulis[1], A. Kargadou[1], D. Stavropoulos[1], A. Spantideas[1], CE. Karageorgiou[1]
[1]*Headache Clinic, Neurology Department, Athens General Hospital, Athens, Greece*

Introduction Menstrual Migraine, according to definition, is the attack of Migraine without aura, only during ± 2 days before or after the menstrual period. Menses are a trigger factor of migraine to 50% of women, but only 10% have real menstrual migraine.

Objective To evaluate the frequency of the menstrual migraine among the population of a headache clinic, we have studied the history of 2000 patients, which have been examined at the clinic.
Patients and Methods Two thousand women have been examined in our Headache Clinic, during the last year. Their ages spanned between 18 and 55 years of age. All women completed a diary card of the headache attacks, the date of the menstrual period' s onset and duration every month, as well as the characteristics of the headache attack, for six months. Women with menopause were excluded.
Results Seven hundred and eighty women (39%) reported the menstrual period as a trigger factor of the headache attack, although only 420 women had pure menstrual migraine. The type of headache was Migraine without aura for 65% of the sufferers. The temporal correlation of the appearance of the attack, to the onset of the menstrual period, was 2 days before for 41% of them.

The management of the menstrual migraine was symptomatic for 62% and prophylactic for 38%.

P4M18

Migraine is associated with menorrhagia and endometriosis

Gretchen Tietjen*[1], Anita Conway[1], Nabiel Herial[1] & Christine Utley[1]
[1]*Medical College of Ohio, Toledo, Ohio, USA*

Objective To determine the frequency of menstrual disorders in migraineurs compared to age-matched controls.
Methods Women, age 22–50 years, with migraine (IHS) and an age and sex matched nonmigraine cohort completed a questionnaire on menstrual disorders, bleeding history, vascular events and risk factors.
Results Migraineurs (50) and controls (52) were similar in OC use (30% v 32%, p 0.77), HRT use (12% v 8%, p 0.69), and prior hysterectomy (24% v 14%, p 0.84). Menorrhagia (> 3 consecutive heavy periods) was more common in migraineurs (63% v 37%, p 0.009) and interfered with ability to work (p 0.017), family activities (p 0.0001), sleep (p 0.003), ability to enjoy life (p 0.001), mood (p 0.022) and quality of life (p 0.003). Bruising (40% v 10%, p 0.0001), rectal bleeding (18% v 2%, p 0.017), and endometriosis (30% v 4%, p 0.0001) was more common in migraineurs, even when controlling for NSAID use. There were trends of hypertension (25% v 10%, p 0.05), TIA/stroke (10% v 2%, p 0.08), and Raynauds (10% v 2%, p 0.08) in migraineurs.
Conclusions Migraineurs experience more menorrhagia, endometriosis, and associated psychosocial consequences, suggesting further study of potential influencing factors, e.g. eicosanoids and platelet function.

Scientific Session 5

Migraine therapy

P5N1

Safety, tolerability, and pharmacokinetics of BIBN 4096 BS, the first selective small molecule calcitonin gene-related peptide receptor antagonist, following single intravenous administration in healthy volunteers

Mario Iovino*[1], Ulrich Feifel[2], Chan-Loi Yong[3], Jan– Markus Wolters[4] & Gudrun Wallenstein[5]
[1]*Human Pharmacology Center, Department of Clinical Research, Boehringer Ingelheim Pharma Gmbh & Co. KG, Ingelheim, Germany,* [2]*Human Pharmacology Center, Department of Clinical Research, Boehringer Ingelheim Pharma Gmbh & Co. KG, Biberach, Germany,* [3]*Department of Drug Metabolismus and Pharmacokinetics, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA,* [4]*Department of Drug Metabolismus and Pharmacokinetics, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany,* [5]*Department of Medical Data Services, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany*

BIBN 4096 BS is the first selective, highly potent, small molecule, nonpeptide calcitonin gene-related peptide receptor antagonist, which has been developed for the treatment of migraine. This double-blind, placebo-controlled, randomized first-in-human study investigated the safety, tolerability and pharmacokinetics of BIBN 4096 BS following single intravenous administration of rising doses (0.1–10 mg) in 55 healthy male and female volunteers. Blood pressure, pulse rate, respiratory rate, ECG, laboratory tests and forearm blood flow did not reveal any clinically relevant changes. Adverse events (AEs) were few, transient and mostly mild in severity. No serious AEs occurred. In summary, intravenously administered BIBN 4096 BS revealed a favorable safety profile and was generally well tolerated. The plasma concentration-time courses of BIBN 4096 BS showed multicompartmental disposition characteristics. Mean C_{max} appeared to be dose-proportional. BIBN 4096 BS exhibited a low total clearance (CL) of 12 L/h and a moderate apparent volume of distribution at steady state (V_{ss}) of 20 L, resulting in a terminal half-life ($t_{\frac{1}{2}}$) of 2.5 h. Renal clearance (CL_R) was 2.0 L/h, suggesting that renal excretion plays only a minor role in the elimination of unchanged BIBN 4096 BS. In conclusion, BIBN 4096 BS is a safe and promising new compound, which might be of major benefit in the treatment of migraine.

P5N2

Comparison of intravenous valproic acid with intravenous lysine-acetylsalicylic acid in acute migraine attacks

Tobias Leniger*[1], Phillip Stude[1], Lutz Pageler[1], Hans Christoph Diener[1] &Volker Limmroth[1]
[1]*Department of Neurology, University Essen, Germany*

Objective To compare the efficacy of intravenous valproic acid (VPA) with intravenous lysine-acetylsalicylic acid (LAS) in acute migraine attacks.
Methods Randomised, double blind, parallel group study, phase II. Twenty patients with acute migraine attacks (onset less than 5 h) received 800 mg VPA or 1000 mg LAS. Headache severity, duration, phonophobia, photophobia, and nausea

were recorded at baseline, 1 h, 2 h, 24 h, and 48 h after treatment (4-step-scale, moderate or severe attacks only). Primary outcome criteria of patients with headache relief or pain free.
Results Patient demographics did not differ between groups: VPA group ($n = 10$, age 30 ± 2.4SD, 6 female/4male), LAS group ($n = 10$, age 36.2 ± 3.8SD, 6 female/4male). Headache relief at 1 h: 60% in the VAL group vs. 80% in the LAS group (2 h: 90% vs. 90%). Both groups showed similar improvements in phonophobia, photophobia and nausea. No recurrence headaches or significant adverse events were reported.
Conclusions The efficacy of VPA is comparable to LAS in acute migraine attacks. VPA may be an important alternative in the emergency setting for patients with contraindications for LAS and triptans or in countries were LAS is not available.

P5N3

Mechanism of botulinum toxin type-A inhibition of calcitonin gene-related peptide secretion from trigeminal nerve cells

Paul Durham*[1], Ryan Cady[1] & Roger Cady[2]
[1]*Department of Biology, South-west Missouri State University, Springfield,* [2]*Headache Care Center, Springfield*

The goal of our study is to determine the cellular mechanisms by which botulinum toxin type A (BTX-A) inhibits calcitonin gene-related peptide (CGRP) release from trigeminal ganglia nerves. BTX-A may have a prophylactic benefit in migraine. While the mechanism by which BTXs block neurotransmitter release from motor nerves is well documented, its effect on CGRP secretion from sensory trigeminal nerves is not known. To determine the cellular events involved in BTX-A inhibition of CGRP release, the amount of CGRP secreted from rat trigeminal ganglia cultures was measured by radioimmunoassay. Interestingly, while overnight treatment of trigeminal cultures with therapeutic concentrations of BTX-A did not affect the amount of unstimulated CGRP release, stimulated release of CGRP following KCl or capsaicin treatment was greatly repressed. Incubation with toxin for shorter time periods (6 or 3 h) was equally effective at repressing stimulated release. The long-term effect of BTX-A on CGRP secretion, the mode of toxin entry, and possible role of vesicle docking proteins are currently under investigation. Results from these studies provide the first evidence that BTX-A can directly inhibit CGRP release from sensory trigeminal nerves, a finding that may explain how BTX-A functions to prevent and decrease the severity of migraine.

P5N4

Ethanol evoked inflammatory responses in trigeminal ganglia and dura mater of the guinea pig: relevance for migraine

Marcello Trevisani[2], Mauro Manconi[1], Selena Harrison[1], Alfredo Bianchi[3] & Pierangelo Geppetti*[1]
[1]*Interdisciplinary Centre of Excellence for the Study of Inflammation (ICSI), University of Ferrara, Ferrara, Italy,* [2]*Department of Critical Care Medicine and Surgery, University of Florence, Florence, Italy,* [3]*Department of Pharmacology, University of Salerno, Salerno, Italy*

Objectives Activation of the trigeminovascular system is considered to playa role in the mechanism of migraine headaches. Ethanol (EtOH), one of the common trigger of migraine, stimulates primary sensory nerves by activating the vanilloid receptor-1 (TRPV1).
Methods In this study we have investigated the role of TRPV1 in EtOH induced: release of substance P (SP) and calcitonin gene related peptide (CGRP) from trigeminal ganglia and dura mater with attached venous sinuses (DMVS) of guinea pigs, and; increase in plasma extravasation (PE) in DMVS.
Results EtOH (0.3–3%) increased SP and CGRP release from trigeminal ganglia and DMVS slices, an effect that was abolished by capsaicin desensitization and by the TRPV1 antagonist, capsazepine (CZP) (SP, by 96%, 97% and CGRP, 83%, 93% inhibition, respectively). Intravenous (560 µL/kg), intraperitoneal and intraesophageal administrations of EtOH (both 1 mL/kg) increased significantly the PE in the DMVS, an effect that was reduced significantly by CZP (by 30%, 72% and 54%, respectively).
Conclusions Our results demonstrate that EtOH activates inflammatory responses in the trigeminovascular system in a TRPV1-dependent manner, thus suggesting a possible role of TRPV1 in the mechanism of EtOH induced attack of migraine and cluster headaches.

P5N5

Treatment of coexisting migraine and chronic tension-type headache with botulinum toxin A: a double-blind placebo-controlled study

Hartmut Göbel*[1], Axel Heinze[1], Vera Zumbroich[1] & Katja Heinze-Kuhn[1]
[1]*Kiel Pain Clinic, Kiel, Germany*

Objectives This study was conducted to determine the efficacy of Botulinum-toxin A [Botox®] in patients suffering from both migraine and chronic tension-type headache with increased tenderness of pericranial muscles.
Methods After a run-in phase of 4 weeks 40 patients fulfilling IHS-criteria for migraine (≥6 days/month) *and* chronic tension-type headache with increased tenderness of pericranial muscles were randomised either to receive 100 U Botox® or placebo injected into 10 individually chosen trigger-points in pericranial muscles. Patients were asked to record occurrence of migraine and tension-type headache in a diary.
Results Compared to the run-in period the average number of migraine days significantly dropped by 41.6% in the 1st, 47.6% in the 2nd and 29.8% in the 3rd month after treatment with Botox®. The corresponding figures for placebo were –5.6% in the 1st month, +2.7% in the 2nd month and ±0% in the 3rd month. The number of days with tension-type headache per month was also significantly reduced by Botox® compared to both run-in phase and placebo: 1st month –19.3% vs. –2.4%, 2nd month –37.8% vs.-2.4% and 3rd month –21.1% vs. –2.0%.
Conclusions Botulinum-toxin A injected into pericranial trigger-points proved to be an effective prophylactic treatment of coexisting migraine and tension-type headache.

P5N6

Topiramate in migraine prophylaxis: results from a placebo-controlled trial including an active comparator-propranolol

Hans-Christoph Diener*[1], Peer Tfelt-Hansen[2], Carl Dahlof[3], Jose Miguel Lainez[4], Giorgio Sandrini[5], Shuu-Jiun Wang[6], Walter Neto[7] & David Jacobs[7], Vijapurkar[7]
[1]*Unversity of Essen,* [2]*Glostrup Amtsssygehus Afd.no1,* [3]*Gothenburg Migraine Clinic,* [4]*Hospital Clinic Universitary Avda Blasco Ibanez, 17,* [5]*University Centre for Adaptive Disorders and Headache,* [6]*The Neurological Institute,* [7]*Johnson & Johnson Pharmaceutical Research and Development*

Introduction Topiramate (TPM) has shown efficacy in migraine prophylaxis in two large placebo-controlled, dose-ranging trials. We conducted a randomized, double-blind, multicenter trial to evaluate the efficacy and safety of 2 doses of topiramate vs. placebo and an active comparator, propranolol (PROP), for migraine prophylaxis.
Methods Subjects with episodic migraine, with or without aura, were randomized to TPM 100 mg/day, TPM 200 mg/day, PROP 160 mg/day, or placebo. The primary efficacy measure was the change from baseline in mean monthly migraine frequency.
Results 575 subjects were enrolled from 68 centers in 13 countries. Based on pairwise comparisons, TPM 100 mg/day was superior to placebo as measured by the reduction in monthly migraine frequency, the overall 50% responder rate, the reduction in monthly migraine days, and reduction in rate of rescue medication use. The TPM 100 mg/day and PROP groups exhibited similar reductions in migraine frequency and other secondary efficacy variables. TPM 100 mg/day was better tolerated than TPM 200 mg/day, and was generally comparable to PROP. No unusual or unexpected adverse events were observed.
Conclusions These findings demonstrate that topiramate 100 mg/day is effective in migraine prophylaxis. TPM 100 mg/day and PROP 160 mg/day exhibited similar efficacy and tolerability profiles.

P5N7

The impact of different antimigraine compounds on platelet and erythrocyte aggregation

Stefan Evers*[1], Thomas Heuel[1], Achim Frese[1], Sonja Schwaag[1] & Ingo-W. Husstedt[1]
[1]*Department of Neurology, University of Münster*

Clinical and experimental data suggest that ergotamine and triptans might contribute to vascular events such as myocardial infarction, stroke, and peripheral arterial occlusion. However, the role of blood cell aggregation in this context is not yet clarified. We therefore designed a cross-over, double-blind, placebo-controlled study to evaluate the impact of different amtimigraine compounds on platelet and erythrocyte aggregation ex-vivo.

Twenty healthy subjects were enrolled. Platelet and erythrocyte aggregation was measured before and two hour after intake of placebo, acetylsalicylic acid, ergotamine tartrate, sumatriptan, and zolmitriptan. Platelet aggregation was measured by the so-called platelet reactivity index, erythrocyte aggregation was measured by photometric assessment in a commercial aggregometer.

Ergotamine tartrate induced a significant increase of platelet aggregation whereas acetylsalicylic acid induced a significant decrease. After placebo, after sumatriptan and after zolmitriptan, no significant changes of platelet aggregation were noted. Erythrocyte aggregation was not affected at all by neither compound.

Our data suggest that ergotamine intake, but not intake of triptans, leads to an increase of platelet aggregation. This might in part contribute to the vascular side-effects of this compound.

P5N8

Efficacy and safety of the feverfew CO_2-extract MIG-99 in migraine prevention – a randomised, double-blind, multicentre, placebo-controlled study

Hans-Christoph Diener*[1], V. Pfaffenrath[2], J. Schnitker[3], M. Friede[4] & H. H. Henneicke-Von Zepelin[4]
[1]*Department of Neurology, University of Essen, Essen, Germany,* [2]*Munich, Germany,* [3]*Institute for Applied Statistics, Bielefeld, Germany,* [4]*Schaper & Brümmer, Gmbh, Salzgitter, Germany*

The efficacy and tolerability of a new CO_2-extract of feverfew (MIG-99) (6.25 mg t.i.d.) was compared with placebo in a randomised, double-blind, multicentre, parallel-group design.

Patients ($N = 170$ ITT; MIG-99: $N = 89$, placebo: $N = 81$) suffering from migraine according to IHS criteria were treated for 20 weeks after a 4-week baseline period. Subsequently, MIG-99 was offered to all patients for another 8 weeks. The primary endpoint was the average number of migraine attacks per 28 days during the treatment months two and three compared to baseline. Safety parameters included the incidence of adverse events, assessment of laboratory parameters, vital signs and physical examination, respectively. The migraine frequency in the MIG-99 group decreased from 4.7 by 1.9 attacks per month, in the placebo group from 4.7 by 1.3 attacks. The difference between treatment groups was statistically significant in favour of MIG-99 ($P = 0.0456$). The rate of adverse events possibly related to study medication was 9/107 (8.4%) with MIG-99 and 11/108 (10.2%) with placebo ($P = 0.654$). The CO_2-feverfew extract MIG-99 is effective in the prophylaxis of migraine and is superior to placebo. MIG-99 shows a favourable benefit-risk ratio. The current data confirm the results of an earlier phase II trial on the efficacy of MIG-99.

P5N9

Pain free efficacy of Sumatriptan in the treatment of migraine at the first sign of pain: prospective, double-blind, placebo-controlled, Canadian multicenter study of Sumatriptan 50 mg and 100 mg vs. placebo

W. J. Becker*[1], S. Christie[2], F. F. Ahmad[3], W. Pryse-Phillips[3] & S. D. Simpson[3]
[1]*University of Calgary and Calgary Health Region, Calgary, Alberta, Canada,* [2]*Ottawa Headache Centre, Ottawa, Canada,* [3]*GlaxoSmithKline, Canada*

Objective To determine the efficacy of sumatriptan 50 mg and 100 mg tablets administered during the mild-pain phase of migraine.
Background While clinical research protocols for migraine therapy have required subjects to await moderate/severe pain before study medication was taken, 2 studies showed that sumatriptan provides effective pain freedom when taken during the mild-pain phase.
Design/methods Subjects with moderate/severe migraine headaches treated their headaches in the mild-pain phase with sumatriptan 100 mg, 50 mg or placebo. Primary end-point was percentage of subjects pain-free at 2 h.
Results

	Pain-Free			% Patients with worsened pain at 2 h	% Required 2nd dose within 24 h	Adverse events
Dose	30 min	60 min	2 h			
Placebo ($n = 109$)	< 1%	7%	16%	56%	17%	6%
50 mg ($n = 126$)	4%	24%**	40%**	34%**	22%	20%#
100 mg	8%*	24%**	50%**	28%**	22%	27%#

($n = 126$), *$P = 0.009$, **$P < 0.001$, #no formal comparisons.

44% and 39% of subjects that were pain-free 2 h following treatment with sumatriptan 100 mg and 50 mg had a return of headache pain compared with 47% for placebo. Majority of returning headaches were mild, 61%, 80% and 50% in the sumatriptan 100 mg, 50 mg and placebo groups, respectively.
Conclusions Sumatriptan 50 mg and 100 mg are well tolerated and effective in providing complete relief of pain when administered in the mild-pain phase for migraine headache.

P5N10

Vasoconstrictor effects of triptans in human thoracic arteries and veins

Angelica Wackenfors*[1], Malin Emilson[1], Richard Ingemansson[2], Lars Edvinsson[1] & Malin Malmsjö[1]
[1]*Department of Internal Medicine, Lund University Hospital, Lund, Sweden,* [2]*Departmente of Cardiothoracic Surgery, Lund University Hospital, Lund, Sweden*

Objectives Chest tightness is experienced by 30% of the patients treated for migraine with triptans. The origin of these side-effects is unknown, although oesophageal and coronary artery contraction may be involved. The aim was to examine if triptans induce vasoconstriction of thoracic arteries and to characterise the 5-HT receptors.
Methods Human left internal mammary arteries and small thoracic arteries and veins were obtained during coronary bypass surgery. 5-HT, 5-CT and triptan-induced vasoconstriction was characterized *in vitro* and receptor mRNA was quantified by real-time PCR.
Results Eletriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan induced contraction in vessels from approximately 40–50% of the patients. The 5-CT contraction was blocked by the 5-HT_{1B} antagonist SB224289 (10^{-7}M), while the 5-HT_{1D} antagonist BRL115572 (10^{-7}M) had no effect. The contractile response to 5-HT was antagonised by the 5-HT_{2A} receptor antagonist ketanserin (10^{-7}M). 5-HT_{2A}, 5-HT_{1B} and 5-HT_{1D} receptor mRNA was detected by real-time PCR in all three vessels.
Conclusion Triptans induce vasoconstriction in thoracic vessels from 40 to 50% of the patients. This is one possible cause of the chest tightness that occurs as a side-effect in 30% of the patients treated with triptans.

P5N11

Placebo-controlled comparison of effervescent Acetylsalicylic Acid (ASA), sumatriptan and ibuprofen in the treatment of migraine attacks

Hans-Christoph Diener*[1], M. Voelker[2] & EMSASI Study Group[3]
[1]*University of Essen, Essen, Germany,* [2]*Bayer AG, Leverkusen, Germany,* [3]*European Migraine Study on Aspirin, Sumatriptan and Ibuprofen*

Acetylsalicyclic acid (ASA) has been frequently used in clinical trials in the treatment of acute migraine attacks in combination with metoclopramide. Recently the efficacy of a new formulation 1000 mg effervescent ASA without metoclopramide was shown. To further confirm the efficacy of this new formulation in comparison with triptans and other NSAIDs a three-fold crossover, double-blind, randomised trial with 312 patients was conducted in Germany, Italy and Spain. 1000 mg effervescent ASA was compared with 50 mg sumatriptan, 400 mg ibuprofen and placebo. The percentage of patients with reduction in headache severity from moderate or severe to mild or no pain (primary objective) was 52.5% for ASA, 60.2% for ibuprofen, 55.8% for sumatriptan and 30.6% for placebo. All active treatments were superior to placebo ($P < 0.001$), whereas active treatments are not statistically different. 27.1%, 33.2%, 37.1% and 12.6% of patients treated with ASA, ibuprofen, sumatriptan or placebo were pain-free at 2 h. With respect to other efficacy criteria and accompanying symptoms no differences between ASA and active treatments ibuprofen and sumatriptan were found. Drug-related adverse events were reported in 4.1%, 4.5%. 5.7% and 6.6% of patients treated with ASA, placebo, ibuprofen or sumatriptan. The study showed that effervescent ASA is as effective as sumatriptan und ibuprofen in the treatment of migraine attacks.

P5N12

The medical care use and costs associated with migraine headache

Jennifer Elston Lafata*[1], Christina Moon[1], Carol Leotta[2], Ken Kolodner[2], Laila Poisson[1] & Richard Lipton[3]
[1]*Henry Ford Health System, Detroit MI, USA,* [2]*IMR, A Subsidiary of Advanced PCS,* [3]*Departments of Epidemiology and Social Medicine, and Neurology, Albert Einstein College of Medicine, New York NY, USA*

Objective To describe the medical care use and costs associated with migraine headaches (IHS 1.1 and 1.2).
Methods A validated telephone survey was used to identify migraine cases ($N = 1265$) and a random sample of nonmigraine controls ($N = 1178$) aged 18–55 enrolled in a managed care organization. Medical care use and cost estimates for the 12 months preceding telephone interview were derived from comprehensive medical/pharmaceutical claims data and linked to survey responses. Unadjusted and adjusted differences in use/costs were estimated using exponential score tests and generalized estimating equations.
Results Migraine cases used more outpatient visits (8.4 vs. 6.1, $p < 0.01$), were more likely to be seen in the emergency department (21.3% vs. 16.6%, $p < 0.01$), and admitted to the hospital (4.6% vs. 2.8%, $p < 0.05$) compared to nonmigraine controls. Likewise, cases incurred significantly higher unadjusted medical care costs ($2761 vs. $2,062, $p < 0.01$). After controlling for patient characteristics, including survey ascertained depressive symptoms and claims data ascertained comorbidities, cases no longer incurred significantly higher medical care costs ($2302 vs. $2,100, $p = 0.30$).
Discussion Although migraine cases use more medical care and incur higher annual medical care costs compared to nonmigraine controls, the presence of psychiatric symptoms and other comorbidities is associated with these increased costs.

P5N13

Treatment priorities among triptan-naive patients with severe headache

Marcelo Bigal*[1,2], Richard Lipton[1], Joshua Liberman[3] & Walter Stewart[4,5]
[1]*Albert Einstein College of Medicine, Bronx, NY, USA,* [2]*The New England Center for Headache, Stamford, CT, USA,* [3]*Advance PCS, USA,* [4]*Geisinger Health Systems, Danville, PA, USA,* [5]*Department of Epidemiology, The John Hopkins University, Baltimore, MD, USA*

Objectives To evaluate a predefined set of treatment attributes among triptan-naive migraine sufferers with moderate or severe disability.
Methods A validated computer-assisted telephone interview was used to identify triptan-naive subjects with moderate or severe disability (MIDAS score ≥ 11). Questions focused on preferences for attributes related to headache treatment. The relative importance of treatment characteristics was rated.
Results Among the 12 555 eligible households contacted, 6181 subjects completed the interview, of which 207 met the MIDAS criteria. Most participants ($n = 163$, 79%) treated headaches exclusively with OTC medications, while just 21% used prescription drugs. The primary medication was reported as less than 100% effective by 189 (91.3%) respondents. The most common reasons for dissatisfaction were recurrence (28%), pain relief that takes too long (26%), and inconsistent relief (26%). Pain-free response at 1 h (58%) was the most important measure of efficacy, followed by sustained pain-free (28%). Cardiovascular side-effects (45 [%?]) were more important than CNS side-effects (19%).
Conclusions 1 – Most triptan-naive disabled headache sufferers are not fully satisfied with their acute treatment, usually an OTC medication; 2 – Disabled triptan-naive headache sufferers are important targets for treatment; 3 – Rapid pain relief is the most important treatment attribute;

P5N14

Tolerability profile of MT 100 during one year of treatment

Egilius Spierings*[1]
[1]*Department of Neurology, Harvard Medical School, Boston, MA, USA*

Objective Assess the long-term safety of single doses of MT 100 (combination of 500 mg naproxen plus 16 mg metoclopramide).
Methods Open-label multicenter study in 1006 patients who ingested single tablet doses of MT100 for the acute treatment of migraine attacks. Safety was assessed by evaluation of adverse events (AEs), clinical labs, and physical examination. 621 patients took at least 12 doses of MT 100 within 6 months and 329 took at least 24 doses within 12 months.
Results No deaths occurred. Dropouts due to AEs were infrequent (8%). 24 subjects experienced serious AEs; none were related to MT 100. Most AEs were mild-to-moderate. Overall rate of AEs declined over time: 14% of 6-month completers had an AE within 24 h of their first dose while 7% reported an AE after their last dose. Similar rates were reported for 12-month completers (13% and 7%). No clinically meaningful changes occurred in any laboratory or physical examination parameter.
Conclusions Single tablet doses of MT 100 administered intermittently over a 12-month period for the treatment of acute migraine are associated with a favorable safety profile.

P5N15

Bodyweight in headache prophylaxis

Filippo Dainese*[1], Federico Mainardi[1], Ferdinando Maggioni[1], Chiara Perin[1], Silvia Ruffatti[1] & Giorgio Zanchin[1]
[1]*Headache Center, Department of Neurosciences, University of Padua, Italy*

Bodyweight gain is not uncommon during prophylaxis, but there are no studies on this undesired side-effect. We studied 336 MO, MA, TTH patients (85% F, 15% M, age 39 ± 14). Controls were made up of 85 patients (79% F, 21% M, age 38 ± 12). For three months patients underwent a prophylactic treatment, which was discontinued in the following three months. Bodyweight was checked weekly. The drugs studied were amitriptyline (20 and 40 mg/day), flunarizine (5 and

10 mg/day), pizotifen (0.5–1.5 mg/day), propranolol (80–160 mg/day), verapamil (160 mg/day) and valproate (600 mg/day). The largest percentage of bodyweight increase was due to flunarizine 10 mg (92%; weight gain: 6.1 ± 4.3 kg) and pizotifen (78%; 3.6 ± 1.9 kg), followed by flunarizine 5 mg (57%; 3.8 ± 1.9 kg), amitriptyline 40 mg (53%; 3.4 ± 2.0 kg) and 20 mg (51%; 3.3 ± 2.5 kg), propranolol (31%; 3.2 ± 2.2 kg), valproate 600 mg (26%; 3.0 ± 1.4 kg) and verapamil (20%; 2.0 ± 0.6 kg). The percentage of patients returning to the starting bodyweight three months after therapy discontinuation was 50% with amitriptyline (20 and 40 mg), 40% with pizotifen, 28% and 29% with flunarizine 10 and 5 mg, respectively. A better knowledge of this problem allows a better tayloring of prohylaxis, according to the patient needs.

P5N16

Diagnosis of migraine headache using corresponding points of Koryo hand therapy

Kyu Hyun Park*[1], Kyung Pil Park[1], Dae Sung Kim[1], Dae Soo Jung[1] & Tae Woo Yoo[2]
[1]*Department of Neurology, College of Medicine, Pusan National University, College of Medicine, Department of Neurology,* [2]*Koryo Hand Therapy Institute, Korea*

Objective It is very important to find location to diagnose migraine headache. The location means side and site. We cannot decide the location with patient's history taken only. We need careful and detailed physical examination. We should allot much time for such procedures. We need to develop new method to determine location using Corresponding Points (CP) of Koryo Hand Therapy found by Yoo.
Methods On detailed physical examination to 400 migraineurs, we observed points of tenderness, tightness and pain sensitivity on the head, shoulder and abdomen. We also checked CP in the both hands with KHT.
Results Among 400 migraineurs, 48 had migraine on both sides, 196 had migraine headache on the right and 156 had on the left side. Migraineurs showed tenderness or pain sensitive response on the head, shoulder (including neck) and abdomen. The CP of Hand showed same pain sensitive response in affected side. Migraineurs had pain sensitive responses at $м^{-1}$, M-2, M-3, M-4, M-5 and M-11 points and specific CP in the palm such as F-19, C-1, A-3 and N-17 in affected side of KHT.
Conclusion Checking the CP on physical examination, we could confirm the location more easily and objectively.

P5N17

Topiramate-related changes in the management of insulin-dependent diabetes mellitus in patients with migraine and diabetes

Pedro A. Kowacs*[1], Elcio J. Piovesan[1], Hudson Fameli[1] & Lineu C. Werneck[1]
[1]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil*

Objective to describe the cases of two female migraine patients with insulin-dependent diabetes mellitus in whom the use of topiramate led to improvement of the diabetes or to significant changes in their diabetes therapy.
Case reports Case #1. A 23-year-old-white female with insulin-dependent diabetes consulted because of transformed migraine. Topiramate 50 mg/day controlled her migraine attacks, but after a month of therapy she started to present clustered hypoglycemic seizures, leading to reduction of topiramate to 25 mg/day and to a significant reduction in her daily dose of insulin. Case #2. A 16-years-old white female with insulin-dependent diabetes reported frequent migraine attacks. Topiramate 25 mg/day resulted in migraine control, as well as better control of her glucose and cholesterol blood levels and, to a lesser extent, of her HbcA1. Her insulin dose could be decreased a little.
Conclusion The possible mechanisms of this supra–addictive interaction between insulin and topiramate may reflect topiramate-induced changes in adipose tissue metabolism and its effects on resistance to insulin. Care should be taken when adding topiramate to insulin-dependent diabetic patients.

P5N18

Topiramate for migraine prevention: a randomized, double-blind, placebo-controlled, multiple-dose study

Jan Brandes*[1], Walter Neto[2], David Jacobs[2] & Suman Bhattacharaya[2]
[1]*Nashville Neuroscience Group,* [2]*Johnson & Johnson Pharmaceutical Research and Development*

Objective To assess the efficacy and safety of three doses of topiramate (50, 100, and 200 mg/day) for migraine prevention.
Methods The primary efficacy measure for this 26-week, randomized, double-blind, placebo-controlled study (MIGR-002) was the change from baseline in mean monthly migraine frequency. Secondary efficacy measures included the 50% responder rate.
Results 468 patients made up the intent-to-treat population (placebo = 114; topiramate 50 mg/day = 117; topiramate 100 mg/day = 120; topiramate 200 mg/day = 117). Mean monthly migraine frequency decreased significantly for patients on 100 mg/day topiramate ($P = 0.008$) and 200 mg/day topiramate ($P < 0.001$) vs. placebo. Significant reductions were evident as early as the first month of treatment. The responder rate was significantly greater for the 50 mg/day (39%, $P = 0.010$), 100 mg/day (49%, $P < 0.001$), and 200 mg/day (47%, $P < 0.001$) topiramate groups than for the placebo group (23%). The most common adverse events in the topiramate groups resulting in discontinuation included paresthesia (5%), fatigue (5%), nausea (3%), and abdominal pain (3%).
Conclusions This study demonstrated the excellent efficacy, and acceptable tolerability profile of topiramate in migraine prevention, confirming results from an additional large, controlled trial (MIGR-001).

P5N19

Potent P2Y6 receptor mediated contractions in human cerebral arteries

Lars Edvinsson*[1], Malin Malmsjö[1], Mingyan Hou[1], William Pendergast[3] & David Erlinge[2]
[1]*Division of Experimental Vascular Research, Department of Internal Medicine,* [2]*Department of Cardiology, Lund University Hospital, Sweden,* [3]*Inspire Pharmaceuticals Inc., Durham, North Carolina, USA*

Background Extracellular nucleotides may be involved in cerebral vasospasm after subarachnoidal haemorrhage. The aim was to characterise the contractile P2 receptors in endothelium-denuded human cerebral and omental arteries by *in vitro* pharmacology. P2 receptor mRNA expression was examined by RT-PCR.
Results In human cerebral arteries, the selective $P2Y_6$ receptor agonist, UDPβS was the most potent of all the agonists tested ($pEC_{50} = 6.8 \pm 0.7$). The agonist potency; UDPβS > αβ-MeATP > UTPγS > ATPγS > ADPβS = 0, indicated the presence of contractile $P2X_1$, $P2Y_2$, $P2Y_4$ and $P2Y_6$, but not $P2Y_1$ receptors, in human cerebral arteries. In human omental arteries, UDPβS was inactive. The agonist potency; αβ-MeATP > ATPγS = UTPγS > ADPβS = UDPβS = 0, indicated the presence of contractile $P2X_1$, and $P2Y_2$ receptors, but not $P2Y_1$ or $P2Y_6$ receptors, in human omental arteries. RT-PCR analysis demonstrated $P2X_1$, $P2Y_1$, $P2Y_2$ and $P2Y_6$ receptor mRNA in cerebral and omental arteries. $P2Y_4$ receptor mRNA was barely detectable.
Conclusions $P2Y_6$ receptors play a prominent role in mediating contraction of human cerebral arteries. Conversely, no such effect can be observed in human omental arteries and previous results confirm the absence of $P2Y_6$ receptors in human coronary arteries. The $P2Y_6$ receptor might be a suitable target for treatment of cerebrovascular diseases such as subarachnoidal haemorrhage and migraine.

P5N20

MT 100 is as effective as Sumatriptan 50 mg in treating acute migraine attacks

Richard Pellegrino*[1]
[1]*Central Arkansas Research Inc. (CARE), Hot Springs, Arkansas*

Objectives We wished to investigate whether there was a relationship between migraine-like headache and two functionally and anatomically closely associated neuropeptides in patients with anterior pituitary (AP) tumours.
Methods An immunoperoxidase method utilised paraformaldehyde-fixed, paraffin-embedded AP tumour tissue from 27 neurosurgical biopsies (M.P.) and 1 control normal post mortem AP. Tissue was cut and reacted on slides with primary antibodies specific for human NPY and Orx B. Observers, blinded to the headache status of each patient, made light microscopic observations of NPY immunoreactive (IR) and Orx B-IR tumour cells.
Results Overall, there was no relationship between headache and NPY-IR ($^{-2} = 0.454$, $P = 0.5$). Specifically, 31% of patients had headache and NPY-IR cells, while 35% had no headache but still had NPY-IR cells. For Orx B, no patients had headache and Orx B-IR cells, while 19% had no headache and Orx B-IR cells. Overall, 100% of patients who had headache had no Orx B-IR cells in their AP tumours ($^{-2} = 4.54$, $P = 0.033$).
Conclusions There was no relationship between NPY-IR and headache. For this cohort, all patients who had headache did not have Orx B-IR cells in their AP tumours.

P5N21

Chronic daily headache and overuse of triptans in patients over 65 years

Miguel J. A. Lainez*[1], Rogelio M. Leira[2], Julio G. Pascual[3], Ana M. Pascual[1] & Miguel J. Santonja[1]
[1]*Department of Neurology, Hospital Clinico Universitario, Valencia,* [2]*Department of Neurology, Hospital Xeral de Galicia, Santiago de Compsotela,* [3]*Department of Neurology, Hospital Marqués de Valdecilla, Santander*

Background Recently, triptans overuse have been implicated in chronic headaches. There are not data about triptans use and its side-effects in patients over 65 years because are contraindicated.
Objective Define triptans' roll in headache chronification in patients over 65 years and cardiovascular complications associated.
Method Prospective program of detection triptans use in patients over 65 years. We selected overusers (>15 days/month) and analysed headaches' characteristics, cardiovascular risk factors and cardiovascular complications.
Results 21 patients fulfilled the criteria, 11 males/10 females, age range 66–75, 10 with migraine characteristics, 11 with criteria of tension-type headache.

Triptans used sumatriptan (9), zolmitriptan (6), naratriptan (4), rizatriptan (2) and almotriptan (3), 15 had previous history of other drugs abuse.

Average daily dose 1.1 tablets (0.5–3).

Mean time of abuse 6.7 months (3–31). 8 patients had one or more cardiovascular risk factors. No cardiovascular effects were registered.
Conclusions Triptans determine headache chronification in patients over 65 years. Dependence mechanism is unknown, but the scarce number of daily doses and the low migraine incidence make improbable a vascular factor. Psychological mechanisms and economic factors (no reimbursed drugs in our country) could play a roll.

Use of triptans in this age group, even with cardiovascular risk factors, would reinforce their cardiovascular safety data.

P5N22

Sustained migraine relief with triptans: how do initial response and headache recurrence contribute?

Charlotte Keywood[1], Gilles Géraud*[2] & Anthony Fox[3]
[1]*Minerva Consulting, London, UK,* [2]*CHU Rangueil, Toulouse, France,* [3]*EBD Group Carlsbad, CA, USA*

Objective To determine the relative importance of initial response (IR) and headache recurrence (HR) in determining sustained migraine relief (SR).

Methods Data were taken from 31 published trials. HR was return of Grade 2/3 headache within 24 h following IR (Grade 1/0) at either 2 h (22 studies) or 4 h (15 studies) postdose. SR = IR(100-RR)/100. Correlation of IR and HR with SR used a least-squares procedure. Sensitivity analysis was performed by finding the mean and upper and lower 95% confidence intervals for IR and HR.
Results IR (2 h) range 46% – 77%, IR (4 h) range 56% – 77%. HR (2–24 h) range 6% – 47%, HR (4–24 h) range 7% – 42%. SR (2–24 h) range 30% – 58%, SR (4–24 h) range 43% – 60%. SR more strongly correlated with HR (2–24 h r = – 0.81, p = 0.0016, 4–24 h r = –0.68, p = 0.044) than IR (2–24 h, r = 0.48, p = 0.029, 4–24 h, r = –0.005, p = ns). 95% CI for SR was narrower for all observed values of HR than for IR. Sensitivity analysis confirmed that HR was superior to IR for estimating SR (P = 0.016) IR and HR were not correlated, r = 0.13, p = ns.
Conclusions HR more powerfully determines SR than IR. Since HR prevention depends on half-life, (1) use of longer-acting triptans can increase patients' probability of attaining sustained migraine relief.

Reference

1 Geraud G et al. Headache 2003; 43 : 376–388.

P5N23

Preliminary evaluation of the relationship of time of headache recurrence to elimination half-life of 5HT 1B/1D agonists

Charlotte Keywood[1] & Gilles Géraud*[2]
[1]*Minerva Consulting, London, UK,* [2]*CHU Rangueil, Toulouse, France*

Objective To evaluate the relationship of time to headache recurrence (THR) with triptan half-life in context of headache recurrence rate (HRR).
Methods Efficacy data were taken from 13 published triptan studies. Recurrence was the return of Grade 2/3 headache within 24 h following headache relief (Grade 1/0) at either 2 or 4 h postdose. Correlations of THR and HRR with half-life used a least-squares procedure.
Results Half-life range 2 h (R10) to 26 h (F2.5), THR range 10.5 h (Z2.5) to 21.4 h (F2.5), HRR range 7% (F2.5) to 47% (R10). THR was less strongly correlated than HRR with half-life. Correlation of half-life with THR r = +0.47, correlation of half-life with HRR r = –0.68 and correlation of THR with HRR r = –0.44.
Conclusions Headache recurrence is less likely and the time to recurrence tends to be longer with long half-life triptans. There is a trend for the greater the risk of recurrence the faster it may occur. This last point emphasizes the relationship between half-life and HRR and strengthens the positive trend seen for THR and half-life.

P5N24

Efficacy of menstrually associated migraine prophylaxis with frovatriptan in true menstrual migraine patients and in patients with menstrually related migraine

Charlotte Keywood[1] & Arthur Elkind*[2]
[1]*Minerva Pharmaceutical Consulting, Thames Ditton, United Kingdom,* [2]*Elkind Headache Center, Mount Vernon, New York, USA*

Objective To compare the efficacy of frovatriptan prophylaxis of menstrually associated migraine (MAM) in patients with True Menstrual Migraine (TMM: patients with migraine attacks Day –2 to Day + 2 of menstruation and at no other time) with that for other patients with Menstrually *Related* Migraine. (MRM: patients with migraine attacks Day –2 to Day + 4 of menstruation, ± migraine attacks at other times).
Methods Double-blind, placebo-controlled three-way crossover study of 6 days perimenstrual treatment with placebo, frovatriptan 2.5 mg o.d. and frovatriptan 2.5 mg b.d. (double loading-dose on dosing day 1). Treatment started 2 days prior to anticipated MAM onset.
Results In TMM (n = 167) and MRM patients (n = 336), both frovatriptan doses effectively prevented MAM, reduced MAM headache severity, its duration and associated functional disability.
Mam incidence TMM patients, 2.5 mg b.d. 38% ($P < 0.0001$), 2.5 mg o.d. 52% ($P = 0.005$), placebo 66%. MRM patients, 2.5 mg b.d. 48% ($P < 0.0001$), 2.5 mg o.d. 59% ($P < 0.0001$) placebo 76%. During all treatments, TMM patients had fewer and milder MAM headaches than MRM patients.
Conclusions Perimenstrual treatment with frovatriptan 2.5 mg o.d. and 2.5 mg b.d. provide effective prophylaxis of MAM for patients with True Menstrual Migraine and Menstrually Related Migraine.

P5N25

Learning from PROMISE study (PROphylaxis of MIgraine with SEglor)

André Pradalier*[1], Michel Lanteri-Minet[2], Christian Lucas[3] & Gilles Geraud[4]
[1]*H. L Mourier, Colombes,* [2]*H. Pasteur, Nice,* [3]*CHRU de Lille,* [4]*CHU Rangueil, Toulouse, France*

The objective of the trial was to evaluate the efficacy of Seglor® (DHE) in migraine prophylaxis. It was a double blind, randomised, multicenter, placebo-controlled and parallel group study conducted in GP practise with a patient management program and according to IHS criteria. 363 patients were evaluated (ITT).

The frequency of attacks was reduced by 57% with Seglor® (from 3.3 ± 1.0 to 1.4 ± 1.4) but without statistical difference against placebo (51%, from 3.3 ± 1.1 to 1.6 ± 1.5). Seglor® demonstrated better efficacy ($P < 0.05$) in most of the secondary endpoints, particularly, the mean duration of an attack, the total duration of attacks per month, the decrease of symptomatic treatments (antalgics level II, OMS) and the patient preference. The tolerance was statistically comparable to the placebo.

PROMISE brings a real question regarding the main criteria to be used in clinical trials with GPs. The frequency would not probably be the best statistical criteria in populations with a number of attacks lower than 4 per month at baseline. The placebo effect seems to be higher when the frequency is lower and any recognised prophylactic treatment has demonstrated an efficacy in this kind of population.

Other variables like duration, intensity and/or symptomatic treatments have to be taken into account too.

P5N26

Comparative effectiveness of intravenous metoclopramide vs. ketorolac in the treatment of acute migraine attacks

Elena Pita Calandre*[1], Juan Jose Luque[2], Salvador Duarte[1] & Aurora Gamez[2]
[1]*Instituto de Neurociencias, Universidad de Granada, Spain,* [2]*Hospital San Augustín de Linares, Jaen, Spain*

Objectives To evaluate the effectiveness of 10 mg intravenous metoclopramide (MTC) vs. 30 mg intravenous ketorolac (KTC) in the symptomatic treatment of migraine attacks.
Methods 25 patients requiring acute migraine treatment received either metoclopramide ($N = 13$) or ketorolac ($N = 12$). Most of them ($N = 19$) had previously tried a triptan, another NSAID or both without reaching significant relief. Headache intensity was assessed in a 5-points scale at 0, 15, 30, 45, 60 and 90 min, and subjects' improvement was scored in a 6-points scale after drug injection. Persistence of associated symptoms was recorded. Two-way analysis of variance was applied to compare group's evolution.
Results Ninety minutes after drug administration 50% KTC and 38% MTC reported mild pain, and 50% KTC and 62% MTC reported no pain; 33% KTC and 16% MTC reported moderate improvement, 17% KTC and 31% MTC very much improvement, and 50% and 46% MTC total recovery; no significant differences were found between groups. As expected, MTC was superior on nausea and/or vomiting; neither drug ameliorated photophobia nor phonophobia. No side-effects were reported by any subject.
Conclusions Intravenous metoclopramide seems highly effective in emergency migraine management, and can be a good choice in patients refractory or intolerant to triptans and/or NSAIDs.

P5N27

A phase III multicenter, randomized, double-blind, parallel-group study of valdecoxib 40 mg vs. placebo in patients with multiple moderate or severe acute migraine headaches with or without aura

H. Mikel Thomas*[1], David Kudrow[2], Elizabeth Ashford[3], Vu Le[4] & Mark Brown[4]
[1]*Clinical Trials Technology, Prairie Village, KS,* [2]*California Medical Clinic for Headache, Encino CA,* [3]*Pharmacia Corporation, High Wycombe, United Kingdom,* [4]*Pharmacia Corporation, Kalamazoo, MI*

The efficacy and safety of valdecoxib 40 mg (+ optional 20 mg) vs. placebo in treating an initial plus up to 2 additional moderate to severe migraine headaches were assessed over a 56-day postbaseline period in an intent-to-treat population of 612 patients (299 V; 313 P). The percentage of patients reporting reduction of headache pain intensity from severe/moderate to mild/none (headache response rate) at 2 h postdose for attack #1 was significantly greater for valdecoxib 40 mg than placebo (46% vs. 32%; $P < 0.001$). More patients were pain-free 2 h postdose for attack #1 with valdecoxib 40 mg than placebo (16% vs. 8%; $P = 0.002$). Migraine-associated symptoms 2 h postdose for attack #1 were significantly reduced with valdecoxib 40 mg compared with placebo (nausea: 30% vs. 40%; $P = 0.011$; phonophobia: 45% vs. 58%; $P = 0.001$; photophobia: 58% vs. 70%; $P = 0.001$). In patients treating 3 migraine headaches, significantly more on valdecoxib than placebo had 2 of 3 or 3 of 3 attacks respond. Fewer patients treated with valdecoxib 40–60 mg than placebo noted an adverse event (AE, 24% vs. 31%) or drug-related AE (8% vs. 11%); one valdecoxib-treated patient withdrew due to an AE. In conclusion, valdecoxib 40 mg is effective and well tolerated in treating single and multiple migraine attacks.

P5N28

Tolerability and efficacy are related after triptan use

Fred Sheftell*[1,2], Marcelo Bigal[1,3], Michel Volcy[4], Stewart Tepper[1,5] & Randall Weeks[6]
[1]*The New England Center for Headache, Stamford, CT, USA,* [2]*New York Medical College, New York, NY, USA,* [3]*Albert Einstein College of Medicine, Bronx, NY, USA,* [4]*University of Antioquia, Medellin, Colombia,* [5]*Yale University School of Medicine, New Haven, CT, USA,* [6]*The New England Research Institute, Stamford, CT, USA*

Objective To analyze the patterns of self-reported tolerability of triptans in regard to headache attributes and efficacy of the drug.
Methods This was a prospective study at a tertiary care headache Center. Subjects using a triptan filled out a standardized questionnaire. The first part of the questionnaire evaluated the usual severity and disability of their headaches. The second part of the questionnaire assessed side-effects. Multiple regression was used to correlate the selected variables with the self-reported tolerability.
Results Our sample consisted of 267 subjects (87% women). When interviewed, 42.6% were using sumatriptan; 21.3%, zolmitriptan; 19.8%, rizatriptan; 8.7%, naratriptan; 7.5%, almotriptan. These groups did not differ in regard of self-reported intensity of headache, disability, and medication effectiveness. Plotting subjects using all triptans ($n = 267$), tolerability was not a function of 'baseline severity of headache', or 'disability of the headache if untreated'. It was, however, significantly and directly related to medication efficacy ($P < 0.01$). All R^2 values were low (< 0.75), indicating that the variables were not significantly correlated and that multicollinearity was not a problem. Sub-analyses indicated the same pattern to the individual triptans.
Conclusion Our data support the concept that tolerability is directly related to and may be a function of efficacy.

P5N29

Randomized, double-blind, placebo-controlled parallel-group evaluation of patient satisfaction with oral sumatriptan administered in mild phase during acute treatment of Menstrually Associated Migraine (MAM)

Andy Dowson*[1], Steve Landy[2], W Jacqueline Kwong[3], Michael Ames[3] & Mary Richardson[3]
[1]*King's Headache Service, London, UK,* [2]*Wesley Neurology and Headache Clinic, Memphis, TN,* [3]*GlaxoSmithKline, Research Triangle Park, NC*

Objective To evaluate patient satisfaction with oral sumatriptan in acute treatment of MAM.
Methods Two identical randomized, placebo-controlled, parallel-group studies were conducted to evaluate the efficacy and tolerability of sumatriptan 50 mg (S50) and 100 mg (S100) when administered during the mild pain phase of a MAM attack. At 24 h after study drug administration, subjects rated their satisfaction with medication in terms of migraine pain relief, other symptoms relief and overall satisfaction using a 7-point rating scale (very satisfied to very dissatisfied).
Results In both studies ($n = 445$ study 1 and $n = 368$ study 2), both S100 and S50 subjects reported significantly ($P < 0.01$) greater satisfaction than placebo in all three questions asked. When pooling the results together, 50% (S50) and 53% (S100) subjects were satisfied/very satisfied with pain relief vs. 24% subjects receiving placebo ($P < 0.001$ for both doses). For other symptoms relief, 42% (both S50 and S100) subjects were satisfied/very satisfied vs. 25% receiving placebo ($P < 0.01$ for both doses). For overall satisfaction, 49%(S50) and 50% (S100) were satisfied/very satisfied vs. 24% receiving placebo ($P < 0.001$ for both doses).
Conclusion Subjects receiving oral sumatriptan for acute treatment of MAM were satisfied with the clinical effectiveness of the medication.

P5N30

Effects of valdecoxib on functional impairment, quality of life and patient satisfaction in patients treated for migraine

Clayton Rowland*[1], Stephanie Barrows[1] & Mark Brown[1]
[1]*Pharmacia Corp., Portage, MI, USA*

The effect of valdecoxib vs. placebo on functional impairment, quality of life (QoL) and patient satisfaction in patients with moderate to severe migraines by IHS criteria was investigated. 702 patients were enrolled in a randomized controlled trial treating up to three migraines in 56 days with either valdecoxib 40 mg or placebo. Functional impairment and patient satisfaction were assessed using instruments developed by Quintiles and QoL was measured using the Migraine Quality of Life Questionnaire (MQoLQ). The Patient Satisfaction Questionnaire consists of two domains – efficacy and side-effects. The MQoLQ consists of five domains – symptoms, work, feelings/concerns, social and energy/vitality. Functional impairment was measured at 2, 4 and 24 h postdose. Patient satisfaction and QoL were assessed at 24 h postdose, or when the patient rescued. Functional impairment improved significantly at two hours for valdecoxib vs. placebo (20%v.5%) for headache one ($P < 0.01$). At 24 h, functional impairment was significantly different (29%v.7%). All five QoL domains showed a significant difference in favor of valdecoxib ($P < 0.01$) for headache one. Patient satisfaction with efficacy was greater for valdecoxib vs. placebo (49%v.33%; $p < 0.01$) in headache one with no difference in bothersomeness of side-effects. Similar results were seen in headaches two and three.

P5N31

Correlation between lipophilicity and triptan outcomes

Julio Pascual*[1] & Pedro Muñoz[1]
[1]*University Hospital Marqués de Caldecilla (UC) and Primary Care Management, Santander, Spain*

Background It has been proposed that triptans achieving higher central nervous system (CNS) levels should have an advantage in efficacy, if central actions are important.
Objectives To correlate efficacy and tolerability results of all triptans with their lipophilicity.
Methods Response, pain-free, recurrence, sustained pain-free, adverse events (AE), CNS AE and thoracic AE results taken from Ferrari et al.'s meta-analysis publications for the optimal doses of all triptans were correlated with their lipophilicity coefficients (log $D_{pH.7.4}$ = – 2.1 almo < – 1.5 suma < – 1.0 zolmi < – 0.7 riza < – 0.2 nara < + 0.5 ele).
Results We found no significant correlation between lipophilicity coefficients and any of the analysed variables. However, there was a clear, almost significant ($P = 0.09$), correlation between lipophilicity and CNS AE ($r = 0.74$) and, to a lesser degree, with a reduction in recurrence rate ($r = 0.46$). The rvalues for response and pain-free with and without placebo ranged from –0.05 and 0.45, suggesting almost no correlation between lipophilicity and efficacy variables.
Conclusions According to this analysis a higher lipophilicity does not seem to be crucial to improve triptan efficacy. This physico-chemical property, however, correlates with a higher incidence of CNS AE and possibly with a lower recurrence rate.

P5N32

Time course of symptom relief with various antimigraine therapies

Ninan Mathew*[1]
[1]*The Houston Headache Clinic, Houston, TX, USA*

Objective To evaluate the percentage of patients with pain, nausea, photophobia, and phonophobia over time for various antimigraine therapies alone and in combination as compared to placebo.
Methods Data from double-blind, randomized, placebo-controlled clinical trials in migraine patients treated with an oral NSAID, sumatriptan, combination NSAID and sumatriptan, combination NSAID and antiemetic, or subcutaneous dihydroergotamine were included in this retrospective analysis. Response to each therapy was compared over time for each migraine symptom.
Results With active treatment the percentage of patients with symptoms decreased at a faster rate than placebo from base-

line to 4 h, with the exception of nausea, which tended to plateau after 2 h in the NSAID, sumatriptan, and combination NSAID and antiemetic groups. The greatest response in all symptoms at 4 h was seen in the group treated with a combination of sumatriptan and an NSAID.

Conclusions The relief of nausea responded differently than the other associated symptoms, indicating that there may be differing mechanisms for migraine pain and associated nausea. Combination therapy, specifically with sumatriptan and an NSAID, produced the fastest and greatest relief of both migraine pain and the associated symptoms during the first 4 h post-treatment.

P5N33

Intranasal zolmitriptan 5 mg is well tolerated and effective during long-term use for the acute treatment of multiple migraine attacks

Andrew Dowson*[1], Bruce Charlesworth[2], Hans-Christoph Diener[3] & Steen Boes-Hansen[4]
[1]*The King's Headache Services, London, United Kingdom,* [2]*AstraZeneca, Macclesfield, United Kingdom,* [3]*Klinik- und Poliklinik fur Neurologie der Universitat Esse, Essen, Germany,* [4]*Kronobergskliniken, Vaxjo, Sweden*

Objectives To assess the long-term safety and tolerability of intranasal zolmitriptan 5 mg in the treatment of multiple migraine attacks over 1 years. A secondary objective was to assess efficacy (2 h pain-free response) during long-term use of intranasal zolmitriptan.

Methods Over a 1-year period, adult patients treated migraine attacks of any baseline intensity with intranasal zolmitriptan 5 mg. Adverse events (AEs) and efficacy outcomes were recorded.

Results The safety population comprised 538 patients (83.8% female) from 52 centres in 6 countries who treated = 1 migraine attack (total 20 717 attacks). AEs were reported in 32.8% of attacks, and were typically mild and transient and resolved spontaneously. The most common AEs were unusual taste and paraesthesia (19.0% and 6.8% of attacks, respectively). Only 24 patients (4.6%) withdrew due to AEs; unusual taste led to withdrawal in only 2 patients (0.4%). The incidence of AEs declined over time. Patients were pain-free 2 h post-treatment in 53.8% of attacks, with this level of response maintained throughout the study.

Conclusions Intranasal zolmitriptan 5 mg was well tolerated and reliably effective when used long-term for the acute treatment of migraine. Withdrawals due to AEs were very rare and the incidence of AEs decreased with increasing duration of treatment

P5N34

Botulinum toxin type -A reduces acute medication use in migraine patients

Maja Relja*[1], Natasa Klepac[1] & Srdana Telarovic[1]
[1]*Department of Neurology, Medical School, Zagreb University, Zagreb, Croatia*

Objective To assess the benefits of botulinum toxin type-A (BTX-*A*) injections in migraine patients by measuring the impact of treatment on normal daily living activities and triptan use.

Background Patients who fail acute therapy should be considered for prophylactic treatment. There are indications that BTX-*A* prophylactic therapy is clinically beneficial in migraine patients.

Design/methods 32 patients with moderate or severe migraine-related disability were randomized to BTX-*A* or placebo for the treatment of migraine pain in this double-blind, placebo-controlled trial. Patients received BTX-A and/or placebo injections (BOTOX^{R} Allergan, Inc., total dose of 100 U) into selected muscles. Two treatments were administered at 3-month intervals. Clinical evaluation and medication use for the 6-month period before and after beginning of treatment were analyzed.

Results The impact of migraine on normal daily activities at 2–4 h after attack was reduced in a significantly higher proportion ($P < 0.01$) of patients treated with BTX-A compared with those receiving placebo. BTX-*A* injections reduced significantly ($P < 0.001$) total triptan use. No adverse events were reported.

Conclusions BTX-*A* application was clinically beneficial for the treatment of migraine patients, as reflected by the decrease of acute medication use and medication cost.

P5N35

Acetaminophen 500 mg, aspirin 500 mg, and caffeine 130 mg (AAC) vs. sumatriptan 50 mg (S50) in the early treatment of migraine

S. Silberstein*[1], J. Saper[2], T. Smith[3], E. Spierings[4], R. M. Gallagher[5], F. Freitag[6], A. Elkind[7] & J. Goldstein[8]
[1]*Jefferson Headache Center, Philadelphia, PA, USA,* [2]*Michigan Head Pain & Neurological Institute, Ann Arbor, MI, USA,* [3]*Unity Health Research, Ryan Headache Center, Chesterfield, MO, USA,* [4]*Boston Clinical Research Center, Wellesley Hills, MA, USA,* [5]*UMDNJ, School of Osteopathic Medicine, Moorestown, NJ, USA,* [6]*Diamond Headache Clinic, Chicago, IL, USA,* [7]*Elkind Headache Center, Mt. Vernon, NY, USA,* [8]*San Francisco Clinical Research Center, San Francisco, CA, USA*

Objectives/methods Compare single doses of AAC ($n = 69$), S50 ($n = 67$), and placebo ($n = 35$) in the early treatment of migraine using a randomized, double-blind, placebo-controlled design. IHS migraineurs vomiting during more than 20%, or requiring bedrest during more than 50% of episodes were excluded. Study medication was taken at the first sign of a migraine episode, as defined by each subject.

Results AAC was significantly superior to S50 ($P < 0.05$) for SPID4 (3.9 vs. 2.1); TOTPAR4 (8.9 vs. 6.9); 2- h response (87% vs. 75%); 24- h sustained response (66% vs. 49%); subject global evaluation (good – excellent) (63% vs. 36%); and rescue (1.4% vs. 11.9%). Reported adverse events were typical of these drug classes.

Conclusions Subjects who took AAC at the first sign of a migraine episode had significantly superior pain relief, more sustained relief, and they required rescue medication significantly less often than subjects who took S50. If corroborated by additional data, these findings could help assure physicians and patients that AAC provides benefits comparable to

those of the leading prescription migraine product in the treated population.

P5N36

True nasopharyngeal absorption of zolmitriptan following administration of zolmitriptan nasal spray

Per-Henrik Zingmark*[1], Roger Yates[2], Cecilia Hedlund[1] & Matts Kågedal[1]
[1]*AstraZeneca R & D Södertälje, Södertälje, Sweden,* [2]*AstraZeneca, Macclesfield, UK*

Objectives To determine the proportion of a 5-mg dose of zolmitriptan nasal spray that is absorbed directly via the nasal mucosa.
Methods Fourteen healthy males received 2 single doses of zolmitriptan 5 mg oral tablet, administered with or without 45 g charcoal. Of these 14 subjects, 12 then received 2 single intranasal doses of zolmitriptan 5 mg nasal spray, administered with or without 45 g charcoal. There was a washout period of 4–14 days between treatments. Blood samples were collected for each treatment period.
Results The validity of the **methodology** was confirmed by the elimination of gut absorption of oral zolmitriptan following charcoal administration.

Using the ratio $AUC_{0-\infty}$ for intranasal dose with charcoal/$AUC_{0-\infty}$ for intranasal dose without charcoal, it was estimated that 28.7% of zolmitriptan 5 mg nasal spray was absorbed intranasally. The corresponding $AUC_{0-1\ h}$ and $AUC_{0-2\ h}$ ratios indicated that intranasal absorption contributed 70.8% and 48.5%, respectively, of the total exposure during these intervals.
Conclusions Approximately 30% of a single dose of zolmitriptan 5 mg nasal spray is absorbed intranasally; > 70% of exposure during the first hour postdose is due to intranasal absorption. These findings support the observations of very fast onset of action following intranasal administration of zolmitriptan.[1]

Reference

1 Abu-Shakra et al. Headache 2002; 42 : 389.

P5N37

Relaxation and hypnosis as prophylactic treatment for children with migraine: a randomised control trial (preliminary results)

Daniel Annequin*[1], Isabelle Celestin Lhopiteau[1], Amouroux Remy[1], Barbara Tourniaire[1] & Tonnelli Anne[1]
[1]*Paediatric Migraine Center Hôpital D'enfants, Paris, France*

Objectives To assess effectiveness of non pharmacological therapy for migraine.
Methods 38 children aged 6–15 years suffering from migraine (IHS classification) with at least 3 attacks/month, received the same usual pharmacological attack treatment (NSAID); they were randomly assigned to one of three groups: control, relaxation, and hypnosis (12 sessions). A headache daily diary was used (duration and pain level). Three evaluations were done (baseline. 3 and 6 months).
Results Migraine was significantly improved with hypnosis and relaxation.

Baseline	Migraine attacks/month	mean VAS pain (0–10)	
Control	5.3 ± 2.0	7.6	
Hypnosis	5.0 ± 2.0	8.1	
Relaxation	5.5 ± 2.2	8.5	
3 months follow up			Relief***
C	3.8 ± 0.9**	6.5	30%**
H	2.3 ± 1.6	5.8	68.9%
R	2.4 ± 1.1	5.9	67%
6 months follow up			
C	4.1 ± 2.7**	6.3	40.6%**
H	1.2 ± 0.9	5.0	75.1%
R	2.1 ± 0.6	5.7	65.9%

** $p < 0.05$ ANOVA. ***Percentage of attacks with more than 50% reduction in pain intensity one hour after pharmacological treatment.

Conclusion Hypnosis and relaxation training appear to be a very effective prophylactic treatment for paediatric migraine. This effect was observed even though the small sample studied.

P5N38

Botulinum toxin type A modified chronic migraine; further long-term experience

Ninan T. Mathew*[1], Alex Kaup[1], Jayasree Kailasam[1] & Lori Meadors[1]
[1]*Houston Headache Clinic, Houston, TX, USA*

Objective To report 'disease modifying' effect of botulinum toxin type A (Botox) in long-term management of disabling chronic migraine based on 3 years experience with a prospective open-label study.
Methods Patients with chronic intractable migraine with high disability (MIDAS above 30) were given 50–100 units of BTX-A in multiple scalp and neck sites. A combination of 'follow the pain' and 'fixed sites' approaches were used.
Results Outcome measures were MIDAS scales, mean headache days and amount of acute medications used. 208 patients were included receiving BTX-A one time to 10 times. Effects of Botox lasted for a mean of 12.5 ± 2.4 weeks. Mean MIDAS score before first injection (N208) was 83.8 ± 12, and 3 months after, 27.2 ± 8.2 ($P < 0.001$). Three months after second injection (N109), MIDAS score was reduced from 31.8 ± 5.1–22.8 ± 3.3 ($P < 0.01$). Third injection resulted in further reduction of MIDAS score from 27.9 ± 3.7–14.2 ± 3.1 ($P < 0.01$). After fourth and subsequent injections, MIDAS scales remained in the range between 10.2 and 15.7.

Number of headache days and use of acute medications showed corresponding reduction. No tachyphylaxis or significant side-effects occurred.

Conclusions BTX-A is an effective therapy for chronic migraine.

P5N39

Comparative efficacy of MT 100 and Sumatriptan 50 mg in treating acute migraine subjects with severe pain or nausea at baseline

Richard Pellegrino*[1]
[1]*Central Arkansas Research Inc. (CARE), Hot Springs, Arkansas, USA*

Objectives Compare the safety and efficacy of MT 100 to sumatriptan 50 mg and placebo in acute treatment of migraine, with a special focus on subjects with severe pain or nausea at baseline.
Methods Double-blind, placebo-controlled study employing a typical triptan study design and patient population. 546 subjects were randomized to receive MT 100 (single tablet), MT 100 (2 tablets), sumatriptan 50 mg (over-encapsulated Imitrex®), or placebo. Data from subjects with nausea or severe pain at baseline were analyzed separately.
Results Pain response data from all subjects, subjects with severe pain at baseline, and subjects with nausea at baseline are displayed below. All agents were well tolerated.

2-h Pain Response	MT 100 1 tab	MT 100 2 tabs	Imitrex 50 mg	Placebo
All subjects ($n = 546$)				
Pain response (%)	53*	58*	53*	29
Subjects with severe baseline pain ($n = 230$)				
Pain response (%)	39	51**	32	31
Subjects with baseline nausea ($n = 337$)				
Pain response (%)	54*	65*	55*	32

* $p < 0.05$ compared to placebo, ** $p < 0.05$ compared to placebo and sumatriptan 50 mg

Conclusions A two-tablet dose of MT 100 appears to be more effective than a single tablet dose or Imitrex 50 mg in patients with severe pain or nausea at baseline.

P5N40

Occipital nerve stimulation for intractable chronic primary headache disorders

David Dodick*[1], Terrence Trentman[2], Richard Zimmerman[3] & Eross Eric[1]
[1]*Department of Neurology, Mayo Clinic, Scottsdale Arizona USA,*
[2]*Department of Anesthesiology, Mayo Clinic, Scottsdale Arizona USA,*
[3]*Department of Neurosurgery, Mayo Clinic, Scottsdale Arizona USA*

Objective There is now clear evidence of functional coupling between nociceptive meningeal afferents and cervical afferents in the greater occipital nerve (GON) at the second-order neuron level (1). The objective of this study is to evaluate the safety and efficacy of occipital nerve stimulation in patients with medically intractable chronic primary headache disorders.
Methods Five patients with medically intractable chronic cluster headache (2 patients), chronic migraine (2 patients), and hemicrania continua (1 patient) underwent a detailed medical, neurologic, psychiatric assessment. Each patient underwent surgical placement of occipital nerve stimulating electrodes.
Results Mean duration of CDH prestimulation was 4.8 years and mean duration of follow-up was 6.2 months. Mean pre and poststimulation MIDAS were 237 (205–270) and 15.5 (0–50). Three of five patients had excellent outcome (90–100% reduction in headache frequency or disability and off medication); one patient had a very good outcome, and one patient had a fair outcome.
Conclusions Occipital nerve stimulation may be safe and effective for patients with disabling primary chronic daily headache disorders. A placebo-controlled study of ONS is warranted in this population of patients.

Reference

1 Bartsch T, Goadsby PJ. Stimulation of the greater occipital nerve induces increased central excitability of dural afferent input. Brain 2002; 125 : 1496–1509.

P5N41

Efficacy and tolerability of eletriptan through the clinical dose range vs. sumatriptan 100 mg for the acute treatment of migraine

Hans-Christoph Diener*[1], Ninan Mathew[2], Jayasena Hettiarachchi[3] & Wei Sun[3]
[1]*University Essen,* [2]*Houston Migraine Clinic,* [3]*Pfizer Inc*

Objective To compare the efficacy and tolerability of eletriptan (20 mg [E20], 40 mg [E40], 80 mg [E80]) with sumatriptan 100 mg (S100) and placebo (PBO) for acute treatment of migraine.
Methods Data from three similar randomized, placebo-controlled, double-blind, comparative studies were pooled ($N = 3398$) for meta-analysis.
Results E40 and E80 were superior to S100 on 2-h and 24-h outcomes ($P < 0.05$, each comparison, E40 or E80 vs. S100). Outcomes at 2 h included headache response (PBO = 26%, S100 = 57%, E20 = 54%, E40 = 67%, E80 = 71%), pain-free rate (PBO = 5%, S100 = 25%, E20 = 19%, E40 = 35%, E80 = 37%) and functional response (PBO = 30%, S100 = 58%, E20 = 53%, E40 = 67%, E80 = 64%). Outcomes at 24 h included sustained response (PBO = 14%, S100 = 34%, E20 = 33%, E40 = 42%, E80 = 48%), sustained pain-free rate (PBO = 3%, S100 = 15%, E20 = 11%, E40 = 22%, E80 = 26%), rescue medication use (PBO = 52%, S100 = 27%, E20 = 30%, E40 = 20%, E80 = 19%) and acceptability (PBO = 27%, S100 = 59%, E20 = 63%, E40 = 67%, E80 = 81%). Eletriptan (all doses) and S100 were superior to PBO (each outcome, $P < 0.001$). Adverse events were generally mild to moderate; comparable among E20, E40 and S100;

and higher with E80. Weighing tolerability and efficacy, patients found E40 and E80 to be more acceptable than S100.
Conclusions E40 and E80 demonstrated superior efficacy to S100 across primary and secondary endpoints and were more acceptable. E20 was comparable to S100. All active treatments were more effective than PBO.

P5N42

Safety assessment of topiramate in migraine prevention: pooled results from over 1500 patients

Jose Miguel Lainez*[1], Walter Neto[2] & David Jacobs[2]
[1]*Department of Neurology, Hospital Clinic Universitary,* [2]*Johnson & Johnson Pharmaceutical Research and Development*

Background The efficacy and safety of topiramate (50, 100 and 200 mg/day) was assessed across 4 double-blind, placebo-controlled studies. Safety measures from the 4 trials were pooled and analyzed.
Methods Safety assessments included clinical laboratory tests, incidence of adverse events, and body weight and vital sign measurements.
Results 1580 patients were included in the pooled safety assessment. The most common adverse events leading to discontinuation in patients treated with topiramate included paresthesia (7%), fatigue (4%), nausea (4%), difficulty with concentration (3%), and insomnia (3%). Although there were isolated reports of visual adverse events, there were no cases of acute myopia or secondary angle-closure. Most adverse events were mild or moderate and transient in nature. Patients lost weight at each dose of topiramate: –1.8 kg at 50 mg/day, –2.5 kg at 100 mg/day, and –2.8 kg at 200 mg/day from baseline. No patients died during the double-blind phase of treatment. There were no clinically significant mean changes in liver function, renal function, or hematology tests. There were no cases of hepatic failure or evidence of direct hepatotoxicity.
Conclusions Topiramate was safe for migraine prevention. The most common adverse event was paresthesia. Topiramate displayed a generally acceptable tolerability profile in these studies.

P5N43

Botulinum toxin A in the prophylactic treatment of migraine – a randomised, double-blind, placebo-controlled study

Sonja Schwaag*[1], Juliane Vollmer-Haase[1], Alexandra Rahmann[1], Achim Frese[1], Ingo-W. Husstedt[1] & Stefan Evers[1]
[1]*Department of Neurology, University of Muenster*

Botulinum toxin has been suggested to be effective in the prophylactic treatment of migraine. We performed a double-blind, placebo-controlled study with a specific focus on different injection sites.

Sixty patients with migraine were randomly assigned to receive either placebo or 16 U botulinum toxin in the frontal muscles and placebo in the neck muscles or in total 100 U botulinum toxin in the frontal and neck muscles. Observation period was three months.

In both verum groups, 30% of the patient showed a reduction of migraine frequency by at least 50%, in the placebo group 25% of the patients showed such a reduction ($P = 0.921$). There were no significant differences between the three study groups with respect to reduction of migraine frequency, number of days with migraine, and the number of total single acute doses. In the posthoc analysis, the reduction of all accompanying symptoms was significantly higher in the 16 U treatment group compared to the placebo group. Adverse events were mild and transient.

Our study did not show any efficacy of botulinum toxin in the prophylactic treatment of migraine. Future studies should focus on the efficacy of botulinum toxin in specific subgroups of patients rather than on a general efficacy.

P5N45

MT 300 is an effective, well tolerated injectable antimigraine therapy

Timothy Smith*[1]
[1]*Ryan Headache Center, Chesterfield, MO*

Objectives Compare the efficacy and safety of MT 300, a new injectable product containing a purified form of dihydroergotamine mesylate (DHE) in a prefilled syringe, with placebo for the acute treatment of migraine.
Methods Two randomized, placebo controlled studies were conducted in patients suffering acute migraine attacks. SQ treatment included MT 300 1 mg ($n = 618$) or placebo ($n = 611$). Primary efficacy was the percentage of subjects with a sustained pain response.
Results Sustained pain responses were significantly higher with MT 300 (36.8% and 33.5%) compared with placebo (18.8% and 21.0%; $P \leq 0.001$). In the subgroup of patients with severe pain at baseline (MT 300, $n = 219$; placebo, $n = 199$), significantly more MT 300 treated patients achieved sustained pain response (31.5% and 29.6%) compared with placebo (10.8% and 13.4%; $P \leq 0.017$). MT 300 adverse events occurred in no more than 6% of patients. In particular, nausea occurred in only 5% and 3% of MT 300 patients vs. 2% and 1% of placebo patients.
Conclusions MT300 is effective for the acute treatment of migraine. Unlike most products, its benefit over placebo was greater in patients with severe pain. Adverse events were reported less frequently than previously reported with older products containing other forms of DHE.

P5N46

Topical anticephalgic premedicated therapeutic mask. A report of a successful double-blind placebo-controlled study of a new treatment for migraines and/or tension headaches with associated frontalis myalgia and photophobia

Morton I. Hyson*[1]
[1]*University of Nevada School of Medicine*

Objective A placebo-controlled double-blind study was performed to determine the efficacy of a topical anticephalgic

premedicated mask in the treatment of migraine and/or tension headaches.

Design/methods The patients were given masks and numbered bottles of topical medication containing topical salicylates or placebo. They were instructed to apply the medication to their frontalis region in the event they should suffer a headache, put on the photoprotective mask, and lie down. Furthermore, they were instructed to take oral medications, if required, for relief of the headache. They subsequently filled out forms rating the degree of relief which they attributed to the topical medications and the masks using a 0–10 scale. They were also simply asked if this form of treatment helped or not.

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 ($P < 0.001$). 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 with associated frontalis pain. Not only did the patients receiving the active medication report significant relief from their headaches, they also noted the period of time during which they suffered from the headaches was reduced as was their need for oral analgesic and/or narcotic medications.

P5N47

Flunarizine and oxidative stress in migraine

I. Ciancarelli*[1], M. G. Tozzi-Ciancarelli[2], C. Di Massimo[2], C. Marini[1] & A. Carolei[1]
[1]*Department of Neurology – Regional Headache Center,* [2]*Laboratory of Applied Physiology, University of L'Aquila, L'Aquila, Italy*

Objectives The prophylactic action of flunarizine on migraine is currently linked to the associated relief of cerebral vasospam and to its powerful antioxidant properties. Vasoactive control of cerebral microcirculation is mediated by NO and by oxygen free radicals generated because of cerebral blood flow changes. In this study we investigated whether the antimigraine action of flunarizine might be ascribed to its influence on NO and oxidative markers.

Methods Twenty-five subjects suffering from migraine without aura and 25 healthy controls were examined. Urinary samples collected before and after treatment with flunarizine (5 mg orally per day for 6 months) were assayed for NO stable metabolites (NO_x) and thiobarbituric acid reactive substances (TBARS). Student's paired and unpaired *t*-tests were used for statistical analyses.

Results Urinary levels of NO_x (0.72 ± 0.15 vs. 0.30 ± 0.11 mmol/mmol creatinine; $P < 0.05$) and TBARS (0.43 ± 0.12 vs. 0.25 ± 0.08 µmol/mmol creatinine; $P < 0.05$) were higher in migraine sufferers before treatment than in controls. No differences were observed in NO_x values in migraine sufferers before and after treatment with flunarizine (0.72 ± 0.15 vs. 0.75 ± 0.10 mmol/mmol creatinine; $P = 0.413$). Urinary TBARS were decreased after flunarizine treatment with respect to levels measured before treatment (0.35 ± 0.07 vs. 0.43 ± 0.12 µmol/mmol creatinine; $P < 0.05$).

Conclusion Our results suggest that flunarizine is not involved in preventing NO-mediated vasodilation and do not support its action as NO-synthase inhibitor. However, flunarizine proves effective in limiting oxidative reactions in migraine sufferers.

P5N48

Socio-economic impact of migraine and other episodic headaches in France. Data from the GRIM 2000 study

André Pradallier*[1], Jean-Paul Auray[2], Abdelkader El Hasnaoui[3], Kazem Alzahouri[2], Jean-François Dartigues[4], Gérard Duru[2], Patrick Henry[5] & Michel lanteri-Minet[6] Christian Lucas[7], Guy Chazot[8], Anne-Francoise gaudin[3]
[1]*Hôpital Louis Mourier, Colombes, France,* [2]*Université Claude Bernard, Lyon, France,* [3]*Laboratoire GlaxoSmithKline, Marly le Roi, France,* [4]*Université de Bordeaux II, Bordeaux, France,* [5]*Hôpital Pellegrin, Bordeaux, France,* [6]*Hôpital Pasteur, Nice, France,* [7]*Hôpital Roger Salengro, Lille, France,* [8]*Hôpital Neurologique, Lyon, France*

The objective of this study was to determine the economic cost of migraine and nonmigraine headache in France. In 1999, 1486 headache sufferers were identified from a representative sample of 10 585 individuals in France, who provided data on healthcare resource consumption. Information on absenteeism and lost productivity was derived from the MIDAS migraine disability questionnaire. Costings were determined for physician consultations, hospitalisation, medication use and laboratory tests, and evaluated both from a societal and a healthcare system perspective. Total annual healthcare expenditure was ¤128 per subject in 1999, corresponding to ¤1044 million when extrapolated to all migraine sufferers in France. Around two-thirds of this cost accrued to the social security system (¤698 million). The principal cost element was physician consultations. The cost per patient rose steeply with increasing severity of headache. The total national annual cost of other forms of episodic headache was ¤125 million. The direct healthcare costs of migraine do not seem to have risen significantly over the past decade.

P5N49

Pain-free results of Sumatriptan 6 mg SC in the treatment of morning migraine

Michelle Lener[4], Paul Winner*[1], Jim Adelman[2], Sheena Aurora[3] & Michael Ames[4]
[1]*Palm Beach Headache Center, West Palm Beach, FL, USA,* [2]*Headache Wellness Center, Greensboro, NC, USA,* [3]*Swedish Headache Clinic, Seattle, WA, USA,* [4]*GlaxoSmithKline, Research Triangle Park, NC, USA*

Objectives To determine the pain-free efficacy of sumatriptan 6 mg SC in the acute treatment of migraine that is moderate or severe upon awakening.

Methods Subjects who were naive to treatment with a SC formulation, were randomized to sumatriptan 6 mg SC or

placebo to treat a single attack within 1 h of awakening with moderate or severe migraine pain. The primary endpoint was the percentage of subjects pain-free at 2 h postdose. Migraine-free relief (free from pain and associated symptoms), patient satisfaction, functional disability, and adverse events were also assessed.

Results **Results** of the individual trials were similar and combined in the following table. Significantly more patients treated with sumatriptan 6 mg than placebo were pain-free and migraine-free beginning 20 and 30 min postdose, respectively. 73% of subjects reported that they would use sumatriptan 6 mg again. The only drug related adverse event reported in = 5% of subjects in any treatment group was injection site reactions (5%). No serious adverse events were reported.

Conclusions Sumatriptan 6 mg SC is effective in providing pain-free relief of morning migraine.

	Results	
	Sumatriptan 6 mg SC ($N = 293$)	Placebo ($N = 291$)
% Pain-Free at 2 h	53%*	19%
% Migraine-Free at 2 h	49%*	17%
% Satisfied	69%*	33%

*$P < 0.001$

P5N50

Sumatriptan 100 mg vs. 50 mg: pain-free efficacy and tolerability across 5 trials

Mary Richardson[2], Paul Winner*[1], Michael Ames[2], Laura Lisk[3] & Martin Jones[3]
[1]*West Palm Beach Headache Center, West Palm Beach, FL, USA,* [2]*GlaxoSmithKline, Research Triangle Park, NC, USA,* [3]*GlaxoSmithKline, Greenford, England, UK*

Objectives To evaluate the efficacy and tolerability of 100 mg vs. 50 mg sumatriptan administered when migraine pain is mild

Methods A combined analysis of double-blind trials where patients received oral sumatriptan 100 mg, 50 mg or placebo during the mild pain phase of a single migraine attack where freedom from pain at 2 h was the primary efficacy endpoint was performed. A weighted average of the estimated odds ratios within each trial was computed. Consistency across trials was explored.

Results The data set included 1865 patients from 5 studies (100 mg = 617; 50 mg = 634; placebo = 614). In all 5 studies, sumatriptan 100 mg and 50 mg provided superior pain-free relief compared to placebo at 2 h. When data from the studies were combined, sumatriptan 100 mg provided pain-free relief in significantly more subjects than 50 mg or placebo (57% vs. 49% and 25%; $p < 0.05$ for both). Sumatriptan was well tolerated. The combined incidence of drug-related AEs was 4%, 10% and 16% (placebo, 50 mg, 100 mg, respectively).

Conclusions Treatment of migraine at the first sign of pain with sumatriptan 50 mg and 100 mg tablets provides consistent superior pain-free relief at 2 postdose compared with placebo.

P5N51

Comparison of pharmacokinetics and safety of Frovatriptan 2.5 mg in adolescents and adults

Andrew Wade[2], Arthur Elkind*[1] & Robert Shaw[2]
[1]*Elkind Headache Center, Mount Vernon, New York, USA,* [2]*Vernalis Ltd, Winnersh, United Kingdom*

Background and objectives Frovatriptan is approved for the acute treatment of migraine in adults. The current study compared the pharmacokinetics and safety of frovatriptan in adolescent migraineurs with (historical) data in adults.

Methods subjects (10 male, 10 female migraineurs aged 12–17 years) were randomized to frovatriptan or placebo stratified by sex and age group (12–14, 15–17) in the ratio of 5 : 1 within each stratum. Blood concentrations of frovatriptan were measured (0–48 h) and vital signs, ECG and adverse event data collected predose, during the study and at 7 days.

Results Frovatriptan 2.5 mg was well tolerated with no safety concerns. Despite greater interindividual variability in adolescents, exposure to frovatriptan was similar to that in adults but with a trend to 20–30% lower exposure. The gender difference (higher exposure in females) and long half-life seen in adults were also observed in adolescents.

Conclusion The pharmacokinetics of frovatriptan 2.5 mg were similar in adolescents (12–14 years and 15–17 years) and adults. Frovatriptan 2.5 mg was well tolerated in adolescent migraineurs.

P5N52

Placebo-controlled comparison of efficacy of effervescent acetylsalicylic acid (ASA) and sumatriptan on accompanying symptoms of migraine attacks

Astrid Eikermann*[1], H. C. Diener[1], M. Voelker[2] & U. Gessne[3]
[1]*University of Essen, Essen, Germany,* [2]*Bayer AG, Leverkusen, Germany,* [3]*Bayer Vital Gmbh, Cologne, Germany*

Recently developed effervescent ASA tablets with high buffering capacity have beneficial effect on migraine accompanying symptoms. In this double-blind, three-armed, multicenter, parallel group study 433 patients were treated either with 1000 mg ASA effervescent or 50 sumatriptan or placebo. Primary objective was the percentage of patients with complete remission of the three accompanying symptoms nausea, photophobia and phonophobia within 2 h 43.8% of patients treated with ASA, 43.7% of patients treated with sumatriptan and 30.9% of patients treated with placebo showed complete remission of all three accompanying symptoms ($P < 0.05$ for ASA and sumatriptan vs. placebo). The percentage of patients with reduction in headache severity from moderate or severe to mild or no pain (secondary objective) was 49.3% for ASA, 48.8% for sumatriptan and 32.9% for placebo. All active treatments were superior to placebo ($P < 0.05$). 25.3%, 24.4% and

14.5% of patients treated with ASA, sumatriptan or placebo were pain-free at 2 h. Drug-related adverse events were reported in 3.9%, 4.7% and 6.7% of patients treated with placebo, ASA or sumatriptan. The study showed that administration of effervescent ASA leads to remission of migraine symptoms nausea, photophobia and phonophobia, reduces migraine headache and is as effective as sumatriptan.

P5N53

'Switching' behaviors in longitudinal use of triptans

Marcelo Bigal* [1,2], Stewart Tepper [2,3], Alan Rapoport [2,4], Michele Feleppa[5] & Fred Sheftell [2,6]
[1]*Albert Einstein College of Medicine, Bronx, NY, USA,* [2]*The New England Center for Headache, Stamford, USA,* [3]*Yale University School of Medicine, New Haven, CT, USA,* [4]*Department of Neurology, Columbia University College of Physicians and Surgeons, New York, NY, USA,* [5]*Primario Unita Operativa di Neurologia e Neurofisiopatologia A. O 'G. Rummo', Benevento, Italy,* [6]*New York Medical College, New York, NY, USA*

Objective To evaluate the patterns of triptan use by migraine sufferers who used more than one triptan at a speciality headache center.
Methods Clinical records and calendars from migraine sufferers who used more than one triptan/formulation (TF), presenting to a tertiary care headache center, were reviewed.

We assessed (1)Number of subjects who switched from one TF to another and returned to the initial one; (2)Number of subjects who switched formulations and did not return; (3)The last triptan used.
Results We evaluated 386 patients. The mean follow-up period was 3.3 years. From those subjects that used sumatriptan SC and were switched to a different TF, 19.5% returned to sumatriptan SC; for the other TF, the percentages were: sumatriptan 25 mg, 7.8%; sumatriptan 50 or 100 mg, 42.3%; sumatriptan NS, 17.7%; zolmitriptan, 17.6%; rizatriptan, 16.5%; naratriptan: 9.4%. For those who used more than 3 TF, the last triptan used was: sumatriptan, 29.5%; zolmitriptan, 31.8%; rizatriptan, 25.0%; naratriptan, 12.5%. Different formulations of sumatriptan were used by 129 (33.4%) subjects. For those who used sumatriptan as the first triptan, it was also the last triptan used in 53.8% of them.
Conclusions Switching behaviors are governed by patient satisfaction based on combined attributes of triptans.

P5N54

Patient satisfaction with oral Naratriptan for intermittent prophylaxis of menstrually associated migraine (MAM): results from two double-blind, placebo-controlled, parallel group studies

Jan Brandes*[1], Naren Savani[2], W. Jacqueline Kwong[3], Steve Shackleford[3] & Diane Boswell[4]
[1]*Nashville Neuroscience Group, Nashville, TN, USA,* [2]*MeDiNova Research; Northwood, Middlesex, UK,* [3]*GlaxoSmithKline, RTP, NC, USA,* [4]*GlaxoSmithKline, Greenford, UK*

Objective Assess patient satisfaction with oral naratriptan for intermittent MAM prophylaxis.
Methods 630 women with MAM participating in two identical multicenter, randomized, double-blind, placebo-controlled studies received placebo or naratriptan 1 mg BID for 6 days starting 3 days before the expected onset of MAM for 4 perimenstrual periods or up to 6 months. Satisfaction with study medication in preventing occurrence, reducing the number, duration and severity of attacks, pain intensity, pain duration, associated symptoms, need for bedrest, helping control migraine attacks, and overall satisfaction was assessed using a 7-point scale before randomization and at study end.
Results Satisfaction ratings were similar between groups before randomization. At study end, significantly ($P < 0.05$) more women receiving naratriptan than placebo reported to be very satisfied/satisfied with study medication in terms of preventing occurrence (44% vs. 29%), reducing number (47% vs. 34%), severity (44% vs. 35%), duration (42% vs. 35%) of attacks, reducing pain intensity (42% vs. 34%), pain duration (40% vs. 32%), nausea (30% vs. 24%), aura (12% vs. 9%), need for bedrest (31% vs. 28%), helping control of migraine attacks (45% vs. 39%), and overall satisfaction (46% vs. 37%).
Conclusion Satisfaction results show that naratriptan is effective and well-tolerated in prophylaxis of MAM.

P5N55

Naratriptan vs. placebo for intermittent prophylaxis for menstrually associated migraine (MAM): analyses of migraine-free days

Jan Brandes*[1], Naren Savani[2], Claire Alderton[3], Michael Ames[4] & Timothy A. Kuhn[4]
[1]*Nashville Neuroscience Group, Nashville, TN, USA,* [2]*MeDiNova Research; Northwood, Middlesex UK,* [3]*GlaxoSmithKline, London, UK,* [4]*GlaxoSmithKline, Research Triangle Park, NC, USA*

Objective To compare the efficacy of naratriptan vs. placebo for intermittent prophylaxis for MAM.
Methods Women reporting regularly occurring MAMs were eligible for two randomized, double-blind, placebo-controlled, international studies. MAM was defined as a migraine beginning during the perimenstrual period (PMP: Day −2 through Day + 4 with onset of menses as Day 1). Women experiencing MAM during the placebo controlled baseline period were randomized to naratriptan 1 mg BID or placebo starting 3 days before expected MAM onset and continuing for 6 days. The primary endpoint was the percentage of PMPs without MAM per woman. Given that the PMP included days when women did not receive study drug, we determined the percentage of women who did not experience migraine on days they received study drug.
Results The intent-to-treat population included women who treated at least one PMP with study drug (311 placebo, 322 naratriptan). The percentage of women who did not experience migraine on the days they received study drug during the first treated PMP was 38% for naratriptan and 20% for placebo ($P < 0.05$).
Conclusion Significantly more women did not experience migraine while receiving naratriptan 1 mg BID for 6 days for intermittent prophylaxis for MAM than placebo.

P5N56

Cardiovascular safety and pharmacokinetics of almotriptan: a randomized, double-blind, placebo-controlled, crossover clinical trial in healthy volunteers

Miquel Salvà*[1], Josep M. Jansat[1] & Antonio Martínez-Tobed[1]
[1]*Almiral Prodesfarma, S.A., Barcelona, Spain*

Objective To assess possible cardiovascular effects of single ascending oral doses of almotriptan and its correlation with the rate and extent of absorption.
Methods In this phase I, randomized, double-blind, placebo-controlled, crossover clinical trial, 24 healthy volunteers (12 females, 12 males) received single oral doses of almotriptan 12.5 mg (therapeutic dose), 25 mg and 50 mg. Almotriptan plasma levels were determined by HPLC and UV detection at 227 nm with the aid of an automated online solid–phase extraction and injection procedure. Cardiovascular safety assessment included, among other variables, QT interval and QT dispersion study from 12-lead ECG.
Results From the results it was demonstrated that the pharmacokinetics of almotriptan is dose- and time-independent, with a linear pharmacokinetic behavior at studied doses. Plasma levels of almotriptan increased proportionally with dose, and mean half-life was around 3 h. There were no statistically significant differences between men and women (except AUC at high dose). There were no clinically relevant cardiovascular findings, thus correlation between plasma levels of almotriptan and cardiovascular effects was not studied.
Conclusions The pharmacokinetics of almotriptan is linear within the studied dose range. Almotriptan did not cause clinically relevant cardiovascular effects.

P5N57

Influence of botulinum toxin treatment on previous primary headaches in patients with cranio-cervical dystonia

Julio Pascual*[1]
[1]*Service of Neurology, University Hospital Marqués de Valdecilla (UC), Santander, Spain*

Background Preliminary data suggest some beneficial effects of botulinum toxin type A (BT) on primary headaches.
Objective To analyse the subjective influence of BT on previous primary headaches of those patients receiving this treatment due to a variety of cranio-cervical dystonia (CD).
Methods All patients receiving BT due to CD were interviewed with and ad hoc questionnaire on the presence or not of headaches prior to BT treatment. Diagnosis and subjective effects of BT on these previous headaches were recorded.
Results Thirty-seven patients (27 females) were interviewed; 21 (18 women) referred to a history of previous primary headache (9 migraine, 8 episodic tension headache and 4 chronic daily headache). Eight (38%) referred to a sustained response (> 50% reduction in headache frequency) since the beginning of BT treatment. Patients with cervical dystonia or receiving doses > 50 U showed the best responses. Age, sex, pain location, duration of BT treatment and headache diagnosis did not seem to correlate with response.
Conclusions BT seems to have a dose-related beneficial effect on primary headaches of some patients with CD.

P5N58

Menstrual and premenstrual migraine – our clinical experience

David Dolezil*[1], Monika Mrazkova[1] & Irena Jezkova[1]
[1]*Department of Neurology, University Hospital Ostrava, Czech Republic*

Objective To investigate menstrual (MM) and premenstrual migraine (PM) in females with headache.
Methods The study population consisted of 94 females with headache connected with menses recruited out of 354 females with headache seen between 1999 and 2002. For diagnosis of headache the criteria of the International Headache Society were used.
Results Only 12 females suffer from true menstrual migraine (TMM) without other type of headaches.1 female had TMM and headache associated with neck disorder. 1 female had migraine with aura. Only 2 females were taking a oral contraceptives. All of the females with TMM were taking triptans for acute treatment with very good response.8 patients were taking preventive treatment (4 times NSAIDs, twice gabapentin, twice valproate) with very good response. 4 patients were without preventive treatment. Other 82 females suffer from MM, PM and other type of migraine and 6 of them had chronic daily headache. Only 4 patients were taking analgesics and antiemetics, the rest was taking triptans. The most frequent migraine triggers were alcohol, weather change and stress.
Conclusion TMM occurs in 13% of females with headache connected with menses. The treatment with triptans and preventive treatment was successful.

P5N59

Clinical characteristics of patients referred to headache specialists in Canada

Werner J. Becker*[1], Rose Giammarco[2], Suzanne Christie[3], Marek Gawel[4], Arnolda Eloff[1] & Michel Aube[5]
[1]*University of Calgary, Calgary,* [2]*McMaster University, Hamilton,* [3]*University of Ottawa, Ottawa, Canada,* [4]*University of Toronto, Toronto,* [5]*McGill University, Montreal, Canada*

Objective To study the clinical features and treatment changes for new patients referred to headache specialists.
Methods The Canadian Headache Outpatient Registry and Database (CHORD) was deployed to four headache centres in Canada (Calgary, Hamilton, Ottawa, and Toronto) and used to study patients referred to headache specialists.
Results Data was available for 566 new referrals, average age 42. 77% were female, 71% had a migraine diagnosis (including 32% with transformed migraine). 53% of patients in the database had headache on > 14 days/month, and 24% of all patients had medication overuse. 21% of medication overusers were triptan overusers.

Triptans were taken by 15% of patients at referral and were prescribed for 44% by the specialist. Prophylactics were taken at referral by 12% and prescribed for 56%.

Conclusions The majority of patients referred to headache specialists received a migraine diagnosis. One quarter of all patients referred were medication overusers and triptan overuse was common. For all patients with headache on > 14 days a month, less than half overused medication. This was also true for patients diagnosed with transformed migraine. Common interventions by the headache specialist included prescription of a triptan and a prophylactic medication.

P5N60

Zolmitriptan produces very high headache response rates in 'typical' migraineurs

Andrew Dowson*[1], Bruce Charlesworth[2] & Graham Wilson[3]
[1]*The King's Headache Services, London, UK,* [2]*AstraZeneca, Macclesfield, UK,* [3]*AstraZeneca R & D Södertälje, Södertälje, Sweden*

Objectives To evaluate the efficacy of zolmitriptan 5 mg nasal spray in subgroups of patients representing those typically seen in clinical practice, and assess the influence of baseline characteristics on response to treatment.

Methods Analyses were performed on 2-h headache response (HR) data obtained from 2 studies: study A – a placebo-controlled study of patients ($n = 235$) treating 2 moderate or severe migraine attacks ($n = 438$) with zolmitriptan 5 mg nasal spray; study B – 1-year extension of study A with patients ($n = 783$) treating attacks ($n = 10\,507$) of any baseline intensity.

Results In study A, the 2- h HR rate for zolmitriptan nasal spray was 70.3% in all patients and 71.7% in female patients. Two-hour HR rates in female patients aged 18–39 years with or without aura were 83.3% and 73.7%, respectively. Female patients with migraine duration typically < 12 h also showed a very high HR rate (84.6%). Data from study B showed that 2- h pain-free rates were highest in patients who treated headaches of mild baseline intensity (73.6%–78.9%), followed by those with moderate (54.0%–58.4%) or severe (33.9%–38.1%) baseline intensity.

Conclusions Zolmitriptan 5 mg nasal spray demonstrated high efficacy across various patient populations, especially in subgroups of patients representing those typically seen in clinical practice.

P5N61

Effects of the CGRP-receptor antagonist BIBN4096BS in experimental migraine models

Kirsten Arndt*[1], Stefan Just[1] & H. Doods[1]
[1]*Boehringer-Ingelheim Pharma KG, Department of CNS Research, Biberach, Germany*

Meningeal vasodilation has been hypothesized as a major cause underlying migraine pain. The physiological trigger of migraine-associated vasodilation is still elusive but evidence suggests an important role of the neuropeptide calcitonin gene-related peptide (CGRP). At this meeting Olesen et al. will be underlining the concepts value by presenting data of the 'proof of concept' trial for migraine pain of the first high-affinity CGRP antagonist BIBN4096BS.

Here, we demonstrate the *in vivo* efficacy of the high-affinity CGRP-antagonist BIBN4096BS (1) in migraine animal models. Facial blood flow changes (FBF) were experimentally induced by electrical stimulation of the trigeminal ganglion or the brainstem. FBF changes were monitored by Laser-Doppler flowmetry. Results show that BIBN4096BS reverses the neurogenically evoked vasodilation in marmoset monkeys and rats with ED_{50}s of 0.003 and 0.1 mg/kg, respectively, reflecting species selectivity of the compound. Furthermore, we show that BIBN4096BS fully reverses the induced FBF in marmoset monkeys, while sumatriptan and zolmitriptan display lower maximal efficacy. Together, these data demonstrate that BIBN4096BS is a potent and highly efficacious compound in migraine animal models.

Reference

1 Doods, H. et al. Br J Pharmacol, 2000. 129(3): 420ff.

P5N62

Zolmitriptan nasal spray exhibits rapid absorption, and similar relative bioavailability to the tablet formulation, in healthy Japanese subjects

Naoto Uemura*[1,2], Tatsuo Onishi[3], Akira Mitaniyama[2], Takeshi Kaneko[4], Koji Ninomiya[4], Koichi Nakamura[5] & Masao Taneno[2]
[1]*University of California, San Francisco, USA,* [2]*Clinical Pharmacology Centre, Niiza Shiki Central General Hospital, Saitama, Japan,* [3]*AstraZeneca KK, Osaka, Japan,* [4]*Japan Clinical Pharmacology Laboratories, Ltd, Saitama, Japan,* [5]*Oita Medical University, Oita, Japan*

Objectives To assess the safety and relative bioavailability of zolmitriptan nasal spray and conventional tablet formulations in healthy Japanese subjects.

Methods In an open, randomised, 2-way crossover study, 48 subjects (32 female) received 2 formulations of zolmitriptan separated by a 2-day washout period. Group 1 ($n = 24$) received one spray and one tablet of zolmitriptan 2.5 mg, while group 2 ($n = 24$) received one spray (5 mg) and two tablets (2.5 mg) of zolmitriptan.

Results Both zolmitriptan formulations and doses were well tolerated and rapidly absorbed. Zolmitriptan was detectable in the plasma after only 2 min with the nasal spray compared to 10 min with the tablet. The ratios of the mean AUCs for nasal spray: tablet were 0.924 (90% CI 0.826–1.033) and 0.960 (90% CI 0.865–1.066) for the 2.5 and 5 mg dose, respectively. The mean elimination half-life was similar for both formulations and doses, ranging between 2.6 and 3.0 h.

Conclusions Zolmitriptan nasal spray was well tolerated and showed a relative bioavailability close to 100% of that of the tablet formulation in healthy Japanese subjects. The detection of zolmitriptan in the plasma as early as 2 min after intranasal dosing suggests a faster onset of action.

P5N63

Topiramate in migraine prophylaxis: results of a double blind placebo controlled study

Alessandro Capuano*[1], Daniele Mei[1,2], Catello Vollono[1], Maurizio Evangelista[1], Diana Ferraro[1] & Girolamo Di Trapani[1]
[1]*Center for the Study of Headaches – Policlinico 'A.Gemelli' – Rome,* [2]*Center for the Study of Headaches – Italian Hospital Group, Guidonia, Rome*

The theory that migraine is the result of neuronal hyperexcitability and the search for prophylactic drugs that are more efficacious in limiting the number of crises and better tolerated, justifies the attempt to use new antiepileptic drugs for the prophylaxis of this pathology which has a great importance due to its high prevalence and due to the disability it causes in part of the sufferers.

In this work we present the results of a randomized double-blind vs. placebo study on the efficacy and tolerability of topiramate in the prophylactic treatment of migraine.

The sample consists of 50 subjects suffering from migraine with and without aura in accordance with the IHS criteria. After randomization, 30 subjects were treated with topiramate in increasing dosages until a maximum of 100 mg a day was reached while the other group, consisting of 20 subjects, was given placebo.

The study was lead in double-blind and it lasted 15 weeks.

At the end of the study we recorded a significant reduction in the monthly frequency and in the intensity of the crises with minimal and transitory side-effects.

Topiramate has thus proven its efficacy in the prophylaxis of migraine with and without aura.

P5N64

Naratritptan vs. naratriptan plus naproxen: a comparison of headache recurrence rates

Hartmut Göbel*[1], Vera Zumbroich[1], Axel Heinze[1] & Katja Heinze-Kuhn[1]
[1]*Kiel Pain Clinic, Kiel, Germany*

Objectives This study investigated whether the headache recurrence rate in patients treating their migraine attacks regularly with Naratriptan could be reduced by adding Naproxen, a NSAID with a long half-life.
Methods 50 patients of the Kiel Pain Clinic fulfilling the IHS-criteria for migraine with/without aura who were regularly using Naratriptan as acute medication and who had experienced headache recurrence in at least 50% of the last 10 attacks were included in the study. According to the open cross-over study design patients treated one migraine attack with Naratriptan and one with Naratriptan plus Naproxen 500 mg. The sequence of treatment was randomised. Headache intensity, AEs and headache recurrence were documented in a diary.
Results A significant higher number of patients experienced a reduction of moderate/severe headache to mild/none within 4 h when taking the combination of Naratriptan plus Naproxen compared to Naratriptan alone (48/50 vs. 36/50). Of these responders significantly less patients reported headache recurrence within 24 h when adding Naproxen to Naratriptan (4/48 vs. 18/36). The few and mild AEs were similar in both treatment regimes and obviously due to Naratriptan.
Conclusions By adding Naproxen to Naratriptan in patients prone to headache recurrence, the recurrence rate can be reduced effectively.

P5N65

Previous use of Sumatriptan influences treatment response in clinical trials

Richard Lipton*[1], Jayasena Hettiarachchi[2], Carolyn Sikes[2] & Michel Ferrari[3]
[1]*Albert Einstein College of Medicine, bronx, USA,* [2]*Pfizer Inc., New York, USA,* [3]*Leiden University Medical Center, Leiden, the Netherlands*

Background Prior exposure to sumatriptan has been suggested as a cause of variability in treatment response in triptan clinical trials.
Methods Data were combined from two trials in which patients were categorized as being either sumatriptan experienced (suma-experienced) or untreated with sumatriptan for at least the previous six months (suma-NE). This exploratory analysis evaluated headache response and pain-free response at 2 h on eletriptan 40 mg ($n = 957$, 58% suma-NE) vs. sumatriptan 100 mg ($n = 960$, 56% suma-NE) vs. placebo ($n = 561$, 54% suma-NE).
Results In the suma-experienced and suma-NE samples, respectively, headache response rates were significantly higher in patients treated with sumatriptan (63% vs. 54%; $P < 0.01$), but were not significantly different with eletriptan (70% vs. 65%) or placebo (23% vs. 28%). Reduction in suma response was correlated with recency of exposure. Pain-free rates were not significantly different for eletriptan (37% vs. 34%), sumatriptan (29% vs. 24%) and placebo (5% vs. 6%). There was no difference in adverse event rates by sumatriptan-exposure status.
Comment The results of this analysis suggest that previous exposure to sumatriptan influences sumatriptan efficacy in clinical trials.

P5N66

Assessment of chronic migraine headache disability

Marcelo Bigal*[1], David Dodick[2], Chris Kozma[3], Ron DeGryse[3], Rozalina Dimitrova[3] & Richard Lipton[1]
[1]*Albert Einstein College of Medicine, Bronx, New York, USA,* [2]*Mayo Clinic Scottsdale, Scottsdale, AZ, USA,* [3]*Allergan, Inc., Irvine, CA, USA*

Objective To measure the headache-related disability in subjects with chronic migraine.
Methods Subjects from two clinical trials of preventive therapy who had ≥ 16 headache days/month had their disability assessed by the Migraine Disability Assessment (MIDAS) Questionnaire.
Results Of 406 subjects, of which the majority were chronic migraine sufferers (81.8% female, with 43.8 ± 10.6 years), 375 completed the MIDAS questionnaire. In the previous 3 months they had headaches on a mean of 64.1 days, missed

3.5 days of paid work or school and had 12.9 days of reduced productivity at work or school. Household work was missed for 12.8 days and was reduced 50% or more on 15 days; family or social activities were missed in 7.6 days. Overall, performance was affected on 52.6 days. Most had severe disability (72.8%, MIDAS IV) (7.5% had little or no disability [MIDAS I]; 6.1% had mild disability (MIDAS II), 13.6% had moderate disability).

Conclusions Subjects with chronic migraine demonstrate high levels of disability. These patients experience severely reduced productivity at work and limitations in other domains as compared to those who suffer from episodic migraine as previously reported in the literature.

P5N67

Zolmitriptan nasal spray improves patient satisfaction by providing fast and effective relief from migraine symptoms

Carl Dahlöf*[1], Steen Boes-Hansen[2] & Andrew Dowson[3]
[1]*Gothenburg Migraine Clinic, Gothenburg, Sweden,* [2]*Kronobergskliniken, Vaxjo, Sweden,* [3]*The King's Headache Services, London United Kingdom*

Objectives To determine patient satisfaction with zolmitriptan nasal spray during long- and short-term studies and in clinical practice.

Methods Patient attitudes to treatment with zolmitriptan 5 mg nasal spray were assessed in: a randomised, placebo-controlled study where patients ($n = 235$) treated = 3 moderate or severe migraine attacks; a 1-year extension of this study where patients ($n = 783$) treated attacks of any baseline intensity; two surveys of migraineurs ($n = 175$ in an interim analysis and $n = 120$) prescribed zolmitriptan nasal spray in clinical practice.

Results Patient satisfaction with zolmitriptan 5 mg nasal spray was rated as good or excellent by 58% of patients during the short-term study and increased to 70% of patients during the long-term extension study. The two patient surveys showed that patients were highly satisfied with zolmitriptan nasal spray, with 71% and 81% choosing to continue with this treatment. The most common reasons for wanting to continue treatment with zolmitriptan nasal spray were fast onset, effectiveness, fewer side-effects and fast return to normal function.

Conclusions Clinical trials show that most patients are highly satisfied with zolmitriptan nasal spray for the acute treatment of migraine. This high satisfaction is borne out in clinical practice, with most patients choosing to continue treatment with zolmitriptan nasal spray.

P5N68

Eletriptan in the treatment of migraine: a comprehensive review of tolerability and safety

Jayasena Hettiarachchi*[1], Ninan Mathew[2] & Jeffrey Alderman[1]
[1]*Pfizer Inc., New York, USA,* [2]*Houston Migraine Clinic, Houston, Texas, USA*

Objective To provide a comprehensive review of the safety and tolerability of eletriptan.

Background Eletriptan, a potent and selective 5-$HT_{1B/1D}$ agonist, is efficacious in the acute treatment of migraine at 20 mg, 40 mg and 80 mg. Despite individual reports, no comprehensive review summarizes the overall safety and tolerability of eletriptan.

Methods Tolerability and safety analyses across the eletriptan development program were reviewed, encompassing > 74 000 migraine attacks in > 11 000 patients throughout the world. In most studies, adverse events (AEs) were recorded concurrently in patient diaries, and standard ECG, laboratory and vital signs data were obtained.

Results Eletriptan was safe and well tolerated across its dosing range, with AEs at the 40-mg dose all within 2% of placebo. Eletriptan was safe and well tolerated regardless of age, sex, concomitant therapy, long-term treatment or coadministration with potent CYP3A4 inhibitors. High intravenous eletriptan doses resulted in no clinically meaningful difference from placebo or standard-dose sumatriptan in angiographically assessed coronary artery diameter.

Conclusions This comprehensive review demonstrates that eletriptan is safe and well tolerated, with a high therapeutic index, indicating that relatively large changes in dose are associated with minimal changes in tolerability.

P5N69

Efficacy of Eletriptan in patients who were dissatisfied with prior medications for acute treatment of migraine: Switch Studies

Soeren Rasmussen*[1], Joao Siffert[1] & Paul Tiseo[1]
[1]*Pfizer Inc., New York, USA*

Objective To assess the efficacy of eletriptan 40-mg (E40) for acute treatment of migraine in patients dissatisfied with NSAIDs, Fiorinal™/Fioricet™ ('FF': butalbital, caffeine, aspirin/acetaminophen), Excedrin Migraine® ('EM': acetaminophen, aspirin, caffeine), or Imigran/Imitrex (sumatriptan).

Methods First-attack, first-dose data were reviewed from four similarly designed studies in which patients dissatisfied with a medication listed above treated a moderate-to-severe migraine with E40. The principal reason for dissatisfaction was lack of efficacy. The primary efficacy assessment was 2-h headache response. Where available, secondary outcomes are provided.

Results Two-hour headache response rates with E40 in patients dissatisfied with other medications were: NSAIDs = 66%, FF = 72%, EM = 81%, sumatriptan = 59%; pain-free rates were: NSAIDs = 25%, FF = 33%, EM = 48%, sumatriptan = 35%.

Functional response rates were NSAIDs = 70%, FF = 73%, EM = 82%. E40 relieved associated symptoms: nausea (NSAIDs = 59%, EM = 76%, sumatriptan = 51%), photophobia (NSAIDs = 70%, EM = 74%), and phonophobia (NSAIDs = 67%, EM = 80%). By 24 h, rescue medication was used by: NSAIDs = 10%, FF = 20%, EM = 16%, sumatriptan = 24%; headache recurrence rates were: NSAIDs = 24%, FF = 17%, EM = 9%, sumatriptan = 26%.

Sustained response rates were NSAIDs = 52%, FF = 59%, EM = 68%, sumatriptan = 39%; sustained pain-free rates were: NSAIDs = 22%, FF = 30%, EM = 39%, sumatriptan = 25%. Adverse events were generally mild-to-moderate and transient.

Conclusion Eletriptan was effective in relieving migraine pain and associated symptoms with good tolerability in patients who previously had unsatisfactory treatment on medications commonly utilized for headache and sumatriptan.

P5N70

Cardiac clearance guideline for migraineurs

Jan Brandes*[1], Susan Roberson[1] & George Scoville[2]
[1]*Nashville Neuroscience Group, P.C., Nashville, TN, USA,* [2]*The Heart Group, Nashville, TN, USA*

Objectives To report long-term cardiac safety experience with triptans and propose guidelines for cardiac clearance in migraineurs.

Background No official cardiac screening guidelines have been proposed for migraineurs despite the need for migraineurs to have migraine specific therapy and to continue triptan therapy as they develop cardiovascular risk factors over the course of their disorder.

Methods Review of 540 patient outcomes was performed. Patients were stratified on the basis of cardiovascular risk factors and known contrain dications to $5HT_{1B\text{-}1D}$ agonists.

Results Treatment outcomes and cardiovascular events will be presented within stratified groups. Data will be discussed on the basis of triptan-related outcomes.

Conclusions Stratification of patients with cardiac risk factors allows for cardiac evaluation based on need. The study suggests the utility of guidelines for cardiac clearance prior to or in the setting of ongoing triptan use in migraineurs. Based on age, risk factors, and IHS migraine characteristics, specific guidelines for triptan cardiac clearance are proposed.

P5N71

Migraine associated to high plasmatic homocysteine levels

Vincenzo Pizza*[1], Domenico De Lucia[2], Giampiero Volpe[1], Umberto Ruggiero[3], Eros Lamaida[1], Anella Agresta[1], Renato de Magistris[5], Alfredo Bianchi[4] & Cesare Colucci d'Amato[3]
[1]*Neurophysiopatoly Service, S. Luca Hospital, Vallo della Lucania (SA),* [2]*Laboratory of Haemostasis and Thrombosis, 2nd University, Naples, Italy,* [3]*Department of Neurological Sciences, 2nd University, Naples, Italy,* [4]*Pharmacology Department, Faculty of Medicine, Catania University,* [5]*1st Surgery Clinic, 2nd University, Naples, Italy*

Objective The aim of our work was to evaluate, in a sample of subjects with migraine, the plasmatic levels of copper, iron, folate, B-12 vitamin and homocysteine. Besides, in hyperhomocysteinemic patients we gave an additional therapy evaluating its efficacy.

Materials and methods 150 consecutive patients (112 women), average age 37.4 (SD 16.8), suffering from migraine with aura (26) and without aura (124) (IHS '88 criteria) were studied and 50 patients with basal hyperhomocysteinemia we gave B12 vitamin and folate for 60 days.

Results We found basal blood hyperhomocysteine in 24% of patients (55% EWA, 45% EwA) with blood values of folates and B12 vitamin lower and normal of copper and iron. Anova test made at follow-up, comparing the migraine indexes of treated subjects to those of controls and both to respective basal values, showed every time significant ($P < 0.05$) differences in patients treated and basal blood homocysteine levels were reduced of 40%.

Conclusions Our data are proving that the administration of folates and B12 vitamin is able to produce a reduction of the migraine index and homocysteine plasmatic levels. Therefore, the homocysteine, by a modification of vasoactive endothelial factors (especially NO and thrombomoduline), could play an important role in migraine.

P5N72

Quality of life measures from a large, randomized, double-blind, placebo-controlled study of Topiramate in migraine prevention

Merle Diamond*[1], Walter Neto[2], David Jacobs[2], Diane Fairclough, Pamela Wolfe & George Papadopoulous[2]
[1]*Diamond Headache Clinic,* [2]*Johnson & Johnson Pharmaceutical Research and Development*

Objective To assess patient health-related quality of life (HRQoL) associated with the use of topiramate in migraine prevention.

Background Initial results from three large controlled trials, consisting of approximately 1500 subjects, indicates that topiramate was associated with significant reductions in monthly migraine frequency.

Design/methods The impact of topiramate treatment on HRQoL was assessed using the Medical Outcomes Study Short-Form 36 (SF-36) and the Migraine-Specific Quality-of-Life questionnaire (MSQ). The primary measures were the Role-Restrictive and Role-Preventive subscales from the MSQ and RP and VT subscales from the SF-36.

Results 468 patients, allocated to 4 treatment groups (placebo, TPM 50 mg/day, TPM 100 mg/day, TPM 200 mg/day), made up the intent-to-treat population. The MSQ Role-Restrictive and Role-Preventive subscales were significantly improved at all TPM doses relative to placebo ($P \leq 0.019$). Significant improvement was also shown in the MSQ Emotional Function subscale at 100 or 200 mg/day TPM ($P < 0.001$). The SF-36 Role-Physical subscale was significantly improved in both the 100 and 200 mg/day groups ($P \leq 0.022$).

Conclusions This study supports the results of a concurrently run study (MIGR-001), demonstrating that treatment with TPM is associated with significant improvements in HRQoL measures.

P5N73

Zolmitriptan nasal spray is highly efficacious and very fast acting in the treatment of acute migraine in a real-life setting: results from phase I of the REALIZE study

Jürgen Aschoff*[1], Marek Gawel[2], John Lee[3] & Bruce Charlesworth[4]
[1]*Department of Neurology, University of Ulm, Ulm, Germany,* [2]*Department of Medicine (Neurology), University of Toronto, Toronto, Canada,* [3]*AstraZeneca, Södertälje, Sweden,* [4]*AstraZeneca, Macclesfield, Sweden, on behalf of the REALIZE study group*

Objectives To compare the efficacy and tolerability of zolmitriptan 5 mg nasal spray with placebo nasal spray in migraine attacks of any intensity, treated at any time during an attack.
Methods Efficacy and tolerability of zolmitriptan nasal spray were assessed in a randomised, double-blind, placebo-controlled, parallel study of zolmitriptan nasal spray in the treatment of a single migraine attack.

Efficacy was assessed by total symptom relief (no pain, nausea, photophobia or phonophobia), headache response (moderate/severe pain becoming mild/none) and pain-free rates.
Results The intent-to-treat population consisted of 912 patients (461 zolmitriptan, 451 placebo). Significantly more zolmitriptan-treated patients experienced total symptom relief at 1 h (primary endpoint; 14.5% vs. 5.1% for placebo; $p < 0.0001$). Significantly more zolmitriptan patients were pain-free and had total symptom relief from 30 min onwards. Importantly, zolmitriptan demonstrated a statistically significant headache response from 10 min, with a 65% response being seen at 2 h. The data did not indicate an unusual tolerability profile and raised no safety concerns.
Conclusions Zolmitriptan nasal spray is highly efficacious and well tolerated in the acute treatment of migraine. Significant headache response from 10 min confirms the very fast onset of this formulation, being the earliest ever reported with a noninjectable triptan.

P5N74

Traditional use of feverfew in migraine prevention

Michael Friede*[1]
[1]*Schaper & Bruemmer Gmbh & Co. KG, Salzgitter, Germany*

Feverfew (*Tanacetum parthenium*) is known as a herbal remedy for migraine prophylaxis.

A database search (MEDLINE, EMBASE, BIOSIS) was performed to evaluate the efficacy and drug safety of feverfew.

The search items were *Tanacetum parthenium*, feverfew, Mutterkraut, migraine. The search was restricted to 1980–2002. Randomized double-blind placebo-controlled trials were included. The methodological quality was evaluated using the criteria of the International Headache Society (IHS).

The results were: **1** Six clinical trials were identified in the database search. Five clinical trials were included in the analysis. The quality can be judged as sufficient (60% of trials). One clinical trial shows a good and a further study shows an excellent methodological quality.

2 There was a statistically relevant reduction in migraine frequency after 3–6 months in three clinical trials. Feverfew decreased the pain intensity of migraine attacks in one trial. Two clinical trials failed to show an effect.

3 The tolerability can be judged as good. Adverse events were mild and transient.

The majority of trials showed a favourable benefit-risk ratio of feverfew compared to placebo. Further clinical trials, according to IHS recommendations, are recommended because of the poor quality of clinical trials.

P5N75

Satisfaction with Sumatriptan 100 mg tablets in patients who are not satisfied with their current triptan

Mary Richardson*[3], Jan Brandes[1], Edmund Messina[2], Steve Shackelford[3] & Pamela Barrett[3]
[1]*Nashville Neuroscience Group, Nashville, TN, USA,* [2]*Michigan Headache Treatment Network, Lansing, MI, USA,* [3]*GlaxoSmithKline, Research Triangle Park, NC, USA*

Objectives To evaluate satisfaction and efficacy of sumatriptan 100 mg tablets in patients not satisfied with their current triptan therapy.
Methods This was a prospective, open-label, multicenter study of patients in the United States who were not satisfied with their current triptan. Patients treated 3 attacks with sumatriptan 100 mg within 1 h of onset of migraine pain. 24 h after treatment of each attack, patients rated their satisfaction with sumatriptan for relief of migraine pain and associated symptoms.
Results 71% of the patients ($n = 817$) who were dissatisfied with their current triptan were satisfied 24 h after treatment with sumatriptan 100 mg tablets' ability to relieve their migraine pain and associated symptoms. Satisfaction appears to be correlated with pain-free efficacy; 83% of subjects who were pain-free at 2 h postdose were satisfied compared with 64% of patients reporting satisfaction in the group who were not pain-free. Sumatriptan 100 mg was well-tolerated, with only 1.9% of patients withdrawing due to adverse events (16/828). Sumatriptan 100 mg was preferred 2 : 1 over the previous triptan by patients who expressed a preference (619/817).
Conclusions In patients not satisfied with their current triptan, 3 out of 4 patients were satisfied with sumatriptan 100 mg. This satisfaction correlated with pain-free efficacy.

P5N76

Gabapentin in migraine prophylaxis

Andrey Danilov*[1], Ravil Sadekov[1] & Alexander Vein[1]
[1]*Department of Neurology, Moscow Medical Academy, Rossolimo 11, Moscow, Russia*

Objective To evaluate efficacy of gabapentin (Neurontin) as a prophylactic agent in patients with migraine without aura and estimate the usefulness of nociceptive flexion reflex as a tool to study antinociceptive control mechanisms.

Study design and treatment The 8-week treatment period of monotherapy with gabapentin consisted of a 2-week starting phase and a 6-week stable-dosing phase. During first 2 weeks, patients were taking 1200 mg/day of gabapentin, next 6 weeks – 2400 mg/day. Medication was given on a three-times-a-day dosing regimen.

Methods Clinical analysis and neurophysiological examination of nociceptive flexion reflex was conducted at the beginning and at the end of 8-week therapy in 11 patients with frequent attacks of migraine without aura. Control group consisted of 10 healthy volunteers.

Results Before starting the treatment the thresholds of pain and nociceptive reflex were significantly lower in patients than in controls. At the end of the 8-week treatment statistically significant increase in thresholds parameters was observed. It was related to significant reduce in frequency and duration of migraine attacks. Gabapentin was well tolerated. Light somnolence and dizziness was observed in two patients.

Conclusion Gabapentin is an effective prophylactic agent for patients with migraine. In addition, gabapentin appears to improve antinociceptive control in migraine.

P5N77

Effect of oral anticoagulation on migraine attacks and the possible relationship with prothrombotic predisposition: a case series

Elisabeth A. van der Heijden*[1], Cees C. Tijssen[2], Annelies R. van't Hoff[3] & Antoine C. G. Egberts[1,4]
[1]*University of Utrecht, Utrecht Institute of Pharmaceutical Sciences – Department of Pharmacoepidemiology and Pharmacotherapy, the Netherlands,* [2]*Department of Neurology, St. Elisabeth Hospital Tilburg, the Netherlands Thrombosis Services Midden-Brabant Tilburg, the Netherlands,* [3]*TThrombosis Services Midden-Brabant Tilburg, the Netherlands,* [4]*Hospital Pharmacy Midden-Brabant, TweeSteden Hospital and St. Elisabeth Hospital Tilburg, the Netherlands*

Objective To investigate the presence of prothrombotic predisposition and the effect of low dose acenocoumarol in patients who spontaneously reported a reduction of their migraine attacks during previous therapeutic use of anticoagulants.

Background The positive effect of anticoagulation on migraine has been described in case reports and observational studies. It remains unclear whether this concerns only a selected group of migraine patients with certain common characteristics.

Methods In four patients with a self-reported strong reduction of their migraine during previous therapeutic use (INR 2.5–4.0) of anticoagulants, the presence of thrombotic risk factors and the effect of low dose acenocoumarol treatment (INR 1.5–2.0) on migraine attacks were prospectively investigated in an open study.

Results Two patients showed Factor V Leiden heterozygosity. The two other patients had an increased level of Factor VIII and von Willebrand factor antigen. One of these patients was also positive for lupus anticoagulant. In both patients with Factor V Leiden heterozygosity, the attack duration was 84%, respectively, 69% reduced during treatment with low dose acenocoumarol. The other two patients discontinued treatment, because, in contrast to previous use, no improvement of migraine was observed.

Conclusion The prothrombotic predisposition in all patients supports the hypothesis that migraine has different etiologic pathways amongst which a prothrombotic tendency. The application of oral anticoagulation in migraine needs further investigation.

P5N78

PROMISE Study (PROphylaxis of Migraine with Seglor®): the quality of life results

Michel Lanteri-Minet*[1], André Pradalier[2], Christian Lucas[3] & Gilles Géraud[4]
[1]*Pain Department Hôpital Pasteur CHU de Nice, France,* [2]*Internal Medicine, Colombes, France,* [3]*Neurology, Lille, France,* [4]*Neurology, Toulouse, France*

Objective The Quality of Life (QoL) is probably the best parameter to initiate migraine prophylaxis. The aim of this work was to confirm it using the results of the PROMISE study. PROMISE was a double blind, randomised, placebo-controlled study conducted in GP practice with HIS criteria. A 4-weeks placebo period (baseline) was followed by a 5-months treatment period with either Seglor® 5 mg bid or placebo.

Methods Two QoL groups were defined in the ITT population of the PROMISE study (MSQ questionnaire): patients with good QoL (gQoL; MSQ = 80; n = 53) and patients with bad QoL (bQoL; MSQ < 80; n = 288).

Results At the inclusion, the QoL was independent of attacks frequency ($P > 0{,}05$) but correlated to their duration ($P < 0{,}05$) and their intensity ($P < 0{,}01$). The frequency and the duration of attacks and the number of days with pain were reduced significantly with Seglor® vs. placebo ($P < 0{,}05$) only in bQoL group.

Conclusions PROMISE brings a real question regarding the main criteria to initiate a migraine prophylaxis. The QoL seems to be the best criteria. In bQoL patients, Seglor® has demonstrated a significant efficacy on the frequency and duration of attacks as well as the number of days with pain.

P5N79

MEDEMIG (II): perception of therapeutical strategies for acute migraine among French general practitioners

Michel Lanteri-Minet*[1], Hélène Massiou[2], Christine Chaffaut[3] & Pierre Clavelou[4]
[1]*Pain Department Hôpital Pasteur CHU de Nice, France,* [2]*Neurology, Lariboisière Hospital, Paris, France,* [3]*AstraZeneca France, Rueil-Malmaison, France,* [4]*Neurology, Clermont-Ferrand, France*

Objective Aim was to investigate perception of the different strategies for acute migraine among general practitioners (GPs) in France.

Methods A telephone survey (algorithm based on IHS criteria, a 76 item questionnaire and a CATI system) was carried out from May to June 2002. MEDEMIG (II) was focused on

the prevailing strategy applied by GPs: step-care strategy across attacks, step-care strategy within attacks or stratified-care strategy based on disability. GPs with migraine (IHS 1.1 and IHS 1.7/$n = 200$) were compared with GPS without migraine ($n = 402$). Student's test was used for statistical analysis.

Results Declared prevailing strategy was the stratified-care strategy for 45% of the GPs, the step-care strategy within attacks for 30% and the step-care strategy across attacks for 21% (4% non responders). No significant difference was found between GPs with migraine and GPs without migraine. Proportion of GPs using triptans was greater in GPs who declared apply the stratified-care strategy (58% vs. 40% and 27%, $p < 0.01$).

Conclusions Results show a good perception of the stratified-care strategy among the French GPs. Nevertheless, it will be necessary to conduct an observational study to verify if such a good perception is correlated to an application in clinical practice.

P5N80

Effectiveness of prophylactic trigger points inactivation in chronic migraine and chronic daily headache with migraine features

Elena Pita Calandre*[1], Javier Hidalgo[1], Juan Miguel Garcia-Leiva[1], Daniel Muñuzuri[1] & Vicente Moreno[2]
[1]*Instituto de Neurosciencias, Universidad de Granada, Spain,* [2]*Servicio de Neurología, Hospital Clínico de San Cecilio, Granada, Spain*

Objectives To evaluate the prophylactic effectiveness of ropivacaine trigger points injection in patients experiencing chronic headache of migraine type.

Methods The sample included 20 patients: 7 suffered treatment-refractory chronic migraine (3–9 attacks per month), 10 experienced transformed migraine (= 10 attacks per month), and 3 suffered new daily persistent headache with migraineous features. They were weekly injected with 2 mg of ropivacaine in temporal and/or occipital trigger points during a 12-week period. Frequency and severity of headache attacks, and rescue medication intake were recorded; patients evaluated their degree of improvement 4 weeks after the last injection.

Results One patient withdrawn after the 8th injection because of non response and adverse reactions. Headache frequency decreased in 32% of the cases, remained unaltered in 47% and increased in 21%. Rescue medication intake decreased in 47% of the subjects. Thirteen patients (68%) reported much or very much improvement, and 6 (32%) slight improvement or no change; improved patients argued that headaches were milder and/or of shorter duration.

Conclusions Anaesthetic trigger points inactivation did not decrease markedly attacks frequency, but relieved significantly the discomfort associated to headache; thus, it can be a valuable tool in the general management of the disease.

P5N81

Rizatriptan 10 mg improves functioning regardless of previous disability status in migraine patients

Arturo Lopez-Gil*[5], Salvador Tranche Iparraguirre[1], Miguel Angel Fuentes Perez[2], Esteban Perez Gutierrez[3] & Francisco Javier Panadero[4]
[1]*CS 'El Cristo', Oviedo, Asturias, Spain,* [2]*ABS Camp De L'Arpa, Barcelona, Spain,* [3]*CS 'Ciudades', Getafe, Madrid, Spain,* [4]*CS Villanueva Del Pardillo, Madrid, Spain,* [5]*Medical Department, MSD Spain, Madrid, Spain*

Objective To evaluate the effect of rizatriptan 10 mg on functional disability in migraineurs stratified by disability status (DS).

Methods Migraine patients were classified by investigators in 3 DS levels according to the percentage of attacks requiring bedrest in the previous 3 months as mild (< 29%), moderate (30–59%) or severe (= 60%). Patients treated one attack with rizatriptan 10 mg and recorded pain intensity and functional disability at baseline, 1 and 2 h. Results are presented as the percentage of patients with normal function from the subgroup of patients with any level of disability at baseline, adjusted by baseline pain intensity and functional disability. A conditional logistics regression model was used to calculate the adjusted probabilities and significance level.

Results 1221 patients completed the study; 378 patients (31.5%) were classified as severe, 649 (54.1%) as moderate and 173 (14.4%) as mild according to DS. DS was associated with baseline pain intensity and functional disability ($P < 0.001$) but not with the likelihood of being normal at 2 h ($P = 0.22$). 71.5% of patients were normal at 2 h following rizatriptan 10 mg ($P < 0.001$).

Conclusions The majority of disabled patients receiving rizatriptan 10 mg regain normal function at 2 h postdose regardless of DS3.

Study funded by MSD Spain.

P5N82

A comparative study of sumatriptan 50 mg, zolmitriptan 2.5 mg and eletriptan 20 mg in Japanese patients with migraine

Hisaka Igarashi*[1] & Fumihiko Sakai[1]
[1]*Department of Medicine (Neurology), Kitasato University, Sagamihara, Japan*

Objective This prospective study compared response rate, tolerability and patients' preference of sumatriptan, zolmitriptan and eletriptan for the acute treatment of migraine.

Methods Sumatriptan 50 mg tablets, zolmitriptan 2.5 mg tablets and eletriptan 20 mg tablets are available in Japan. They were prescribed to the outpatients with migraine. Patients recorded their headache diary including severity, duration and associated symptoms of migraine, effectiveness and adverse events of triptans.

Results A total of 80 patients (men 8, women 72, the mean age 40 years) took triptans for their migraine attacks. Effective response after 2 h was noted in 65% of 195 attacks taking

sumatriptan, in 76% of 192 attacks taking zolmitriptan and in 64% of 142 attacks taking eletriptan. The recurrence rate was 24% for sumatriptan, 32% for zolmitriptan and 25% for eletriptan. The adverse events were 49% for sumatriptan, 63% for zolmitriptan and 40% for eletriptan. In 42 patients who took three triptans, 9 patients preferred sumatriptan, 9 preferred zolmitriptan and 12 preferred eletriptan. The main reason of preference was effectiveness (sumatriptan), faster onset of recovery (zolmitriptan) and fewer adverse events (eletriptan). The remaining 12 patients did not show any preference.

Conclusions 71% patients differentiated among three triptans. Doctors should prescribe the best medicine for each patients.

P5N83

H3 receptor sites and the management of migraine

Maria Nicolodi*[1] & Federigo Sicuteri[1]
[1]*Interuniversity Headache Centre, Foundation 'Prevention and Therapy of Primary Pain and Headache', Florence, Italy*

In mammalian brain, histaminergic neuron system is suggested to be involved in various physiological functions including antinociception. Animal data have shown that histamine crosses blood–brain barrier and induce analgesia or hyperalgesia depending on doses. Our aim was to activate central histaminergic analgesia by using doses of histamine acting on autoreceptors.

Histamine chloride 0,048/kg/ h 24 h/day/continuous infusion was subcutaneously administered by an infusion pump to 113 (78 females, mean age 35.8 ± 7.9) patients with migraine without aura (5–7 attacks A2/months) who were refractory (benefit less than 30% vs. baseline) to conventional therapies: beta-blockers, antiepilects, Ca-antagonists. After 1 month run-in, the patients underwent a 4-weeks treatment. Vascular/visceral hyperalgesia was evaluated at the end of run-in, at the end of the treatment period by using elsewhere described vein over-distension test.

A decrease ($P > 0.0001$) of migraine attacks followed the treatment. Decrease ($P > 0.0001$) of vascular/visceral hyperalgesia was independent of the degree of amelioration.

The relatively low doses of histamine likely act on H3 receptor sites, auto-receptors controlling histamine release and turn-over.

P5N84

MIDAS scores and response to Triptans in migraine patients on Topiramate

Rachel Hering-Hanit*[1]
[1]*Headache Unit, Department of Neurology, Meir General Hospital, Kfar Saba, Israel*

Objectives Evaluation of topiramate efficacy, the MIDAS scale and response to triptans in patients suffering from migraine with and without aura.

Methods Sixty-nine patients with migraine with and without aura, who have experienced 4–8 migraine attacks during a 4-week prospective baseline, were included in the study. Topiramate, 50–150 mg daily, was given in 2 divided doses for 12 weeks. Patients started with one 25-mg tablet at night in the first week and increased the dose by 25 mg every week in 2 divided doses until relief was obtained or adverse events occurred. Headache frequency, duration and severity were recorded. The MIDAS questionnaire was completed before and at the end of the study, and the response to triptans was recorded.

Results Sixty-six patients completed the trial. Results demonstrated topiramate to be effective in 72.6% with ≥ 50% reduction in headache frequency from baseline. Mean MIDAS scores were 19.3 at baseline and 5.8 after 12 weeks of treatment. Sixteen out of 29 patients who had not responded to triptans before initiating topiramate, responded well following topiramate administration. Three patients withdrew from topiramate treatment due to adverse events.

Conclusions Topiramate seems to be effective in migraine prophylaxis with a significant decrease in the mean MIDAS scale values. Patients who had previously not responded to triptans responded well following topiramate administration. The drug is well tolerated with no serious adverse events.

P5N85

Determinants of triptan preference in a tertiary care migraine population: patterns of use

Fred Sheftell*[1,6], Marcelo Bigal[1,2], Michele Feleppa[3], Alan Rapoport[1,4] & Stewart Tepper[1,5]
[1]*The New England Center for Headache, Stamford, USA,* [2]*Albert Einstein College of Medicine, Bronx, NY, USA,* [3]*Primario Unita Operativa di Neurologia e Neurofisiopatologia A. O 'G. Rummo', Benevento, Italy,* [4]*Department of Neurology, Columbia University College of Physicians and Surgeons, New York, NY, USA,* [5]*Yale University School of Medicine, New Haven, CT, USA,* [6]*New York Medical College, New York, NY, USA*

Objective To evaluate the patterns of triptan use in migraineurs presenting to a speciality center.

Methods We reviewed the clinical records and calendars of migraine sufferers who had used more than one triptan. All subjects were followed for at least one year. For every triptan/formulation used, information regarding patient satisfaction, duration of use and reasons for discontinuation were obtained according to a predefined set of questions.

Results Our sample consisted of 386 patients (87.8% females). Sumatriptan in various formulations was used by 90.4% of the patients; zolmitriptan, by 61.5%; rizatriptan, by 50.5%; naratriptan, by 35.4%, and almotriptan, by 8.0%. Almotriptan was excluded from this analysis. More subjects wanted to try another triptan amongst those initially using sumatriptan 25 mg, compared to all the other triptans ($P < 0.01$). Subjects using naratriptan were less likely to report recurrence as a reason for switching. Incomplete relief was reported more often by those using sumatriptan 25 mg and naratriptan. Inconsistency was a reason for switching in those using sumatriptan NS, sumatriptan 25 mg and naratriptan. Side-effects were important factors for those using sumatriptan 100 mg, NS and SC.

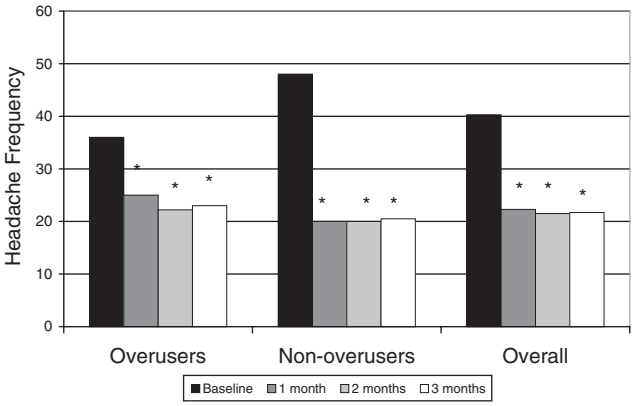
Conclusions Patients balance a variety of treatment attributes when assessing the overall acceptability of a headache medication.

P5N86

Botulinum Toxin type A in the preventive treatment of refractory headaches – comparison between medication overusers and nonmedication overusers groups

Stewart Tepper*[1,2], Marcelo Bigal[1,3], Fred Sheftell[1,4] & Alan Rapoport[1,5]
[1]*The New England Center for Headache, Stamford, CT, USA,* [2]*Yale University School of Medicine, New Haven, CT, USA,* [3]*Albert Einstein College of Medicine, Bronx, NY, USA,* [4]*New York Medical College, New York, NY, USA,* [5]*Department of Neurology, Columbia University College of Physicians and Surgeons*

Objectives A previous study of our group supported the role of BTX-A in the treatment of refractory headaches. Since some of the subjects in this study were medication overusers, part of the assessed benefits could have been due to analgesic discontinuation. Thus, subgroup analysis about overusers vs. non overusers is presented.
Design/methods Clinical records and headache calendars with the following inclusion criteria were reviewed: 1 – Ages from 18 to 65 years old; 2 – Primary headache with previous failure of at least four preventive treatments; 3 –Have received 100 units BTX-A and have being followed for at least 6 months. Outcomes included frequency of pain; intensity of pain, days with severe headache, and headache index (frequency × intensity).
Results Our sample consisted of 100 subjects (65 overusing acute medications). The evolution of the headache index is displayed in the figure (*: $p < 0.01$ compared to baseline) (Fig.). The response was not as dramatic in the first month in the group of overusers, but similar patterns of improvement were found in overusers and non overusers at all endpoints.



Figure

Conclusions BTX-A was found to be effective in subjects overusing or not acute care medication. Prospected controlled studies are required to confirm these data.

P5N87

Improved migraine treatment outcomes with rizatriptan 10 mg compared to nontriptant treatment (I-Max migraine disability assessment program – Spain

Miguel Torrecilla*[1], Antonio Castellanos[2], Milko Torres[3], Teresa Caloto[5], Gonzalo Nocea[5] & Gerth William[4]
[1]*CS San Juan, Salamanco, ES,* [2]*CS Gerena, Sevilla, ES,* [3]*CS Buenos Aires, Madrid, ES,* [4]*Worldwide Outcomes Research, Merck & Co., Inc, Whitehouse Station, NJ, USA,* [5]*Outcomes Research, MSD, Madrid, ES*

Objectives To evaluate the impact of rizatriptan 10 mg on migraine treatment outcomes relative to nontriptan treatment in primary care practice.
Methods This was an observational, open-label study of 118 triptan-naïve patients recruited by 22 primary care physicians in Spain. Patients completed a diary at baseline for their most recent prestudy attack and for 3 consecutive attacks: 1st and 3rd treated with rizatriptan 10 mg (wafer); 2nd with previous nontriptan therapy. The diary contained questions at 24 h after dosing on pain relief, associated symptoms, and return to usual activity.
Results Previous migraine treatment included NSAIDs (43.2%), analgesics (30.5%), ergotamines (16.8%) and combinations (9.5%). Pain relief, associated symptoms, and return to usual activity are reported in the table. All 2- h outcome measures were statistically greater ($P < 0.01$) for rizatriptan 10 mg compared with nontriptan treatment.
Conclusions Improvement in migraine outcomes was faster and more complete for attacks treated with rizatriptan 10 mg than for attacks treated with nontriptan medications.

	Pre-Study	1st Attack (rizatriptan)	2nd Attack (Previous Tx)	3rd Attack (rizatriptan)
(Previous Tx)				
Onset of headache relief	48.3%	83.4%	45.8%	78.1%
Pain completely gone	17.8	40.1	12.1	46.7
Migraine Sx completely gone	13.1	37.7	10.0	43.8
Return to normal activities	17.6	35.5	18.4	47.8

P5N88

Patient satisfaction greater with rizatriptan 10 mg compared to nontriptant treatment (I-Max migraine disability assessment program – Spain)

Adalberto Serrano*[2], Montserrat Nieto[3], Paloma Ruis[3], Teresa Caloto[4], Gonzalo Nocea[4] & William Gerth[1]
[1]*Worldwide Outcomes Research, Merck & Co., Inc, Whitehouse Station, NJ, USA,* [2]*CS Repelega, Vizcaya, ES,* [3]*CS La Ventilla, Madrid, ES,* [4]*Outcomes Research, MSD, Madrid, ES*

Objectives To evaluate patient satisfaction with rizatriptan 10 mg and nontriptan medication in a primary care setting.

Methods This was an observational, open-label study of 118 triptan-naïve patients recruited by 22 primary care physicians in Spain. Patients completed a diary at baseline for their most recent prestudy attack and for 3 consecutive attacks: 1st and 3rd treated with rizatriptan 10 mg (wafer); 2nd with previous nontriptan therapy. Patients reported satisfaction with medication on a seven-point scale at 24 h after dosing and at the end of study.
Results Reported attack frequency was < 1/month in 8.2%, once or twice/month in 45.3%, and ≥ 3/month in 46.5% of patients. Previous migraine treatment included NSAIDs (43.2%), analgesics (30.5%), ergotamines (16.8%) and combinations (9.5%). The percent of patients' completely/very satisfied was higher in attacks treated with rizatriptan 10 mg than with nontriptan therapy ($P < 0.001$). At end of study, more patients were completely/very satisfied with rizatriptan 10 mg (62.4%) than with nontriptan therapy (17.2%; $p < 0.001$). The majority of patients were more satisfied with rizatriptan 10 mg (86.1%) than their previous nontriptan medication (13.9%; $p < 0.001$).
Conclusions Migraine sufferers, given the opportunity to try rizatriptan 10 mg, were more satisfied with rizatriptan than with nontriptan medication.

P5N89

Lack of pharmacokinetic interaction between almotriptan and oral contraceptives: a double-blind, placebo-controlled, crossover study in healthy female volunteers

Xavier Cabarrocas*[1] & Jean-Paul Macher[2]
[1]*Almirall Prodesfarma, S.A., Barcelona, Spain,* [2]*Forenap Pharma, Rouffach, France*

Objectives To assess if a single dose of almotriptan 12.5 mg interacts with the pharmacokinetic profile of a low-dose combined monophasic oral contraceptive in healthy women.
Methods In this phase I, single center, double-blind, randomized, two-period crossover, placebo-controlled study, 21 healthy female volunteers received two cycles of 21 days of oral contraceptive treatment (ethinylestradiol 30 µg and desogestrel 150 µg) and one single dose of either almotriptan 12.5 mg or matching placebo between days 8 and 12 of each cycle. Blood samples were taken periodically up to 24 h after almotriptan or placebo administration, and serum profiles of ethinylestradiol and desogestrel as well as sex hormone binding globulin (SHBG) plasma levels were determined.
Results Similar profiles of ethinylestradiol and desogestrel were obtained under almotriptan and placebo, and there were no significant differences on $AUC_{(0-24)}$, C_{max}, and T_{max}, nor on SHBG plasma concentrations. Almotriptan was well tolerated and the incidence of adverse events was the same with almotriptan as with placebo. No clinically significant changes were observed with almotriptan, neither on laboratory parameters, on vital signs and ECG parameters, or on physical examination.
Conclusions A single dose of almotriptan 12.5 mg did not alter the pharmacokinetics of the oral contraceptive hormones ethinylestradiol and desogestrel in healthy female volunteers. Furthermore, almotriptan was safe and well tolerated.

P5N90

Topiramate in 100 refractory migraine patients

Julio Pascual*[1], Margarita Sanchez del Rio[2], Valentin Mateos[3], Jose M. Lainez[4], Jesus Hernandez-Gallego[5], Rogelio Leira[6] & Maria Dolores Jiménez[7]
[1]*University Hosp. Marqués de Valdecilla (Santander),* [2]*Hosp. Ruber Internacional (Madrid),* [3]*Asturias General Hospital (Oviedo),* [4]*University Hosp. Valencia (Valencia),* [5]*Hosp. Dr Negrín (Las Palmas de Gran Canaria),* [6]*University Hosp. Santiago de Compostela (Santiago de Compostela),* [7]*Hosp. Ntra. Sra. de Valme (Sevilla)*

Objectives To report our experience with topiramate in the treatment of patients with refractory migraine.
Methods We offered treatment with topiramate to patients with the diagnosis of IHS migraine who have not responded to or tolerated beta-blockers, amitriptyline, flunarizine and/or valproate. This series included 100 patients (women), between 16 and 81 years. Variables analysed were 'response' (reduction in frequency > 50%), excellent response (> 75%) and tolerability.
Results After 3 months daily maintenance doses of topiramate varied between 25 and 400 mg, with most taking 100 mg. Twenty withdrew due to adverse events at doses as low as 25–50 mg, while 23 patients found topiramate inefficacious. The remaining 57 cases responded, 31 of them with excellent effect. Fourteen patients lost significant weight (3–13 kg).
Conclusions Topiramate is a good therapeutic option for around half of patients with refractory migraine. If there is clinical response, this is normally excellent, whilst topiramate intolerance usually occurs from onset and at low dosage.

P5N91

Efficacy of topiramate in a patient population with refractory menstrual associated migraine

Edmund Messina*[1], Christina Calabrese[1], Kellie Murry[1] & Jayne Messina[1]
[1]*The Michigan Headache Treatment Network, Lansing, Michigan USA*

Objective To assess the effect of prophylactic topiramate on migraine frequency and severity in a patient population with menstrual associated migraine (MAM) patterns who failed to respond to other treatment attempts. This group was selected as a particularly challenging migraine treatment group.
Methods A retrospective review was performed on the electronic medical records of 143 female patients with MAM who had received topiramate for migraine prophylaxis for at least 6 weeks. Multiple parameters were evaluated, including: demographics, number of previous prophylactic agents, concurrent agents, use of abortive medications and analgesics, global patient headache evaluation, number of headache days/month, adverse effects, dosing regimen, duration of topiramate treatment.
Results The data was divided into groups, including those based on headache frequency (ranging from almost daily to less than weekly), severity (ranging from mild to severe), previous treatment failures with other agents (AEDs, antidepressants, etc.).
Conclusion Preliminary findings suggest that topiramate was a well tolerated and effective migraine preventative in

our grouping of patients with refractory menstrual associated migraine.

P5N92

Efficacy of topiramate in prophylactic treatment of migraines: first open label, multicenter, study in Czech Republic

David Dolezil*[1], Jiri Mastik[2], Rudolf Kotas[3] & Ivana Novotna[2]
[1]*Department of Neurology, University Hospital Ostrava,* [2]*Department of Neurology, University Hospital Brno,* [3]*Department of Neurology, University Hospital Plzeñ*

Objective To evaluate the efficacy and safety of topiramate (TPM) in migraine prophylaxis.
Methods 26 patients aged 18–65 having migraine with or without aura fulfilling IHS criteria participated in the study (4-week baseline phase, 8-week titration phase, 12-week maintenance phase). Migraine presents more than 6 months with 2 and more attacks per month. Primary efficacy outcomes included frequency of migrainous attack per month, number of days with migraine per month, migraine severity at scale 0–3 (0 no pain, 3 severe headache) and MIDAS. All patients recorded information on their migraine to their patients diaries. Dose of TPM were titrated in 25-mg increments to TMP 100 mg BID or 200 mg BID.
Results 3 patients were excluded from the study due to TPM adverse effects (twice very mild), 15 patients had mild adverse effects of TPM during titration phase. TPM was administered at dose of 100 mg/day (23 patients) or 200 mg/day (2 patients), with the average value 108 mg/day. Number of migrainous attack/patient/month improved from 6,56 to 2,73. Average of MIDAS improved from 3,47 before treatment of TMP to 1,6 after treatment of TMP.
Conclusion This study demonstrated that TPM was effective in the prophylactic treatment of migraine. 17 patients were taking TMP after end of the study.

P5N93

Zolmitriptan orally disintegrating tablet (ODT) is a highly effective migraine therapy and is preferred over conventional sumatriptan tablets and rizatriptan wafer

Andrew Dowson*[1] & Bruce Charlesworth[2]
[1]*The King's Headache Services, London, UK,* [2]*AstraZeneca, Macclesfield, UK*

Zolmitriptan ODT dissolves on the tongue without the need for fluid intake, providing a convenient and discreet treatment for migraineurs who have nausea or difficulty swallowing conventional tablets, or require a treatment that can be taken immediately, wherever a migraine strikes. A randomised, double-blind study of 471 patients who treated a single moderate or severe migraine with zolmitriptan 2.5 mg ODT or placebo demonstrated high headache response rates 2 h post-dose with zolmitriptan (63% vs. 22% placebo; $p < 0.0001$). Pain-free responses were also significantly higher than placebo at 1, 2 and 4 h (8% vs. 3%, 27% vs. 7% and 37% vs. 11%, respectively; all $p < 0.05$). Of 469 patients stating a preference, 70% preferred zolmitriptan ODT to conventional tablets, 92% considered the ODT easy to handle, and 80% liked its orange taste. A comparator study showed that, compared with sumatriptan, significantly more patients preferred zolmitriptan ODT overall (60% vs. 40%; $p = 0.013$) and in terms of convenience and ease of use. Similarly, two comparator studies found that significantly more patients preferred zolmitriptan ODT to rizatriptan wafer. These studies show that zolmitriptan ODT is an effective and convenient alternative to conventional tablets, and is preferred to sumatriptan tablets and rizatriptan wafer by migraineurs.

P5N94

Botulinum Toxin Type A in the treatment of chronic daily headache

Fabrizio Balestrieri*[1], B. Chiocchetti[1], S. Canova[1], M. Bartelli[1], F. Pinto[2] & G. Arnetoli[1]
[1]*Centro Cefalee ed Algie Faciali-II °Clinica Neurologica,* [2]*Dip Neurofisiopatologia. A.O. Careggi University of Florence Institute*

There are a several works that investigated the role of botulinum toxin type A (BTX-A) in the prophylactic treatment of headache. Our aim was to study the possible benefit of the use of BTX-A in the prophylactic therapy of chronic daily headache (CDH). The first objective consist in reduction of frequency, intensity and duration of headache attacks, the second one was the evaluation of use of symptomatic drugs during the treatment. In the present study 7 patients (6 Female 1 Male mean age 47.3 ± 12 years [ys]) has been evaluated with diary in the three preceding months and after injection of BTX-A Disport® 200 U in specific muscular sites. The treatment had been repeated 3 months after the first injection. Frequency, intensity and duration of headache are reduced in patients, the use of symptomatic drugs had been reduced in all patients; in the pre injection period the mean consumption of sintomatic drugs is 77 and after the second treatment with BTX-A is 8. Our work shows that repeated injections of BTX-A in the prophylactic treatment of CDH establish a significant improvement of frequency, intensity and duration of headache, and also a marked reduction of the use of symptomatic drugs.

P5N95

The effectiveness of repetitive Naratriptan or Frovatriptan in intractable migraine

Carla Rubingh*[1], Susan Baggaley[1] & Kathleen Digre[1]
[1]*University of Utah Health Sciences Center, Salt Lake City, Utah*

Introduction The purpose of this study was to evaluate whether naratriptan or frovatriptan were effective in breaking intractable migraine. While intravenous dihydroergotamine is limited by the need for hospitalization or frequent office visits, naratriptan and frovatriptan have long plasma half-lives and may be an outpatient alternative to break status migrainosis.
Methods We reviewed charts on patients with an underlying IHS diagnosis of migraine with and/or without aura, who experienced intractable daily migraine. They received nara-

triptan 1.25 mg TID × 3–5 days or frovatriptan 2.5 mg QD-BID × 3–5 days. We reviewed migraine frequency, rescue dosing and patient's subjective report. We defined success by migraine frequency less than 3 days per week and rescue dosing less than 3 times per week.
Results There were 24 total patients, 7 males and 17 females. Nine patients had been given naratriptan and 15 had been given frovatriptan. Fifty-six percent of patients (5/9) given naratriptan responded with decreased migraine frequency and rescue doses. Sixty-six percent of patients (10/15) demonstrated a successful response to frovatriptan. All patients were on preventive medications. There was no significant difference between agents (one sample chi squared test $p = 0.221$).
Conclusions Naratriptan and frovatriptan are both effective at breaking intractable migraine, however, larger scale studies are needed.

P5N96

The significance of clinical and laboratory characteristics in etiology and pathogenesis of migraine

Ranko Raicevic*[1], Ljubo Markovic[2], Toplica Lepic[1], Evica Dincic[1], Dragana Veljancic[1] & Aleksandar Radisavljevic[2]
[1]*VMA Clinic of neurology, Belgrade,* [2]*Institute of radiology, VMA, Belgrade*

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 disarrythmia 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%),overbridged 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 diagnostic criteria and in selection of drugs and procedures in prophylaxis and treatment of migraine attacks.

P5N97

Zolmitriptan conventional and orally disintegrating tablets achieve headache response as early as 30 min post-treatment: results of a pooled data analysis

Alan Rapoport*[1], Andrew Dowson[2], Bruce Charlesworth[3], Janette Hughes[3] & Nick Syrett[3]
[1]*New England Center for Headache, Stamford, USA,* [2]*The King's Headache Services, London, UK,* [3]*AstraZeneca, Macclesfield, UK*

Objectives To evaluate headache response rates 30 min after treatment with zolmitriptan 2.5 or 5 mg conventional or orally disintegrating tablets (ODT).
Methods Data were pooled from eight placebo-controlled studies of oral zolmitriptan in order to assess headache response rates 30 min after treatment.
Results Zolmitriptan 2.5 mg produced a significantly higher 30-minute headache response rate than placebo in an analysis of all 6 studies using the 2.5 mg dose as either the conventional tablet or ODT (15.1% vs. 11.2%; $p < 0.001$). Headache response rates were greater than placebo in the 4 studies using the conventional zolmitriptan 2.5 mg tablet (13.3% vs. 10.3%; $p < 0.05$) and in the 2 using the ODT (20.1% vs. 12.7%; $p < 0.01$). Similarly, 30-minute headache response rates were higher than placebo in all 4 studies using zolmitriptan 5 mg as either the conventional tablet or ODT (16.0% vs. 11.8%; $p < 0.05$) and in 3 studies using the conventional tablet (15.5% vs. 11.0%; $p < 0.05$). The one study utilising zolmitriptan 5 mg ODT also showed a significant headache response at 30 min (17% vs. 13% placebo; $p < 0.05$).
Conclusions Both the conventional tablet and ODT formulations of zolmitriptan 2.5 and 5 mg provide a significantly greater headache response rate than placebo seen as early as 30 min after treatment.

P5N98

Relationship between preference for Rizatriptan or Sumatriptan and function

Franck Skobieranda*[1], Norman Bohidar[1] & Filippa Karcewski[1]
[1]*Merck & Co., Inc. West Point, PA, USA*

Objective Evaluate the relationship between patient preference for rizatriptan or sumatriptan and function.
Methods This was a two-attack crossover study of rizatriptan orally disintegrating tablet 10 mg or sumatriptan 50 mg tablet in 524 patients. Patients recorded function on a 0–3 scale. Post-study, patients expressed their treatment preference. A prespecified comparison of treatments and the proportion of patients reporting normal ability was performed. This posthoc analysis was conducted to evaluate the relationship between preference and function.
Results 370 patients treated two attacks and reported preference and function. At two hours, more patients using rizatriptan reported normal ability vs. sumatriptan (70.0% vs. 63.7%, $p = 0.029$). Eighty percent of patients who returned to normal ability faster using rizatriptan preferred rizatriptan. Sixty-six percent of patients who returned to normal ability faster using sumatriptan preferred sumatriptan. Eighty-four

percent of patients noted that restoration of function contributed to their preference choice.
Conclusions Although a causal relationship cannot be concluded, based on results from this analysis, patients tended to prefer the acute migraine treatment which provided a more rapid return to function.

P5N99

Prioritization of triptan treatment attributes by Spanish neurologists

Rogelio Leira*[1], David Ezpeleta[2] & Jordi Galván[3]
[1]*Department of Neurology, Hospital Clínico Universitario, Santiago de Compostela, Spain,* [2]*Department of Neurology, Hospital 'Mútua de Terrassa', Terrassa Barcelona, Spain,* [3]*Medical Department. Almirall Prodesfarma, Barcelona, Spain*

Objectives To evaluate the relative importance of triptan treatment attributes for Spanish neurologists and determine which triptans fit best with their preferences.
Methods Neurologists attending a migraine symposium were asked to review the case history of a triptan naïve migraineur and evaluate the relative importance of efficacy, consistency, and tolerability attributes in the prescription decision for that patient. Importance weights were collected using an electronic audience response system and fed into a multi-attribute decision model (TOPSIS), together with placebo-corrected data from a recent meta-analysis of 53 clinical trials. For each triptan the model calculated average similarity with respect to a hypothetic ideal triptan and the frequency with which it featured among the 'top-3' closest to this ideal.
Results Useable data were obtained from 42 respondents. Attribute importance weights for efficacy, consistency, and tolerability were 37%, 33%, and 30%, respectively. According to the TOPSIS analysis, almotriptan 12.5 mg, eletriptan 80 mg, and rizatriptan 10 mg were found to be most similar to the hypothetic ideal. Only almotriptan featured in the 'top-3' of 100% of the respondents.
Conclusions Spanish neurologists consider efficacy the most important attribute when selecting an oral triptan, followed by consistency, and tolerability. Almotriptan, eletriptan, and rizatriptan fit best with their preferences.

P5N100

The role of personality in transformed migraine in Turkish patients

Basak Karakurum*[1], Ozlem Soylu[1], Mehmet Karatas[1], Zulfikar Arlier[1], Meliha Tan[1] & Semih Giray[1]
[1]*Baskent University Medical Faculty Adana Teaching and Medical Research Center, Department of Neurology, Adana, Turkey*

Since the transformation from episodic into chronic pattern of migraine attack may be associated with depression, anxiety, panic disorder, personality, analgesic overuse, determination of risk factors are very important. We conducted this prospective, randomized, case-controlled study to assess the role of personality in patients with transformed migraine (TM) and episodic migraine (EM). Fifty patients with TM and 50 patients with EM were included in the study. We analyzed age, gender, previous migraine history, number of years with daily headaches, pain intensity, medication overuse and personality of the cases with Minnesota Multiphasic Personality Inventory (MMPI). TM was diagnosed according to the Silberstein and Lipton criteria. The mean ages in EM and TM group were 32.6 ± 9.7 and 33.8 ± 9.0 years, respectively. The sex distributions were similar ($P > 0.05$). In TM group, the score of hysteria, hypocondriasis, psychastenia, depression, and social introversion were higher than EM. There was statistically difference between two groups ($P < 0.05$). These personality characteristics may be predictor for transformation from EM into TM.

P5N101

The outcome of headache management following nurse intervention: assessment in clinical practice using the MIDAS Questionnaire

Andrew J. Dowson*[1,2] & Rebecca Salt[1]
[1]*Surrey Headache Service, C/o Merrow Park Surgery Guildford, Surrey, Unitd Kingdom,* [2]*Kings College Hospital Headache Service, London, United Kingdom*

Objectives To assess the outcome of a nurse intervention strategy in patients presenting to the surgery with headache.
Methods All patients aged 18–65 years attending the surgery who reported headache in the previous 3 months were assessed by a nurse and completed a Migraine Disability Assessment (MIDAS) Questionnaire and a questionnaire investigating headache features and physician consultations. All patients were given oral and written advice by the nurse on headache management. Patients with MIDAS Grade III–IV (moderate-severe disabling headache) were also offered an appointment with a headache specialist physician. Patients were reviewed after 3 and 6 months with the questionnaires.
Results 195 patients took part. At baseline, 136 (69.7%) were MIDAS Grade I/II and 59 (30.3%) were Grade III/IV. Compared to baseline, patients reported significant mean reductions at 6 months in: total MIDAS scores (5.9 vs. 9.6; $p = 0.014$); headache frequency (MIDAS A: 7.0 vs. 12.6; $p = 0.009$); headache severity (MIDAS B: 5.0 vs. 6.0; $p = 0.003$); and physician consultations for headache (3-month period: 0.05 vs. 0.30; $p = 0.05$).
Conclusions Advice on headache management given by a nurse can lead to significantly improved patient outcomes. Additionally, MIDAS was shown to be a sensitive outcome measure for reduction in disability in headache sufferers.

P5N102

Effervescent acetylsalicyclic acid in the treatment of acute migraine

Hartmut Göbel*[1], Axel Heinze[1], Marianne Petersen-Braun[2] & Uwe Gessner[2]
[1]*Kiel Pain Clinic, Kiel, Germany,* [2]*Bayer Vital Gmbh, Bayer, Germany*

Objectives Soluble preparations of analgesics are recommended in order to promote gastric emptying and thereby

enhance the effect of analgesics. This study was conducted to collect information about the efficacy and tolerability of a new effervescent formulation of acetylsalicylic acid [Aspirin®Migräne] in the treatment of acute migraine.
Methods According to the open, prospective design patients fulfilling IHS-criteria for migraine were asked to treat up to 3 migraine attacks with 2 × 500mg Aspirin®Migräne and to record headache intensity, accompanying symptoms and AEs.
Results 296 patients treated at least one migraine attack. The responder rate 2 h postdose (reduction of moderate/severe headache to mild/none) was 58.4% for the first, 61.0% for the second and 62.7% for the third attack. The percentage of patients suffering from nausea dropped from 49.3% to 10.6%. Other accompanying symptoms such as vomiting, photophobia and phonophobia were also relieved effectively. The tolerability of the study drug was assessed as 'very good' or 'good' by 87.3% of the patients. The most common AE was 'stomach pain' in 5.9% of all attacks followed by fatigue (3.1%).
Conclusions This new effervescent formulation of acetylsalicylic acid [Aspirin®Migräne] with a high buffering capacity relived both pain and accompanying symptoms and was well tolerated.

P5N103

Parecoxib I.V. in the treatment of acute migraine as escape medication after nonresponse to triptans

Hartmut Göbel*[1], Axel Heinze[1] & Katja Heinze-Kuhn[1]
[1]*Kiel Pain Clinic, Kiel, Germany*

Objectives Parecoxib is the first selective COX-2-inhibitor available for intravenous use. Administered intravenously in the treatment of acute postoperative pain onset of action has been demonstrated already after 7–10 min and lasts up to 24 h. Because of this fast and sustained analgetic effect it was investigated whether Parecoxib is effective as an escape medication after nonresponse to triptans in the treatment of acute migraine.
Methods In an open design 21 patients suffering from migraine with or without aura according to IHS-criteria were treated with 40 mg Parecoxib i.v. after nonresponse to a triptan within 4 h, i.e. headache still of at least moderate intensity. Accompanying symptoms, migraine disability and AEs were documented in a diary as well as headache intensity (0 = no pain, 1 = moderate, 2 = severe, 3 = very severe) every 15 min for 4 h post-treatment.
Results The average pain intensity before treatment was 2.9. After 30 min the average pain intensity dropped to 1.5, after 1 h to 1.0 and after 4 h to 0.6. Headache recurrence was not seen. Tolerability was very good.
Conclusions Parecoxib i.v. proved to be an effective and well tolerated escape medication in the treatment of acute migraine attacks after nonresponse to triptans

P5N104

Specialised comprehensive treatment of patients with chronic headache and pain disorders: long-term evaluation of cost effectiveness and quality of life

Hartmut Göbel[1], Axel Heinze[1], Katja Heinze-Kuhn[1], Andrea Roth[2], Hans-Heinrich Rüschmann[2] & Peter Buschmann[3]
[1]*Kiel Pain Clinic, Kiel, Germany,* [2]*Gesellschaft für Systemberatung im Gesundheitswesen GSbG, Kiel, Germany,* [3]*AOK Schleswig-Holstein, Germany*

Objectives (A) Long-term analysis of cost-effectiveness of specialised comprehensive treatment of patients with chronic headache and pain disorders in the Kiel Pain Clinic. (B) Long-term analysis of the quality of life before and after treatment.
Methods 238 consecutive patients admitted to the Kiel Pain Clinic because of either frequent migraine, tension-type headache, drug-induced headache or other pain disorders were included in the analysis. Patients were asked to complete a standardised quality-of-life-questionnaire (SF-36 Health Survey) before inpatient treatment, after discharge and 1 and 2 years later. Any costs for the German health system caused within 2 years before and after treatment were calculated and compared with patients treated in other nonspecialised clinics for the same diagnoses.
Results A significant improvement in all categories of the SF-36 Health Survey was found after inpatient treatment, an improvement which proved long-lasting over 2 years. Compared to nonspecialised treatment patients included in the specialised comprehensive program made significantly less demands on the German health insurance in the two years following inpatient treatment.
Conclusions A specialised comprehensive treatment of patients with chronic headache and pain disorders according to modern treatment standards can improve the patients quality of life and is distinctive cost-effective compared to nonspecialised treatment.

P5N105

Episodic migraine: customized prophylactic treatment improves performance on quality of life test

Carlos Bordini*[1], Hilton Mariano Da Silva[1], Roberta Garbelini[1] & José Speciali[1]
[1]*Department of Neurology, Sao Paulo University, School of Medicine at Ribeirao Preto, Ribeirao Preto, SP, Brazil*

Objectives To study of the impact of preventative treatment on HRQL in migraine suffers.
Subjects and methods Thirty-five consecutive episodic migraine without aura patients attending to a tertiary care Unit (Batatais Headache Clinic) entered the study. Inclusion criteria no previous prophylactic treatment, ages ranging from 18 to 65 years, history of migraine from at least one year and attack frequency from two to six per month. A complete neurological exam was performed and the SF-36 questionnaire was complete. Except for the **introduction** of the prophylactic drug, no other changes were made in the migraine current treatment. Four-to-six months later, patients were asked to sign the SF-36 test. Pretreatment and post-treatment

variables were compared. Statistical methods the Kolmorov – Smirnoff, Student *t*-test and Wilcoxon's test.
Results The mean age of the 35 patients (32 female and 3, male) was 40,2 years (range 18–60 years). There was a significant improvement in the domains Role physical, Bodily pain, General health, Vitality, Social function and Mental health after the preventive treatment.
Conclusion An important improvement of the quality of life was found in our group of patients giving support to the current view that customized treatments is an useful tool for migraine managing.

P5N106

Preference for oral Eletriptan vs. subcutaneous Sumatriptan: results of an open crossover trial

Jayasena Hettiarachchi*[1], John Morrow[1], Jean Denaro[1], Wei Sun[1] & Carolyn Sikes[1]
[1]*Pfizer Inc., New York, USA*

Background Patient preference studies provide useful practical information regarding the optimal choice of medication for patients and physicians.
Methods In an open crossover study, subjects with previous subcutaneous sumatriptan experience ($n = 311$) were randomized to eletriptan 80-mg or subcutaneous (sc) sumatriptan 6-mg for two treatment periods consisting of three attacks each, followed by an optional treatment period of three attacks with the treatment of their choice. The primary endpoint was medication preference rated on a five-point global scale.
Results Headache response at 2 h was higher for sc sumatriptan vs. eletriptan (87% vs. 81%; $P < 0.01$), while pain-free response at 2 h was similar (61% vs. 58%, not significant). Patients preferred eletriptan to sc sumatriptan (51% to 43%), with the leading reasons cited being ease of use (24%), absence of adverse events (22%) and lack of recurrence (12%). Given a choice between the two treatments, a significantly higher proportion of patients elected to continue eletriptan (70%) compared to sumatriptan (30%). Eighty percent of patients rated eletriptan as an acceptable treatment compared to previous therapy.
Conclusion The higher frequency that patients chose to continue on eletriptan compared to sc sumatriptan demonstrates the importance of assessing efficacy in the broader context of overall patient preference.

P5N107

Low-dose topiramate in migraine and transformed migraine prophylaxis

Pedro André Kowacs*[1], Elcio Juliato Piovesan[1], Djon Rober Watzko[1], Hudson Fameli[1] & Lineu Cesar Werneck[1]
[1]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil*

Objective To evaluate the efficacy and tolerability of low-dose topiramate (up to 50 mg/day) as a prophylactic to migraine and transformed migraine.
Methods One hundred and seventeen migraine and transformed migraine out-patients using up to 50 mg of open-label topiramate were evaluated through telephone calls. In the survey, patients were asked about their attack frequency, headache intensity, improvement, use of analgesic and adverse events. Fifteen patients were excluded because of noncompliance. Of the remaining 102 (women = 95, men = 7; aged 14–70y, mean = 42y), 61 had migraine and 41 transformed migraine. Duration of therapy ranged from 1 to 13 month (mean = 7 month) with doses of 25 mg/day ($n = 46$) and 50 mg/day ($n = 56$).
Results Eleven patients became headache-free, and 66% reported an improvement ≥75% (16.6% improved between 50% and 75%). Intense headaches dropped from 88.2% to 17.6%. Mild headaches, not initially reported, were reported by 60.8% of the patients at the final survey. Fifty-five percent of the patients presented some side-effect, mostly weight loss (3–20 kg in 90 days)(33%), attention deficit (13.7%), somnolence (11.7%), dizziness (11.7%), paresthesiae (10.78%), amnesia (9.8%), confusion(8.8%), changes in thought(7.8%), in 10 patients severe enough to lead to withdrawal.
Conclusion Low-dose topiramate therapy can be regarded as a safe and effective in the prophylaxis of migraine and transformed migraine.

P5N108

Repeated intransal capsaicin application to treat chronic migraine

Bruno Marcello Fusco*[1,2], Giorgio Barzoi[1] & Felice Eugenio Agrò[1]
[1]*School of Medicine, University 'Campus Biomedico', Rome, Italy,*
[2]*Department of Pharmaceutical Science, University of Salerno, Salerno, Italy*

Capsaicin activates the peripheral nociceptive fibres, acting on the polymodal vanilloid receptor-1. Repeated administrations of capsaicin result in a block of the VR1 and refractoriness of the fibres. Capsaicin was suggested as a therapeutic tool in pain. Repeated nasal administrations of capsaicin improve cluster headache. Data from episodic migraine are unclear. The effect of repeated intranasal administration of capsaicin was evaluated in 10 patients affected by chronic migraine (double blind randomized design). Five patients ((2 men and 3 women, age from 32 to 48) were treated with an emulsion containing capsaicin in both nostrils, once a day for seven days; five patients (1 men and 4 women, age ranged from 24 to 45), with seven decreasing citric solutions as placebo which mimicked the decreasing burning sensation, observed during capsaicin treatment. The headache severity (numeric scale 1–10) and self satisfaction were evaluated 30days after the treatment. All patients treated with capsaicin reported an improvement, between 40% and 70%. One patient treated with placebo reported a 20% amelioration. Statistical evaluation (chi-square, $p < 0.01$) showed a significant efficacy of capsaicin as compared to placebo. This preliminary study indicates a therapeutic effect of nasal application of capsaicin in chronic migraine.

P5N109

Which migraineurs can be prevented from attacks by Lomerizine?

Michio Yamaguchi*[1]
[1]*Yamaguchi Clinic, Nishinomya, Japan*

Objective Calcium entry blockers are used widely for prevention of migraine attack. Lomerizine-HCl (LM) successfully reduces frequency of attacks in some patients, but others respond poorly. The author wants to find key factor(s) influencing LM effect in the *patients' side*.
Methods Migraineurs (57 females and 13 males, mean age: 36. Range: 14–64 y.o.) diagnosed by IHS criteria as migraine with or without aura (MO or MA, respectively) received daily 40 mg of LM orally for 12 weeks. Patients divided into 3 groups by headache severity as severe (needs bed rest for hours), moderate, and mild (no rest required) ones. Number of attacks and severity change were considered for effectiveness. Significance was checked by Chi square test with Yates' correction.
Results Difference between MO and MA, and between old group (36 y.o. or over) and young ones were insignificant. Only 6 severe-attack cases out of 9 (40%) improved by LM, while 48 out of 55 mild-attack cases responded ($P < 0.001$). Although 2 patients with dysmenorrhea out of 6 responded to LM, 42 in 51 cases without menstrual trouble improved successfully ($P < 0.05$).
Conclusion In the patients' side, severity of migraine and complicated dysmenorrhea were significant factors against the migraine prevention.

P5N110

Botulinum toxin, type A: effects on pain and headache

John Claude Krusz*[1] & William Knoderer[1]
[1]*Anodyne Headache and PainCare*

Introduction Botulinum toxin, type A, can decrease pain and headache. The mechanism is unclear; effects on sensory afferent or noncholinergic fibers is a possibility. Intradermal administraton of type A toxin was chosen to test this hypothesis.
Methods 23 patients were selected with painful conditions: (migraines, back, neck, CRPS, diabetic neuropathy, TMJ, scar pain, carpal tunnel syndrome). 100 units of botulinum toxin was administered intradermally. 12 had coexistent IHS migraines. All had muscle spasm. A skin wheal was raised with toxin.
Results All but one migraine patient responded. 20 patients (87%) had pain reduction. Neck pain ($n = 10$) was 70% diminished. Back pain ($n = 2$) did not respond. CRPS response in 2 of 3 patients. Diabetic neuropathy ($n = 1$), carpal tunnel syndrome ($n = 2$), TMJ ($n = 3$) and scar pain ($n = 2$) saw all patients respond. 3 patients had no pain reduction. Pain reduction across all categories was 62%; average duration was 8.5 weeks (range 3–20). All patients reported relief of spasm.
Conclusions Botulinum toxin, type A, given intradermally, reduces headache and pain in many conditions. Results are comparable to intramuscular administration, and raises new questions about mechanisms(s) of action of botulinum toxin. Double blind studies are warranted to replicate these findings.

P5N111

Eletriptan: switching triptans for greater efficacy

John Claude Krusz*[1]
[1]*Anodyne Headache and PainCare*

Introduction Eletriptan has just been introduced for migraine-specific therapy. This study was done in a headache clinic population where prior triptan therapy, though successful, was felt to be suboptimal over time.
Methods 30 patients who used triptans successfully to treat migraines were given eletriptan, 40 mg at onset of migraine. A repeat dose was allowed after 1 h. Patients kept diaries or rated migraine characteristics as they treated 5 or more migraines with eletriptan.
Results 24 patients (80%) reported that eletriptan was equal to or better than prior therapy. 15 patients (63%) had a definite preference for eletriptan with respect to degree of migraine relief. This was consistent in 90% of migraine attacks treated with eletriptan. 6 patients utilized a second dose consistently. 3 patients rated eletriptan as slightly less efficacious than prior therapy and 3 preferred other triptan therapy as superior. No side-effects, other than dry mouth in 2 patients, were noted.
Conclusions Eletriptan is quite effective as acute migraine-specific therapy. It can recapture a strong degree of efficacy where prior triptan therapy has decremented. One can make a strong case to switching therapy to eletriptan where prior therapies are suboptimal, or where repeat dosing occurs frequently.

P5N112

Transcranial Doppler examination in migraine children with pharmacoprophylaxis of lamotrigine

Ewa Pilarska*[1] & M. Lemka[1]
[1]*Developmental Neurology Department, Medical University of Gdansk*

Objectives In the recent years lamotrigine has started to play an important role in pharmacoprophylaxis. Blood flow disturbances connected with increased cerebrovascular reactivity in children with migraine can be observed. Pharmacoprophylaxis with lamotrigine probably may have an influence on these hemodynamic changes and the clinical status.
Methods Hemodynamic changes assessed by transcranial Doppler examination were detected in migraine headaches in pain-free periods before and after prophylactic treatment by lamotrigine in 10 children (6 boys, 4 girls) aged 8–15 years. Six of them had migraine with aura, 4- without aura. Control group consisted of 10 children without headache in similar age. Doppler examination including evaluation of BFV and PI of MCA's and ACA's was performed. The dose of lamotrigine was 50 mg/day. The duration of pharmacoprophylaxis was 3 months.

Results Compared to the control group, children with migraine presented significantly higher BFV of MCA and ACA. Migraine attacks became less frequent and shorter; aura less intensive after lamotrigine prophylaxis. No side-effects were observed during lamotrigine administration. There were no significant differences in cerebral blood flow parameters after 3 months of prophylactic treatment.
Conclusions Lamotrigine may be efficient and safe in preventive medications for migraine in children. Transcranial Doppler examination may be useful in determining children's headache pathomechanism.

P5N113

Efficacy and preference of sumatriptan,zolmitriptan and elertiptan in a Japanese Headache Clinic

Haruko Araki*[1], Takao Takeshima[1], Tamami Ijiri[1], Yoko Fukuhara[1], Kumiko Ishizaki[1], Masayoshi Kusummi[1], Hisanori Kowa[1] & Kenji Nakashima[1]
[1]*Department of Neurology, Tottori University Faculty of Medicine*

Background and objective Three oral triptans, sumatriptan(S), zolmitriptan(Z), and eletriptan(E), have become available in Japan. We surveyed efficacy of three triptans for acute migraine attacks.
Methods A series of 164 migraineurs (43 with aura; 121 without aura, mean age 36.5 years), who visited the headache clinic of Tottori University hospital from September 2001 to December 2002, were studied. Three triptans were randomly assigned as an open-trial manner. We evaluated 2- h efficacy of triptans.
Results Eighty-four patients was prescribed one or more triptans (S67; Z37 and E32). In trials of sumatriptan (S-trial), 35 of 67 patients (52.2%; mean dosage 54.5 mg) responded at 2 h, 17 (25.4%) did not respond and the other 15 (22.4%) did not complete trial. In Z-trial, 20 of 37 patients (54.1%, mean dosage 2.8 mg) responded, 12 (32.4%) did not respond, and 5 (13.5%) did not complete. In E-trial, 21 of 32 (65.6%, mean dosage 30 mg) responded, one (3.1%) did not respond, and 10 (31.3%) did not complete. Sixty-four of 84 migraineurs completed two or three trials of different triptans. Only nine patients (10.7%) stated that the triptans used were equally effective and equally preferable.
Conclusions We demonstrated a piece of evidence that S, Z and E are equally effective in Japanese migraineurs and that the effectiveness and preference of triptans may differ among patients.

P5N114

Efficacy of topiramate in the prophylaxis of high frequency migraine in children

Niranjan Narain Singh*[1] & Surendra Misra[2]
[1]*Institute of Medical Sciences, Banaras Hindu University,* [2]*Institute of Medical Sciences BHU Varanasi India*

Objective To determine the efficacy of Topiramate as a prophylactic agent in children with high frequency migraine.
Methods We studied the incidence of headache relief in children with migraine .52 children with high frequency migraine (headache frequency more than once per week)were treated with slowly increasing Topiramate 2 mg/kg/day for at least three months. The frequency, severity and duration of headache were evaluated at subsequent visits. Average age of patient was 9.2 year. Average frequency of headache was 8.2 days/month. Average severity was 6.84/10. Average duration was 2.5 h (± 1.5) per attack.
Results Two patients dropped out from follow-up. Forty-five (90%) children had an overall perception of well being. The frequency of headache improved to 1.5(– + 1.5) while average severity to 1.3 (– + 1.1). Average duration was reduced to 0.4(0.9) hours per attack. Long-term follow-up up to three months showed consistent relief. In 5 patients, the medication was withdrawn because of side-effects: Diarrhea and pain abdomen (4) and perioral paresthesia (1).
Conclusion Topiramate is an effective prophylactic treatment even in children with very high frequency migraine. Once daily dosing gave a very good compliance. Diarrhea being the major limiting side-effect.

P5N115

Topamax for refractory headache and migraine patients

Reto Agosti*[1] & Sonja Eugster[1]
[1]*Headache Center Hirslanden, Zurich, Germany*

Introduction Topiramate (Topamax®) is in migraine prophylaxis. At the Zurich University Hospital and Headache Center Zürich/Hirslanden highly therapy refractory headache patients are treated in a specialized headache facility.
Methods Retrospective analysis of patients with various types of resistant and chronic secondary headaches under topiramate. Demographic data and data on outcome and body weight were collected and analyzed.
Results Of 27 treated patients 10 were lost for follow up. Of the remaining 17 patients 10 patients responded in a favorable way and 7 did not. Headache were mixed in both groups and contained migraine, tension type and other headaches. Mean dosage of favorable group was 325 (25–700). Most significant side-effects were tiredness and dizziness. Weight gain was not observed but a weight loss in the PO group.
Conclusions Topiramate is a valuable alternative for resistant headaches. Weight loss is a very strong motivation to try a new medication. Tolerability seems to be the key to success: the average dose of the responders was almost five time that of the non responder group.

P5N116

Anticephalgic premedicated mask

Morton I. Hyson[1]
[1]*University of Nevada, School of Medicine, Nevada, USA*

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

Design/methods The patients were given masks and numbered bottles of topical medication containing topical salicylates or placebo. They were instructed to apply the medication to their frontalis region in the event they should suffer a headache, put on the photoprotective mask. Furthermore, they were instructed to take oral medications, if required, for relief of the headache.
Results Seven out of 20 of the patients who received the placebo stated the medication and mask helped and gave it an average rating of 4.31 on a 0–10 scale. Twenty-eight out of 34 of the patients receiving the active medication stated it was effective, rating it 7.42 on the 0–10 scale ($P < 0.001$). 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 with associated frontalis pain.

P5N117

Unlicensed and off-label prescribing of drugs in specialty headache practice

Elizabeth Loder*[1] & David Biondi[1]
[1]*Harvard Medical School, USA*

Objective To assess the extent of off-label prescribing in headache practice.
Methods A prospective record was kept of all prescriptions written during a single month in a tertiary care headache program affiliated with two Harvard teaching hospitals. Each drug was categorized as 'off-label' – that is, not approved or licensed by the United States Food and Drug Administration (FDA) for a headache or pain indication or 'on-label' –approved by the FDA for a headache or pain indication.
Results A total of 399 prescriptions were written during a 30-day period. 208 (52%) were used off-label. The largest percentages of prescriptions written for approved, on-label indications were for triptans ($n = 74$; 39% of all on-label prescriptions), and nonsteroidal anti-inflammatory drugs ($n = 64$; 32% of all on-label prescriptions).

191 off-label drugs were prescribed. The largest percentages of prescriptions written for unapproved, off-label indications were for newer antiepileptic drugs such as topiramate ($n =$ 26;% of off-label prescriptions), newer antidepressants, especially venlafaxine ($n = 25$;%), and botulinum toxin type A ($n =$ 13;% of off-label prescriptions).
Conclusions Off-label prescribing is common in the speciality management of headache conditions. We conclude that it is within the current standard of care to use off-label medications in the treatment of complex headache conditions.

P5N118

Peripheral nerve stimulation in treatment of neuropathic trigeminal pain

Konstantin Slavin*[1]
[1]*University of Illinois, Chicago, USA*

Despite advances in pharmacological pain treatment, management of neuropathic pain syndrome in the facial region remains problematic. Several years ago, we presented our technique of treatment neuropathic trigeminal pain with implanted peripheral nerve stimulation. In this presentation we summarize 3-year experience of a single institution in using this pioneering technique.

Out of 12 patients with neuropathic pain in supraorbital and/or infraorbital area due to trauma, sinus surgery, or other surgical interventions, 7 were considered for a trial of stimulation. With stimulation electrodes inserted percutaneously, a week-long trial of stimulation allowed us to select 6 patients that underwent implantation of the permanent system. All of them experiences improvement or disappearance of their pain for prolonged period of time, and some were able to return to normal activities with or without medications.

We present details of our technique of peripheral nerve stimulation for treatment of trigeminal neuropathic pain and discuss indications, screening procedure, associated risks and long-term results of its clinical application.

In our opinion, peripheral nerve stimulation may be a useful nondestructive option for treatment of medically intractable neuropathic pain in the trigeminal nerve distribution. It may be considered for patients with post-traumatic or postsurgical neuropathy involving distal trigeminal nerve branches.

Pharmacology

P5O1

Contractile 5-HT 1B receptor responses to triptans in human cerebral and coronary arteries and the possible relationship with clinical mechanisms of action

Lars Edvinsson*[1], Angelica Wachenfors[1], Jenny Longmore[2], Anthony Davenport[3] & Erik Uddman[1]
[1]*Division of Experimental Vascular Research, Department of Internal Medicine, Lund University Hospital, Lund, Sweden,* [2]*Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Harlow, U.K,* [3]*Department of Clinical Pharmacology, Centre for Clinical Investigation, Addenbrooke's Hospital, Hills Road, Cambridge*

The aim of the present study was to compare vasoconstrictor potency (EC_{50}) of triptans (measured using human isolated coronary and cranial arteries) and examine whether there was any relationship with the plasma concentrations (Cmax, nM) of the drugs achieved following oral administration.

Cerebral and coronary artery ring segments were mounted in organ baths for isometric tension recording and cumulative concentration effect curves to either sumatriptan, rizatriptan or eletriptan were obtained and the pEC_{50} obtained from nonlinear regression analysis. The ratio of Cmax/EC_{50} was calculated where the Cmax was the maximum concentration of the

drug detected in plasma following oral administration. Fresh frozen sections of coronary artery were subjected to standard immunohistochemical techniques using specific 5-HT_{1B} and 5-HT_{1D} receptor antibodies.

The triptans were equally strong vasoconstrictors of cerebral arteries; rank order of agonist potency was, eletriptan > rizatriptan > sumatriptan. In coronary arteries the triptan potency was rizatriptan = sumatriptan > eletriptan; the maximum effect was sumatriptan > rizatriptan = eletriptan. In cerebral arteries the ratio of $Cmax/EC_{50}$ was not significantly different from unity indicating a relationship. For coronary artery, the ratios were significantly less than unity indicating no direct relationship. Thus, plasma levels are likely to be below concentrations usually required for coronary artery contraction. Immunohistochemistry did not reveal any obvious difference in 5-HT_{1B} receptor expression between normal and diseased coronary arteries.

P5O2

The effect of the nonpeptide CGRP-antagonist, BIBN4096BS on human-alphaCGRP induced headache and hemodynamics in healthy volunteers

Kenneth Ahrend Petersen*[1], Lisbeth Hjorth Lassen[1], Steffen Birk[1] & Jes Olesen[1]
[1]*Danish Headache Center, University of Copenhagen and Department of Neurology, Glostrup University Hospital, Glostrup, Denmark*

The CGRP-antagonist BIBN4096BS has been tested in the treatment of acute migraine. To further elucidate the mechanism of action, we investigated the ability of BIBN4096BS to inhibit h-αCGRP induced headache and cerebral hemodynamic changes in man.

Ten participants completed this double-blinded placebo-controlled crossover study. The participants were randomised to receive BIBN4096BS 2.5 mg or placebo as pretreatment before a 20-minute intravenous infusion of h-αCGRP ($1.5\ \mu g \cdot min^{-1}$). Transcranial Doppler was used to measure blood flow velocity in the MCA; regional and global cerebral blood flow was measured by ^{133}-Xenon-inhalation SPECT. The temporal and radial artery diameters were measured by high-resolution ultrasound. Systemic hemodynamics, $P_{et}CO_2$, and headache were monitored.

BIBN4096BS did not affect the changes in the diameter of the MCA or changes in global and regional CBF induced by h-αCGRP. Vasodilatation of the extra-cranial arteries was significantly inhibited ($P = 0.0012$ and $P = 0.008$, respectively, the temporal and radial artery), however.

Six of the 10 participants experienced a 'CGRP-induced headache' after placebo pretreatment, none with BIBN4096BS ($P = 0.031$).

These results show that BIBN4096BS effectively prevents 'CGRP-induced headache' and extra-cerebral vasodilatation, but does not significantly affect the induced cerebral hemodynamic changes. This supports an extra-cerebral site of action of BIBN4096BS's potential antimigraine effect. Future studies are warranted.

P5O3

Triptans cause cutaneous allodynia

Mattias Linde*[1,3], Carl Dahlöf[1,3], Mikael Elam[2,3] & Håkan Olausson[2,3]
[1]*Gothenburg Migraine Clinic,* [2]*Department of Clinical Neurophysiology, Sahlgren University Hospital,* [3]*Institute of Clinical Neuroscience, Gothenburg University, Sweden*

Objectives Patients commonly report dysesthesia after intake of triptans. We tested if sumatriptan can cause allodynia.

Methods Prospective, randomized, double-blind, placebo-controlled, cross-over design. Twenty-four ($n = 24$) participants: 12 (10 women, 2 men, mean age 41.2 years) with migraine according to the International Headache Society and a history of cutaneous allodynia after sumatriptan. 12 healthy subjects (10 women, 2 men, mean age 38.7 years) without migraine. TSA-2001™ (Medoc), SenseLab-Brush-05™ (Somedic) and tactile directional sensibility (TDS) hand-held stimulator. Left hand. Pain- and medication-free intervals. Before and 20 + 40 min after injection of 6 mg sumatriptan or saline (placebo).

Results Significant ($P = 0.008$, sign-test) placebo-subtracted (suma > placebo = 8, ties = 16, suma < placebo = 0) increase in brush-evoked discomfort after 20 min, mainly in the subgroup of migraineurs ($P = 0.031$). Disappeared by 40 min Significant ($P = 0.031$, Wilcoxon sign-rank test) lowering of HPT after 20 min, more marked among migraineurs (meanΔ –1.0 °C, suma > placebo = 10, suma < placebo = 2, p = 0.06) than nonmigraineurs (meanΔ –0.5 °C, suma > placebo = 7, suma < placebo = 5, NS). Disappeared at 40 min ($P = 0.068$). Cold pain thresholds and TDS unchanged.

Conclusions Sumatriptan can cause tactile and thermal, cutaneous allodynia. This raises further questions concerning other sensory side-effects of triptans and warrants consideration in the interpretation of studies on migraine-induced allodynia.

P5O4

Endothelium Dependent relaxant responses to selective 5-HT 1B/1D receptor agonists in the isolated middle cerebral artery of rat

Lars Edvinsson*[1,2], Natalie Loevland Hoel[1,2], Jacob Schwartz[1,2], Elizabeth Nilsson[1] & Peer Tfelt-Hansen[3]
[1]*Department of Internal Medicine, University Hospital of Lund, Lund, Sweden,* [2]*Department of Clinical Experimental Research, Copenhagen University Hospital, Glostrup, Denmark.,* [3]*Department of Neurology, Copenhagen University Hospital, Glostrup, Denmark*

Agonists for 5-$HT_{1B/1D}$ receptors are used in the treatment of migraine attacks in part due to their selective vasoconstrictor effects on intracranial arteries. To study the vasomotor effects of triptans in middle cerebral artery of rats (MCA), we used the *in vitro* ring segments technique and the pressurized arteriography method allowing discrete investigation of the contribution of endothelial cells and smooth muscle cells to vascular tone.

MCAs from Sprague-Dawley rats were mounted onto two glass micropipettes, pressurized to 85 mmHg and luminally

perfused. Luminally added 5-HT, sumatriptan and rizatriptan induced *dilatations* of 27 ± 4%, 11 ± 4% and 16 ± 6%, respectively, compared to the resting diameter. The relaxant effect of sumatriptan was mediated through 5-HT $_{1B/1D}$ receptors since the selective antagonists GR55562 (10^{-6} M) blocked the response. The use of L-NOARG and charybdotoxin revealed that the dilatation was dependent on both NO and endothelially derived hyperpolarizing factor (EDHF).

Using the ring segments in tissue baths, MCA segments were mounted on two metal wires. The relaxant responses to sumatriptan could no be reproduced using this model; instead weak contractile responses (6 ± 3% of submaximal contractile capacity) were observed.

The experiments show that the expression of 5-HT$_{1B/1D}$ immunoreactivity in the endothelium thus translates into relaxant responses to 5-HT and triptans, a response mediated via NO or EDHF.

P5O5

Blockade of calcitonin gene-related peptide (CGRP) receptors in the trigeminocervical complex reduces trigeminovascular nociceptive traffic

Robin James Storer*[1], Simon Akerman[1] & Peter James Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London, UK*

Objective We sought to determine whether CGRP modulated craniovascular nociceptive pathways using *in vivo* microiontophoresis onto neurons in the trigeminocervical complex and intravenous administration of the CGRP the antagonists α-CGRP$_{8-37}$ and BIBN-4096 in the cat.
Methods Cats were anaesthetised with α-chloralose, which was supplemented with halothane during surgical preparation. Extracellular recordings of activity in the trigeminocervical complex evoked by supramaximal electrical stimulation of the superior sagittal sinus (SSS) were made. Seven- or nine-barrelled glass micropipettes incorporating tungsten recording electrodes were used for microiontophoresis.
Results Cell firing was increased by microiontophoretic application of L-glutamate ($n = 43$ cells). Microiontophoresis of CGRP excited 7 of 17 tested neurons, an effect inhibited by BIBN-4096. BIBN4096 inhibited the majority of units (26 of 38 cells) activated by L-glutamate. CGRP$_{8-37}$ inhibited a similar proportion of units (5 of 9 cells). Intravenous administration of BIBN-4096 resulted in a dose-dependent inhibition of trigeminocervical SSS-evoked activity.
Conclusions The data suggest that there are nonpresynaptic, probably postsynaptic, CGRP receptors in the trigeminocervical complex that can be inhibited by blockade of the CGRP receptor. The data are consistent with a CGRP receptor antagonist being effective in the acute treatment of migraine and cluster headache.

P5O6

Topiramate inhibits trigeminovascular traffic in the cat: a possible locus of action in the prevention of migraine

Robin James Storer*[1] & Peter James Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London*

Objectives To examine the effect of topiramate on trigeminocervical activation in the anaesthetised cat.
Methods Cats ($n = 7$) were anaesthetised with α-chloralose, supplemented with isoflurane during surgical procedures, and prepared for physiological monitoring. The superior sagittal sinus (SSS) was isolated and electrically stimulated to produce a model of trigeminovascular nociceptive activation. Cumulative dose–response curves for the effect of topiramate at doses of 3, 5, 10, 30 and 50 mg/kg intravenously on SSS-evoked trigeminocervical neurons were constructed.
Results Topiramate reduced SSS evoked firing of neurons in the trigeminocervical complex in a dose-dependent fashion. The maximum effect was seen over 30 min for the cohort taken together, although for some animals and doses the maximum effects were seen earlier. At 3 mg/kg after 15 min firing was reduced by 35 ± 13%. At 5 mg/kg after 30 min firing was reduced by 48 ± 5%. At 50 mg/kg firing was reduced 63 ± 15% by 30 min.
Conclusions Topiramate inhibited the activation of trigeminocervical neurons in response to stimulation of the superior sagittal sinus. Inhibition of the trigeminocervical complex directly, or neurons that control sensory input is a plausible mechanism of the action of preventative medicines in migraine, or cluster headache.

P5O7

Post-synaptic high threshold Voltage Dependent Calcium Channels (VDCC) modulate trigeminovascular nociceptive transmission in the TrigeminoCervical Complex (TCC)

Kevin Gerald Shields*[1], Robin James Storer[1], Simon Akerman[1] & Peter Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London*

Objectives To investigate the role of P/Q, L and N-type VDCCs in postsynaptic action potential generation in trigeminovascular nociceptive afferents in the trigeminocervical complex (TCC) of the cat.
Methods Trigeminovascular nociceptive afferents were identified in the TCC by electrical stimulation of the superior sagittal sinus. Cell bodies were identified by their response to microiontophoresis of $_{L}$-glutamate. Selective antagonism of VDCC was accomplished by microiontophoresis of ù-agatoxin IVa/TK (P/Q), ù-conotoxin GVIa (N) and calciseptine (L-type). Non-selective antagonism was also studied with cadmium ions. The response to $_{L}$-glutamate was then studied during coadministration of vehicle (control) and active compound.
Results Non-selective blockade of high threshold VDCC with cadmium resulted in a reduction in L-glutamate-evoked neuronal activity ($n = 5$, $t_4 = 4.33$; $P = 0.01$). Selective antagonism of P/Q ($n = 19$, $t_{18} = 9.88$; $P < 0.0001$), L ($n = 8$, $t_7 = 8.03$; $P < 0.0001$) and N-type ($n = 13$, $t_{12} = 7.18$; $P < 0.0001$) VDCC's each resulted in significant reductions in postsynaptic action potential generation in response to L-glutamate.

Conclusions Post-synaptic high threshold VDCCs in general, and specifically of P/Q, L and N-type, can modulate nociceptive transmission in the trigeminocervical complex *in vivo*.

P5O8

Effects of BIBN4096BS on cardiac output distribution and on calcitonin gene-related peptide (CGRP)-induced carotid haemodynamic changes in anaesthetised pigs

Udayasankar Arulmani*[1], Kapil Kapoor[1], Jan P C. Heiligers[1], Edwin W. Willems[1], Henri Doods[2], Carlos M. Villalón[3] & Pramod R. Saxena[1]
[1]*Department of Pharmacology, Erasmus Medical Centre, Rotterdam, the Netherlands,* [2]*Boehringer Ingelheim Pharma KG, Biberach, Germany,* [3]*Department of Pharmacobiology, CINVESTAV-IPN, Mexico D.F., Mexico*

Objectives CGRP released during migraine attacks dilates the cranial blood vessels, thereby causing headache. We therefore investigated the effects of BIBN4096BS, a CGRP receptor antagonist, on cardiac output distribution and on α-CGRP induced carotid haemodynamics in porcine model predictive for antimigraine activity.
Methods Pigs were anaesthetised with sodium pentobarbital. The cardiac output distribution of BIBN4096BS (100, 300 and 1000 μg/kg; i.v) was determined by radioactive microsphere method. In carotid haemodynamic experiments, phenylephrine (10 μg/kg min^{-1}) was infused into the carotid artery (i.c). The systemic and carotid haemodynamic responses were measured at baseline and after α-CGRP (100 pmol/kg min^{-1}, i.c) infusions, given before (control) and following three i.v. injections of vehicle or BIBN4096BS.
Results BIBN4096BS produced a small decrease in cardiac output and, at its highest dose, the vascular conductance to the lungs, kidneys and adrenals decreased moderately. α-CGRP infusion increased the total carotid conductance, but decreased mean blood pressure. These responses were blocked by BIBN4096BS (see Fig. 1).
Conclusion BIBN4096BS behaves as a potent antagonist. The slight haemodynamic changes with the high doses of BIBN4096BS suggest that endogenous CGRP does not play an important role in regulating the basal vascular tone. BIBN4096BS may be effective in migraine therapy without overt cardiovascular liability.

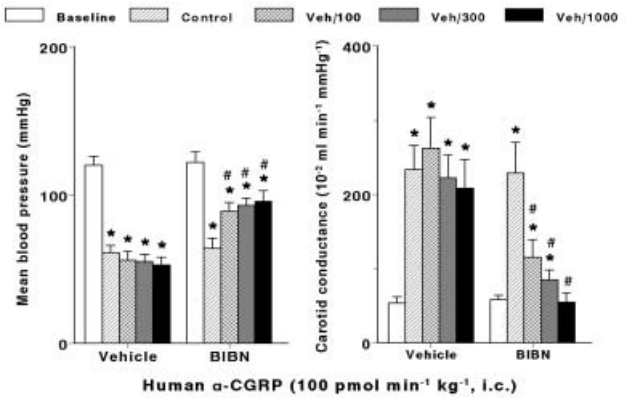


Figure 1

P5O9

Pharmacological analysis of existing prophylatic migraine agents: inhibition of sympathetic nervous system activation as a common mechanism of action

Stephen Peroutka*[1]
[1]*Synergia Pharma, Inc., South San Francisco, CA, USA*

More than 50 pharmaceutical products have been reported to be effective in the prophylactic treatment of migraine. However, none of these drugs eliminates the majority of headaches in the majority of patients, let alone eliminates all migraine attacks. In an attempt to determine if a common mechanism of action and/or common site of action exists for migraine prophylactic drugs, the pharmacological effect of beta-adrenergic receptor antagonists, anticonvulsants, tricyclic antidepressants, calcium channel blocker, 5-hydroxytryptamine receptor antagonists, angiotensin-converting enzyme antagonists and angiotensin receptor antagonists were reviewed. All existing therapeutic agents display a wide variety of both desirable and undesirable pharmacological effects.

Only a single pharmacological effect could be identified that is shared by this diverse group of prophylactic agents: the induction of orthostatic hypotension. Moreover, all classes of prophylactic agents interact with receptors, enzymes and channels that either directly or indirectly stimulate the sympathetic nervous system. By inhibiting these receptors, enzymes and channels, prophylactic drugs share an ability to inhibit sympathetic function. As a result, suppression of SNS activity is a common pharmacological property of migraine prophylactic agents. This observation provides for a testable hypothesis that could lead to the development of more effective migraine prophylactic agents.

P5O10

Antinociceptive effect of amitriptyline is not directly related to serotonin reuptake inhibition

Sait Ashina*[1], Lars Bendtsen[1], Inge Hindberg[2] & Rigmor Jensen[1]
[1]*Department of Neurology and Danish Headache Center, Glostrup Hospital, University of Copenhagen, Copenhagen, Denmark,* [2]*Department of Clinical Chemistry, Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark*

Objective To explore possible mechanisms of action of the analgesic effect of amitriptyline we investigated prophylactic efficacy together with platelet 5-HT levels during treatment with amitriptyline, the SSRI citalopram, and placebo. Low platelet 5-HT levels are assumed to reflect a high degree of neuronal 5-HT reuptake inhibition.
Methods Forty patients with chronic tension-type headache were included. The study was a double-blind, placebo-controlled, three-way crossover trial.
Results Thirty-four patients completed the study. The area under the headache curve was significantly lower during treatment with amitriptyline, 308, than during treatment with citalopram, 377 ($P = 0.04$) and placebo, 441 ($P = 0.002$). There was no significant difference between citalopram and placebo. Platelet 5-HT was significantly lower during treatment with

citalopram, 0.4×10^{-18} mol/platelet, than during treatment with amitriptyline, 1.7×10^{-18} mol/platelet ($P < 0.001$), and placebo, 3.5×10^{-18} mol/platelet ($P < 0.001$).

Conclusion The lower platelet 5-HT during treatment with citalopram than amitriptyline indicates that 5-HT reuptake was most effectively inhibited by citalopram. In contrast, amitriptyline was most effective in reduction of headache. This suggests that the analgesic effect of amitriptyline in chronic tension-type headache can not solely be explained by serotonin reuptake inhibition.

P5O11

GABA receptors modulate trigeminovascular nociceptive transmission in the ventroposteromedial (VPM) thalamic nucleus of the rat

Kevin Gerald Shields*[1], Holger Kaube[1] & Peter Goadsby[1]
[1]*Headache Group, Institute of Neurology, Queen Square, London*

Objectives To investigate the postsynaptic profile of GABA receptors in relay cells, responsive to trigeminovascular activation in the VPM thalamic nucleus, and determine if sodium valproate was able to modulate responses of these cells.

Methods Trigeminovascular nociceptive afferents were identified in the VPM by electrical stimulation of the superior sagittal sinus (SSS). $_{L}$-glutamate was microiontophoresed onto the cell body in 5 s pulses and the response was studied during coadministration of saline (control), GABA, $GABA_A$ agonist (muscimol), $GABA_B$ agonist (baclofen), sodium valproate and $GABA_A$ (bicuculline) and $GABA_B$ (OH-saclofen), antagonists.

Results In all cells tested GABA suppressed the response to $_{L}$-glutamate ($n = 26$, t_{25} 6.4; $P < 0.0001$) and to SSS stimulation ($F_{1.4,16.8} = 15.42$, $P < 0.0001$). This effect could be antagonised with bicuculine but not OH-saclofen. Sodium valproate was able to inhibit the response to $_{L}$-glutamate ($n = 14$, $t_{13} = 11.04$; $P < 0.0001$) and to SSS stimulation ($F_{2,12} = 24.0$; $P < 0.0001$).

Conclusions The response of VPM thalamic relay cells activated by trigeminovascular nociceptive afferents can be modulated by both $GABA_A$ and $GABA_B$ receptors, though $GABA_A$ receptors appear to predominate. The response of these cells can also be inhibited by microiontophoretic application of sodium valproate.

P5O12

Circulating nociceptin levels during the cluster headache period

Csaba Ertsey*[1], Mónika Hantos[2], György Bozsik[1] & Kornélia Tekes[2]
[1]*Department of Neurology, Semmelweis University, Budapest, Hungary,* [2]*Department of Pharmacodynamics, Semmelweis University, Budapest, Hungary*

The trigeminovascular system has a prominent role in the pathomechanism of cluster headache. Nociceptin (NC), an opioid neuropeptide, is the endogenous ligand of the OP-4 receptor, with both algesic and analgesic properties depending on the site of action. NC and the OP-4 receptor are expressed by CGRP-positive trigeminal ganglion cells. Moreover, NC was shown to inhibit neurogenic dural vasodilatation, a phenomenon related to trigeminovascular activation. To explore its possible involvement in cluster headache, we studied NC plasma levels when attack-free during the cluster period. In 14 cluster headache patients NC levels were significantly lower than in an age-, and sex-matched group of controls (4.91 ± 1.96 vs. 9.58 ± 2.57 pg/mL, $p < 0.0001$). NC levels showed no correlation with age, length of disease or episode length. There may be a defective nociceptin-mediated regulation of trigeminal activity during the cluster period, which may contribute to the genesis of the attacks.

P5O13

Supratherapeutic doses of eletriptan vs. a therapeutic dose of sumatriptan and vs. placebo: effect on human coronary arteries

James Goldstein*[1], Kenneth Massey[2], Simon Kirby[3], Michael Gibson[4], Jayasena Hettiarachchi[5], Andrew Rankin[6] & Neville Jackson[6]
[1]*WM Beaumont Hospital,* [2]*Pfizer Global Research & Development,* [3]*Pfizer Global Research and Development, UK,* [4]*Harvard Clinical Research Institute,* [5]*Pfizer Inc,* [6]*Global Research and Development, Pfizer Ltd*

Objective To assess eletriptan's cardiovascular safety at high plasma concentrations by evaluating effects on coronary artery diameter after supratherapeutic-dose intravenous eletriptan, therapeutic-dose subcutaneous sumatriptan and placebo.

Design/methods Patients ($n = 60$) undergoing diagnostic coronary angiography with normal arteries were randomized to intravenous eletriptan (plasma concentrations 3–5X C_{max} of 80-mg oral eletriptan), subcutaneous sumatriptan (6-mg therapeutic dose) or placebo, in a double-blind, double-dummy, parallel-group design. Serial coronary angiograms and drug plasma levels were analyzed. The primary outcome was maximum percentage change in coronary artery diameter expressed as percentage of baseline diameter.

Results The mean maximum change in left anterior descending (LAD) coronary artery diameter for eletriptan, –22% (95% CI:26%,-19%) was similar to sumatriptan, –19% (95% CI:22%,-16%) and placebo, –16% (95% CI:20%,-12%). The maximum percentage reduction in mid-LAD diameter for eletriptan was similar to placebo, even at eletriptan C_{max} 5-times an 80-mg dose during migraine. Noninferiority analysis demonstrated equivalence of high-dose eletriptan with therapeutic-dose sumatriptan. All patients completed the study without significant adverse events.

Conclusions Eletriptan exerts a clinically insignificant effect on coronary artery tone, even at supratherapeutic concentrations administered intravenously, and demonstrates a high coronary safety margin, even at high plasma concentrations exceeding those potentially seen with concomitant use of potent CYP3A4 inhibitors.

P5O14

The novel CGRP-antagonist, BIBN4096BS does not affect the cerebral hemodynamics in healthy volunteers

Kenneth Ahrend Petersen*[1], Steffen Birk[1], Lisbeth Hjorth Lassen[1], Christina Kruuse[1], Olga Jonassen[2] & Jes Olesen[1]
[1]*Danish Headache Center, University of Copenhagen and Department of Neurology, Glostrup University Hospital, Glostrup, Denmark,*
[2]*Department of Clinical Physiologies and Nuclear Medicine, Glostrup University Hospital*

The nonpeptide CGRP-antagonist BIBN4096BS has been tested in the treatment of acute migraine. Blocking the receptor of a strong vasodilator entails a theoretical risk of causing cerebral vasoconstriction, a probability not previously investigated with BIBN4096BS.

Seven participants completed this double-blind crossover placebo-controlled study. The subjects received in random order 10 min infusions of either placebo, 2.5 mg or 10 mg of BIBN4096BS on 3 separate days. Transcranial Doppler was used to measure the middle cerebral artery blood flow velocity ($V_{mean\ (MCA)}$); regional cerebral blood flow (rCBF) was measured by ^{133}-Xenon inhalation SPECT. The temporal and radial artery diameters were measured by high-resolution ultrasound. Systemic hemodynamics, end-tidal pCO_2, and adverse events were monitored.

BIBN4096BS had no influence on either global or $rCBF_{MCA}$, or $V_{mean\ (MCA)}$. There was no effect on the systemic hemodynamics. Adverse events were minor. We conclude that there is no effect of CGRP-receptor blockade on the cerebral or systemic circulation in humans; indicating that circulating CGRP is not exerting vasodilatatory activity in the resting state. Thus, the use of BIBN4096BS for acute migraine seems to be without risk of cerebral vasoconstriction.

BIBN4096BS may be the first potential antimigraine drug proven to be a nonvasoconstrictor. Future studies are warranted.

P5O15

A dose–response study of nitric oxide synthase inhibition in man

Lisbeth Hjorth Lassen*[1], Helle Klingenberg Iversen[1] & Jes Olesen[1]
[1]*Danish Headache Center, Department of neurology, Glostrup University Hospital, 2600 Glostrup, Denmark*

Nitric oxide (NO) is implicated in several disorders. N^G monomethyl L-arginine (L-NMMA), is an inhibitor of all 3 Nitric Oxide Synthases (NOS). The present study was performed to find the maximal tolerated dose of L-NMMA for further studies of NOS inhibition in man.

In a double blind, placebo controlled, cross over design six healthy volunteers were randomised to receive three different doses of L-NMMA (0.3 mg/kg, 1 mg/kg, 3 mg/kg) or placebo i.v over 5 min on four different days. On a fifth study day, in an open design, the same subjects received L-NMMA in the dose 6 mg/kg i.v over 15 min The effect of L-NMMA on the maximal mean blood velocity (V_{mean}) in the middle cerebral artery (MCA) (transcranial Doppler), the luminal diameter of the radial artery (high frequency ultrasound), mean arterial blood pressure (MAP), heart rate, and electrocardiogram were repeatedly followed. Inhibition of NOS had no effect on Vmean in MCA or on the diameter of the radial artery, but MAP increased and heart rate decreased dose dependently. After L-NMMA 6 mg/kg over 15 min maximum MAP increase was 20% at 20 min after start of L-NMMA infusion. Maximum decrease of heart rate was 24% at 15 min after start of the L-NMMA infusion

We conclude that L-NMMA in a dose that caused marked changes in systemic blood pressure and heart rate had no effect on cerebral and radial arteries in man.

P5O16

Effects of the CGRP antagonist BIBN4096BS on capsaicin-induced carotid haemodynamic changes in a porcine migraine model

Udayasankar Arulmani*[1], Kapil Kapoor[1], Jan P C. Heiligers[1], Edwin W. Willems[1], Henri Doods[2], Carlos M. Villalón[3] & Pramod R. Saxena[1]
[1]*Department of Pharmacology, Erasmus Medical Centre, Rotterdam, the Netherlands,* [2]*Boehringer Ingelheim Pharma KG, Biberach, Germany,* [3]*Department of Pharmacobiology, CINVESTAV-IPN, Mexico D.F., Mexico*

Objectives Calcitonin gene-related peptide (CGRP), a potent vasodilator released from capsaicin-sensitive trigeminal sensory nerves, seems to play an important role in the pathogenesis of migraine (1). We have therefore investigated the effects of BIBN4096BS, a CGRP receptor antagonist (2), on capsaicin-induced carotid haemodynamic changes and plasma CGRP release in pigs.

Methods 22 pigs (10-14 kg) were sedated with azaperone (120 mg, i.m) and midazolam (10 mg, i.m) and then anaesthetised with pentobarbital (600 mg, i.v). Phenylephrine (10 μg/kg min^{-1}) was infused into the carotid artery (intracarotidly; i.c). Total and arteriovenous anastomotic (AVA) blood flows (determined with and electromagnetic flow meter and radioactive microspheres, respectively) and plasma CGRP concentrations (radioimmunoassay) were measured at baseline and after capsaicin (10 μg/kg min^{-1}, i.c) infusions, given before (control) and following three i.v. injections of vehicle or BIBN4096BS (100, 300 and 1000 μg/kg).

Results In animals treated with vehicle, the capsaicin infusion increased the total carotid/AVA blood flows and plasma CGRP levels. In contrast, after BIBN4096BS, the capsaicin-induced carotid haemodynamic changes were attenuated, but those in plasma CGRP levels were, interestingly, enhanced by the highest doses of BIBN4096BS (Fig. 1).

Conclusion BIBN4096BS blocks the capsaicin-induced carotid haemodynamic changes, but not the associated CGRP release. The compound may prove effective against acute migraine.

References

1 Edvinsson et al. CNS Drugs 2001; 15: 745–53.
2 Doods et al. Br J Pharmacol 2000; 129: 420.

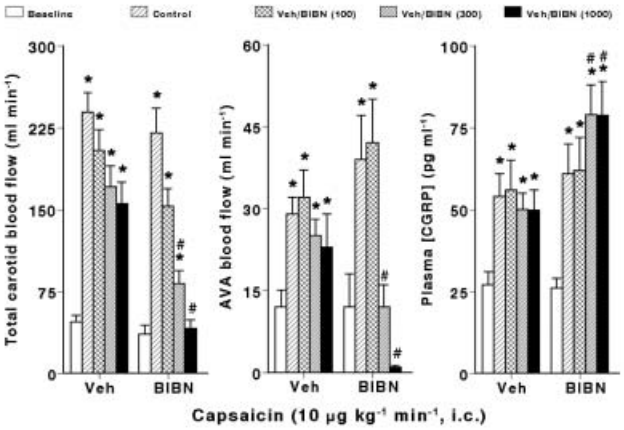


Figure 1

P5O17

CGRP and substance P are not involved in the relaxation of human and porcine coronary arteries by capsaicin

Saurabh Gupta*[1], Antoinette MaassenVanDenBrink[1] & Pramod R. Saxena[1]
[1]*Department of Pharmacology, Erasmus Medical Center, Rotterdam, the Netherlands*

Objectives Capsaicin activates sensory nerve fibres via vanilloid VR_1 receptor to release neuropepetides, like calcitonin gene related peptide (CGRP) and substance P. Capsaicin sensitive nerves are present in coronary arteries. Therefore, we examined the role of these peptides in capsaicin-induced relaxation of coronary arteries.
Methods Segments (inner diameter 250–600 µm) were mounted in Mulvany myograph. Dose–response curves of capsaicin were constructed before (control) or after endothelium denudation, the CGRP receptor antagonists BIBN4096 and $CGRP_{8-37}$, the neurokinin NK_1 receptor antagonist L-733060, the voltage-sensitive calcium channel inhibitor ruthenium red as well as the cyclic GMP inhibitor methylene blue. Relaxant responses were measured isometrically and are expressed as percentage of precontraction with 30 mM K^+ (mean ± SEM).
Results Capsaicin relaxed both human and porcine vessels in a dose dependent manner, with E_{max} values of 85 ± 10% (n = 7) and 92 ± 3% (n = 8) and pEC_{50} values were 5.2 ± 0.03 and 5.7 ± 0.13, respectively. The removal of endothelium or the blockade of CGRP or NK_1 receptors, calcium channels or cyclic GMP did not modify the relaxant response to capsaicin (Table 1).
Conclusion The capsaicin-induced relaxations of the human and porcine coronary arteries are not mediated by CGRP or substance P. The failure of ruthenium red to block these responses suggests the lack of involvement of VR_1 receptor.

P5O18

CGRP8-37 inhibits CGRP-induced vasodilation in the human forearm

Floris Vanmolkot*[1] & Jan de Hoon[1]
[1]*Center for Clinical Pharmacology, University Hospital Gasthuisberg, Leuven, Belgium*

Objectives *In vitro* and animal studies have shown that calcitonin gene-related peptide (CGRP)-induced vasodilation is inhibited by the CGRP fragment $CGRP_{8-37}$. The aim of this study was to investigate the effects of $CGRP_{8-37}$ on resting forearm blood flow (FBF) and on CGRP-induced vasodilation *in vivo* in humans.
Methods Increasing doses of CGRP (1-3-10 ng- $min^{-1}.dL^{-1}$) were infused into the brachial artery of 12 healthy subjects. After washout, CGRP infusions were repeated during simultaneous infusion with placebo (NaCl 0.9%, n = 6) or $CGRP_{8-37}$ (333 $ngmin^{-1}.dL^{-1}$, n = 6). FBF and FBF-ratio (FBF infused/FBF noninfused arm) were assessed using bilateral venous occlusion plethysmography.
Results CGRP increased FBF from 3.2 ± 0.3 (baseline) to 4.8 ± 0.3, 7.7 ± 0.7 and 12.7 ± 1.0 $mLmin^{-1}.dL^{-1}$, respectively (P < 0.001, n = 12). FBF-ratio during the first (1.9 ± 0.2, 3.1 ± 0.3 and 5.2 ± 0.8) and second (2.1 ± 0.1, 3.0 ± 0.1 and 4.7 ± 0.3) series of CGRP infusions with placebo did not differ. Baseline FBF did not change during $CGRP_{8-37}$ infusion (3.1 ± 0.3 vs. 3.1 ± 0.3 $mLmin^{-1}.dL^{-1}$). $CGRP_{8-37}$ attenuated CGRP-induced increase in FBF ratio (2.2 ± 0.3, 3.3 ± 0.2 and 5.7 ± 0.4 vs. 1.6 ± 0.1, 2.0 ± 0.3 and 3.5 ± 0.6, P = 0.012).
Conclusions Intra-brachial CGRP infusion results in a dose-dependent and repeatable FBF response. The CGRP-receptor antagonist $CGRP_{8-37}$ does not affect resting FBF, but effectively inhibits CGRP-induced vasodilation in the human forearm.

P5O19

How 140 reduces significantly the FOS immunoreactivity (FOS-IR) in the trigeminal nucleus caudalis (TNC) in response to the electrical stimulation of the rats Superior Sagittal Sinus (SSS): a new therapeutic target for the primary headaches

Marcelo Ciciarelli*[1] & A. P. Corrado[2]
[1]*Department of Neurology, University of Sao Paulo, Ribeirao Preto, Brazil,* [2]*Department of Pharmacology, University of Sao Paulo, Ribeirao Preto, Brazil*

Objectives The pathophysiology of primary headache involves activation of the trigeminal-vascular system which induces a neurogenic inflammation(NI) with FOS-IR into TNC. However the pain origin remain unclear. We have reported in a dog model of pain, that only Bradykinin(BK) and S-nitrosocysteine(SNOc) are able to trigger a nociceptive response(NR).In this study we evaluated the role of the BK-SNOc pathway in the FOS-IR into TNC.
Methods Anesthetized rats(250–300 g) were submitted to SSS stimulation(20 V; 0,3Hz; 250 µs) and intracarotid injection of algogenic endogenous agents, BK(3 µg-n = 6,10 µg-n = 8) and SNOc(1,5 mg, n = 6), in absence or presence of L-NAME (10 mg/kg,i.p)-a NOS inhibitor- or HOE 140(400 µg/kg,i.p)-a selective BK_2 antagonist.

Results 1-BK induced a dose-dependent FOS-IR into TNC(n = 14,P < 0.05); 2-SSS stimulation caused significant FOS-IR(n = 5,P < 0.05); 3-L-NAME reduced the FOS-IR caused by BK10 μg(n = 6,P < 0.05) and SSS stimulation(n = 3,P < 0.05) but not by SNOc(n = 3,P > 0.05); 4-HOE 140 also inhibited the FOS-IR induced by BK(n = 4,P < 0001) and SSS stimulation(n = 3,P < 0.05).

Conclusions Results indicate the participation of NO in the NR induced by BK and SSS stimulation and suggest the involvement of BK-SNO pathway in the pathophysiology of this nociceptive stimulus, with possible implications in the mechanisms of primary headaches. Since it has been demonstrated that HOE 140 is well tolerated in humans, its use would be suggestive as a new therapeutic alternative for the treatment of the vascular headaches.

P5O20

Cyclo-oxygenase-2 inhibitors as short-term prophylaxis of menstrually related migraine. A pilot study

Franco Granella*[1], Gianni Allais[2] & Chiara Benedetto[2]
[1]*Department of Neurosciences, University of Parma, Parma, Italy,*
[2]*Woman's Headache Centre, Department of Gynaecology, University of Turin, Turin, Italy*

Objectives A short-term preventive treatment may give substantial benefit to women with menstrually related migraine (MRM). In this pilot study we treated MRM patients with cyclo-oxygenase (COX)-2 inhibitors (coxibs).

Methods After a two-month run-in period, we treated 20 women with MRM (defined as attacks beginning from – 2 to + 3 days after the onset of menses) with coxibs (celecoxib 200 mg daily, n = 12; rofecoxib 25 mg daily, n = 8) for 2–6 months (67 cycles treated). Women were required to have regular menstrual cycles and to be able to predict the onset of menses. Treatment was started 2 days prior to the expected onset of MRM and continued for 7–10 days. The primary efficacy outcome was the number of days with MRM (ND-MRM).

Results ND-MRM was significantly reduced, passing from 4.0 ± 2.2 days during run-in to 1.8 ± 1.6 days during treatment (P < 0.0001). Also the number of MRM attacks (run-in: 2.1 ± 1.1, treatment: 1.2 ± 1.0; p < 0.0001) and the number of escape medications (run-in: 5.3 ± 2.9, treatment: 2.0 ± 2.0; p < 0.0001) decreased significantly. Adverse events (AEs), mainly GI symptoms, were reported by 8 women, but only 2 patients dropped due to AEs.

Conclusions Coxibs may be useful in the short term prophylaxis of MRM.

P5O21

Circulating nociceptin levels in migraineurs: preliminary data

Csaba Ertsey*[1], Mónika Hantos[2], György Bozsik[1], Judit Áfra[3] & Kornélia Tekes[2]
[1]*Department of Neurology, Semmelweis University,* [2]*Department of Pharmacodynamics, Semmelweis University,* [3]*National Institute of Neurosurgery, Budapest, Hungary*

Nociceptin (NC), the endogenous ligand of the opiate-4 type (OP-4) receptor, has received substantial interest as it can have both analgesic and algesic effects in the CNS. Recently, NC immunoreactivity and OP-4 receptor mRNA were found in trigeminal ganglia neurons. All the CGRP-, SP-, NOS-, or PACAP-positive neurons of the ganglia showed NC-immunoreactivity. In a rat trigeminovascular model, NC dose-dependently suppressed neurogenic dural vasodilatation, while it had no effect on baseline vessel diameter. These results raise the possibility that NC might be involved in trigeminally mediated headaches such as migraine. To test this hypothesis we studied circulating NC levels in attack-free migraineurs (n = 15, including 8 with MA and 7 with M0). This group of migraineurs had significantly lower NC levels than matched controls (5525 ± 2053 vs. 9,58 ± 2,57 pg/mL, p < 0,0001). M0 patients tended to have lower NC levels than MA patients (4479 ± 0505 vs. 6,44 ± 2482 pg/mL, p = 0065) but the small sample sizes do not allow a definite conclusion. These preliminary results, however, seem to indicate that NC may have a role in migraine pathogenesis, possibly by modifying the activity of the trigeminovascular system.

P5O22

Contractile effects induced by triptans in the basilar and uterine arteries

Carlos Alberto Fontes Ribeiro*[1], Sónia Alexandra Silva[1] & Francisco Batel Marques[1]
[1]*Department of Pharmacology, Faculty of Medicine, University of Coimbra, Portugal*

Efficacy and ischemic adverse reactions to triptans have been linked to their interaction with 5-HT_{1B} and/or 5-HT_{1D} receptors. This work aimed to verify the role of these receptors in the contractile response to triptans in different vascular settings.

Macroscopically normal basilar arteries were obtained from autopsies and experiments were carried out within 48 h post mortem. Uterine arteries were obtained from patients undergoing surgery. Isometric concentration-response curves were performed, in the presence of cocaine, deoxycorticosterone and L-NAME.

The rank order of agonist efficacy or affinity was 5-HT > sumatriptan ≥ zolmitriptan > naratriptan. Pindolol (5-$HT_{1A,B}$ antagonist) did not alter the contractile responses induced by 5-HT or triptans, and ketanserin (5-HT_2 antagonist) did not antagonise the contractile responses induced by the triptans, but significantly inhibited contractions caused by 5-HT (a reduction of 20 and 90% in the basilar and uterine artery, respectively). BRL 15572 (5-$HT_{1B,D}$ antagonist) did significantly antagonise, in an insurmountable way, the contractile responses induced by triptans. Tachyphylaxis to the triptan-induced contractile effects was observed in the uterine but not in the basilar artery. These findings indicate that 5-HT_{1D} and 5-HT_2 are the predominant serotonergic receptors involved in the *postmortem* basilar artery and in the *ex vivo* uterine artery, respectively, which mediate contraction. Moreover, in peripheral arteries the tachyphylaxis to triptans may be another factor of safety for these drugs.

P5O23

EP4 prostanoid receptors mediate PGE2-induced vasodilatation of human cerebral artery

Richard Davis*[1], Colin Murdoch, Robert Sheldrick, Kenneth Clark & Robert Coleman
[1]*Pharmagene Laboratories, Royston, Hertforshire, United Kingdom*

Enhanced levels of prostaglandin E_2 (PGE_2) are reported in migraineurs during an attack. Also implicated in the pathophysiology of migraine is dilatation of the cerebral vasculature. The aim of the present study was to characterise the effects of PGE_2 on the regulation of vascular tone in human cerebral arteries. Human cerebral arteries were obtained with informed consent of the donor's next of kin and local ethical committee approval. Middle cerebral artery rings were mounted under isometric conditions in organ baths in Krebs solution containing indomethacin (3 μM), at 37 °C. Following precontraction with a submaximal concentration of phenylephrine (1 μM), increasing concentrations of PGE_2 concentration-dependently induced vasodilatation. Rank order of potency of prostanoid receptor agonists suggested the involvement of prostanoid EP_4 receptors (see Table). More direct evidence that PGE_2 was acting via EP_4 receptor stimulation was achieved by demonstrating significant rightward shifts in the PGE_2 concentration response curves in the presence of the EP_4 receptor antagonists, AH23848 (10 μM, pA_2 5.8, $n = 3$) and EP_4A (1, 3 10 μM, pK_B 7.0, $n = 3$). These data demonstrate that PGE_2-induced relaxation of precontracted human cerebral artery is predominantly mediated via EP_4 receptors.

	Selectivity	pEC_{50}	*n*
PGE_2	$EP_1/EP_2/EP_3/EP_4$	8.0 ± 0.1	6
11-deoxy PGE_1	$EP_4 > EP_2$	7.6 ± 0.3	6
PGE_1-OH	$EP_2 > EP_4$	5.9 ± 0.2	4
Butaprost $EP_2 < 63$			

P5O24

Expression of serotonin receptor and calcitonin gene-related peptide in neuronal PC12 cells

Yoshiko Furiya*[1], Makito Hirano[1], Shingo Kariya[1], Tomohisa Nishiwaki[1] & Satoshi Ueno[1]
[1]*Nara Medical University, Department of Neurology, Kashihara-city, Nara, Japan*

Objective Serotonin receptor (5-HTR) 1b/1d agonists, triptans, abort migraine attacks by inhibiting the release of calcitonin gene-related peptide (CGRP) from trigeminal sensory neurons. These findings were obtained from previous studies using primary cultures of heterogeneous trigeminal ganglion of sacrificed animals. To establish a simple assay system, we estimated the expression of 5-HTR and CGRP in rat pheochromocytoma 12 (PC 12) cells and tested the availability of the homogeneous PC12 preparations to evaluate the pharmacological effetcs of antimigraine drugs.
Methods Total RNA was isolated from naive and treated PC12 cells with nerve growth factor (NGF). We amplified 5-HTR and CGRP mRNAs by using reverse-transcribed PCR, and performed immunostaining of neuronal PC12 cells with antibodies to 5-HTR 1b and 1d.
Results 5-HTR 1b/1d mRNA was not detectable in naive PC12 cells. NGF induced neuronal PC12 cells expressed mRNAs of 5-HTR 1d and CGRP, but no. 5-HTR 1b. The expressions were confirmed by the immunostaining.
Conclusions Differentiated PC12 cells may be useful to examine pharmacological effects of antimigraine drugs including triptans.

P5O25

Propranolol in migraine prophylaxis in children

Valentina Jakovljevic*[2] & Zarko Martinovic[1]
[1]*Institute of Mental Health, Belgrade, Yugoslavia,* [2]*Health Center, Cuprija, Serbia and Montenegro*

The purpose of this paper was to study the prophylactic effect of propranolol in children with severe migraine.

All patients in this open study satisfied IHS criteria for migraine. Inclusion criteria also included age 6–14 years at the study onset, severe migraine headaches requiring prophylaxis and the willingness of parents to keep headache diary regularly. The group treated with propranolol where compared with the control group without prophylactic treatment. Both groups were comparable in age and severity of migraine during 6 weeks baseline periods. The severity and duration of migraine headache in two groups during a 12-month period were compared and analysed for statistical significance.

After 3 months of treatment, the severity of headache decreased slightly and the difference between groups was not significant. However, the comparison after 6, 9 and 12 months showed a significantly higher improvement in the group treated with propranolol ($\chi^2 = 5.80$, $p < 0.05$ and $\chi^2 = 17.50$, $p < 0.001$). The effective doses of propranolol ranged from 2 to 4 mg/kg and side-effects were mild.

The results confirmed the efficacy and safety of propranolol in migraine prophylaxis in children.

P5O26

Topiramate in the treatment of chronic daily headache

Amnon Mosek*[1] & Marina Dano[1]
[1]*The Headache Clinic, Department of Neurology, Sourasky Medical Center, Tel Aviv, Israel*

Objective To report on our experience with topiramate treatment in patients with chronic daily headache (CDH).
Methods Patients chart review. Data was collected from follow-up headache diaries.
Results Eleven patients with CDH were treated with topiramate (average age 51 ± 13 years, 64% women). In all topiramate was initiated after failure of previous treatments. The CDH (median duration 5 years, range 2–25 years) was of transformed migraine type (5 patients) and tension type headache. Topiramate treatment was effective in 7 (64%) patients. Five patients achieved an average of 77% (range 66–96%) reduction in headache days and a 72% (range

50–96%) decrease in analgesics consumption. In 2 patients whom daily headache continued, 50% reduction in the severity and the hours of headache per day resulted in 50 and 100% reduction of the daily analgesics. The average effective dose was 100 mg/day. These effects continued for an average follow-up of 9 months (range 5–13.5 months). Side-effects of topiramate were reported by 9 (82%) patients and were well controlled when 12.5 mg increments every 1–2 week were used.

Conclusion Topiramate was found to be an effective treatment for patients with CDH in whom previous treatments were unsuccessful. Slow increments of the dosage well controlled the drug side-effects.

Scientific Session 6

Trigeminal neuralgia and paroxysmal facial pains with autonomic signs

P6Q1

Deep brain stimulation in chronic cluster headache: a study of efficacy and mode of action in the first Belgian patients

Michel Vandenheede*[1], L. Di Clemente[1], A. Fumal[1,2], V. De Pasqua[1], A. Maertens De Noordhout[1], M. Mouchamps[3], J-M. Remacle[3] & J. Schoenen[1,2]
[1]*University Department of Neurology, University of Liège, Citadelle,*
[2]*University Department of Neuroanatomy, University of Liège,*
[3]*Department of Neurosurgery, CHR Citadelle, Liège, Belgium*

Background Hypothalamic activation during a cluster attack was demonstrated by PET studies. Posterior hypothalamic stimulation was found effective in 5 resistant chronic cluster patients published up to now.

Objectives To confirm these results and explore the underlying mechanisms in a pilot-study of 5 patients. Clinical evaluation was combined with algometric studies (pain thresholds, nociceptive reflexes), determination of hormone levels at baseline and after a 1-month attack-free period.

Results We implanted the two first patients in January and March 2003 using published stereotactic coordinates. After weekly modifications to obtain a therapeutic response, the final stimulation parameters were: bipolar mode, 3.8 mV, pulse width 90 μsec, 185 Hz. The patient who had 3 attacks/day unremittingly since 2 years, had a 20-day attack-free period followed by 3 attacks triggered by long high altitude excursions. At 2 months postimplantation, headache frequency was therefore decreased by 96.4%. Algometric tests and nociceptive reflexes were not significantly modified by the hypothalamic stimulation. Hormone changes will be presented as well as the results obtained in subsequent patients.

Conclusion Deep hypothalamic stimulation seems to be a promising therapeutic option for resistant chronic cluster headache patients. Its beneficial effects are unlikely to be related to diffuse analgesia.

P6Q2

Neuromuscular transmission in cluster headache patients: a single-fiber EMG study

Laura Di Clemente*[1], Michel Vandenheede[1], Gianluca Coppola[1] & Jean Schoenen[1]
[1]*Headache Research Unit, Departments of Neuroanatomy & Neurology, University of Liège*

Background The precise etiopathogenesis of cluster headache (CH) is not known. A genetic component is likely in certain cases (1), and a common pathophysiologic denominator may exist with migraine. Subclinical impairment of neuromuscular transmission was reported in subgroups of migraine with aura patients (2) and was recently found in CH (Ertas, personal communication).

Objective To search for abnormalities of neuromuscular transmission in CH patients using stimulation single-fiber EMG (SFEMG).

Results Five CH patients were recorded up to now. Among these, 2 had subtle SFEMG abnormalities: 1 patient had conduction blocks in 5% of fibers, the other had a single fiber with an abnormal MCD = 55 μs. Both patients had episodic CH and were females; the first one received verapamil. There were no other clinical peculiarities.

Conclusions Subtle abnormalities of neuromuscular transmission may exist in CH patients. Further studies are necessary to evaluate their prevalence and severity, as well as the influence of drug treatments.

References

1 Leone M, Russel MB, A, Attanasio A, Grazzi L, D'Amico D et al. Increased familial risk of cluster headache. Neurology 2001; 56: 1233–6.
2 Ambrosini A, Maertens de Noordhout A, Schoenen J. Neuromuscular transmission in migraine: a single-fiber EMG study in clinical subgroups. Neurology 2001; 56: 1038–43.

P6Q3

Validation of selective interview method to estimate prevalence of familial cluster

Massimo Leone*[1], Andrea Rigamonti[1], Eliana Mea[1], Domenico D'Amico[1], Licia Grazzi[1], Michael B. Russell[2] & Gennaro Bussone[1]
[1]*Istituto Nazionale Neurologico Carlo Besta, Milano, Italy,* [2]*Copenhagen University, Copenhagen, Denmark*

Recent genetic-epidemiological studies showed a significantly increased risk of cluster headache (CH) in relatives of CH patients (Kudrow et al. 1994, Russell et al. 1995, Leone et al. 2001). In these studies information on relatives was obtained from the proband but it does not seem likely that one person will to be aware of the state of health his/her entire family. We studied whether direct interview of *all* the first degree relatives of a series of CH patients provided a more accurate estimate of the prevalence of CH in families than the method of simply interviewing the sample of relatives indicated by the proband as possibly suffering from the disease. We telephone-interviewed all the first degree relatives ($N = 299$) of 87 CH

patients (Leone et al. 2001) with the aid of a previously validated questionnaire. Only one new case with episodic CH was found (1/299 = 0.3%). This result validates the methodology of our previous study, i.e. using only information supplied by the proband, and subsequent interview of those indicated, to identify relatives suffering from CH. We have shown that this earlier method: 1. does not require excessive investment of time or resources; 2. may be confidently used in future family studies of CH.

P6Q4

Specific hypothalamic activation during a spontaneous cluster headache attack

Massimo Leone*[2], Thomas Sprenger[4], Henning Boecker[3], Gennaro Bussone[2], Arne May[1] & Thomas Toelle[4]
[1]*Department of Neurology, University of Regensburg,* [2]*Instituto Carlo Besta, Milano,* [3]*Department of Nuclear Medicine, University of Munich,* [4]*Department of Neurology, University of Munich*

Based on clinical grounds, a role of the hypothalamus has been proposed in the pathology of cluster headache. Especially the seasonal pattern of bout periods and the neuroendocrine changes led to this assumption. Recently, using positron emission tomography (PET), a specific activation increase of the hypothalamus has been shown in nitrate-induced cluster headache. These data supported the view, that the inferior hypothalamic grey may act as primum movens triggering pain attacks. However, it was a matter of debate, whether these data were confounded by the vasoactive properties of nitrates.

We report regional cerebral blood flow (rCBF) changes induced by a spontaneous cluster headache attack. As hypothesized, activations were found in the hypothalamic grey matter. Moreover, during the attack, the periaqueductal gray matter (PAG), medial thalamus, pallidum and prefrontal cortex (PFC) as well as in the contralateral perigenual cingulate cortex (ACC), cerebellum, and PFC showed increases of rCBF. These data provide strong evidence supporting the crucial role of the hypothalamus in the pathogenesis of this disease.

P6Q5

Decision making in cluster headache

Alejandra Mazzola[1], Tristan Bekinschtein[1], Manes Facundo[1], Salvat Fernando[1] & Leston Jorge*[1]
[1]*Cognitive Neurology and Pain Section, Department of Neurology, FLENI Institute, Buenos Aires, Argentina*

Objective To evaluate the cognitive profile in cluster headache patients with emphasis in decision making processes.
Background It has been suggested that prefrontal cortex plays a critical role in cognitive decision-making. Prefrontal dysfunction has been found in patients with cluster headache.
Methods Twenty-three patients in cluster headache period without pain and 20 matched healthy controls received a general neuropsychological evaluation and a decision making task.
Results Patients with cluster headache displayed deficits in the Decision Making Test despite remaining unimpaired on others areas of cognition.
Conclusions These findings suggest that cluster headache patients during cluster period without pain have decision making deficits. They also provide new evidence that decision-making processes can be dissociated from other cognitive domains. The clinical relevance of these results will be discussed.

P6Q6

Suboccipital (GON) injection with long-acting steroids in cluster headache: a double-blind placebo-controlled study

Anna Ambrosini*[1], Michel Vandenheede[2], Paolo Rossi[3], Fulvio Aloj[4], Enzo Sauli[3], Maria Gabriella Buzzi[5], Francesco Pierelli[1,6] & Jean Schoenen[2]
[1]*INM Neuromed – Headache Clinic, Pozzilli (Isernia), Italy,* [2]*Headache Research Unit – Departments of Neurology and Neuroanatomy, University of Liège, Belgium,* [3]*INI, Grottaferrata (Rome), Italy,* [4]*INM Neuromed – Intensive Care Unit, Pozzilli (Isernia), Italy,* [5]*S. Lucia Foundation, Rome, Italy,* [6]*Department of Neurology and Otorhinolaryngology, University of Rome La Sapienza, Italy*

Oral steroids are efficient as preventative treatment during bouts of cluster headache (CH). Unfortunately, withdrawal from steroids may cause attack recurrence in many patients. Steroid injection in the Greater Occipital Nerve region ipsilateral to the pain side may be an effective 'single shot' treatment (Anthony 1987, Peres et al. 2002), but no placebo-controlled study was available up to now.

The aim of this study was to conduct a double-blind study on the preventive effect of an ipsilateral suboccipital injection of a mixture of long- and rapid-acting betametasone 9.06 mg/mL (Diprophos©, Schering-Plough) and 0.3 mL 2% xylocaïne in CH attacks.

Twenty-three patients with Episodic ($n = 16$) (bout lasting since less than 2 weeks) or Chronic ($n = 7$) CH were included: 13 received Diprophos© (D-group; 4 CCH, 9 ECH), 10 physiological saline (P-group). During the postinjection week, 12 D-group patients (92.3%) had at least a 50% reduction of attack frequency compared to the preinjection week (4 were attack-free), whereas only 1 P-group patient had a similar improvement ($P = 0.0004$). Four weeks after the injection, 9 D-group patients, including 3 CCH, were attack-free without prophylaxis.

This study demonstrates that a single suboccipital steroid injection significantly suppresses attacks in ECH and CCH, inducing a remission in 70% of patients.

P6Q7

Melatonin as treatment for indomethacin–responsive headache syndromes

Todd Rozen*[1]
[1]*Michigan Head-Pain and Neurological Institute, Ann Arbor, MI, USA*

Objective To use melatonin as therapy for indomethacin-responsive headaches.

Background Melatonin has a chemical structure similar to indomethacin. Melatonin has anti-inflammatory properties in animal models. Melatonin was given to patients with indomethacin-responsive headaches to assess effectiveness.
Methods case reports results Case 1: 45-year-old-woman with new onset headache postrenal transplant. Hemicrania continua was diagnosed but the patient's renal status contraindicated an indomethacin trial. On melatonin 9 mg/day she became pain free, off melatonin her pain returned.

Case 2: 38 years-old woman with idiopathic stabbing headache. She averaged 10–18 pain spikes per day. Indomethacin was started but she could not tolerate above 125 mg. This reduced attack frequency 25%. On melatonin 12 mg she became pain free and remained so through follow-up.

Case 3: 23 years-old woman with ice pick headaches occurring 2–6 times per day. She was on warfarin so indomethacin could not be initiated. On melatonin 9 mg the ice-picks ceased. Off melatonin the headaches returned.
Conclusion Melatonin is effective in alleviating the pain of hemicrania continua and idiopathic stabbing headache both known indomethacin–responsive syndromes. Melatonin may be an alternative treatment to indomethacin and has a more favorable side-effect profile.

P6Q8

Effective treatment of episodic cluster headache with Frovatriptan

Charles Kelly*[1]
[1]*Department of Neurology, Womack Army Medical Center, Fort Bragg, North Carolina, USA*

While the use of long-acting 5-HT receptor agonists are widely accepted for migraine, little is known about their effectiveness in the prevention of cluster headaches. Four consecutive male patients presented with an average of 3.5 cluster attacks per day that were poorly controlled with traditional pharmacotherapy. To determine the effectiveness of a long-acting 5-HT receptor agonist in the prevention of their episodic cluster headaches, all patients initiated daily prophylactic treatment with frovatriptan (2.5 mg QD). Three out of four patients experienced immediate and complete resolution of their attacks within 24 h of starting frovatriptan. The remaining patient had a 50% reduction in headache frequency within 24 h and complete resolution by 72 h. No adverse experiences were reported. One patient reported rare breakthrough headaches five days later that were less severe and were treated with one additional frovatriptan tablet on an as-needed basis. Another patient experienced a single breakthrough in the early morning that was treated with a change to QHS dosing. The remaining two patients were free of attacks for the duration of their 7–20 day treatment.
Conclusion Daily frovatriptan therapy may be an effective treatment for refractory episodic cluster headaches.

P6Q9

The stimulation of posterior hypothalamic gray matter in patients with intractable cluster headache alters orthostatic tolerance

Pietro Guaraldi*[1], Pietro Cortelli[1], Giulia Pierangeli[2], Massimo Leone[3], Angelo Franzini[3] & Gennaro Bussone[3]
[1]*Università Di Modena E Reggio Emilia*, [2]*Università di Bologna*, [3]*Istituto Neurologico Carlo Besta Milano*

Four patients (3 males; 36 ± 9 years) with intractable chronic CH with bilateral (1 pz) or monolateral (3 pz) posterior hypothalamic gray matter stimulator underwent 30 min HUT, in 3 conditions: (A) preoperatively (B) after implantation stimulation 'off' (C) after implantation stimulation 'on'. Results are summarized in the table * = $P < 0.05$.

HUT test	A ('pre')	B ('off')	C ('on')
n =	3	4	3
Age	34 ± 9 (27–45)	36 ± 9 (27–45)	38 ± 9 (27–45)
Delta SBP (mmHg)	–1 ± 3	–12 ± 9	–18 ± 1*
Delta DBP (mmHg)	4 ± 1	5 ± 2	–0.5 ± 3
Delta HR (bts/min)	13 ± 5	29 ± 8*	29 ± 7*
Rest HR variability			
LF (nu)	61 ± 27	54 ± 26	51 ± 25
HF (nu)	36 ± 28	38 ± 24	43 ± 24
LF/HF ratio	3.15 ± 3.05	2.32 ± 2.21	2.54 ± 3.42
Tilt HR variability			
LF (nu)	74 ± 16	94 ± 1*	91 ± 3*
HF (nu)	22 ± 15	4.5 ± 1*	5 ± 1*
LF/HF ratio	6 ± 6	21 ± 3*	17 ± 2*
Rest DBP variability			
LF (nu)	66 ± 14	75 ± 3	78 ± 6
HF (nu)	28 ± 15	16 ± 4	16 ± 6
LF/HF ratio	3.05 ± 2.1	4.92 ± 1.18	5.32 ± 1.82
Tilt DBP variability			
LF (nu)	82 ± 8	96 ± 2	86 ± 9
HF (nu)	13 ± 6	3.5 ± 1	12 ± 9
LF/HF ratio	8.2 ± 5.9	30.7 ± 13*	10.6 ± 6,5

P6Q10

Side shifting hemicrania continua with aura (chronic migraine with aura with autonomic symptoms responsive to indomethacin?)

Mario Peres*[1] & William Young[2]
[1]*São Paulo Headache Center, São Paulo, Brazil*, [2]*Jefferson Headache Center, Philadelphia, PA USA*

Atypical features of HC, including both visual aura and side shifting have been reported previously, however, auras and variable unilaterality have never been reported together in HC. We report two patients with side shifting HC with aura. The clinical presentation of our patients can also be classified as chronic migraine with aura, with autonomic symptoms and responsive to indomethacin. Both migraine subtypes and side shifting hemicrania continua with aura are not included in the current IHS classification, so these patients are not classifiable.

Side shifting hemicrania continua with aura implies the need to revisit the traditional IHS categorization of headaches into unique diagnostic groups.

The modular headache theory explains how headaches with the features of several different primary headache disorders may occur. These patients' headaches would activate aura modules, bilateral unilaterality modules, autonomic symptom modules, and in case 1 at least the throbbing pain module and the nausea and the photophonophobia modules. One could speculate that the unilaterality modules are indocin responsive and that perhaps that they differ from the unilaterality module of cluster headache. While these patients had a low probability assortment of modules, learned stereotypy stabilized their headache pattern allowing for the persistence of this unusual phenotype.

P6Q11

Co-existence of migraine and cluster headache – suggestions to the nosology based on observations in 70 patients

Krishnamurthy Ravishankar*[1]
[1]*Jaslok and Lilavati Hospitals, Bombay, India*

Objectives The IHS Classification includes Migraine and Cluster Headache as two distinct primary headaches, but one often encounters patients with mixed features of both. This study analyses the pattern of coexistence of these two primary headaches.

Methods 6000 patients from our Headache Clinic who were diagnosed using the HIS criteria were included in this study. 70(1.1%) had coexisting features of both migraine and cluster headache and were analysed.

Results 59 out of 70 (84%) had mixed features of both cluster headache and migraine *simultaneously* during the acute attack(Group A) and 11 (16%) had features of both not simultaneously but at *separate* points of time (Group B). 34 out of 59 in the larger group A had cluster headache with migrainous features and 13 had migraine with cluster headache features while 12 had mixed features of both with neither dominating.

Conclusion As compared to earlier studies, there was a greater number of patients with mixed features during the acute attack. Based on this observation, an attempt has been made to clarify the nosological status of this subset rather than label them all as cluster–migraine syndrome. This can have implications for specific treatment.

P6Q12

Trigeminal autonomic cephalgias and pituitary adenomas

Anne Donnet*[1], Thierry Brue[2], Isabelle Morange[2] & Philippe Jaquet[2]
[1]*Neurosurgery Department, CHU Timone, Marseille, France*, [2]*Department of Endocrinology, CHU Timone, Marseille, France*

Objective The objectives of this study were to analyse the characteristics of headaches with ipsilateral autonomic symptoms in patients with pituitary adenoma and to investigate the mechanisms involved. The correlation between tumor size, suprasellar extension, cavernous sinus invasion and headache is discussed.

Results: Seven patients (five females, two males) were examined in 2002.

Headache was more prevalent in patients with a prolactin-secreting adenoma (5 patients).

SUNCT was reported in 3 patients, episodic cluster headache in one; for three patients, the trigeminal autonomic cephalalgia was not specifically identified.

Conclusion Both extension of the tumor into the cavernous sinus and/or hyperprolactinemia may be responsible for trigeminal activation leading to a homolateral autonomic cephalalgia.

P6Q14

SUNCT syndrome responsive to Gabapentin

Pedro A. Kowacs*[1], Elcio J. Piovesan[1], Marcos Christiano Lange[1], Lineu C. Werneck[1] & Marcelo Rezende Young[1]
[1]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil*

Objective To describe the case of a patient presenting a SUNCT syndrome, refractory to most of the usual therapy for headaches except to gabapentin.

Case report A 41-years-old white male had started having at the age of 25 a left trigeminal-autonomic cephalalgia, involving the 1st division of his left trigeminal nerve. The neuralgic pain was excruciating, lasting from a few seconds to minutes, and was triggered when touching the left nasal alae. There were prominent associated ipsilateral autonomic phenomena. He had been submitted to an unsuccessful alcoholization of the nerve. His pain worsened over the years, with some episodes of status, and he was initially diagnosed as having a cluster–tic syndrome. Clonazepam, carbamazepine, oxcarbazepine, baclofen, phenytoin, methysergide failed to control his pain. Chlorpromazine would significantly relieve the pain. High–dose celecoxib (600 mg/day), indomethacin (100 mg/day) and lamotrigine (350 mg/day) resulted each in partial and temporary pain control. Gabapentin 1800 mg/day led to a complete and consistent pain control after two months of follow-up.

Conclusion SUNCT syndrome remains elusive to diagnosis and therapy. Gabapentin must be considered as a useful therapeutic option to treat this rather uncommon condition.

P6Q15

IV Levetiracetam: efficacious for cluster headache

John Claude Krusz*[1] & Jane Cagle[1]
[1]*Anodyne Headache and PainCare, Dallas, USA*

Introduction Levetiracetam is a unique molecule used for control of seizures and has been shown to be useful for refractory headaches and pain, both orally and intravenously[1–3]. We currently describe treatment of an acute flareup of cluster headache with IV levetiracetam.

Methods Three case reports are described at this point. All were males who had onset of cluster headaches. 1 patient had coexistent migraines. They came to the headache clinic; an IV was placed and levetiracetam was given IV. 400–800 test dose was given. Then, 800 mg was given every 10 min with monitoring. Patients rated their cluster severity on a 0–10 NRS scale.
Results All 3 patients reported cessation of cluster headache attacks with treatment. All were placed on oral levetiracetam for prophylaxis. Average dose was 8400 mg over 45–50 min Side-effects were not reported other than transient drowsiness in 1 patient.
Conclusions IV levetiracetam is a potential option for treating acute cluster headaches. Safety, tolerability and, most importantly, efficacy have been well demonstrated in this and other open-label studies[3] treating migraines and cluster headaches. Double-blind studies are warranted for levetiracetam IV.

P6Q16

Acute stabbing headache confined to the retroauricular regions in adults

Hong-Ki Song*[1]
[1]*Department of Neurology, Hallym University*

Objectives Paroxysmal stabbing or icepick-like headache located in the extratrigeminal areas are not uncommon in clinical practice. However, clinical characteristics of acute stabbing headache confined to retroauricular regions have rarely been investigated carefully.
Methods Among subjects referred to university hospital because of acute-onset paroxysmal stabbing headache during last five years, 63 patients in which symptoms were confined to the unilateral retroauricular regions were included. All the patients underwent a general, neurological, and otological assessment. Brain imaging studies were performed in 25 cases including all five subjects with past history of similar attacks.
Results All patients were neurologically and otologically free. Preceding symptoms of flu-like or upper respiratory tract infection were reported in 35%. All but one had a self-limited course recovering completely in 1–2 weeks. During the course, subsequent Bell's palsy was disclosed in 4, and otic zoster infection in two cases. Brain imagings were nonspecific except small schwannoma at the cerebellopontine angle in a recurrent case. Headache was not affected or partially relieved by acetaminophen or cafergot, but responded successfully to indomathacin or naproxen alone or with amitriptylline.
Conclusions Most of acute stabbing headache confined to retroauricular regions were idiopathic in etiology, and showed self limiting benign course. However, possibility of subsequent auricular zoster or facial palsy should be considered.

P6Q17

Microvascular decompression for trigeminal neuralgia – the patient's perspective

Joanna Zakrzewska*[1], Benjamin Lopez[1], Sung Kim[2] & Hugh Coakham[3]
[1]*Barts the London NHS Trust, London, United Kingdom,* [2]*University of Cincinnati, Cincinnati, USA,* [3]*Frenchay Hospital, Bristol, United Kingdom*

Objectives this study aimed to review patients with trigeminal neuralgia who had undergone a microvascular decompression (MVD) by one neurosurgeon with the aim of ascertaining their satisfaction with the procedure.
Methods as part of a larger study on the post operative satisfaction of 284 patients who underwent a MVD at one centre patients' views were independently ascertained using a self complete questionnaire.
Results replies were obtained from 162 female and 122 male patients mean age 60 with a mean duration of symptoms of 6.5 years followed up for a median of 5 years. They reported that 74% should have had the operation earlier with 26% stating that the operation was performed at the right time. This was irrespective of whether they had recurrence of pain. They had seen an average of 3.7 health care professions before seeing the neurosurgeon. The procedure resulted in 89.2% reporting satisfaction and 74% said the operation was better than they had expected.
Conclusion patients with trigeminal neuralgia are very satisfied with outcomes after MVD and would welcome an earlier opportunity for this procedure.

Others

P6R1

Neurotransmitter pattern of patients who experienced headache after lumbar puncture

Luana Vaianella[1], Laura Pierguidi[1], Andrea Alberti[1] & Paola Sarchielli*[1], Giovanni Mazzotta[1], Virgilio Gallai [1]
[1]*Department of Neuroscience, University of Perugia, Italy*

Study aim The present research was aimed at identifying the biochemical ground predisposing to post-LP headache.

Patients 145 patients with different diagnostic suspicions for diseases of the CNS were included. Thirty percent of them have a past history of migraine or tension-type headache.
Methods Sensory neuropeptides Neurokinin A (NKA), Substance P (SP), and calcitonin gene-related peptide (CGRP) were determined by ELISA methods. Amino acids (glutamate, aspartate, glycine and taurine) and monoamine metabolites, 5-hydroxyindolacetic acid (5HIAA), and homovanillic acid (HA) were determined by HPLC.
Results Independently from the diagnosis at discharge, significantly lower levels of NKA and CGRP were found in the CSF of patients with and without a past history of headache, who developed post-LP headache with respect to patients without headache ($P < 0.04$ and $p < 0.03$).

No significant differences were found in the levels of biogenic amine metabolites between patients with and without

LP headache. Patients with a history of migraine, who in the majority of cases experienced a post-PL headache, had higher levels of glutamate and aspartate compared with patients without ($P < 0.04$ and $p < 0.05$).

Discussion Reduced levels of CGRP and NKA and, to a lesser extent SP, in patients with PL headache, support the concept of a hypersensitivity to trigemino-vascular neuropeptides in patients who developed post PL headache. Higher levels of excitatory amino acids seem to be specific for the subgroup of patients suffering from migraine.

P6R2

Intravenous lidocaine is effective in the treatment of SUNCT syndrome

M. S. Matharu[1], A. S. Cohen[1] & P. J. Goadsby*[1]
[1]*Headache Group, Institute of Neurology, London, United Kingdom*

Objective To determine whether intravenous lidocaine is an effective treatment of SUNCT syndrome.

Methods Four patients with SUNCT syndrome were recruited into an open-label trial of intravenous lidocaine. An infusion of intravenous lidocaine was started at a rate of 1 mg/minute and gradually increased in increments of 0.5–1 mg/minute until the headaches were suppressed, significant side-effects intervened or a maximum infusion rate of 3.4 mg/kg/h was achieved. Continuous cardiac monitoring was performed while the treatment dose was being titrated.

Results Intravenous lidocaine at 1.3–3.3 mg/kg/h completely suppressed the headaches for the duration of the infusion in all four patients. The head-ache recurred rapidly after cessation of treatment. Three patients developed side-effects. Nausea was reported by three patients and was partially or completely controlled with antiemetics. Two patients developed cognitive decline, in the form of depressive thoughts and paranoia; these symptoms reversed with cessation of the treatment. No patients developed cardiac problems.

Conclusions Intravenous lidocaine is an effective treatment for SUNCT syndrome. It can be considered when acute intervention is required to suppress a severe exacerbation of SUNCT.

P6R3

Different impairment of crossed and uncrossed visual pathways in migraine with aura patients during the interictal phase

G. Coppola*[1], G. Fiermonte[1,2], V. Parisi[3] & F. Pierelli[2,4]
[1]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy,* [2]*University Centre for Adaptive Disorders and Headache (UCADH), University of Rome 'La Sapienza', Rome, Italy,* [3]*Oculistic Clinic, University 'Tor Vergata', Rome, Italy,* [4]*IRCCS, NEUROMED, Pozzilli (IS), Italy*

Objectives In the headache-free period of the migraine with aura (MA) patients, asymmetries of cerebral blood flow (1), of the visual evoked potentials (VEPs) (2) and of the spontaneous EEG activity (3) were observed.

To evaluate the neural conduction along crossed and uncrossed visual pathways in MA patients.

Methods VEPs were recorded in 13 MA patients and 20 control subjects. Visual stimuli were full field checkerboard patterns, reversed at 2 Hz and the single check edges subtended 60, 30, 15, and 7.5 min of visual angle. The bioelectrical cortical responses were recorded simultaneously in homolateral (HC) and controlateral (CC) visual cortices, with respect to the stimulated eye. We considered as 'Interhemispheric difference (ID)' the difference between the P100 implicit time and N75-P100 amplitude recorded in HC and in CC in absolute values.

Results We found an asymmetry in the bioelectrical responses obtained in HC and CC, and the ID were significantly higher than controls for N75-P100 amplitudes at 60 min of arc ($P = 0.02$) and for P100 implicit times at 60 ($P = 0.001$) and 15 min of arc ($P < 0.05$).

Conclusion In MA patients crossed and uncrossed visual pathways may impaired differently, and magnocellular might more impaired than parvocellular visual pathways during the interictal period.

P6R4

Effect of rizatriptan on CGRP level in migraine

Adam Stepien*[1], Piotr Jagustyn[1], Anna Trafny[2] & Krzysztof Widerkiewicz[3]
[1]*Department of Neurology, Aviation Institute of Medicine, Warsaw, Poland,* [2]*Military Institute of Hygiene and Epidemiology, Warsaw, Poland,* [3]*Merck Sharp, *Dohme Idea INC, Poland*

Calcitonin gene-related peptide (CGRP) is one of the most abundant neuropeptdes in the nervous tissue. Local cranial release of CGRP, which marks the trigeminovascular system, play more important role in the pathophysiology of migraine attacks and cluster headache. In some studies the level of CGRP are elevated in the cranial venous blood of patients with an acute spontaneous attack of migraine. Sumatriptan abolish increasing level of this peptides. The aim of our study was to determinate influence of rizatriptan on CGRP release in migraine. We also investigated plasma levels of CGRP in 45 patients with migraine attack, before and two hours after administration of rizatriptan – the drug from new generation of triptans. In the examined group of patients the level of CGRP was higher before treatment than two hours after administration of rizatriptan. There was no difference between migraine with and without aura. The decreasing of the CGRP levels was corresponding witch migraine relieve. This results indicate that probably all triptans abolish increasing level of this peptide in migraine attacks.

P6R5

NMR spectroscopy in patients suffering from migraine

J. Papatriantafyllou*, S. Gotsis, P. Toulas, A. Robotis & K. Karageorgiou
Headache Clinic, Neurology Department, General Hospital of Athens 'G. Gennimatas', Athens, Greece

Aim of the study NMR spectroscopy in patients suffering from migraine.

Material / Methods In this study participate 6 women with migraine for more than 10 years according to the IHS criteria.

The patients underwent an MRI scan of brain in a scanner of 1.5 Tesla. We obtained NMR spectra (TR/TE = 1500/35) from voxels of preselected areas of the brain. These areas are the left hippocampus, the grey and the white matter of the occipital lobes, the left cingulated and the prefrontal cortex. We measured the concentrations of the metabolites NAA (N-acetyl-aspartate), creatines, MI(myo-inositol), choline and calculated the ratio to total creatine (because of the small normal variations). The same procedure was applied to 10 normal volunteers who did not suffer from any CNS disease (neurological or psychiatric).

Results The Mi/Cr ratio in patients is higher in many areas indicating metabolic deviation in the substrate.

There is a positive correlation between the Mi/Cr ratio and the duration of the migraine.

P6R6

Duration of migraine illness is a predictor for response to Botulinum Toxin Type A

Eric J. Eross*[1] & David W. Dodick[1]
[1]*Department of Neurology, Mayo Clinic, Scottsdale, AZ, USA*

Objective The objective of this study is to determine if the duration of migraine illness alters the effectiveness of botulinum toxin type A (BoNT-A) on disability in patients suffering from episodic or chronic migraine

Methods We followed 61 patients with episodic and chronic migraine after treatment with BoNT-A. For all 61 patients, baseline and 3 month follow-up information on migraine associated disability (MIDAS) was recorded. The percent change in disability was determined for all patients. The percentage of patients who experienced at least a 50% improvement in disability (responders) was determined. Finally, the duration of migraine illness was determined and an analysis was performed to determine if response to BTX-A was dependant on duration of illness.

Results Of the 61 patients studied, 62% were responders. The average duration of illness for responders was 21.9 years compared to 31.4 years for nonresponders ($P < 0.05$). Patients who had suffered from migraines for less than 30 years had a response rate of 79% compared to 46% in the group who have had headaches for 30 or more years. This is a statistically significant (< 0.05) difference.

Conclusions Duration of migraine illness appears to be a clinical factor, which is predictive of treatment response to BoNT-A.

P6R7

I.V Depacon and P.O. Depakote ER for treatment of status migrainosis and prevention of episodic migraine

Charles A. Popeney*[1]
[1]*Fort Bend Neurology, Sugar Land, USA*

Objective To assess the efficacy and safety of I.V Depacon (Valproate Sodium) to abort Status Migrainosis and Depakote ER (Valproate ER) for prophylactic treatment in these same patients.

Design/methods 31 consecutive patients ((27/31) female (4/31) male) were included in this retrospective study. All patients met the IHS criteria for status migrainosis. Age(m = 33 r:13–57), migraine type, length of time with migraine, and length of status migrainosis was obtained. All patients received 1000 mg I.V Depacon over 5–10 min (rapid infusion) in an outpatient setting. Vital signs were monitored. Pain free status was assessed. Those patients that did not achieve pain free status over the time of infusion were given additional Depacon 500 mg I.V. q. 8 h for 5 additional doses. At the end of these additional infusions, pain free status was assessed. Those patients who needed prophylactic treatment were started on p.o 500–1000 mg Depakote ER at the time of their last I.V Depacon dose (to sustain levels).The need for prophylactic treatment was based on ineffective prior prophylactic agents or no present prophylactic use. Headache frequency was followed over 3 months and recorded. Adverse events and side-effects were recorded for both I.V. Depacon and Depakote ER.

Results A reduction in pain from moderate to severe to mild or pain free was seen in 71% of patients treated with a one time 1000 mg Depacon infusion. Of those patients that did not achieve pain free status after 1000 mg Depacon achieved pain free status after 5 additional doses of Depacon. Thus, 71% of patients received pain free status after one time 1000 mg Depacon or additional 5 Depacon doses as outlined in our protocol. 11 patients were started on 500–1000 mg Depakote ER. 82% had a greater than 50% reduction in frequency of their migraines over a 3-month period. 2 patients had recurrence of their status migrainosis. There were no adverse events seen with I.V. Depacon. One patient had hair loss, another a rash with Depakote ER.

Conclusions Depacon I.V is safe and effective for treatment of status migrainosis. Using the Depacon protocol we chose was highly efficacious. This was done in an outpatient setting with no adverse events. Implementing Depakote ER after Depacon infusions is also effective to reduce frequency of the now, episodic migraine patients.

P6R8

Epidemiology of children migraine in Vojvodina

Marija Knezevic-Pogancev*[1]
[1]*Institute for Child and Youth Health Care, Novi Sad, Yugoslavia*

Migraine is the most frequent recurrent headache in children and adolescents. The objects of examination were to present rate of recurrent headaches of migraine type and the type of the migraine syndrome in Children of Vojvodina.

In the period from 1988 to 1999, 24035 children aged 3–16 years living in the region of Vojvodina were examined. The examination was conducted by giving the population examined to fill in a carefully constructed and standardized questionnaire and by interviewing directly children and parents of the children who had recurrent headaches.

The migraine syndrome shows in 3.87% of children aged 3–7 years, and in 8.63% of children aged 3–16 years. The

migraine syndrome in children population of the same age appears as the migraine with aura in 25.55%, as the migraine without aura in 67.21% and as other migraine syndromes in 7.23% of children with migraine headache.

The presence rate of the migraine syndrome increases with age from 2.65% to 11.72% in boys and from 2.71% to 15.86% in girls. The migraine with aura shows a continuos linear rise from 1.8% to 32.7%, whereas the migraine without aura reaches its peak at prepuberty stage (79.7% of migraine syndromes. Migraine equivalents reach their peak at the age of five (67.3% of migraine syndromes).

P6R9

Estrogens are able to modulate facial inflammatory pain: a study in aromatase knock-out mice using the Formalin Model

Sylvie Multon[1], Estelle Rikir[1], Sandrine Halleux[1], Jeanine Mosen[1], Arpad Pardutz[1] & Jean Schoenen*[1]
[1]*Research Center for Cellular and Molecular Neurobiology, Neuroanatomy Section, Headache Research Unit, University of Liège, Belgium*

The mechanisms by which estrogens may be responsible for the higher prevalence of certain head and facial pains in females are not known. We studied the role of gender and of estrogens on inflammatory pain using the orofacial formalin test in mice. We measured the frequency of rubbing of the formalin-injected lip in male and female estrogen-deficient aromatase knock-out mice (ArKO, *Cyp19*) with and without pretreatment with β-estradiol (5 µg, s.c.) and in their wild-type littermates (WT).

There was no difference in nociceptive behaviour between male and female WT mice. By contrast, lip rubbing was significantly more pronounced in ArKO than in WT females during the second 'tonic' pain phase. ArKO males did not differ significantly from their WT littermates regarding phases 1 and 2, but they displayed a third phase of pain behaviour 36 min after the formalin injection. In β-estradiol-treated ArKO mice no differences could be detected anymore.

These results confirm the role of estrogens in the modulation of inflammatory facial pain. They indicate that estrogens have an antinociceptive effect and that the different behaviour in ArKO mice is not due to developmental changes. The differences between male and female ArKO mice suggest that underlying control mechanisms differ between genders.

P6R10

Cortical elaboration of experimental pain by selective trigeminal nociceptive fibres activation during nytroglicerin-induced headache in migraine patients

Marina De Tommaso*[1], Rosanna Cerbo, Giuseppe Libro[1], Marco Guido[1], Luciana Losito[1], Olimpia Difruscolo[1], Michele Sardaro[1] & Francomichele Puca[1]
[1]*First Neurologic Clinic, Psychiatric and Neurologic Department, University of Bari, Italy*

Previous studies showed that cortical processing of CO2 laser aδ fibers activation is suppressed during experimental pain (Romaniello et al. 2002): otherwise during spontaneous pain occurring during migraine attack, the cortical responses by trigeminal laser stimulation {LEPs) were increased (de Tommaso et al. 2002), showing a cortical facilitation of trigeminal nociceptive inputs processing. The aim of the present study was to record LEPs during nytroglicerine induced headache in migraine without aura patients, in respect with the spontaneous migraine attack. Seven patients were selected and evaluated during at least 2 h after the onset of migraine attack and 72 h after its resolution. In all patients headache was induced by oral administration of 0.3 mg of nytroglicerine. In all conditions the LEPs were recorded by CZ-A1/A2 scalp electrode, stimulating the right and left suprorbital skin. The tracks were blindly examined. The N-P cortical complex was increased in amplitude during spontaneous migraine attack in comparison with the interictal phase, but appeared suppressed during the experimental-induced headache.

These results may suggest that the facilitation of trigeminal inputs elaboration at cortical level is a peculiar phenomenon occurring during spontaneous migraine attack, probably based upon the dysfunction of the inhibitory pain control which caused the suppression of LEPs during nytroglicerine-induced headache.

P6R11

Sleep and nocturnal primary headache: polysomnographic findings

Raffaele Manni*[1], Michele Terzaghi[1], Natascia Ghiotto[2] & Giuseppe Nappi[2,3] & Grazia Sances[2]
[1]*Unit of Sleep Medicine and Epilepsy, University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [2]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH), IRCCS C. Modino Institute of Neurology, Pavia, Italy,* [3]*Department of Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

It is widely accepted that sleep is a functional factor in the precipitation/induction of headache attacks. Relationship between headache and sleep is still not completely clear. Our study set out to evaluate the relationship between nocturnal headache attacks and sleep macro/microstructure.

Thirty-nine headache patients (24 males; 15 females; mean age 54.51 years), suffering from nocturnal attacks, were studied. All underwent a clinical structured interview and were evaluated by means of continuous 24- h ambulatory polysomnography (A-PSG) paralleled by a sleep log. Fifty-seven per cent of the subjects were affected by migraine without aura, 20% by hypnic headache, 15% by cluster headache; in 8% of the patients the diagnosis has still not been determined.

Sleep was preliminarily scored according to standard macrostructural analysis criteria.

In 15 patients, headache occurred during the 24-h A-PSG, globally 20 attacks were recorded: 17 of these occurred during sleep, all but one at night-time; 3 in patients with hypnic headache (2 in REM sleep, 1 in NREM sleep); 7 with cluster headache (1 in REM, 6 in NREM); and 7 with migraine without aura (1 in REM; 6 in NREM).

Our data suggest a sleep stage-dependence of headache attacks that differs according to the headache syndrome.

This study was supported by a grant from the Italian Ministry of Health (PF 2001/151).

P6R12

Abnormal modulatory influence (facilitation instead of inhibition) by diffuse noxious inhibitory controls in migraine and chronic tension-type headache patients

Paolo Rossi*[1], Giorgio Sandrini[2], Alberto Proietti Cecchini[2] & Giuseppe Nappi[3]
[1]*Headache Clinic, INI, Grottaferrata, Italy,* [2]*Headache Diagnosis and Treatment Centre, University Centre for Adaptive Disorders and Headache (UCADH) IRCCS C. Mondino Institute of Neurology, Pavia, Italy,* [3]*Department of Clinical Neurology and ORL, University of Rome 'La Sapienza', Rome, Italy*

Objectives The aim of this study was to evaluate the function of pain modulating systems subserving the Diffuse Noxious Inhibitory Controls (DNICs) in primary headaches.
Methods 24 migraineurs and 17 patients with chronic tension-type headache have been evaluated by means of nociceptive flexion RIII reflex and cold-pressor test (CPT) as heterotopic noxious conditioning stimulation. Twenty healthy subjects were studied as controls.
Results The subjective pain thresholds and the RIII reflex threshold were significantly lower in CTTH patients as compared to controls. In controls a significant inhibition of RIII reflex was observed during the cold stimulation (–30%, $p < 0.05$). On the contrary migraine and CTTH.
Patients instead of inhibition showed facilitation (+ 31%, $p < 0.05$ and + 40%, $p < 0.01$, respectively) of RIII reflex during the CPT. The results of subjective pain perception during CPT paralleled those of RIII reflex area in both headache and controls subjects.
Conclusions The present study demonstrates a dysfunction in systems subserving DNICs in headache patients. We suggest that an impairment of endogenous supraspinal pain modulation systems may be an important common denominator in the pain mechanism of both migraine and CTTH possibly contributing to the development and/or maintenance of central sensitization of nociceptive pathways observed in primary headaches.

This work was supported by a grant from the Italian Ministry of Health (RC 2001).

P6R13

The cerebral hemodynamics of headache associated with sexual activity

Stefan Evers*[1], Oliver Schmidt[1], Achim Frese[1], Ingo-W. Husstedt[1] & Erich-B. Ringelstein[1]
[1]*Department of Neurology, University of Muenster*

Headache associated with sexual activity is an idiopathic headache disorder and regarded to be a vascular headache. However, no pathophysiological studies have been performed to support this hypothesis.

We investigated 12 patients with the explosive type of sexual headache according to the IHS criteria during a headache-free state by means of acetazolamide test and of stress Doppler sonography. Twelve age-matched migraine patients and 14 healthy subjects served as control groups. Changes of blood pressure, of cerebral blood flow velocity and of pulsatility index were evaluated.

Patients with sexual headache showed a significantly higher increase of blood pressure during standardized physical exercise as compared to healthy subjects and migraine patients. Changes of cerebral blood flow velocity by physical exercise were not different between the three examination groups. After 1 g acetazolamide, cerebral blood flow velocity showed a significantly higher increase in patients with sexual headache (plus 66%) than in healthy subjects (plus 46%), and pulsatility index showed a significantly lower decrease as compared to healthy subjects and migraine patients. These data suggest that in patients with sexual headache the metabolic rather than the myogenic component of the cerebral vasoneuronal coupling is impaired.

P6R14

Quality of life in whiplash headache: a 6 and 12 month follow-up

Fabio Antonaci*[1], Sara Ghirmai[1], Giorgio Bono[2], Francesca Caprioli[1] & Giuseppe Nappi[3]
[1]*Department of Neurological Sciences, University of Pavia, IRCCS 'C. Mondino', Pavia, Italy,* [2]*Department of Neurology, University of Insubria, Varese, Italy,* [3]*Department of Neurological Science. University 'La Sapienza', Rome, Italy*

Although disability has been largely studied in patients with whiplash (W) injury, a systematic assessment of quality of life (QL) is required. This report describes the health related QL in W headache. 66 females and 18 males diagnosed according to the QTF of WAD (1995) as grade 2 and grade 3 entered the study. Quality of life was measured using the SF36. Health Survey and Migraine-specific quality of life questionnaire (MSQ). W were tested at the time of first consultation (T0), 6 and 12 months later (T12). In patients with W injury the QL was significantly impaired in all categories compared to a control group population. Females and males were significantly more impaired in all items than sex matched controls. On MSQ questionnaire the categories Role Restrictive and Emotional were significantly less impaired in patients with longer illness duration than in those with a recent whiplash headache. A trend towards amelioration emerged at T12 in all categories on SF36 and on MSQ, with a few the exception. W is a condition affecting negatively the QL even if patients show a tendency to improve over time.

This work was supported by a grant of Ministry of Public Health No.57.2/RF93.28.

P6R15

Hyperhomocysteinemia in patients with migraine with aura

Domenico D'Amico*[1], Franca Moschiano[2], Angelo Attanasio[1], Nicoletta Erba[2], Emilio Ciusani[1], Ferdinando Schieroni[2] & Gennaro Bussone[1]
[1]*C. Besta National Neurological Intitute, Milan, Italy,* [2]*L. Mandic Hospital, Merate, Italy*

The reasons of the increased risk for stroke which has been demonstrated in patients with migraine, and particularly with migraine with aura (MA) are not known. Hyperhomocistinemia has been proposed a risk factor for stroke (Kelly PJ et al. 2002). The aim of the study was to investigate homocysteine levels in MA patients. Only one study evaluated homocysteine in migraine (Hering-Hanit R et al. 2001).

One-hundred-nine patients (70 women – 39 men; mean age 36 years), and 86 healthy controls (40 women – 46 men; mean age 36 years) were studied.

Mean values of homocysteine serum levels (expressed in μmol/L – evaluated by Abbott reagent) were 12.28 ± 1,1 in patients with MA, and 9.76 ± 0.4 in controls. Statistical analysis by Student-Newman-Keuls Method, showed significantly higher values in MA vs. controls ($P < 0{,}03$). The proportion of subjects with hyperhomocysteinemia (homocysteine > 10 in women, > 15 in men) was significantly higher ($P < 0.05$ at chi-square test).in MA vs. controls (considering the total groups, and also in both sexes separately).

Our results showed that patients with MA tend to show higher homocysteine levels. These findings suggest that hyperhomocysteinemia may play a role in predisposing subjects with MA to ischemic stroke.

P6R16

Blood nitric oxide metabolites in patients with migraine during headache-free period

Nobuo Araki*[1], Hotaek Kim[1], Daisuke Furuya[1], Misato Takahama[2], Harumitsu Nagoya[1], Masamizu Yamazato[1] & Kunio Shimazu[1]
[1]*Department of Neurology, Saitama Medical School,* [2]*Department of 4th Internal Medicine, Saitama Medical Center*

Objective Previous studies showed migraine patients have supersensitivity to glyceryl trinitrate. The purpose of this study is to analyze the serum level of nitric oxide metabolites in patients with migraine during headache-free period.
Methods Twenty-five migraine patients (both with aura and without aura) during headache free interval and 12 healthy volunteers were included in this study. Blood samples from patients and controls were obtained and divided into serum. A microdialysis probe was put into each serum and dialysate samples were obtained for 10 minutes. Nitrite and nitrate levels in each sample were determined by the Griess reaction.
Results Serum nitrite levels of migraine patients (1.8 ± 1.0 μmol/L) were higher than those of the healthy volunteers (1.2 ± 0.2 μmol/L). Serum nitrate levels of migraine patients (12.5 ± 6.6 μmol/L) were significantly higher than those of the healthy volunteers (7.6 ± 3.0 μmol/L). Total NO metabolites (NO_2^- + NO_3^-) in patients with migraine (14.3 ± 6.9 μmol/L) were significantly higher than that of the healthy volunteers (8.8 ± 3.0 μmol/L).
Conclusion These data suggest that nitric oxide production in patients with migraine is enhanced during headache-free period.

P6R17

Lack of intracortical inhibition in migraine – a transcranial magnetic stimulation study

Michael Siniatchkin*[1], Hartmut Heinrich[1], Birgit Kröner-Herwig[1] & Aribert Rothenberger[1]
[1]*Child and Adolescent Psychiatry and Clinical Psychology, University of Göttingen*

Objective and methods The TMS studies in migraine provided contradictory results. The aim of the study was to investigate intracortical inhibitory mechanisms using a suprathreshold TMS (Magstim 200 HP; EMG from the right abductor digiti minimi) in a paired-pulse paradigm with long interstimulus intervals (ISI = 20, 120 ms, 10 trials for each ISI, randomized) and measurement of the cortical silent period (CSP; 40% above active motor threshold) in women suffering from migraine without aura ($n = 10$; 28.2 ± 8.6 years), episodic TTH ($n = 11$; 29.7 ± 9.4 years) and in healthy women ($n = 12$; 27.8 ± 8.1 years).
Results We found no differences for CSP between migraineurs and other subjects ($F(2, 32) = 1.12$; $p = 0.179$). Concerning suprathreshold stimulation, migraine patients demonstrated a significantly increased facilitation ($P = 0.02$ compared with healthy subjects) and a reduced intracortical inhibition ($P = 0.05$).
Discussion The findings suggest a lack of central inhibitory mechanisms in migraine. Because the long ISI intracortical inhibition and the CSP were related to the $GABA_B$ and dopaminergic systems, the role of these systems in the pathogenesis of migraine may be discussed.

P6R18

Headache prevalence related to hemoglobin, erythrocyte count levels and ferritin. The HUNT-Study

Anne Hege Aamodt*[1], Berit Borch-Iohnsen[2], Knut Hagen[1], Lars Jacob Stovner[1], Arne Åsberg[3] & John-Anker Zwart[1]
[1]*Department of Neurology and Clinical Neurophysiology, St. Olav Hospital, Trondheim University Hospital, Trondheim, Norway,* [2]*Institute for Nutrition Research, University of Oslo, Norway,* [3]*Department of Clinical Chemistry, St. Olav Hospital, Trondheim University Hospital*

Headache is a common symptom in several hematological diseases, and clinical based studies show an association between headache and both high and low levels of hemoglobin. To investigate the association between headache and hemoglobin further, we analysed these parameters in an unselected population.

In a cross-sectional population based study (the HUNT Study) a total of 2385 women aged 20–55 years responded to a headache questionnaire and had blood samples for measuring hemoglobin, erythrocyte count levels and ferritin.

In the multivariate analyses, adjusting for age and education, there was a linear trend of decreasing prevalence of headache ($P = 0.02$) and migraine ($P = 0.01$) with decreasing hemoglobin. In particular, migraine was less likely among women with low hemoglobin (values < 11.5 g/dL) (OR = 0.4, CI 0.2–0.9). A tendency of the same trend was found for erythrocyte count level, but not for ferritin.

The reason for the increased prevalence of headache with higher hemoglobin levels is unknown, but one may speculate that it is related to increased blood viscosity of the. Further investigations are needed to study this association.

P6R19

Effect of botulinum toxin type A (BoNT-A) therapy on pain frequency and intensity in patients with cervical dystonia

Mitchell Brin*[1], Allison Brashear[2] & Julie Mordaunt[1]
[1]*Allergan, Inc., Irvine, CA, USA,* [2]*Indiana University Hospital, Department of Neurology, Indianapolis, IN, USA*

Background Head, face, and/or neck pain are frequently associated with craniocervical dystonia (CD), as described in the IHS 11.2.3 classification.
Objective To evaluate the impact of BoNT-A therapy on pain in CD patients.
Methods One hundred and seventy CD patients were randomized to double-blind placebo (PBO) or BoNT-A treatment. Pain frequency and intensity were assessed at 2,4,6,8, and 10 weeks after injection using a 0 (never or none) to 4 (constant or very severe) scale. Change from baseline analyses were performed on observed data.
Results At baseline, 91% and 93% of BoNT-A patients and placebo patients, respectively, reported some frequency or intensity of pain. At the primary endpoint (week 6) the mean reduction in pain frequency was significantly greater in BoNT-A patients (–0.31 from 1.79) vs. PBO patients (–0.01 from 1.91); p = 0.018. At week 6 there were significant differences in the mean changes in pain intensity (BoNT-A: –0.36 from 1.78) vs. (PBO; +0.06, from 1.8); p < 0.001). A greater proportion of BoNT-A patients had at least one grade decrease in pain frequency (29.5% vs. 12.5%) and intensity (32.1% vs. 6.9%).
Conclusion BoNT-A effectively reduces craniocervical pain frequency and intensity, and may be useful for neck and/or headache pain associated with CD.

Reference

1 Allergan, Inc., Irvine, CA, [2]Indiana University Hospital, Department of Neurology, Indianapolis, IN.

P6R20

Critical Flicker Frequency – a study comparing migraineurs with normal controls

Pedro Andre Kowacs*[1], Elcio Juliato Piovesan[1] & Hudson Fameli[1], Hamilton Pereira da Silva[1], Anderson Cesar Zani[1] & Lineu César Werneck[1]
[1]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil*

Objectives To determine and compare the critical flicker frequency (CFF) of individuals with migraine with aura (MA), migraine without aura (MWA) and healthy controls (HC).
Methods Twenty-six migraineurs, aged 31.1 ± 11.3 years, 12 with MA and 14 with MWA and 30 HC aged 30.9 ± 8.9 years were included. Equipment consisted of a 100 × 12.5 × 12.5 cm box with four flickering LEDs in their back wall. Under the continuous flicker method (CFM) three ascending sequences from 20Hz to 70Hz and three descending sequences from 70Hz to 20Hz were alternately performed, the mean of six measurements being considered. Under the forced choice method (FCM), stimuli lasting 4 s, 2 s in a fused frequency (70Hz) and the other two in a randomly chosen frequency (from 20 to 60) were delivered. Individuals pressed a locking switch while perceiving the CFF.
Results Migraineurs presented a mean CFF lower than healthy controls at the CFM (40.45 vs. 44.33, respectively; p = 0.019) and at the FCM (34.16Hz vs. 38.5Hz, respectively, p = 0.019). MA individuals presented thresholds significantly lower than those presented by HC ($P = 0.008$ and p = 0.0001, under the CFM and the FCM, respectively).
Conclusions Our results show migraineurs to react abnormally to flickering stimuli. Flickering lights may play a role in the expression of migraine.

P6R21

Changes in visual field performance after migraine measured with flickering stimuli

Allison McKendrick*[1] & David Badcock[1]
[1]*School of Psychology, University of Western Australia*

Objectives To determine whether sensitivity deficits to flickering stimuli in migraineurs are greater closer to a migraine.
Methods Twenty-two migraineurs (12 migraine with aura, and 10 without) and 22 nonheadache controls aged 18–45 years participated. Controls were tested twice to determine test-retest variability. Migraineurs were assessed at baseline (minimum 4 days postmigraine, range 4–120 days, mean 25 days), then at 24 h, and 7 days after the cessation of a migraine. Flicker sensitivity was measured across the central 30° of the visual field using the Auto-Flicker test of a Medmont M600 perimeter. Groups were compared using the perimetric global indices Age Defect and Pattern Defect [PD], as well as on a point-wise basis across the visual field.
Results The PD index was significantly higher for migraineurs than controls at baseline ($P = 0.03$) demonstrating areas of localized reduced sensitivity. A further significant reduction in sensitivity relative to baseline was present in the

migraine group at both 24 h and 7 days postmigraine ($P < 0.01$).

Conclusions Localised deficits of flicker sensitivity are present in migraineurs relative to nonheadache controls. Sensitivity deficits are even greater 24 h postmigraine, particularly in locations with lower baseline sensitivity, and do not recover to baseline within 7 days.

P6R22

Headache during endovascular procedures

Raquel Gil-Gouveia*[1], Isabel Pavão-Martins[1], Lenor Lopes[2], Rita Sousa[2] & Jorge Campos[2]
[1]*Centro de Estudos Egas Moniz, Avenue. Professor Egas Moniz, Hospital de Santa Maria, Lisboa, Portugal*, [2]*Serviço de Neurorradiologia, Hospital de Santa Maria, Lisboa, Portugal*

Objectives Cerebral endovascular procedures can elicit headache in some patients. This can be a model to study vascular headaches. We aim to describe such headaches controlling intervening variables.

Methods Patients submitted to cerebral angiography were included by completion of a headache questionnaire before the procedure, with clinical data and previous headache history. Headaches during angiography were characterized in conscious patients.

Results Preliminary results of the first 63 procedures (54 diagnostic angiographies, 9 embolizations) are presented, including 55 patients (34 females) with an age average 48.4 years. Twenty-seven patients (49.1%) had previous headache history, classified as migraine (10 patients), tension type headache (15) and other headache (2). Twenty-two subjects had subarachnoid haemorrhages. Ten patients complained of headache during the procedure that was associated to vascular manipulation in all cases (6 contrast injection, 4 embolization). Headache was brief (mean duration 6.7 s, 2–30 s) and vessels most frequently involved were the internal carotid (5 cases) and vertebral artery (2). Headaches were mostly ipsilateral (six cases) and varied locations and intensities.

Conclusions Headaches during endovascular procedures are related to sudden vascular distension and are transient and ipsilateral to the manipulated vessel. Further characterization with more cases can allow us to understand such headaches.

P6R23

Headache in patients with benign positional vertigo

Byung Kun Kim*[1], Hee Joon Bae[1], Ja Seong Koo[1] & Ohyun Kwon[1]
[1]*Department of Neurology, Eulji University School of Medicine, Eulji Hospital, 280–1, Hagye-dong, Nowon-gu, Seoul, Korea*

Objectives Benign positional vertigo (BPV) is most common cause of episodic vertigo and episodic vertigo is frequently reported in migraineurs. This study attempts to clarify the clinical features of headache accompanied by idiopathic BPV and the prevalence of primary headache in patients with BPV.

Methods A prospective study was conducted on a consecutive series of 351 patients with BPV. The diagnosis of BPV was based on typical findings of vertigo and nystagmus by Dix-Hallpike maneuver and head turning in supine position.

Results Headache accompanied by idiopathic BPV was found in 46% of subjects. It was mild or moderate in 99% of subjects. 22% of patients still suffer from a dull headache up to several months after BPV was cured with canalith repositioning treatment. The 1-year prevalence of primary headache in idiopathic BPV according to the International Headache Society criteria was 8% with migraine and 30% with tension type headache. Migraine was not more frequent in idiopathic BPV than in post traumatic BPV.

Conclusions Patients with BPV frequently complain with headache, which may last for several days after episodic vertigo stopped. It is unlikely that migraine and idiopathic BPV is interrelated.

P6R24

Computerized and topographic EEG analysis in migraine patients

Andrea Alberti*[1], Francesca Galletti[1], Paola Sarchielli[1], Giovanni Mazzotta[1] & Virgilio Gallai[1]
[1]*Headache Centre, Neuroscience Department, University of Perugia, Italy*

The aim of this research is to investigate, by computerized and topographic EEG analysis, electroencephalographic abnormalities in migraine patients during the intercritical period and to verify whether there are differences between migraine with aura (MwA) and without aura (MwoA).

Material and method 27 migraine patients attending our Headache Center, 15 with MwA (average age: 34.3 ± 8.9) and 12 with MwoA (average age: 33.6 ± 11.4), were examined. No patient was affected by other neurological disorders and no patient was undergoing prophylactic treatment for migraine. 22 apparently healthy individuals (average age: 32.6 ± 12.2) were assessed as a control group. Patients were studied at least 72 h from the last attack. Computerized analysis was applied on chosen free-artefact epochs for at least 2 min The signal was processed by Fast Fourier Transform analysis to give the power spectrum, the values of absolute and relative power of delta, theta, alfa and beta bands and topographic activity maps. *T*-test was used for the comparison of the means of all parameters between patients and controls and between MwA and MwoA subgroups. The results of the statistical analysis were visualized on significance maps.

Results Migraine patients showed a statistically significant increase in the relative power of the theta band on temporal-parietal regions, bilaterally ($P < 0,05$). No significant differences were found for the other parameters examined between MwA and MwoA patients.

Conclusions Electroencephalographic abnormalities found in migraineurs may be interpreted as an expression of altered neuronal reactivity, perhaps due to a peculiar biochemical milieu favouring the greater susceptibility to depolarization. These alterations, during intercritical period, could indicate a fleeting equilibrium between exciting and inhibitory stimuli, a sort of bioelectrical 'migraine threshold'.

P6R25

Migraine aura status after closure of cardiac right-to-left shunts

Giulia Pierangeli[1], Sabina Cevoli*[1], Elena Minguzzi[1], Fabiola Magnifico[1], Pietro Cortelli[2], Pasquale Montagna[1], Andrea Donti[3] & C. Canali[1]
[1]*Department of Neurological Science, University of Bologna, Bologna, Italy,* [2]*Department of Neurology, University of Modena and ReggioEmilia, Modena, Italy,* [3]*Department of Cardiology, S. Orsola-Malpighi Hospital, Bologna, Italy*

Objective To describe a case of migraine aura status, responsive to Acetazolamide, arising after closure of an interatrial defect type II.

Background An association between migraine with aura and cardiac right-to-left shunts has been reported. Closure of large right-to-left shunt seems to decrease the frequency and severity of attacks.

Results We studied a 46-year-old-man affected, since the age of 15 years, by attacks of migraine with visual aura that occurred once a month and were responsive to Sumatriptan. An interatrial defect type II was detected at the age of 18 years. The patient underwent closure of the shunt by transcatheter techniques at the age of 46 years. There was no residual shunt one month after closure. Immediately after the closure procedure a migraine aura status began, characterized by one or two auras, seldom accompanied by migrainous headache, recurring nearly every day for three months. Neurological examination and brain MRI were normal. Aura symptoms disappeared shortly after the start of oral Acetazolamide (250 mg twice a day). An attempt to lower the dose resulted in a return of attacks.

Conclusion Our patient had a remarkable worsening of visual auras after the intervention of closure of interatrial defect type II, which lasted several months and responded to Acetazolamide. This association suggest a relationship between migraine with aura and cardiac right-to-left shunt which should be studied systematically.

MURST(R.F.O.) ex-60% 2000-2001-2002 grants.

P6R26

Familial hemiplegic migraine in adolescents: neuropsychologic deficits

Michele Roccella*[1] & Lucia Parisi[1]
[1]*Department of Psychology, University of Palermo, Italy*

Familial Hemiplegic Migraine (FHM) is a rare autosomal dominant-type migraine with aura.

A single familial hemiplegic migraine locus has been previously mapped to 19p13.1. Studies in different FHM families showed that additional causative genes must reside in other regions of the genoma, including the long arm of chromosome 1. FHM is characterised by attacks of transient hemiparesis followed by a migraine headache. It is typically divided into pure familial hemiplegic migraine and familial hemiplegic migraine with permanent cerebellar signs. CACNA1A gene mutations on chromosome 19 are involved in approximately 50% of FHM families. Headache attacks may be preceded, accompanied, or followed by hemiparesis or hemiplegia with other neurologic signs including altered consciousness, psychic symptoms, aphasia, and even coma.

Neuropsychologic deficits concerning functions such as: memory, attention and psychomotor abilities were reported in patients with migraine with aura in the intercritical period. Cognitive deficits concerning memory and psychomotor abilities were reported also in subjects with migraine without aura. The physiopathological mechanism underlying cognitive deficits is still unknown. A complex neurotransmitter disorder might account for impairment of both short- and long-term memory in headache patients. The purpose of this study was to very, through a set of multisectorial tests (WISC-R, Raven's Progressive Matrices, Zazzo's 'Deux Barrages' test, Benton's D-form of Visual Retention test, Frostig's Development of Visual Perception test, Bender's test, Rey's Complex Figure tes B-form), the damage the neuropsychological functions in three adolescents with FHM. The neuropsychologic assessment of the subjects was carried out six moths after the latest FHM episode. No cognitive deficit was detected in any subject. All the subjects reported an average IQ score with the WISC-*R*-test. In one case a mild and not significant impairment of the long-term verbal memory as well as a minor attention deficit were detected.

P6R27

Changes in disability and in quality of life scores in migraine patients after prophylaxis

Domenico D'Amico*[1,2], Patrizia Santoro[2], Fabio Frediani[2], Paolo Bernardoni[2], Salvatore Misceo[2], Rosa De Marco[2], Clara Tonini[2], Franca Mosciano[2], Enrico Ferrante[2], Susanna Usai[1], Alessandra Solari[1,2] & Gennaro Bussone[1,2]
[1]*C. Besta National Neurological Institute, Milano, Italy,* [2]*'Progetto Cefalee Lombardia' Group*

Migraine is characterized by low health-related quality of life (HRQOL) and disability in every-day activities. The aim of this study was to investigate if the functional impact of migraine changed after preventive treatment, using standardized instruments to assess disability in daily activities and to measure HRQol.

A group of subjects with migraine without aura attending 9 Headache Centers in Lombardia (Northern Italy), and in whom a preventive treatment was needed, entered the study. All patients completed the Italian versions of the Migraine Disability Assessment Score (MIDAS) questionnaire and of the SF-36 survey at their first consultation. After a 2-month run-in period, they were given a prophylactic treatment, and they came back after 3 months to give back the diary cards and to complete MIDAS and SF-36. Seventy-three patients completed the study.

Statistical analysis showed significant changes after treatment intervention: $p < 0.001$ at Student *t*-test for headache frequency, number of symptomatic drugs and MIDAS score; $p < 0.001$ at Wilcoxon signed-rank test for all SF-36 scales but two (PF and GH).

Our data showed that preventive treatment induced a marked reduction of the impact of migraine, with a significant

improvement in ability to function and in most quality of life domains.

P6R28

Migraine-related disability in the workplace: data from an Italian company-wide based study

Domenico D'Amico*[2,1], Sergio Genco[2], Francesco Perini[2], Vito Toso[2], Franco Michele Puca[2] & Gennaro Bussone[2,1]
[1]*C. Besta National Neurological Intitute, Via Celoria 11, 20133, Milan, Italy,* [2]*EMIKRONOS Study Group*

The 837 employees (714 women, 123 men; mean age 44.2 years) of the Italian company La Perla (Bologna) were interviewed by a headache specialist at work. Consultation rate, headache characteristics, drug use, and work disability over the preceding three months were assessed in the 107 (12.8%; 102 women, 5 men; mean age 38.7 years) with migraine (IHS criteria).

29.9% patients had 1–3 headache days/month, 41.1% had 4–6 days/month, 25.6% 7 or more days/month. Pain was mild in 4.7%, moderate in 54.2%, severe in 39.3%. 53% never consulted, 29% consulted a GP, 27.1% one or more specialists. 86.9% used symptomatic drugs, 81.3% only NSAIDS, 5.6% used NSAIDS and triptans. 24.5% missed at least one day due to headache; mean days/month missed were 0.6. 98.6% worked on headache days (23.4% for 1–3 days; 50.5% for 4–12 days); mean days/month with headache at work were 8.2. On such days productivity was reduced by 30–40% in 33.6%, by 40–50% in 33.6%.

Migraine is common at work and seriously reduces productivity. A quarter of migraineurs lost at least one working day, and most experienced headache at work with negative effects on productivity. The consultation rate and use of triptans and preventive drugs were surprisingly low.

P6R29

Cognitive function is not significantly impaired in older people with a long history of migraine

Jane Pearson*[1], Edward Chronicle[1], Elizabeth Maylor[2] & Lucy Bruce[2]
[1]*Department of Psychology, Lancaster University, Lancaster, UK,*
[2]*Department of Psychology, University of Warwick, Coventry, UK*

Objectives Migraine is characterised by acute and severe disruptions to the brain parenchyma. It is possible that there may be some cumulative effect on the cortex, manifesting itself in later life. This study aimed to examine measures of cognitive function in older patients and matched controls.
Methods Volunteers were recruited from an existing database of 595 people over 50 years of age who had previously undertaken cognitive testing. All members of the database were approached and asked to respond if they had ever suffered from migraine.
Results 16% of the members of the database identified themselves as current or previous migraine sufferers. In 85%, an IHS diagnosis of migraine was confirmed by telephone interview. There was no significant difference between migraine and control groups in self-rating measures of current general health, eyesight or hearing. No significant differences were seen between the groups on cognitive measures of (a) fluid intelligence (b) crystallised intelligence and (c) processing speed.
Conclusions This study provides preliminary evidence that measures of general cognitive function are unaffected in patients with long history of migraine. It will be of interest to assess more specific cognitive and neurophysiological measures of cortical function in this population.

P6R30

VNS therapy shows long-term improvement in patients with chronic daily headache

Jack Klapper*[1] & Timothy Smith[2]
[1]*Colorado Neurology & headache center, Denver, CO, USA,* [2]*Ryan Headache Center, St. Louis, MO, USA*

Objectives We report the long-term results of a pilot study of VNS therapy in patients with chronic daily headache (CDH).
Methods Seven patients diagnosed with CDH received up to 1 years of VNS therapy including the 3-month acute study. Changes in headache prophylactic medications and VNS stimulus parameters were allowed during the long-term study. Patients served as their own controls for comparison of outcome, disability, and quality of life.
Results Median age was 47 year (range, 29–56), median number of years diagnosed with headache was 23 (range, 12–50), median headache-free hours/day was .12 (range, 0–5.69) At 6 months, statistically significant improvement was seen in total MIDAS scores ($P = 0.0156$) and in the SF-36 Social Functioning subscale ($P = 0.0469$). Average Daily Headache Index (frequency × duration × usual severity) shows 1 patient > 50% and 1 patient > 25% improvement at 6 months. 4 of 7 patients showed an increase in headache-free hours per day at 6 months. Data on all 7 patients at 1-year will be presented.
Conclusions Long-term VNS therapy was associated with both a distinct reduction in headache-related disability and an overall improvement in quality of life.

P6R31

Radiofrequency treatment for cervicogenic headache: a randomised, double-blind, sham-controlled study

Lars Jacob Stovner*[1], Frode Kolstad[2] & Grethe Helde[1]
[1]*Norwegian National Headache Center,* [2]*Division of Neurosurgery, Department of Clinical Neurosciences, Trondheim University Hospital, Trondheim, Norway*

Cervicogenic headache is still a controversial disease entity, and good and reliable treatment is lacking. Previously, an open study has indicated a transitory effect of facet joint radiofrequency neurotomy in the neck, but no blinded and controlled study has been performed.

In the present study, 12 patients with disabling, and previously treatment-resistant headache fulfilling the criteria for the disorder were included. Six patients were randomised to receive facet joint neurotomy from C2 to C6 ipsilateral to the pain, and 6 were randomised to sham treatment with a very

similar procedure but with no lesions given. Patients were followed for 2 years with diary registration of pain for 14-day periods after 1, 3, 6, 12, 18 and 24 months, and also followed with algometry and neck mobility measurements at 3, 12 and 24 months.

Patients treated with neurotomy were somewhat improved (not statistically significant) at 3 months, but later there were no marked differences between the groups. There were only short-lasting side-effects, but after 24 months, the sham treated group tended to have less pain.

In conclusion, cervical facet joint radiofrequency neurotomy is probably not beneficial in cervicogenic headache.

P6R32

rTMS modulation of visual cortex in healthy subjects undergoing short-term light deprivation. A model to study the hypothesis of under-inhibition in migraine?

Filippo Brighina*[1], Aurelio Piazza[1], Tony Vitello[1], Giuseppe Giglia[1], Simona Scalia[1], Michele Gennuso[1] & Brigida Fierro[1]
[1]*Neurophysiological Unity, University of Palermo, Italy*

Background we reported a facilitatory effect of 1 Hz rTMS on the occipital cortex in migraineurs, likely dependent on deficient inhibitory circuits, unable to be up-regulated.
Light deprivation (LD) increases cortical excitability reducing efficiency of GABA circuits in normal subjects.
Objective to evaluate the effects of 1 Hz rTMS on visual cortex of healthy subjects undergoing LD
Methods 8 subjects underwent LD for 60 min. On a different session, they underwent 1 Hz rTMS (900 stimuli) over Oz at phosphene threshold (PT) intensity, in the last 15 min LD. In a control experiment, 3 subjects underwent 10 Hz rTMS (600 stimuli). In all conditions, PT was measured before, after 45 and 60 min LD and every 5 min after light re-exposure to evaluate PT recovery time (RT).
Results PT values were significantly decreased after 45 and 60 min LD.; mean RT was about 20 min 1 Hz rTMS significantly increased RT as compared to baseline. 10 Hz rTMS reduced RT and increased PT values at 60 min LD.
Conclusions reduced cortical inhibition induced by LD determines facilitation to 1Hz rTMS as found in migraineurs. This supports the hypothesis of visual cortex under-inhibition in migraine with aura. Deficient inhibitory circuits could be perhaps up-regulated by high-frequency rTMS

P6R33

The patterns of health-resource utilization and treatment for chronic migraine sufferers participating in a clinical trial

Marcelo Bigal*[2], Fred Freitag[1], Richard Lipton[2], Chris Kozma[3] & Ron DeGryse[3]
[1]*Diamond Headache Clinic, Chicago, IL, USA,* [2]*Albert Einstein College of Medicine, Bronx, NY, USA,* [3]*Allergan, Inc., Irvine, CA, USA*

Background Chronic migraine headaches (≥16 days/month) are commonly seen in the speciality practice yet the impact on healthcare utilization is not well-described.
Objective To describe healthcare resource utilization of subjects with chronic migraine headaches.
Methods Subjects from two similar preventive trials who were 18–65 years old, with a primary headache disorder > 15 headache days/month by history and diary, and stable medical conditions completed a questionnaire on healthcare utilization for headache over the past year.
Results A sample of 406 patients, the majority of whom were chronic migraine sufferers (81.8% female, age 43.8 ± 10.6 years), made an average of 16.1 annual healthcare visits for headache, most frequently to neurologists (65.2%, mean of 2.7 visits/year), and general practitioners (62.2%, 5 visits/year) and others (29.4%). Other use of healthcare services included 1.4 ± 5.96 emergency room visits and 0.08 ± 0.37 hospitalizations annually. Most patients used OTC medications (77%), followed by triptans (63%), prescription non-narcotic analgesics (46%) and narcotics (39%).
Conclusions Chronic migraine sufferers use substantial health-care resources; strategies to reduce its burden on the healthcare system are needed. In contrast with previous data from episodic migraine populations, patients with chronic migraine tend to visit neurologists rather than GP's and use OTC medications more frequently.

P6R34

Similarity of chronic migraine patients with and without a history of migraine

Marcelo Bigal*[1], Richard Lipton[1], Ron DeGryse[2], Rozalina Dimitrova[2] & Stephen Silberstein[3]
[1]*Albert Einstein College of Medicine, Bronx, NY, USA,* [2]*Allergan, Inc., Irvine, CA, USA,* [3]*Thomas Jefferson University Hospital, Philadelphia, PA, USA*

Background The Silberstein-Lipton criteria for chronic migraine (CM) provide 3 alternative links to migraine: (1) A prior history of migraine; (2) A transformation period; (3) Current superimposed attacks of migraine. CM sufferers with and without a previous history of migraine have not been compared.
Objective To compare the demographic and clinical features of CM patients with (CM+) and without (CM-) previous history of migraine.
Methods Participants in a trial of preventive migraine therapy who met criteria for CM completed a demographic questionnaire and the MIDAS. CM+ and CM- subjects were contrasted.
Results Of 286 subjects, 110 (38.4%) were CM+ and 176 (61.5%) were CM-. The groups did not differ in age (42.5vs.44.2),% female (86.4 vs.78.3), monthly headache-free days (6.8 vs.6.2), monthly migraine days (13.6 vs. 12.6), MIDAS grade or Beck Depression Inventory scores. CM+ and CM- differed in the time since CDH onset (10.6 vs. 17.5 years, respectively; $p < 0.001$).
Conclusions These results suggest that CM with and without a history of migraine represent the same disorder and support the revised Silberstein-Lipton criteria for CM. The divergence between CM+ and CM- in time since onset of CM suggests that patients with longer duration CM may forget their history of migraine.

P6R35

The effect of Flunarizine on visual evoked potentials in migraine: a 3-month follow up study

Dheraj Khurana*[1], S. Prabhakar[1], V. Lal[1], P. S. Kharbanda[1], C. P. Das[1] & R. Bhatia[1]
[1]*Postgraduate Institute of Medical Education and Research, Chandigarh, India*

Objective To determine abnormalities in VEPs in migraineurs and study effect of Flunarizine on them.
Methods 50 patients of migraine with or without aura as per criteria laid down by the IHS, attending Neurology OPD at our Institute were prospectively enrolled between June 2001 and October 2002. VEPs to a 2-Hz Checkerboard stimulation were recorded before and after flunarizine at 6 weeks and 12 weeks of therapy. The N1, P100 and N2 latencies and N1-P100, P100-N2 amplitudes were recorded.
Results 34 patients turned up at 6 weeks while 23 patients returned 12 weeks. Most patients reported significant improvement in headaches. At baseline only the mean N1 latency showed a significant reduction as compared to controls. At 6 weeks postflunarizine, the mean N1 latency and P100-N2 latency of both eyes combined showed an increase ($P < 0.005$) while at 12 weeks postflunarizine the N1 latency, N1-P100 and P100-N2 amplitudes showed a significant increase ($P < 0.001$, $p < 0.05$, $p = 0.01$, respectively) as compared to baseline values.
Conclusions An increase in the amplitudes and latencies of VEPs in migraineurs following flunarizine therapy indicates an increase in cortical excitability on treatment. This implies a worsening of the underlying pathophysiology despite an apparent clinical improvement. This electrophysiological paradox has not been elaborated earlier and it may cast newer insights into the pathophysiology of migraine.

P6R36

Transcranial Doppler and near infrared spectroscopy for evaluating cerebral blood flow and vasomotor reactivity in patients affected by migraine with aura

Francesco Tibuzzi[1], Patrizio Pasqualetti[1], Francesco Passarelli[1], Claudia Altamura[1,2], Nicola Rosato[1], Paolo Maria Rossini[1,2] & Fabrizio Vernieri*[1,2]
[1]*AFaR Dipartimento Di Neuroscienze, Ospedale Fatebenefratelli, Isola Tiberina, Roma, Italy,* [2]*Clinica Neurologica, Università Campus Biomedico, Roma, Italy*

Migraine with aura (MWA) is associated with a reduction in cerebral blood flow (CBF). The importance of the autoregulation mechanism in migraineous patients is still to be determined.

Near InfraRed Spectroscopy (NIRS), deriving information about the concentrations of hemoglobin (Hb), is a noninvasive technique able to measure cerebral blood volume (CBV) and vasomotor reactivity (VMR).

We performed transcranial Doppler (TCD) and NIRS in order to obtain CBF and CBV changes in 18 control subjects and in 18 MWA patients (9 with no side prevalence of attacks and 9 with unilateral headache). All subjects underwent a simultaneous examination of flow velocity (FV) measured by TCD and of oxyHb, deoxyHb and total hemoglobin content (THC) evaluated by NIRS at rest and during hypercapnia.

Our results failed to show any significant difference in terms of FV and VMR measured by TCD and of THC increase, as a measure of regional CBV, evaluated by NIRS, between migraineous patients and controls. Patients with unilateral headache presented lower THC increase in the headache (3.7%) than in the non headache side (6.4%) and than in controls and patients with no side prevalence. NIRS could represent a technique able to detect significant CBV changes in patients with MWA.

P6R37

The Korean migraine study

Chin-Sang Chung*[1], Byung-Chul Lee[2], Bum-Hee Yu[3], Jong-Won Kim[4], Gyeong-Moon Kim[1], Hye-Sun Park[5] & The Korean Migraine Study Group
[1]*Department of Neurology, Samsung Medical Center,* [2]*Department of Neurology, Hallym University School of Medicine,* [3]*Department of Psychiatry, Samsung Medical Center,* [4]*Department of Diagnostic Laboratory Medicine, Samsung Medical Center,* [5]*Paichai University, Taejon, Korea*

Despite the high prevalence rate and impact on quality of life (QoL) of migraine in Korea, it has never been studied comprehansively. The Korean Migraine Study (KMS) is the first government-funded, 4-year (2002–06) nationwide migraine study supported by the Korean Ministry of Health and Welfare. The KMS is composed of clinical, epidemiological, genetic, and molecular studies. The clinical studies include characterization of Korean migraineurs (issues on diagnostic criteria, trigger factors, transformation of migraine, chronic daily headache, and patterns of health care utilization), development of QoL measures specific for Koreans, reflecting the Korean cultural aspects, development of web-based nationwide migraine network and database, epidemiologic survey, psychologic and nonphamarcological aspects of migraine management, genetic studies for migraine genes and heredity (genetic markers and pharmacogenomics of migraine using single nucleotide polymorphism), and animal experimental study for pathophysiological mechanisms of migraine (role of nitric oxide and new therapeutic challenges). The authors will present the basic structure and strategies of the KMS and the summary of the first-year results.

P6R38

Clinical features of headache associated with sexual activity

Achim Frese*[1], Astrid Eikermann[2], Katrin Frese[1], Sonja Schwaag[1], Ingo-W. Husstedt[1] & Stefan Evers[1]
[1]*Department of Neurology, University of Münster,* [2]*Department of Neurology, University of Essen*

Objectives To provide data about the clinical features of headache associated with sexual activity (HSA).
Methods 51 patients with the diagnosis of HSA (type 1, dull subtype = 11, type 2, explosive subtype = 40) were questioned by a structured interview.

Results There was a clear male preponderance (2.9 : 1). The age at onset had two peaks with a first peak between the 20th and 24th ($n = 13$), and a second peak between the 35th and 44th ($n = 20$) year of life. The pain was predominantly bilateral (67%), and diffuse or occipital (76%). The quality was nearly equally distributed between dull, throbbing, and stabbing. HSA was not dependant on special sexual habits. There was a high comorbidity with migraine (25%), benign exertional headache (29%), and tension-type headache (45%). HSA type 1 and 2 did not significantly differ except a higher probability to stop the attack by breaking off sexual activity in HSA type 1.

Conclusion Mean age at onset, a male preponderance, a predominantly bilateral and occipital pain, and a high comorbidity with other primary headaches are in concordance with case reports in the literature. However, we found two peaks for the age at onset. From the clinical point of view, we found no evidence proving subtype 1 and 2 to be distinct disorders. HSA type 1 and 2 may be different manifestations of the same disease rather than distinct entities.

P6R39

Interhemispheric transfer dysfunctions in migraine patients

Gianluca Bruti*[1], Laura Di Clemente[1], Costanza Rossi[1], Claudio Mostardini[1], Fabrizio Di Stani[1], D'Agostino Vittoria[1], Veronica Villani[1], Gian Luigi Lenzi[1], Rosanna Cerbo[1] & Vittorio Di Piero[1]
Department of Neurological Sciences, University of Rome La Sapienza

Psychomotor subclinical dysfunctions were observed in migraineurs and could be correlated with white matter abnormalities and callosal atrophy. Poffenberger's paradigm is a visuomotor task able to evaluate interhemispheric transfer time (ITT). It is based on the concept that in unimanual RT to lateralized flashes, contralateral responses tend to be slower than the ipsilateral responses (Crossed-Uncrossed Difference-CUD).

We evaluated the reaction times (RT) and ITT in migraineurs by using Poffenberger's paradigm.

Sixty migraineurs and 30 controls were recruited. Migraineurs showed a significant higher mean RT than controls ($P < 0.00001$). Furthermore it was observed a positive correlation between CUD and the frequency of attacks. Migraineurs with high frequency of attacks (HF = 4 attacks/month) showed a significant higher CUD than both migraineurs with low frequency of attacks (LF = 4 attacks/month) ($P < 0.005$) and controls ($P < 0.02$).

These data suggest a subclinical psychomotor dysfunction in migraineurs. In particular, we observed a positive correlation between CUD and the frequency of migraine attacks without a significant differences between the means RT of migraineurs with HF and those with LF of attacks. The close relationship between the frequency of migraine attacks and the increase of ITT might suggest a selective impairment of the corpus callosum.

P6R40

Asymmetric hemispheric activation in response to visual stimuli migraineurs with unusual aura

Alix Padron*[1], Pedro Coutin[1] & Dhanpat Mohnot[1]
[1]*Clínica de Cefaleas y Migraña, Unidad de Neurología, Hospital Universitario de Los Andes, Mérida-Venezuela*

Introduction The migraines with unusual visual auras are not different forms of the disease, but when combined with other types of aura can cause diagnostic doubts. They have the same pathophysiology and respond to the same treatment.
Methodology Flash visual evoked potentials were recorded in 21 patients with ages between 14 and 50 years affected by migraine with unusual visual aura fulfilling with the criteria of the Headache International Society and 10 normal control subjects. Three -dimensional intracranial current source densities during the evoked responses were estimated using the low resolution electromagnetic tomography (LORETA) algorithm.
Results While in control subjects the active areas during the evoked response included both calcarine cortices and occipital convexities, in 15 patients the right occipital convexity showed little or no activation, being restricted to the left occipital lobe, while 2 patients showed only right activation, and the other 4 showed symmetrical activation of both occipital lobes.
Conclusion It is concluded that asymmetrical cortical excitability may underlie some of the pathological phenomena associated with unusual visual aura in migraineurs patients.

P6R41

Psychological and sleep quality differences between chronic daily headache and temporomandibular disorders patients

E. Vazquez-Delgado*[1], J. E. Schmidt[2], C. R. Carlson[2], R. DeLeeuw[1] & J. P. Okeson[1]
[1]*Orofacial Pain Center, College of Dentistry,* [2]*Department of Psychology, University of Kentucky, Lexington, Kentucky, USA*

The aim of this study was to investigate whether chronic daily headache (CDH) and temporomandibular disorders (TMD) patients present with different psychological and sleep quality characteristics. Sixty-seven patients diagnosed with CDH according to Silberstein et al.'s classification criteria were matched by age, sex, pain intensity, and pain duration with 67 patients who had a primary diagnosis of myofascial pain (MP), and 67 patients with a primary diagnosis of TMJ intracapsular pain (IC) according to the Research Diagnostic Criteria for TMD. The CDH group was comprised of three mutually exclusive diagnostic groups, that is transformed migraine ($n = 35$), chronic tension-type headache ($n = 26$), and 'other CDH' ($n = 6$). All CDH subgroups showed similar psychological and sleep quality profiles. All patients completed a battery of psychological and sleep quality questionnaires. The CDH and MP groups revealed higher levels of psychological distress than the IC group on most psychological domains. The MP group also revealed numerically higher levels of psy-

chological distress in most psychological domains than the CDH group, although these differences where not statistically significant. We did not find statistically significant differences between the three groups on post traumatic stress symptoms either. Sleep quality was significantly worse in the MP group than in the CDH and IC groups. These results are discussed in the context of multimodal patient evaluation and treatments that are necessary for successful clinical management.

P6R42

Cutaneous allodynia in chronic migraine

Fidel Ernesto Sobrino*[1]
[1]*Clinical Neurologist, Colsubsidio Headache Clinic, Bogotá-Colombia*

Introduction The Migraine is a progressive disorder mediated by activation and sensitization of peripheral pain fibers and central neurons that process information from meninges intracranially and extracranially. The Cutaneous Allodynia (CA) is pain resulted from a non-noxious stimulus to normal skin. The most migraine patients exhibit CA inside and outside their pain-referred areas.
Objective We aim was to prove the presence of CA in Chronic Migraine (CM) patients, its localization, and its probable relation with drug overuse.
Methods and results A total of 135 patients with CM (Silberstein, 1996), were interviewed with two singles questions. 76 (56.3%) patients had CA of them 65 (85.5%) patients had CA inside their pain-referred areas, while 11(14.5%) patients had CA outside their pain-referred areas. The mean age of the patients with CM + CA was 39.2 years and 34.5 for CM without CA patients. The average of the used medications for the attacks in group with CM + CA patients was 6.4 and 4.8 for CM without CA.
Conclusions CA is not only a common find in episodic migraine. The age average and amount medications for acute attacks used in the group the CM + CA patients although were majors compared with CM without CA patients none were statistically significant.

P6R43

The migraine disability assessment (MIDAS) questionnaire: reliability of the French version

Michel Lanteri-Minet*[1], Haiel Alchaar[1], Gerard Besson[2], Frederique Brudon[3], Anne Donnet[4], Pierric Giraud[5], Jacques Valance[6], Françoise Bille-Turc[4] & Jean-Louis Gaustaut[4]
[1]*Pain Department, Hôpital Pasteur, CHU Nice, France,* [2]*Neurology, Grenoble, France,* [3]*Neurology, Villeurbanne, France,* [4]*Neurology, Marseille, France,* [5]*Neurology, Annecy, France,* [6]*Neurology, Toulon, France*

Objective Aim of this work was to test a French version of the MIDAS questionnaire.
Methods A classical multistep process was used to translate MIDAS questionnaire into French. Test-retest reliability was tested on 100 French migraine without aura patients according to IHS criteria. They completed French MIDAS version twice (at the consultation and at home 21 days later) without therapeutical changes between the first (fc) and the second (sc) compilations. Test-retest reliability between fc and sc was evaluated by Spearman and Pearson tests. Student *t*-test was used to compare differences between scores on fc and sc. Stability was evaluated as percentage concordance of sc relative to fc. The internal consistency of MIDAS scoring was assessed using Cronbachs alpha.
Results Of the 100 patients enrolled, 85% completed the MIDAS form twice and 15% did not return sc (dropouts). Cronbach's alpha exceeded 0.70, indicating good internal consistency. Total MIDAS scores correlated highly from one compilation to the next (Pearson's 0.80 and Spearman's 0.76). For each question, mean score was lower at sc; however, differences were never significant.
Conclusions French version of MIDAS maintains the brevity and simplicity of the English version and is characterized by a good test-retest reliability.

P6R44

Familial ice cream headache without migraine

Germán Morís*[1]
[1]*Service of Neurology, Hospital Alvarez-Buylla, Mieres, Asturias, Spain*

Frontal pain caused by ingestion of a cold stimulus, called ice cream headache, is a common headache entity. Conflicting results are reported about relationship between cold stimulus headache and migraine. We reported an ice cream headache family without migraine. A 41-year-old man consulted due to a pain in the frontal area provoked by eating or drinking cold foods. His mother had suffered from migraine but he had not migraine attacks. He suffered a occipital fracture without cerebral lesion in 1999. The pain started in his childhood. The headache always began in a few seconds when he applied cold foods to the soft palade. He describe a sharp and excruciating pain over the midfrontal area, it lasted 10–20 s and disappeared when he finished eating cold beverages. He denied a cold-induced toothache. There were no associated features. He had 3 children of 12, 10 and 8 years-old. Two of them referred the same headache after ingesting cold beverages but they had never experienced migraine. As inheritance of this family shows, migraine facilitates headache provoked by ingestion of cold stimulus, although is not essential the development of active migraine in susceptible persons.

P6R45

Activation of the coagulation system in migraine patients

Domenico D'Amico*[1], Andrea Rigamonti[1], Elena Corsini[1], Eugenio Parati[1] & Gennaro Bussone[1]
[1]*C. Besta National Neurological Intitute, Milan, Italy*

Migraine is considered a risk factor for stroke. The reasons for this association are unknown. Activation of the coagulation system has been reported in migraine with aura (MA) (Hering-Hanit R et al. 2001).

We investigated prothrombin factor (F1.2) levels in a group of migraine patients. F1.2 is a cleavage product of prothrombin: elevated plasma F1.2 is a marker of ongoing thrombin generation. Fifty-six patients, 24 with migraine without aura (MO) and 32 with MA, and 57 controls were studied.

The mean ± SD F1.2 levels (nmoli/L) were: 1.1 ± 1.3 in migraineurs (MA 1.2 ± 1.6, MO 1.1 ± 0.7), 1.0 ± 1.7 in controls. The differences were statistically significant as far as the total group (migraineurs vs. controls, ANOVA on ranks: $p = 0.006$), and also when the different forms of migraine were considered (MA and MO vs. controls, Dunn's method $p < 0.05$). Higher percentages of subjects with elevated $F_{1.2}$ (> 1.1) were present among patients than among controls (MA 31.2%, MO 29.2%, controls 19.3%).

In conclusion, we found an increase in F1.2 levels in migraine patients. Studies on larger samples are needed to confirm these data. Activation of the clotting system may be involved in the increased risk for stroke in these patients.

P6R46

State and nociceptive behavior in chronic migraine. Hypersensitization state or sensitization process?

Elcio Piovesan*[1], William Young[1], Liciane Piovesan[1], Pedro Kowacs[2], Lineu Werneck[2] & Marcos Lange[2]
[1]*Thomas jefferson University, Philadelphia, USA,* [2]*Headache Unit, Neurology Division, Internal Medicine Department, Hospital de Clinicas da UFPR, Curitiba, Brazil*

Objectives In order to evaluate the state (SN) and the nociceptive behavior (NB) in chronic (CM) and episodic migraine (EM) we introduce a new method to assess pain pressure threshold (PPT) called the algometric repetitive assessment test (ARAT).

Methods The ARAT consist of 30 consecutive measurement of PPT in infraorbital nerves (ION) and index fingers (IF).

Three groups were studied normal control ($n = 6$); interictal EM ($n = 10$); and CM ($n = 20$). The NB compares the results of the first, second and third sets of 10 PPTs in each patient. The NS was studied, comparing the 30 PPT among groups.

Results The NS is greater in the control group than CM for trigeminal points ($P = 0.013$ and $p = 0.007$). The NB did not change in the control and CM groups, but did change in the EM group, for trigeminal points ($P < 0.001$ and $p < 0.001$).

Conclusion The NB in CM did not change, because these patients were in a hypersensitive state, as showed when compared the NS with control group. In EM the NB reduce during the ARAT test suggesting a sensitization process, a time that NS is the same that the control group.

P6R47

Naratriptan in the preventive treatment of refractory chronic migraine

Alan Rapoport*[1,2], Marcelo Bigal[1,3], Fred Sheftell[1,4], Michel Volcy[5], Michele Feleppa[6] & Stewart Tepper[1,7]
[1]*The New England Center for Headache, Stamford, CT, USA,* [2]*Department of Neurology, Columbia University College of Physicians and Surgeons, New York, NY, USA,* [3]*Albert Einstein College of Medicine, Bronx, NY, USA,* [4]*New York Medical College, New York, NY, USA,* [5]*University of Antioquia, Medellin, Colombia,* [6]*Primario Unita Operativa di Neurologia e Neurofisiopatologia A. O 'G. Rummo' Benevento, Italy,* [7]*Yale University School of Medicine, New Haven, CT, USA*

Objective To review the efficacy of naratriptan in the preventive treatment of refractory chronic migraine (CM).

Design/methods Clinical records and headache calendars with the following inclusion criteria were reviewed: 1 – Age from 18 to 65 years old; 2 – Diagnosis of CM according the criteria proposed by Silberstein et al. 3 – Previous failure of at least four preventive treatments; 4 – Have used daily naratriptan for no less than two consecutive months. The dose of naratriptan prescribed was 2.5 mg bid.

Results Our sample consisted of 27 subjects (74.1% females). All subjects were followed for at least one year after being given naratriptan. A significant reduction of headache frequency was obtained in 2 months (15.3 vs. 24.1 at the baseline, $p < 0.001$), 6 months (9.1, $p < 0.001$) and 1 years (7.3, $p < 0.001$). A significant reduction in the number of severe days with pain was obtained in 1 month (5.6 vs. 12.5 at baseline, $p < 0.01$), 2 months (5.7, $p < 0.01$), 6 months (2.8, $p < 0.01$) and 1 years (2.7,$P < 0.01$). Of the 20 subjects that continued to use naratriptan after 6 months, 13 (65%) reverted to migraine.

Conclusions This study supports the role of naratriptan in the preventive treatment of intractable CM, pending prospective studies.

P6R48

Patients' management of migraine, migraine with aura and chronic daily headache

Michele Peters*[1], Huda Huijer Abu-Saad[1,2], Ian Robbins[1,3], Vasso Vydelingum[1], Andrew Dowson[4] & Margaret Murphy[1]
[1]*European Institute of Health and Medical Sciences, University of Surrey, UK,* [2]*School of Nursing, American University Beirut, Lebanon,* [3]*St George's Hospital, London, UK,* [4]*King's College, London, UK*

Objectives To compare headache management between migraine (M), migraine with aura (MWA) and chronic daily headache (CDH) patients over the last 12 months. Management related to health care consultations, medication use, use of alternative therapies, use of general (acute and prophylactic) management and social support.

Methods A postal questionnaire was sent to members of the Migraine Action Association (UK). M ($n = 117$) and MWA ($n = 239$) patients were classed according to IHS. CDH ($n = 83$) was diagnosed when patients suffered more than 15 headache days per month. Descriptive analysis, ANOVAS, Chi-square and Kruskal–Wallis tests were used for statistical analysis ($P < 0.05$).

Results The groups did not differ in age, gender, ethnicity, qualifications and employment status. Significant differences in management strategies between the groups were found in consultations with headache specialists and neurologists; the number and types of acute medications (e.g. triptans); the use of antidepressants and some acute and prophylactic avoidance techniques. No significant differences were found in consultations with other health professionals (e.g. GP) and alternative health professional and the use of general acute management and social support. However, all 3 groups actively used these strategies.

Conclusion M, MWA and CDH patients are active users of management strategies. The strategies used can be related or independent to diagnosis.

P6R49

Spanish General Practitioner's attitude to the headache

Salvador Tranche*[1], Jose Manuel Martinez[2], Jesus Castillo[3], Sebastian Calero[4], Maria Luisa Garcia[5] & Marta Iturbe[2]
[1]*C.S. El Cristo, Gijón, SESPA, Spain,* [2]*C.S. Billabona, Osakidetza, Spain,* [3]*C.S. Camargo, Servicio Cantabro de Salud, Spain,* [4]*Servei d'Atenció Primària de L'Hospital de Llobregat, Barcelona, Spain,* [5]*C.S. Mendiguchia Carriche, Madrid, INSALUD, Spain*

Objectives The aim of this study was to know the attitude of the Spanish general practitioners to the headache and investigate the relation between the attitude and the fact of suffering headache.
Methods An inquiry was posted until three times to 1185 general practitioners chosen randomly. This questionnaire was dealing with questions about epidemiology, knowledge, attitude to the headache and treatment.
Results From 1185 general practitioners, 721 (60,84%) returned the questionnaire. Of these, 56% were male, 44% female, mean age 43 ± 9.6. 70% reported a high/very high interest in headache. 80% dedicated more time in the first visit than in other type of visit. 85% examined the patient always/almost always. 75% followed up the patient. 10% followed his/her centre's protocol. The IHS classification was known by 52%, used occasionally by 27% and usually by 5%. The chronic daily headache followed by secondary headaches were considered the most interesting training. There was no relation between the fact of having headache and showing interest in the headache.
Conclusions 70% Spanish GP's reported a high/very high interest in headache. The IHS classification was known by more that 50%, but it was hardly used. The protocols were not widespread in the different primary care centres. The chronic daily headache was considered the most interesting training. There was no relation between the fact of having headache and showing interest in the headache.

P6R50

In-patient treatment of the chronic daily headache

Seymour Diamond*[1] & Alexander Feoktistov[1]
[1]*Diamond Headache Clinic, Chicago, Illinois, USA*

The study involved 103 patients with chronic daily headache (CDH) with 69% abusing pain medications. We used following admission criteria to the Diamond Headache In-patient Unit at St. Joseph Hospital.

1 Patients diagnosed with CDH according to classification proposed by Silberstein, Lipton, and Solomon, 1994;
2 Steady CDH with poor response to treatment or
3 Use of habit forming pain medications on a daily basis for at least 3 consecutive months.

The mean duration of treatment was 11 days.
We used the following treatment:

1 Detoxification
2 Reversal pharmacotherapy
3 Preventive pharmacotherapy
4 Non-pharmacological methods.

For evaluation, we used Headache Index (HAI) formula: (HA frequency*HA severity*HA duration)/30 days. We calculated HAI for both severe HA and background HA. We assessed HAI before, 1 and 3 months after the hospitalization. After 3 months, HAI for both severe and background HAs decreased from 72 and 62, respectively, to 26 ($P < 0.001$). Average HAI had changed more than 50% in 63% of the patients. Considering that all patients were 'nonresponders' for different types of outpatient treatment, we conclude that inpatient management of the difficult HA patients is a highly effective type of treatment.

P6R51

Headache-related quality of life in episodic cluster headache

Csaba Ertsey*[1], György Bozsik[1] & Ilona Jelencsik[1]
[1]*Department of Neurology, Semmelweis University, Budapest, Hungary*

Health-related quality of life (QoL) represents the effect of illness on the patient. Disease-specific QoL instruments measure the particular impact of a selected condition. They also allow the comparison of conditions which share the leading symptom.

Personal accounts of cluster headache (CH) patients suggest that this headache type can severely affect QoL. To test this hypothesis we studied headache-related QoL in 30 episodic CH patients and compared the results to those of age-, and sex-matched migraineurs ($n = 43$) and healthy persons ($n = 70$). We used MSQ 2.1, a headache-specific instrument, originally devised to study QoL in migraine. This instrument measures the limitations in role and emotional functioning in 3 domains, termed role function restrictive (RFR), role function preventive (RFP), and emotional function (EF). CH patients had significantly lower scores on all three scores compared to controls (RFR 39.9, RFP 52.17, EF 49.19 vs. RFR 97.14, RFP 100.0, EF 99.16, $p < 0.0001$). CH patients also had lower scores than migraineurs, but the difference was not statistically significant. After the termination of the CH period QoL scores of CH patients were similar to those of healthy persons. – Headache-specific QoL is severely impaired in CH and this impairment is at least as severe as in migraine.

P6R52

Cortical function in migraine: what can performance on visual tasks reveal?

Alex Shepherd*[1]
[1]*School of Psychology, Birkbeck College, University of London, London, UK*

Models of cortical function in migraine include hyperexcitability and heightened responsiveness, hypoexcitability and low cortical preactivation, and/or a disruption of intracortical inhibition and excitation. Clarifying these alternatives is possible with performance measures, notably visual, that compare migraine and healthy control groups. Shepherd (2001) reported larger aftereffects in migraine in a study that

examined the altered appearance of test gratings following adaptation, which suggested a prolonged suppression of neuronal response. Another consequence of adaptation is elevated detection thresholds for similar patterns unless they are presented very briefly, suggesting that the effects of the cellular and synaptic components of adaptation are separable (Wilson and Humanski, 1993). The first study presented here examined the separable cellular and synaptic components of adaptation, by determining threshold discriminations for very brief and longer test patterns, before and after adaptation. The second examined heightened responsiveness as a factor in any abnormal cortical response by comparing perceptual asymmetries in migraine and control groups. The third comprised an assessment of pattern sensitivity. The same migraine and control participants completed each task, as correlations between different tasks also inform on models of cortical function in migraine.

P6R53

Effect of preventive headache therapy with botulinum toxin type A (BoNT/A) on emergency room utilization

Andrew Blumenfeld*[1]
[1]*Southern California Permanente Medical Group, San Diego, CA, USA*

Background Emergency room (ER) visits contribute substantially to the direct cost of treating chronic headache disorders.
Objective To compare ER utilization before and after preventive headache treatment with botulinum toxin type A (BoNT/A).
Methods ER visits during the 6-month periods before and after BoNT/A treatment for chronic, disabling headache disorders were determined by retrospective chart review of patients in the Kaiser Permanente Healthcare System.
Results ER utilization data were available for 79 patients pre-BoNT/A and 77 patients post-BoNT/A. Pre-BoNT/A, 65% of patients had no ER visits, 25% made 1 visit, and 10% had > 1 ER visit. In contrast, post-BoNT/A 84%, 13% and 3% had 0, 1, and > 1 ER visits, respectively. There was a decrease in the number of ER visits for 23 patients and an increased ER utilization in 8 patients. This shift in ER utilization after BoNT was statistically significant; Chi-square = 7.258, d.f. = 1, P = 0.007.
Conclusions These results indicate that BoNT/A treatment for chronic disabling headaches significantly reduced emergency room utilization. Further research is needed to identify the headache population at high risk for ER utilization and the potential impact of BoNT/A on these patients and on the overall burden of headache.

P6R54

Cost-effectiveness analysis of six triptans using data from a published meta-analysis

Kathi Weis*[1]
[1]*Pfizer Inc., New York, USA*

Objectives To compare the cost-effectiveness of six triptans using data from a published meta-analysis.
Methods Efficacy and recurrence rates in a meta-analysis by Ferrari et al. were used as a basis to calculate cost-effectiveness. The Eletriptan efficacy rate was updated to include studies completed after -publication of the meta-analysis. The cost-effectiveness measure – cost per successfully treated patient (CPSTP) – was the ratio of total triptan cost of treatment to number of successfully treated patients. The measure of success is 2-h pain free sustained for 24 h.
Results The most cost-effective triptans were Eletriptan 40 mg at Euro 14.85 CPSTP followed by Almotriptan 12.5 mg (16.81 Euros) and Sumatriptan 50 mg (18.93 Euros). The least cost-effective triptans were Sumatriptan 100 mg (35.71 Euro) and Rizatriptan 5 mg (33.17 euro).
Discussion Efficacy and recurrence rates directly impact cost-effectiveness results. Including the Eletriptan studies completed after publication of the meta-analysis provided additional information on which to make informed decisions about therapies that provide successful outcomes.
Conclusion The price of a dose of triptan does not provide information on the outcome of therapy, only cost-effectiveness analyses provides empirical evidence of the value for resources spent on triptan therapy, and Eletriptan was the most cost-effective migraine therapy.

P6R55

Improvement of migraine with aura after migrainous infarct onset: report of three cases with one-year follow-up

Hilton Mariano Da Silva*[1], Mário Alberto Filho[2], Eric Paschoal[2], Carlos Bordini[1] & Jose Speciali[1]
[1]*Department of Neurology, Psychiatry and Medical Psychology, School,*
[2]*Department of Neurology and Neurosurgery, Hospital Municipal Mário Gatti, Campinas, Brazil*

Objectives We prospectively evaluated three consecutive patients with MS who fulfilled the IHS criteria. Others causes of stroke in young people were ruled out.

Cases A 33-year-old woman developed right weakness and scotoma during a typical attack that did not recover. A MRAI showed narrowing of the left calcarin artery. Since then, there was a reduction of the frequency and severity of headache attacks (5 in 2001 and 4 in 2002), despite no changes on the prophylactic treatment. A 43-year-old woman developed a left scotoma during a typical attack. A computerized static perimetry (CSP) discloses an enlargement of the blind spot with a left inferior central scotoma. Since then, there was reduction of the frequency of pain (three attacks/year). A 25-year-old woman was seen due to a permanent right temporal scotoma that was occurred during an attack of MA. A CCT scan discloses a left occipital infarct. The patient experienced two more attacks and became free three months after the MS onset.
Conclusion Our patients experienced an important improvement following the MS. This fact may be a hint for new studies aiming to unveil the inner mechanisms of MS.

P6R56

Coupling between visually evoked flow responses and visually evoked potentials in migraineurs

Marjan Zaletel*[1], Zoran Rodi[2], Martin Strucl[3] & Bojana Zvan[1]
[1]*University Clinical Center, Department of Neurology, Ljubljana, Slovenia,* [2]*Institute of Neurophysiology, Ljubljana, Slovenia,* [3]*School of Medicine, Institute of Physiology, Ljubljana, Slovenia*

Neurovascular coupling could be altered in patients with migraine. We studied the coupling between visual evoked potentials (VEP) and visually evoked flow responses (VEFR) in migraineurs interically.

30 volunteers and 10 age matched migraineurs participated. The stimulus was checkerboard with contrast of 1%, 10% and 100%. VEFR were measured in the PCA using TCD monitoring system. VEPs were recoded from the scalp according to recommendations of the International Society for Clinical Electrophysiology of Vision. We determined the mean amplitudes of the VEPs and VEFR, which were further statistically analysed. We introduced coupling index VEFR/VEP.

Paired *t*-test showed significant differences ($P < 0.001$) between VEFR, VEP and VEFR/VEP to 100% contrast stimuli and VEFR, VEP, VEFR/VEP to 10% contrast stimuli ($P < 0.01$) as well as VEFR, VEP, VEFR/VEP to 10% contrast stimuli and 1% contrast stimuli ($P < 0.01$) in both groups. Between subject effect was no significant for VEP, while for VEFR as well for VEFR/VEP appeared to be significant ($P < 0.05$). *T*-test showed significant differences in VEFR and VEFR/VEP ($P < 0.05$) at 1%, 10% and 100% contrast.

We found that VEFR as well ratio VEFR/VEP are increased in migraineurs implicated hyperactive neurovascular coupling and tendency toward functional hyperemia.

P6R57

III.-Social and labour impact of headache conditions in the Spanish Mail Service employees

Mª Teófila Vicente-Herrero*[1], Miguel JA Láinez[2], Samuel Díaz[3] & Correos Headache Study Group[4]
[1]*Médico Área de Salud Laboral Correos. Valencia.,* [2]*Servicio de Neurología. Hospital Clínico Universitario. University of Valencia.,* [3]*Servicio de Neurología. Hospital San Francisco de Borja. Gandia. Valencia,* [4]*Correos Headache Study Group*

Objectives After to send a headache survey to 61.665 Spanish Mail Service employees, we select among the positive reply, 446 of them and after their protocol and treatment, we value: Repercussions of headache in daily life: family, social, changes of character and behaviour. Repercussion at work: Days and hours lost, decline in productivity, changes in jobs and labour conflict.

Material and methods A program during 2001–02 was applied based on 446 employees with migraine with or without aura and chronic migraine with medication overuse, from 20 Spanish provinces, with an average age of 43, 66% female, 34% male. The average time of suffering was 20 years.

Results Improvement of all aspects studied, in daily life and repercussion at work, with reduction of work days lost (1/month/worker vs. 0/month/worker) and hours of work lost (0.92/month/worker vs. 0.23/month/worker), increase in productivity (59% vs. 94%) and reduction of indirect costs (744 927 E vs. 219 289 E).

Conclusions The saving in labour costs due to headache before and after the protocol justifies the implication of the company and application of pharmacological criteria as well as medical formation and information. 97% of the work force consider necessary to continue periodic controls of the illness by the company doctors.

P6R58

Migraine and E-TTH: do they have similar clinical features and pathophysiologic mechanisms?

Necdet Karli*[1], Mehmet Zarifoglu & Nermin Caliskan
[1]*University of Uludag, Medicine Faculty, Neurology Department,* [2]*University of Uludag, Medicine Faculty, Neurology Department,* [3]*University of Uludag, Medicine Faculty, Neurology Department*

It's difficult to differentiate episodic tension type headache (E-TTH) and migraine in 15% of patients. They share similar clinical features, which makes differential diagnosis more complicate. Some investigators suggest that, similar clinical features might have been caused by similar pathophysiologic mechanisms.

We aimed to find out whether these headache patients share similar prodromal and aura symptoms, and trigger factors.

Three groups of headache patients (E-TTH, migraine with and without aura) included into the study. Patients were given a questionnaire and asked to answer it alone. Later, they were questioned by a neurologist according to the same form in order to prevent misunderstanding.

There wasn't statistically significant differences between all groups in prodromal symptoms and trigger factors. Most prodromal symptoms and trigger factors were similar in all groups. Nearly half of the aura symptoms were similar in E-TTH and migraine without aura groups.

Our study showed that E-TTH and migraine patients share similar prodromal symptoms and trigger factors. According to our findings, we suggest that E-TTH and migraine may share the same pathophysiologic mechanisms. These findings also support the continuum theory.

P6R59

Eagle syndrome – possible entrapment of the glossopharyngeal nerve?

Konstantin Slavin*[1]
[1]*University of Illinois, Chicago, USA*

Eagle syndrome is a rare condition characterized by sharp lancinating pain in the side of the neck, throat, ear and face. It is usually caused by an elongation of the styloid process or ossification of the stylohyoid ligament. Underlying mechanism of the pain production is thought to be local irritation of the glossopharyngeal nerve that passes in the vicinity of the styloid process tip.

Recently, we treated two patients with Eagle syndrome. Both them presented with characteristic pain pattern and had

elongation of styloid process documented with CT scan of the skull base. During the diagnostic workup, local block of the area of the styloid tip produced temporary pain relief along with the numbness in the tonsillar area and impaired swallowing mechanism. The symptoms were permanently eliminated with open surgical resection of the styloid process through a lateral transcutaneoous approach.

Based on this clinical picture and results of local anesthetic block, we postulate that Eagle syndrome is an example of entrapment neuropathy that involves the glossopharyngeal nerve as it travels through a narrow anatomical path around the styloid process. With this presentation, we wanted to raise awareness of physicians and headache specialists about this rare but easily treatable pain syndrome.

P6R60

Occipital nerve stimulation for treatment of severe occipital headaches

Konstantin Slavin*[1]
[1]*University of Illinois, Chicago, USA*

Treatment of chronic occipital headaches and occipital neuralgia remains challenging; few available options for medically intractable cases generally include occipital neurectomy, upper cervical ganglionectomy and various percutaneous destructive procedures on the occipital nerves or the upper cervical nerve roots. A nondestructive alternative of occipital pain treatment with long-term stimulation of the occipital nerve with implanted electrodes is gradually gaining popularity in medical and surgical circles.

We present our latest 12 months experience with occipital nerve stimulation. Out of large number of patients with occipital pain who were referred to us for surgical consideration, 8 were selected for the occipital nerve stimulation trial. Six of them had more than 50% improvement of pain intensity during the trial and underwent implantation of the permanent stimulation system. These patients were followed up for at least six months, and the results of the follow up are presented here.

In our opinion, long-term occipital nerve stimulation is a safe and effective modality that may be particularly useful for medically refractory cases of occipital neuralgia and disabling occipital headaches. This presentation summarizes our indications, screening protocol, and technical details of the occipital nerve stimulation procedure. Strict adherence to minute details allowed us to minimize complication risks.

P6R61

Qigong Yangsheng – traditional Chinese medicine exercises for migraine and tension headache

Elisabeth Friedrichs*[1], Beate Pfistner[2] & David Aldridge[3]
[1]*General Practitioner, Augsburg, Germany,* [2]*Bonn, Germany,* [3]*Chair of Qualitative Research in Medicine, University of Witten-Herdecke, Germany*

Objective The aim of this pilot study was to assess whether any evidence can be found that qigong exercises can provide supplementary treatment for tension headache and migraine.

Methods 95 volunteers participated in exercises from '15 Formulas of Taiji Qigong Exercises' by Jiao Guorui, an 'active part' of Traditional Chinese Medicine.

Results Number of days with headache, standardized over 28 days, was 8 at baseline; during the follow-up, it was 5 (median; $P < 0.001$). Median number of days with pain per participant was reduced by 1 day.

With a reduction in days with headache of at least 50%, 27 of all participants (28%) qualified as responders. In the group with 3–7 days with headache at baseline, 30% qualified as responders; in the group with 8–14 days, 34%. Together, these two groups represented 75% of the Participants Secondary efficacy measures such as 'pain intensity' were also found to provide significant evidence of clinical improvement.

Conclusions This study provides supportive evidence suggesting that qigong exercises can be an effective supplementary treatment in headache.

Acknowledgements The study was supported by the German Medical Acupuncture Association and the German Medical Association for Qigong Yangsheng.

P6R62

Precipitating events and accompanying symptoms in migraine and TGA

Mira Bucuk[1], Ksenija Willheim[1], Ante Jurjevi?[2], Dubravka Sepic-Grahovac[1] & Zoran Tomic*[1]
[1]*Department of Neurology, Clinical Hospital Center Rijeka,* [2]*Medixal School Rijeka*

According to the hypothesis of the same patophysiological mechanism of migraine and TGA our intention was to determinate common precipitating events and accompanying symptoms during migraine and TGA attacks.

33 migraineurs, 25 female and 8 male (mean age 45.73) and 33 patients with TGA, 24 female and 9 male (mean age 60.39) were examined.

Patients underwent the following laboratory tests, EEG (26 patients), cerebral CT (19 patients) and SPECT (6 patients). Detailed anamnesis and heteroanamnesis were taken which included information about precipitating events and accompanying symptoms.

The results showed that the most often precipitants in migraineurs and in TGA patients were: physical excercise (18.2% vs. 15.2%), emotional stress (63.6% vs. 30.3%), cold bath (6.1% vs. 12.1%), sexual intercourse only in TGA group (6,l%). Spontaneous onset had 1.2% migraineurs and 36.4% TGA patients; the most often accompanying symptoms were vegetative symptoms (90.0% vs. 24.2%), headache (100% vs. 24.2%), vertigo (3.0% vs. 12.1%) and photo/phonophobia only in migraineurs (63.6%). 12.1% migraineurs and 39.4% TGA patients were without these symptoms.

Our results are in concordance with the results of other authors confirming the presence of the same common precipitants and accompanyng symptoms in migraine and TGA.

P6R63

Improvement with sumatriptan in menstrually related migraine-like headache: a case report

Pierric Giraud*[1], J. H. Ruel[1], M. Sindou[2] & G. Chazot[3]
[1]*Service de Neurologie A, Hôpital de la Région Annecienne, Annecy,* [2]*Service de Neurochirurgie A,* [3]*Service de Médecine Nucléaire et Service de Neurologie D, Hôpital Neurologique, Lyon*

When all IHS criteria for migraine as well as triptan response are present, radiological examination is unnecessary as the probability of finding another disease is very low (*The US Headache Consortium, AAN, 1999*). We report an observation fulfilling IHS criteria for migraine without aura improved by sumatriptan associated with a right cavernous sinus meningioma.

Case 125618: A 44-years-old female suffered from with migraine without aura during menstruation. Clinical examination was normal but onset at the age of 42 and a nonalternating localization of pain led the physician to conduct a contrast CT-scan that proved normal. Good response to 100 mg sumatriptan reinforced diagnostic certainty of migraine without aura. Seven years later, a sudden onset right cluster-like headache appeared. Clinical examination was normal outside attacks. Brain MRI disclosed a meningioma that had developed in the right cavernous area invading the cavernous sinus and expanding into the right temporal lobe. Surgery was performed and patient was headache-free for 15 days. Nevertheless, intense neuralgic trigeminal pain progressively reappeared.

This observation addresses the question of the relationship between migraine and meningioma and prompts us to review the literature reporting symptomatic migraine improved by triptan.

P6R64

Withdrawal therapy followed by prophylaxis for transformed migraine

Licia Grazzi*[1], Domenico D'Amico[1], Susanna Usai[1], Frank Andrasik[2], Andrea Rigamonti[1], Massimo Leone[1] & Gennaro Bussone[1]
[1]*C. Besta National Neurological Institute, Milan, Italy,* [2]*Institute for Human and Machine Cognition, University of West Florida, Pensacola, FL*

Objective Purpose of the study was to assess disability using MIDAS questionnaire in a sample of TM patients with drug overuse and to investigate if disability changes after treatment intervention.

Methods 106 patients were included into the study. They completed the MIDAS questionnaire. They underwent an inpatient withdrawal treatment and then were given prophylaxis antimigraine and/or antidepressant compounds. The came back 6 and 12 months after discharge and the headache diary was checked and the MIDAS questionnaire was completed again.

Results Days of headache per month and analgesics consumption per month decreased significantly at 6 months follow up and this was confirmed at the 12 months follow up. Also MIDAS scores decreased significantly at 6 and 12 months.

Conclusions Our results showed than most TM patients with drug overuse were highly disabled in their daily activities.

Withdrawal of the overused drug followed by prophylactic treatment lead to a dramatic change at 6 months follow-up confirmed at 12 months follow-up (more than 50% reduction in headache activity and symptomatic drug consumption). Also MIDAS score was reduced (more than 40%) at the last follow-up. Midas seems an effective instrument as outcome measure in following TM patients with drug overuse.

P6R65

Posttraumatic SUNCT status

Sebnem Bicakci*[1], Hacer Bozdemir[1], Yakup Sarica[1] & Gamze Almak[1]
[1]*Cukurova University, Balcali Hospital, Department of Neurology, Adana, Turkey*

SUNCT syndrome is characterized by unilateral, particularly periorbital burning, electrical or stabbing-like pain, congestion and tearing. Less commonly frontal sweating, nasal obstruction or rhinorrhea, eyelid oedema, diminished palpebral fissure, blushing, tachipnea, photophobia, blepharospasm and ipsilateral myosis may occur. Status-like form of this rare syndrome has been reported in six cases in the literature so far.

A 50-year-old-male patient had left orbital and periorbital stabbing and burning-like pain lasting for 60–90 s, associated with tearing, congestion, rhinorrhea and ptosis. He relieved from attacks spontaneously or with antineuralgic medication lasting for 2–3 months. Following a severe, blunt trauma to his painful region 3 months ago, attack frequency and duration increased remarkably, occurring 5–10 times hourly, approximating more than 100 times/day. Neurologic examination at his admission was normal except typical attack signs. Blood analysis, maxillofacial and cranial CT, MRI and brain SPECT were normal. He was given lamotrigine, topiramate and indomethacin for 5 months. He underwent trigeminal ganglion blockade due to failure of the medical therapy. He was out of status. The severity and number of attacks subsided at least 50%.

This case is noteworthy because of status pattern following blunt head trauma and the management challenges.

P6R66

The use of Topiramate in cluster headache

Rachel Hering-Hanit*[1]
[1]*Headache Unit, Department of Neurology, Meir General Hospital, Kfar Saba, Israel*

Objectives Assessment of topiramate efficacy in cluster headache.

Background Cluster headache is a rare, clinically well-characterized disabling disorder that occurs in both episodic and chronic forms. A large number of drugs such as ergotamines, steroids, methyser-gide, lithium carbonate, verapamil, valproate and baclofen are considered beneficial for prophylaxis. Nonetheless, this extremely painful condition is occasionally refractory to conventional treatment. Topiramate has

been shown in several cases to be effective in the prevention of cluster headache.

Methods Twenty-seven symptomatic episodic cluster headache patients (23 males), aged 16–54 years, were treated with daily topiramate, 25–100 mg, in 1–2 divided doses for the cluster period and 2 weeks after.

Results Within three days to two weeks, 19 patients reported cessation of attacks. No adverse events were observed or reported while on topiramate. In the remaining 8 patients, the attacks did not change or worsened, and corticosteroids, valproate and verapamil were prescribed.

Conclusions Topiramate seems to be effective, safe and well tolerated for cluster headache.

P6R67

Representations of headache on the internet: the importance of gender imagery

Joanna Kempner*[1]
[1]*Department of Sociology, University of Pennsylvania, Philadelphia, USA*

Self-help medical websites are proliferating on the Internet. The unregulated character of these sites raises questions about the quality of their content. These websites form patients' understanding of the prototypical headache patient, which in turn affects patient decisions to seek care. This research study seeks to assess how the typical headache patient is represented on the Internet. A database of websites was compiled and included sites created by headache advocacy organizations and medical professionals, as well as sites where headache sufferers exchange information and experiences. The content analysis revealed that almost all websites represented headache sufferers as Caucasian women, although this was a less prevalent practice in websites sponsored by professional headache organizations. Further, supposedly gender-neutral language that described headache syndromes often used feminine language to describe migraine patients. While this language reflects an epidemiological reality of headache prevalence among women, it may also unduly perpetuate the myth that only women get migraine. This study provides insight into how scientific information is disseminated to the public. This study is also useful for the practitioner who wishes to understand the assumptions that patients may bring to the clinic.

P6R68

Validity and reliability of Migraine Disability Assessment (MIDAS) Questionnaire in Turkish patients with migraine

Umit Gedikoglu*[1], Serap Ücler[1], Ozlem Coskun[1], Tugba Tunc[1], Ufuk Emre[1], Hülya Yildiz[1] & Levent Inan[1]
[1]*Ministry of Health, Ankara Research Hospital, Department of Neurology, Ankara, Turkey*

Background The Migraine Disability Assessment (MIDAS) questionnaire is a brief, self administered questionnaire designed to quantify headache related disability over a 3-month period.

Materials and methods We have tested a Turkish version of the MIDAS questionnaire in 60 migraine patients. Sixty clinically diagnosed migraine headache sufferers were enrolled in a 90-day diary study and completed the MIDAS questionnaire 1., 21. days and end of the study (90.day).

Results We found that overall MIDAS score had good reliability. Internal consistency was good (cronbach's alpha 0,87).

Conclusions These findings support the use of the MIDAS questionnaire as a clinical and research tool with Turkish patients.

P6R69

Ophthalmoplegic migraine – a case report

Graça Sousa*[1], Sara Vieira[1] & Castro Neves[1]
[1]*Neurology Department – Hospital de S. Joâo – Porto, Portugal*

Background Ophthalmoplegic migraine is a rare periodic migraine headache that is accompanied by paresis of the ocular nerves, usually transient and outlasting the headache. Normally occurs in children and has a male preponderance. No clear genetic pattern is present and etiology is poorly understood: it is believed to be due to a neuro-ischemic, neurocompressive or demyelinating mechanism. The diagnosis is reliant on clinical grounds and exclusion of other disorders: aneurysm, arteriovenous malformation, tumor or granulomatous inflammation. Patients over the age of 10 years should undergo a neuroradiologic evaluation.

Clinical presentation A 49-year-old female with a 8-year history of migraine without aura developed a complete left III nerve palsy at the onset of an ipsilateral throbbing headache. She experienced further two similar episodes: left headache with ipsilateral VI cranial nerve palsy, that resolved gradually within 3 weeks, and a right III nerve palsy 4 days after the onset of ipsilateral headache; with normal pupil. Laboratory findings, cerebrovascular Doppler-ultrasound, cerebral CT scan, MR and angiography were unremarkable.

Conclusion We emphasize the rarity of this clinical condition affecting a woman with history of migraine without aura who developed, on adult life, three episodes of paresis of ocular nerves, ipsilateral with the headache.

P6R70

Research into headache treatment and levels of patient satisfaction in Japan

Takayuki Kitamura*[1]
[1]*Department of Neurosurgery, Nippon Medical School, Tokyo, Japan*

The study group 'ADITUS Japan' comprised of doctors who seek to improve diagnosis and treatment of headache conducted 'Research into Headache Treatment and Levels of Patient Satisfaction' from May 2002 to September 2002. This research was conducted in order to clarify the condition of the headache medical examination after the launch of Triptan in Japan.

The target includes neurologist, neurosurgeon and general physician in Japan, as well as their patients. The reply was obtained from 149 doctors and 252 patients.

One of the points discovered in this research is a significant change in doctors' medicine prescription patterns after a Triptan came to the market. Many doctors usually prescribe nonsteroid anti-inflammation drugs and an Ergotamine tablet to treat minor migraine. However, doctors prescribe Triptan at a much higher frequency when treating severe migraines. The tendency to use a curative medicine properly according to the degree of serious illness can be seen.

Also patients' satisfaction with Triptan is high in predominance compared with other medicines. This demonstrates the high satisfaction level of Triptan among doctors and patients in Japan.

P6R71

Low serum level TNF-α in patients with chronic headache during headache-free period

Tamami Ijiri*[1], Takao Takeshima[1], Kumiko Ishizaki[1], Haruko Araki[1], Yoko Fukuhara[1], Masayoshi Kusumi[1], Hisanori Kowa[1] & Kenji Nakashima[1]
[1]*Department of Neurology, Tottori University, Faculty of Medicine, Yonago, Japan*

Objective To explore the contribution of cytokines to the pathophysiology of chronic headache, we have evaluated the serum levels of interleukin (IL)-6, IL-10, IL-13, tumor necrosis factor (TNF)-α in patients with migraine and in patients with tension-type headache (TH) during headache – free period.
Methods ELISA was used to determine the serum levels of IL-6, IL-10, IL-13 and TNF-α in 69 patients with migraine (48 women and 21 men) and in 36 patients with TH (24 women and 12 men) during headache-free period and in 55 healthy controls who were headache free (31 women and 24 men). The serum cytokine levels of the patients and controls were compared using ANOVA.
Results Both the TNF-α levels of sera in the patients with migraine and with TH were significantly lower than in the controls ($P < 0.001$, $p < 0.01$), and the TNF-α levels of sera in the patients with migraine were significantly lower than in the patients with TH ($P < 0.001$). No differences were found in IL-6, IL-10 and IL-13 levels between samples.
Conclusions Our findings suggest that TNF-α plays a role as a proinflammatory cytokine in chronic headache.

P6R72

Management of headache among the Spanish general practitioners

Maria Luisa Garcia*[1], Sebastian Calero[2], Jesus Castillo[3], Jose Manuel Martinez[4], Salvador Tranche[5] & Marta Iturbe[4]
[1]*C.S. Medniguchia Carriche, Madrid, INSALUD, Spain,* [2]*Servei d'Atencio Primaria de L'Hospital de Llobregat, Barcelona, Spain,* [3]*C.S. Camargo. Servicio Cantabro de Salud, Spain,* [4]*C.S. Billabona, Osakidetza, Spain,* [5]*C.S. El Cristo, Gijón, SESPA, Spain*

Objectives The aim of this study was to know the management of the different types of primary headache by the Spanish General practitioners.
Methods An inquiry was posted until three times to 1185 general practitioners chosen randomly. This questionnaire was dealing with questions about epidemiology, knowledge and treatment choice of headache.
Results From 1185 doctors, 721 (60,84%) returned the questionnaire. Of these, 56% were male, 44% female, mean age 43 ± 9.6. 22% reported a good/very good management of headache against 5.4% poor/very poor management. 12% sent to the neurologist the first episode of migraine without aura; 42% migraine with aura; 52% cluster headache; 32% chronic daily headache without drug abuse and 55% chronic daily headache with drug abuse. No relation was found between the fact of being a doctor suffering headache, and sending to neurologist. The first choice analgesic in the mild migraine was paracetamol (61%); in the moderate migraine: nonsteroidal anti-inflammatory drugs (64%) followed by triptans (17.5%) and paracetamol (10%). In the severe migraine: triptans (80%), nonsteroidal anti-inflammatory drugs (12%) and ergotamine (2.5%). There were no differences regarding the preventive treatment of migraine: Calcium Channel Blockers (41%) and β adrenoceptor antagonists (41%). No relation was found between the fact of being a doctor suffering headache, and prescribing drugs.
Conclusions Only 5% reported a poor/very poor management of headache. A very high per cent of chronic daily headache were sent to the neurologist. The most used analgesic for the mild migraine by 61% of the doctors was the paracetamol; nonsteroidal anti-inflammatory drugs for the moderate migraine and triptans for the severe. No relation was found between the fact of being a doctor suffering headache, and prescribing drugs or sending to the neurologist.

P6R73

Migraine therapy: a survey of pharmacists

Richard Wenzel*[1], Richard Lipton[2], Merle Diamond[3] & Roger Cady[4]
[1]*Diamond Headache Center Inpatient Unit, Chicago, IL, USA,* [2]*Albert Einstein College of Medicine, Bronx, USA,* [3]*Diamond Headache Center, Chicago, IL, USA,* [4]*Primary care Network, Springfield, USA*

Objective Assess pharmacists' knowledge, attitudes, and practice patterns of migraine therapy.
Methods 171 self-administered surveys.
Results Among community pharmacists, 85% make one to five OTC headache product suggestions per day while 12% made six or more suggestions daily. Only 38% view migraine as a neurobiological disease; 46% consider headache an important part of their practice. Fifty-one percent feel patients should try OTC medication prior to prescription drugs; 47% teach patients to guard against over-use of OTC drugs. 61% feel that migraine-specific drugs should be reserved for patients who have failed at least two other prescription drugs. Only 41% always ask patients about headache-related disability.
Conclusion Community pharmacists interact with headache sufferers frequently and are well positioned to improve care. Pharmacists are not well versed in current and evolving treatment strategies and would benefit from further training.
Acknowledgements This project was supported by the Diamond Headache Clinic Research & Educational Foundation and GlaxoSmithKline Pharmaceuticals.

P6R74

Changes in attack frequency and cluster headache type after prolonged sumatriptan treatment

Csaba Ertsey*[1], György Bozsik[1], Judit Áfra[2] & Ilona Jelencsik[1]
[1]*Department of Neurology, Semmelweis University,* [2]*National Institute of Neurosurgery, Budapest, Hungary*

Clinical, hormonal and PET data suggest that a hypothalamic pacemaker has a prominent role in the timing of cluster headache attacks. Within the hypothalamus, the suprachiasmatic nucleus (SCN) is known to govern endogenous rhythms. Serotonergic drugs can modify biological rhythms in humans and can alter SCN activity in animal models.

Sumatriptan, which poorly penetrates the blood–brain barrier, is highly effective in the acute treatment of cluster headache. Quite often, abortive sumatriptan treatment leads to a change in cluster attack frequency. A similar effect of other, more lipophylic triptans has also been documented.

We describe a patient who had a 12-year history of primary chronic cluster headache with no response to a number of preventive agents. During a 5_ month abortive sumatriptan treatment, after an initial rise in headache frequency, he gradually became headache-free. After 3 years' remission he developed ipsilateral secondary episodic cluster headache.

This case illustrates that sumatriptan can change the frequency of cluster headache attacks and also cluster headache type, possibly by altering the function of the hypothalamic pacemaker. This, in turn, would suggest that sumatriptan may penetrate the blood–brain barrier during the active phase of cluster headache.

P6R75

Headaches in multiple sclerosis Patients

Daina Jegere*[1] & Jolanta Kalnina[1]
[1]*Latvian Maritime Medicine Center, Riga, Latvia*

Objectives Headaches are more common in patients with multiple sclerosis (MS) than in controls. They have been associated with tumor-like giant plaque formation and with plaques of the brain stem and periductal gray matter.

The purpose of study was to investigate the headache-types in MS patients and to evaluate the effectiveness of MS therapy on headaches.

Methods We examined 112 patients (aged 18–50 years, 65% female and 35%- men) with clinically definite MS (according the Schumacher criteria) from Latvian Multiple Sclerosis Center. All patients had physical and neurological examinations and MR investigations of brain. Data on specific headache diagnosis, testing and treatment were analyzed.

Results From 112 MS patients headache- free were eight, 16 had migraine, 73 had tension-type headaches, 12 patients had signs of trigeminal neuralgia and in 8 patients headaches were caused by optic neuritis, 18 patients had mixed headaches. In 43 patients the signs of depression were founded out.

Conclusions The headaches in SM patients with signs of depression are more frequent and severe. Different headaches improves during the course of prophylactic treatment of MS. The trigeminal neuralgia is more often in MS patients than in general population.

P6R77

Pain coping strategies of the patients with rebound headaches

Alexander Feoktistov*[1] & Elena Filatova[1]
[1]*Neurology Department of FPPE of Moscow Medical Academy, Moscow, Russia*

The study involved 65 patients with rebound headaches (RHA) according to diagnostic criteria proposed by Diener and 15 healthy controls. We assessed coping strategies using questionnaire 'Pain coping strategies' which includes 3 scales: emotional (emotional reactions on pain), cognitive (patient's type of thinking during pain) and behavioral.

Scales are valued from 1 up to 6 points and show frequency of different coping strategies use during the headache.

We revealed, that from emotional scale patients with RHA most frequently use strategies of depression and fear – 4.6, while rarely use strategies of 'well-being' – 2.6. From cognitive scale patients often use strategies of hopelessness and despair – 4.9. Among behavioral scale most popular were strategies of avoidance of social and physical activities – 5.9. Also, patients with RHA rarely use strategies of active or passive relaxation – 2.3. All changes were significant comparing with controls ($P < 0.05$). Results indicate that patients with RHA add emotional components to the pain and form restrictive behavioral pattern. These peculiarities play an important role in decreasing patient's quality of life, which form pathological circle: HA – decreased quality of life – HA. Considering these changes we conclude that cognitive psychotherapy should be an important part of treatment process.

P6R78

Headache treatment in the emergency room with Endovenous Ketorolac and Tiapride

Samuel Díaz-Insa*[1], Esther Romero[2], Carles Navarro[2], Cristina Soriano[1], Sandra García[2] & Juan Carlos Martín-Baena[2]
[1]*Neurology Section, Hospital 'Francesc de Borja' de Gandía, Gandía, Spain,* [2]*Emergency Department, Hospital 'Francesc de Borja' de Gandía, Gandía, Spain*

Objectives To prove the efficacy of endovenous (ev) ketorolac + tiapride in patients with headache attending the Emergency Room (ER).

Methods During 4 months we evaluated all patients attending ER with headache as prior symptom. We recommended ev ketorolac + tiapride as symptomatic treatment. We considered age, gender, IHS type of headache, time with headache till ER arrival, previous treatment, time staying in the ER, drug use in the ER and finally, outcome as maintaining similar headache, pain-relief or pain-free.

Results 315 patients attended ER with headache. 164 were administered the recommended treatment, with 17.68% (29) not evaluable and the rest (135) had the following outcome: 73 (54.07%) pain-free, 60 (44.44%) pain-relief and just 2 (1.48%)

maintaining similar headache. All headache types benefit: tension-type headache 60% pain-free/40% pain-relief; migraine 59%/41%; Chronic daily headache 32%/68% and Secondary headaches 78%/22%.
Conclusions The use of ev ketorolac + tiapride for any patient with headache arriving to the ER improves 98.5% of them with 54% pain-free. It allows a good management, even unspecific, of all kinds of headache. Despite this, afterwards, an specific management of each individual headache is desirable.

P6R79

Dystonia and headaches: the response to botulinum toxin therapy

Nestor Galvez-Jimenez*[1], C. Lampuri[1], R. Patino-Piccirilo[1] & M. Hargreave[1]
[1]*The Cleveland Clinic Florida, Weston, Florida, USA*

Background Headaches and other pain syndromes frequently associated with cranio-facio-cervical dystonias may respond to botulinum toxin type A (BoNT/A) treatment.
Objective To determine the prevalence and clinical features of the different types of IHS headaches associated with cranio-facio-cervical dystonias and the response to BoNT/A.
Methods An examination of our movement disorders database between 1996 and 2001 identified 70/234 patients with cranio-facio-cervical dystonias treated with BoNT/A. Headache pain severity was assessed before and after treatment (visual analog scale [VAS]; 0 = no pain; 10 = the worst).
Results Forty-one/70 patients (58.5%) (mean age of 57.19 years) (45 cervical dystonia, 17 blepharospasm, 8 oro-mandibular dystonia) had headaches (34 tension type [TTH], 19 cervicogenic, 6 migraine). Some patients had more than 1 type. Pain was located in the following areas: 65.8% frontal; 48.7% cervical; 12.1% shoulder, 34% top of head, 73% temporal; 46.3% occipital; 7.3% masseter; and 4.8% jaw. VAS pain scores dropped from 7.4 to 1.79 after BoNT/A treatment (a 75% improvement). Mild injection-site pain and transient forehead heaviness were the only adverse events reported.
Conclusion TTH and other headaches are common concurrent complaints in patients with cranio-facio-cervical dystonias. BoNT/A therapy appears to be effective and well-tolerated as preventive treatment in dystonic patients.

P6R80

Recurrent eosinophilic meningitis revealed as hypereosinophilic syndrome

Ji Yeon Ryu*[1] & Kyung So Jeon[1]
[1]*Hanil Medical Center*

We report a 37-year-old female patient with recurrent eosinophilic meningitis revealed as idiopathic hypereosinophilic syndrome, who showed the severe headache with vomiting. She had similar severe headache history 2 years ago diagnosed as viral meningitis. At this time, total CSF WBC count is 1000/mL (eosinophilic portion is 67%) and previous CSF WBC count is 22/mL with 70%). Total peripheral eosinophil count has been always over 3000/mL during 2 years. There was no organ involvement. Bone marrow biopsy was done and revealed the normocelluar marrow with eosinophilic hyperplasia. Her severe headache was improved with corticosteroid pulse therapy. A well-documented case of the hypereosinophilic syndrome has not been previously reported in association with recurrent cerebrospinal fluid eosinophilia and biochemical evidence for meningitis.

P6R81

Prevalence and clinical characteristics of experimental model of 'ice cream headache' in migraine and episodic tension-type headache patients

Hamit Macit Selekler*[1], Sarper Erdo_an[2] & Faik Budak[1]
[1]*Department of Neurology, Kocaeli University Faculty of Medicine,*
[2]*Department of Public Health, Kocaeli University, Faculty of Medicine,*
[3]*Department of Neurology, Kocaeli University Faculty of Medicine*

This study was designed for the investigation of prevalence and clinical characteristics of 'ice-cream headache' or headache caused by 'ingestion of cold stimulus' between migraine and episodic tension-type headache patients. 76 migraine and 38 episodic tension-type headache patients were included in the study. An experimental model of 'ice-cream headache' was developed for the study. Pain occurrence period, its localization and quality were recorded for each patient who felt pain in their head during the test procedure. Pain in the head occurred in 74% of migraine and percentage32 of 'tension-type headache' patients. Pain was evoked in more than half of the migraine patients in the first 20 seconds, while pain was evoked in between 20 and 50 s in 75% of the patients with 'episodic tension-type headache'. Most frequent pain localization was the temple in migraine patients. According to results obtained from this study, it seems that experimental model of 'ice-cream headache' is not only more frequent in migraine patients, but also its localization, quality and speed of occurrence differ from 'tension-type headache'.

P6R82

Aggravation of the headache by physical effort, bending down and head movements during the migraine attacks

Hamit Macit Selekler*[1] & Sezer Komsuoðlu[1]
[1]*Kocaeli University Faculty of Medicine,* [2]*Kocaeli University Faculty of Medicine*

Aggravation of the headache by routine physical activity during the attacks is the subcriterion of the 'C' criteria which is among the 'migraine without aura' criteria. While questioning patients about this subcriterion, sensitivity of 'walking stairs' and 'carrying a heavy object' vs. 'head movements' and 'bending down' in regard of aggravation of headache was aimed to be determined. Fifty patients with migraine without aura with 'throbbing quality' of headache were questioned about the aggravation of their headaches with two sets of question groups. (Group 1: 'walking stairs' and 'carrying a heavy object'; Group 2: 'head movements' and 'bending

down'). The first group of questions were answered positively by 46 patients and, four patients answered these questions as 'I don't know'. The second group of questions were answered positively by 26 patients, 'I don't know' by 18 patients and 'no' by 6 patients. Some patients with severe migraine headaches may prevent themselves from rigorous daily activities while they could bend or make sudden head movements inadvertently during the attack. Questioning 'head movements' and 'bending down' could help us in this 'C' subcriterion.

P6R83

Idiopathic stabbing pain and migraine

Hamit Macit Selekler*[1]
[1]*Kocaeli University Faculty of Medicine*

Frequency of ISH in migraine patients indicates this part of their pain control system is defective, permitting a high frequency neuronal discharge spontaneously. Persistent disinhibition of a segment of the trigeminal pathways suggests the trigeminal system could also discharge excessively for hours or days to provide a neural origin for migraine. Clinical characteristics of ISH and its relationship to migraine by means of precipitants, aggravators, localization and temporal relationship to migraine headache were questioned in 55 patients with ISH and migraine. 26 patients reported precipitating factors for ISH like hunger, tiredness and less sleep. 11 patients reported that stabbing pain occurred just before the migraine headache. ISH began just before migraine headache ($n = 11$), at the beginning of migraine headache ($n = 7$), ISH as migraine headache intensifies ($n = 11$), ISH when migraine headache is the most severe ($n = 17$) were reported. Aggravation of ISH as bending down and relieving of ISH with applying pressure to head, sleep and rest were also reported. As we review the findings of this study, precipitants, regional and temporal relationship of two pains as well as aggravators and relievers of ISH during migraine attack give some hints about the relationship between trigeminal firing due to disinhibition and migraine attacks.

P6R84

Irritant stimulus headache: ingestion of an irritant stimulus

Hamit Macit Selekler*[1] & Sezer Komsuoðlu[1]
[1]*Kocaeli University Faculty of Medicine*, [2]*Kocaeli University Faculty of Medicine*

Ingestion of a cold stimulus, previously called as 'ice-cream headache', was described as 'a pain produced in susceptible individuals by the passage of cold material, solid or liquid, over the palate and posterior pharyngeal wall' by IHS. Occurrence of ice cream headache was explained by means of defective pain control mechanisms in migraine patients. Two patients who suffer from both migraine and 'ice-cream headache' reported hot and soft fizzy drinks such as coke also caused a similar pain. A 35-year-old man reported ingestion of hot liquids and coke cause headache in temporal region which is the same when he drinks cold liquids in temporal region only when he is under stress which also causes insomnia and alcohol intake. A 20-year-old woman reported ingestion of hot liquids cause headache as well as ingestion of irritants to her pharynx such as coke and it has the same quality as 'ice cream headache'. She suffers hot/irritant induced headaches during almost all her migraine attacks. It seems that individuals must be sensitized before for hot/irritant induced headache to occur. However, we think irritation of the pharynx plays a major role in this kind of headaches.

P6R85

Non-medicinal therapy methods for the primary headaches

Hamit Macit Selekler*[1], Basak Gürp_nar[1] & Hüsnü Efendi[1]
[1]*Kocaeli University Faculty of Medicine Department of Neurology*

Migraine and tension-type headaches have different pathophysiologies.

Patients methods for relieving symptoms that arise during these attacks differ as well. This study consisted of 108 migraine, 65 chronic migrainous-type headache, 32 episodic tension-type headache and 21 chronic tension-type headache patients whose methods of coping with pain were investigated. Darkness, silence, applying pressure to head and applying heat to head were more frequent methods in migraine and chronic migrainous-type headache patients. Applying cold to head was the most frequent method in patients with tension-type headaches. Lying and massage during the attack were the methods that were preferred in similar ratios among headache groups. Sleeping and provoked vomiting were specific coping methods in migraine patients.

P6R87

Clock like periodicity as the most important feature of cluster headache

Niranjan Narain Singh*[1] & Surendra Misra[1]
[1]*Institute of Medical Sciences, Banaras Hindu University*, [2]*Institute of Medical Sciences BHU Varanasi India*

Objective This study was undertaken to know the incidence of seasonal as well as diurnal periodicity of pain in cluster headache.
Method Profile of CH was analyzed by retrospective analysis of CH patient attending neurology clinic from January 1995 to December 2001 over 3881 patients of headache. Diagnosis of CH was based on HIS criteria and 15 patients were picked up.
Results The most consistent finding in CH patient was periodicity of cluster period which showed the peak in February – March (8) and August – September(14) which was also the time when most of the patient contacted. Maximum cluster was seen during August – September, which is in contrast with western countries where this season has the lowest record.

Which may be because of difference in daylight hours. Similarily diurnal periodicity was also marked-9–11($n = 5$),13–16 h($n = 9$),21–01 h($n = 11$).

Such periodicity of attacks where not seen in any other patient.

P6R88

Suandok Headache Score (SHS) and Suandok Headache Questionnaire (SHQ) in diagnosing migraine

Siwaporn Chankrachang*[1], Surbsai Kongsaengdao[1], Helen Ling[1] & Ruedeewan Kaewlai[1]
[1]*Chiang Mai University Hospital, Thailand*

Background We designed Suandok-Headache-Questionnaire (SHQ) to develop Suandok-Migraine-Score (SMS) to assist physicians in approaching the most common headache syndrome efficiently. SMS is intended to be a simple, self-administered equation to give migraine diagnosis.
Objective To develop SMS and test its reliability.
Methods We designed SHQ with 21 factors related to medical history of headache. 302 patients with complaint of headache were enrolled and SHQ was completed for each patient. Clinical diagnoses were made separately by independent neurologists following I.H.S. criteria. SHQ data from patients with migraine and nonmigraine diagnoses were analyzed by statistical correlation (SPSSV11.5). Factors with *P*-values less than 0.05 were selected and reapplied to SPSS programme to get SMS equation. Factors were removed and retested until remaining factors in combination provide *P*-value < 0.05.
Results N. Factors per se were: **1** Nausea (N), **2** Family history (FHx), **3** Gender: male (M) and female (F), **4** Pulsatile quality (PQ), **5** Improvement with anti-migraine medication (MGD), **6** Muscle spasm (MS).

SMS equation with a reliability coefficient of 0.55** was 1.621 (N) + 1.261 (FHx) + 7.3 (RH) + 1.377 (PQ) + 0.967 (MGD) – 3.103(MS) – 8.989(F) – 10.722(M).
Conclusion We designed SHQ to obtain SMS, which has a reliability coefficient of 0.55. Following this preliminary result, our next step is to test its validity by applying in different population samples.
Keywords Suandok Migraine Score, Suandok Headache Questionnaire, International Headache Society (IHS) criteria, Migraine, tension type headache.

* The *P*-value was calculated by paired *t*-test, ** The reliability coefficient was calculated by Alpha (Cronbach) model.