

IS THE HEADACHE AS A SERIOUS COMPLAIN IN MS INVOLVED PATIENT?

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Introduction More than 170 years passes from first clinical description of Multiple sclerosis, But its etiology is Remain unknown. Headache and vertigo were rare complains in M.S. patients. But it seem headache become a serious problem in new studies. This retrospective study try to show that clinical view of M.S. is changing.

Materials and Methods This retrospective study was conducted on 96 known cases that hospitalized from 2002 June to 2005 May, in Zanjan Vali-e-Asr hospital. We collected data (Age, Gender, Geographic area, Clinical Signs and Symptoms) and then analyzed data by spss.

Results From ninety six patients, there were 57 female (59%) and 39 male (41%).Paresthesia (77 cases, 80%) was the common problem that we recoded in sings and symptoms. Movement difficulties in lower limbs and with lower range occurrence in upper extremities were about 58% and 34% respectively. Vision problems were recorded as a frequent complain in patients, (42%). Headache was occurred in 12 (13%) patients as a first and single manifestation before their hospitalization.

Conclusions On the new studies results basis, it seems M.S. is changing its view in new recent years. New researches on background of M.S involved patients are highly recommended.

NUMMULAR HEADACHE

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Background Nummular headache has recently been included in the International Headache Classification. We report a series of 6 cases. To the best of our knowledge nummular headache has not been previously been described in the UK literature. One possibility is that it is under-recognised.

Clinical data The source of patients was those presenting to general neurological and headache clinics at Derriford Hospital, Plymouth.6 patients fulfilling the diagnostic criteria for nummular headache were identified over an 18-month period. The mean age range of patients was 30–50 years and duration of symptom was 2–3 years. 2/6 patients also had history of migraine. There was no associated history of head trauma. During the consultation patients typically finger-pointed and delineated a rounded, painful area in 2–6 cm in diameter. Pain quality was mild-moderate, continuous and persisting from days to months with allodynia in the area of pain in 2/6 patients. Neurological examination was otherwise normal. No structural abnormalities were identified. Symptoms resolved after treatment with gabapentin or nonsteroidal anti inflammatory drugs in 4/6 patients. Partial response occurred in 2/6 patients

Conclusions Patients value accurate diagnosis and explanation of their symptoms. Furthermore, correct classification of disease process may be of therapeutic importance. This case series indicates that nummular headache may be under recognised. It suggests (as reported in the original case series) that ‘finger-pointing’ is a useful clinical sign in the diagnosis of nummular headache.

GNAS1 T393C POLYMORPHISM IS ASSOCIATED WITH MIGRAINE

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Introduction Sympathetic nervous system (SNS) disbalance has been proposed as a mechanism underlying migraine pathophysiology. Objective: To investigate if GNAS1 T393C polymorphism, previously associated with a different SNS sensitivity, plays a role in migraine.

Subjects and Methods We performed both case-control, and family-based association studies using two independent sets of subjects.

Results Case-control study. A total of 712 subjects (365 migraineurs; 347 healthy controls) entered the study. Significant genotypic differences were observed ($\chi^2=11.381$, 2 df; $p=0.003$). Using logistic regression analysis, GNAS1 T393C significantly contributed to migraine prediction (OR 1.79. CI 95% = 1.27–2.53; $p=0.001$ for CC genotype vs TC/TT genotypes). Family-study. 558 subjects (384 affected; 174 unaffected) belonging to 117 pedigrees were genotyped. Significant sTDT and combined z' scores were obtained (Table 1), which suggest linkage but not association, since we employed multiplex families.

Table 1 Results of family study. TDT, sTDT and combined scores (see image) In conclusion: We suggest here in two independent samples that the GNAS1 gene is implicated in migraine. Since T393C variant is a conservative polymorphism, it may be in linkage disequilibrium with another functional genetic variation. Granted by IFIMAV API/05/22, CIEN Foundation nodo-HUMV, and FISS PI050388.

GNAS1-393 allele	T*	NT**	p	Y***	sTDT z' p	Combined z' p		
T	58	52	NS	57	3.108	0.001	2230	0.026
C	52	58	NS	53	2.857	0.001	1.069	NS

*transmitted and **not transmitted alleles; ***numbers of families where sTDT was available

DIFFERENCE IN BLOOD FLOW IN THE BRAIN RELATED TO MIGRAINE PATIENTS

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Purpose To investigate the difference between blood flow in the cerebral hemispheres in migraine patients measured by ultrasound dopplerography of the mild cerebral artery (MCA).

Methods 69 people – 21 males and 48 females from ages 18 to 65 were studied. We have three groups for investigation- 1. Migraine patients- 45 - ultrasound dopplerography was performed during migraine attacks and between the attacks 2.First control group - patients with other kinds of headache- 17. Most of them had Tension-type headaches 3. The second control group were healthy people without headaches – 7. An MRI of the brain was made for all patients in order to exclude secondary headache disorders. The ultrasound dopplerography was made in all vessel regions of the brain (carotids and vertebral). The test was performed twice in the first group, once before and once after the treatment of 3 migraine attacks. For groups two and three, only one ultrasound dopplerography was performed. All patients with migraines were treated with Eletriptan 40 mg for their attacks.

Results The difference between the blood flow in the hemispheres was found only in patients with migraines. The difference occurred only in the MCA. The blood flow in the MCA was higher in both

sides of the brain both during and between attacks, but the increase was more significant during the attack on the headache side. This difference was measured at approximately 30% during migraine attacks and approximately 15% between attacks. After treating three consecutive attacks, blood flow returned to more normal levels and the difference in blood flow became less significant, being measured at approximately 5%–10%.

Conclusions 1. Measuring the difference in blood flow in the MCA using ultrasound dopplerography, gives the practitioner an objective diagnostic method for migraine treatment. 2. Blood flow differences could be reduced with proper treatment.

NEUROPHYSIOLOGICAL AND NEUROPSYCHOPHYSIOLOGICAL FINDINGS IN A GROUP OF PATIENTS WITH EPILEPSY AND MIGRAINE

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Background We investigated patients with epilepsy of different kinds who suffered from migraine in the same time, with aim to establish the specifics of the neurophysiological and neuropsychophysiological findings in a group of patients with epilepsy and migraine.

Materials and Methods We investigated 37 patients with epilepsy and migraine. The patients were at the age ranged between 42–56 years old. The type of epileptic seizures were classified by Ilae 1989 on generalized and partial complex seizures, and migraine headache by ICDH II 2004. EEG, evoked potentials (VEP, SEP, BAEP), psychological tests and CNV paradigm was used as a neuropsychophysiological correlate of the cognitive-mnemonic function. CT-scan and MRI were also made.

Results In a group of 37 patients epileptic seizures associated with migraine had in 36% of patients. EEG was normal in 12 patients, in 21 we found different abnormalities, mostly diffuse theta-delta dysrhythmia in frontal and temporal lobe, and focal unspecific activity in 5 patients. VEP was pathological in 27 patients, 21 on the one eye, and in 4 bilaterally with prolonged latency and decreased amplitude. SEP was normal in the hall group, and BAEP was with prolonged latency in the early complex in 16 patients. CT-scan and MRI showed hippocampal sclerosis in 3 patients with partial complex seizures, and in 8 patients showed cortical and subcortical reductive changes, while in all the other patients were normal. CNV paradigm showed prolonged latency, reaction time and almost 50% reduction of the amplitude in 35 of 37 patients.

Discussion This research did not show specifics of the neurophysiological and neuropsychophysiological findings in a group with epilepsy and migraine nor according to the type of seizure, nor according to the time connection of the attacks between the two diseases. We only find some relationship between two diseases by the changes of latency, amplitude and reaction time in CNV paradigm which can arise further investigations in the future in this field.

NEUROVASCULAR COUPLING IN MIGRANEURS DURING HEADACHE FREE PERIOD

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Background Neurovascular coupling may be altered in migraineurs. Therefore, visual evoked potentials (VEP) and visually evoked cerebral blood flow velocity responses (VEFR) were simultaneously recorded and their relationship was analysed.

Methods Thirty healthy controls and 30 age matched migraineurs during headache free interval participated in the study. The VEFR were measured in the posterior cerebral artery using transcranial Doppler and VEP were recorded from occipital leads. Neuronal activity was changed by using a visual stimulus with increasing contrast of 1%, 10% and 100%.

Results We found an increase in VEFR and VEP in both the healthy and migraineurs groups ($p < 0.01$). VEFR were significantly higher in migraineurs ($p < 0.01$), while VEP did not significantly differ between the groups ($p > 0.05$). Regression showed a significant association between VEP and VEFR in both healthy controls ($r = 0.66$, $p < 0.01$) and migraineurs ($r = 0.63$, $p < 0.01$). The regression coefficient of migraineurs ($b = 0.88$, $SE = 0.08$) was significantly higher than that of healthy controls ($b = 0.55$, $SE = 0.07$) ($p = 0.04$).

Conclusions We conclude that neurovascular coupling is increased in migraineurs interictally.

SELF DIAGNOSIS OF SINUS HEADACHES: ECONOMIC IMPACT

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Background Sinus headache is often self-diagnosed based on vasomotor rhinitis and periorbital pressure, with or without other head pains. Patients will often report “sinus headache” to their primary care providers after trying non-prescription analgesics, antihistamines and/or decongestants. As most providers are not aware of the IHS criteria for this condition, treatment may include antibiotics or other sinus-related medications. When this is unsuccessful in reducing the frequency or intensity of the symptoms, imaging of the sinuses may be ordered. When symptoms still persist, a referral to a headache specialist often follows.

Methods Patients referred to our Headache Clinic are given a detailed questionnaire and interviewed by a medical team experienced in headache care and the IHS criteria. One question asks what the patient thinks is their headache diagnosis. We identified 101 consecutive patients who listed “sinus headache” as their self-diagnosis and further reviewed their use of medical services 2 years prior to referral to our clinic and up to one year after referral. We assessed their headache type by IHS criteria.

Results 67 patients had migraine, 20 had tension headaches, 16 had cervicogenic headaches, 15 had medication overuse. Some had multiple types of headaches. Prior to being seen in our clinic, 47 had CT scans of their sinuses, 45 of which were normal. 36 had at least one course of antibiotics. 58 were symptomatic for greater than 10 years and 12 for 6–10 years. The proportion of males was higher than expected.

Conclusions Self diagnosis of “sinus headache” is associated with delayed diagnosis of the true headache type, overuse of inappropriate diagnostic tests and treatments. Further education of both the public and the primary care providers may help improve headache diagnosis and care.

THE ASSOCIATION BETWEEN HEADACHE AND VAL158MET POLYMORPHISM IN THE CATECHOL-O-METHYLTRANSFERASE GENE. THE HUNT STUDY

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Background and aims The Catechol-O-methyltransferase (COMT) gene contains a functional polymorphism, Val158/108Met, that has been found to influence human pain perception, and one study has found that migraine was less likely among those with

Val/Val polymorphism. The aim of this population-based study performed among unselected adults was to evaluate the relationship between Val158Met polymorphism and headache, migraine included.

Methods In the 1995–1997 Nord-Trøndelag Health Study (HUNT), the association between Val158Met polymorphism and headache was evaluated in a random sample of 2,451 individuals.

Results Among women lower prevalence of non-migrainous headache was found among individuals with Val/Val genotype than among those with the other genotypes (26.2% vs. 33.6%, $p=0.025$). No association between Val158Met polymorphism and migraine or headache frequency was found.

Conclusions In this population-based study, lower prevalence of non-migrainous headache was found among women with Val/Val genotype at the COMT gene than among those with the other genotypes.

SICK LEAVE IS RELATED TO FREQUENCIES OF MIGRAINE AND NON-MIGRAINOUS HEADACHE. THE HUNT STUDY

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Background and aims Few population-based studies have evaluated the influence of non-migrainous headache and headache frequency on sick leave. The aim of this large cross-sectional population-based study was to examine the association between sick leave and headache.

Methods Between 1995–1997, all 92,566 adults in Nord-Trøndelag County in Norway were invited to participate in a health survey. Out of 73,327 invited individuals below 67 years of age, a total of 38,192 (52%) responded to questions about headache, work situation and sick leave during the past year. Associations between sick leave and headache, migraine included were assessed in multivariate analyses, estimating prevalence odds ratios (ORs) with 95% confidence intervals (CIs).

Results There was increasing prevalence of sick leave with increasing frequency of migraine and non-migrainous headache. Sick leave more than 8 weeks during the past year was more than three times likely among individuals with headache >14 days per month compared with those without headache.

Conclusions There was a higher prevalence of short and long term sick leave during the last year among headache sufferers as compared to headache-free individuals. Duration of sick leave was positively associated with frequency of migraine and non-migrainous headache. The results may indicate that better treatment of individuals with chronic headache may have beneficial economical implications.

EFFECTS OF TOPIRAMATE ON INTERICTAL EEG ABNORMALITIES IN MIGRAINE PATIENTS

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Background and aims Migraine is characterized by reduced habituation of multi-modal evoked potentials, which is the expression of an abnormal pattern of cortical excitability [1]; the question about reduced or increased cortical excitability is still debated [2]. Recently the efficacy of topiramate as a migraine-preventive therapy was assessed [3]. In migraine patients, an effect on cortical hyper-excitability was suggested [4]. The aim of the present study

was to examine the effects of topiramate on the Contingent Negative Variation (CNV) habituation and Steady State Visual Evoked Potentials (SSVEPs) amplitude in a cohort of migraine without aura (MA) patients.

Methods Twenty MA patients, eligible for migraine prophylaxis, were recorded in a pain-free state before and after 2 months of 100 mg topiramate therapy assumption. Fifteen control subjects, age and sex matched, were also selected. The EEG was recorded by 19 channels, according to the 10–20 International System. The CNV habituation and SSVEPs amplitude patterns were assessed, according to previous reports [5, 6]. The basal EEG data, computed in the MA group, were compared to normal controls group and to the data obtained after topiramate treatment. The EEG data were examined in blind.

Results Topiramate induced a 50% or more reduction in monthly migraine frequency. The CNV reduced habituation pattern was reversed by topiramate, approaching the normal values. The SSVEPs amplitude was also significantly reduced after 2 months of topiramate therapy, as well as the EEG synchronization in alpha band.

Conclusions Topiramate was able to reverse the neurophysiological abnormalities subtending migraine: its modulatory action on ion channels and non-NMDA receptors may reduce the cortical hyper-excitability which is confirmed to be a predisposing factor for migraine.

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ZOLMITRIPTAN ORALLY DISINTEGRATING TABLET (ODT) DEMONSTRATES EXCELLENT PATIENT AND PHYSICIAN SATISFACTION IN PRIMARY CARE MIGRAINE THERAPY

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Background In order to provide effective and practical treatment strategies for migraine patients in primary care, physicians require information on more patient-relevant endpoints than those typically used in clinical trials. Objective: To evaluate zolmitriptan ODT 2.5 mg for the acute treatment of migraine in a primary care setting.

Methods This multinational, multicentre, 6-month, open-label study of zolmitriptan ODT 2.5 mg recruited patients with an established diagnosis of migraine. Patients treated 1–3 migraine attacks per month with study medication, and all other attacks with usual therapies. Investigator-led questionnaires recorded preferences and treatment experiences.

Results 595 patients treated a total of 7171 migraine attacks. 75.4% of patients wished to continue using zolmitriptan ODT; common reasons were effectiveness (70.2%), ease of use (60.9%) and rapid effect (59.1%). Most patients (70.9%) preferred zolmitriptan ODT to previous therapies. Almost all (95.4%) reported that zolmitriptan ODT was convenient to use and enabled early treatment (84.3%). Physicians wanted to continue prescribing zolmitriptan ODT for 67.7% of patients; common reasons were effectiveness (64.1%), rapid effect (50.1%) and ease of use (49.9%).

Conclusions Patients and physicians are highly satisfied with the effectiveness, rapid effect and ease of use of zolmitriptan ODT in a primary care setting.

KYNURENIN IN COMBINATION WITH PROBENECID PREVENTS STIMULATION-INDUCED INCREASE IN C-FOS IMMUNOREACTION IN THE CAUDAL TRIGEMINAL NUCLEUS

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Electrical stimulation of the trigeminal ganglion is known to induce increase of c-fos immunoreactive second-order neurons in the caudal trigeminal nucleus which forward nociceptive impulses to the thalamus. Systemic administration of nitroglycerine, often used as a migraine model, also results in an increase of the number of c-fos immunoreactive secondary sensory neurons in the caudal trigeminal nucleus. Since it is supposed that synapses between first- and second-order trigeminal neurons are mediated by excitatory amino acids, post-synaptic NMDA receptors are bound to be inhibited by kynurenic acid, which, beside Mg²⁺, is the only known endogenous NMDA receptor antagonist. Kynurenic acid, however, does not pass the blood-brain barrier; therefore, it cannot be used as a protective agent. In contrast, kynurenine, from which kynurenic acid is formed by the action of kynurenine aminotransferases, passes the blood-brain-barrier without difficulty. In our investigations we tested the hypothesis whether kynurenine administered systematically together with probenecid, known to increase brain tissue concentration of kynurenic acid, provides protection of second order neurons against stimulation arriving from central processes of the trigeminal ganglion cells and, consequently, whether this combination inhibits increase of c-fos immunoreactive nerve cells in the caudal trigeminal nucleus. We found that after i.p. injection of kynurenine and probenecid, the electrical stimulation-induced increase of c-fos immunoreactivity of secondary sensory neurons fails to ensue; the same treatment prevents also the nitroglycerine-induced increase of c-fos immunoreactive neurons. These results suggest that migraine headache might be blocked by a combined application of parenteral kynurenic acid and probenecid treatment.

EFFICACY OF AN INSTRUCTION PROGRAM ON HEADACHE AND FACE, NECK AND SHOULDER PAIN IN A WORKING COMMUNITY. A LONGITUDINAL CONTROLLED STUDY

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Aims Our main purpose was to examine the effect of an instruction program on frequency of headache and face, neck and shoulder pain in a working community. **Methods.** 343 employees of the city of Turin whose working activity involves public contact (registry and tax office) were distributed in two groups: study group (n=167) and controls (n=176). In all subjects data were taken of headache, and facial, neck and shoulder pain, if present. They were then given a diary on which to record, on a daily basis, frequency, severity and duration of the headache and facial, neck and shoulder pain episodes, from March to October 2005. At month 3 an instruction program was administered to the study group: it consisted of brief shoulder and neck exercises to be performed several times a day, a relaxation exercise and instructions of how to reduce hyperfunction of the craniofacial and cervical muscles during the day. Both groups kept the diary for further six months (months 3–8). For each subject, the difference between the frequency of symptoms at months 7–8 and at months 1–2 was calculated, and the mean differences between the two groups were compared (Student t test).

Results The monthly frequency of headache significantly decreased over time in the study group compared to controls (from 5.9 to 3.5 vs 6.5 to 6.4, $p < 0.000$); the same pattern was observed for the frequency of facial pain ($p = 0.03$) and neck and shoulder pain ($p < 0.000$). Such significant decrease was confirmed in a multiple regression analysis adjusted by sex and age.

Conclusions It is concluded that the administration of a simple instruction program can significantly reduce the prevalence of headache and facial and cervical pain in a working community.

CHRONIC DAILY HEADACHE IN ADOLESCENTS

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Background and aims Chronic daily headache (CDH) in adolescents is poorly understood and difficult to treat. This study was designed to compare demographics, psychological factors and pain response in adolescents with CDH with those who have less frequent recurrent pediatric headache (RPH).

Methods In a hospital-based behavioral treatment program, 155 adolescents with CDH and 228 with RPH completed questionnaires regarding headache characteristics and activity, the Spielberger State-Trait Anxiety Inventory (trait form), the Children's Depression Inventory and the Childhood Somatization Inventory. Cold pressor testing (CPT) at 10°C was also performed over four 10-second intervals. Statistical analysis included Chi square and independent sample T-testing.

Results CDH adolescents were older, more frequently girls, missed more school due to headache, had significantly higher scores on all psychological measures and lower CPT scores when compared to adolescents with RPH.

Conclusions In comparison with RPH, adolescents with CDH referred to a behavioral treatment program tend to be older girls who report more symptoms of anxiety, depression and somatization. Although they report less functional disability related to headache, they have higher rates of school absenteeism due to headache. CDH adolescents report lower CPT scores than RPH adolescents; thus not appearing to augment pain sensation. The relationship between psychological factors and CDH in adolescents needs further study.

USE OF ZOLMITRIPTAN IN SPAIN: A SATISFACTION SURVEY

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Background and aims Efficacy, tolerability and safety are all important parameters when evaluating the utility of a drug substance. Equally important, however, is to explore patients' treatment experience of the drug. The primary objective of the study is to explore migraine patient treatment satisfaction with zolmitriptan ODT.

Methods Non-interventional, cross-sectional study on treatment satisfaction with zolmitriptan ODT by migraine patients in Spain, managed by primary care physicians. The target population were patients diagnosed with migraine with or without aura or with probable migraine with or without aura, according to IHS diagnostic criteria (2004), who had used zolmitriptan orally disintegrating tablet (ODT) 2.5 mg to treat at least 3 migraine attacks over the previous 3 months. Treatment satisfaction was measured using a 17-item questionnaire.

Results Of 291 patients included, (77.5% women, mean age 43.5 years) 94.9% of patients reported that they were satisfied or very satisfied with zolmitriptan ODT. 93.8% of patients wanted to continue

with the treatment, with effectiveness, rapid effect and ease of use being the main reasons (75.6%, 64.6% and 63.6%, respectively). For the majority of patients, the Primary Care Physician stated that they wanted to continue prescribing zolmitriptan ODT in future, the main reasons being effectiveness (85.2%), rapid effect (64.6%) and ease of use (54.6%). Most of the patients (61.3%) reported an onset of action within the first 30 minutes and were pain free within the first hour (67.9%). The impact of migraine on daily activities was reduced within the first 60 minutes in 71.4% of patients. 94.8% of patients either had no side effects or stated that these were of little or no concern.

Conclusions The vast majority of patients expressed a high satisfaction with zolmitriptan ODT as a migraine treatment and both patients and doctors wanted to continue using it.

HYPERTENSION AND HEADACHE

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Aims To investigate the frequency of hypertension in patients with headache, characterized as tension type and migraine like.

Methods A total of 78 consecutive outpatients were examined, and blood pressure was determined in all patients. Headache and its subtypes were defined according to International Headache Society criteria. Patients were considered hypertensive, if blood pressure was higher than 140/90 mmHg several times without an acute crisis present.

Results There were 54 male and 22 female, aged 33–76 years. 59 patients had tension type headache (TTH) and 19 patients had migraine. Prevalence of hypertension was 32% among all patients, 35.5% among TTH patients and 15.7% among patients with migraine. After adjustment for age and gender, hypertension was found to be more common in TTH patients than in migraine.

Conclusions Hypertension could be one of the factors leading to exacerbation of the frequency and severity of attacks, especially in patients with TTH. Hypertension has important therapeutic implications and should be actively sought in headache patients, and more thoroughly investigated in the general population.

SYNDROME OF HEADACHE AND “ALARMING” NEUROLOGICAL DEFICITS WITH CEREBROSPINAL FLUID LYMPHOCYTOSIS AND SPONTANEOUS RECOVERY: HANDL SYNDROME

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We report of two young male patients (29 and 35 yrs), with acute onset of severe headache, aphasia and right-sided hemiparesis. The differential diagnosis consisted migraine with aura, encephalitis or a localised epileptic syndrome. In a lumbar puncture we found lymphocytic pleocytosis (82 and 52 cells/microliter). The symptoms recovered completely within several hours. The EEG showed in both patients intermittent theta waves in the fronto-temporal regions and no epileptic discharges. The clinical features in our patients are similar to those in the HaNDL syndrome, reported by Berg et al (1995). The HaNDL syndrome is previously referred to as pseudomigraine with lymphocytic pleocytosis (PMP) by Gometz-Aranda et al. or solely as Pseudomigraine by Bartleson et al (1981). In the 2nd Edition of the International Classification of Headache Disorders (ICHD-II), HaNDL is defined and classified in Group 7.8: “Headache attributed to non-vascular intracranial disorder”. The diagnostic criteria for HaNDL syndrome are: I at least one episode of moderate or severe headache accompanied by or shortly followed by transient neurological deficits; II CSF pleocytosis with lymphocytic predominance (>15 cells/ μ l); III episodes of headache

and neurological deficits recur over <3 months; IV normal neuroimaging, CSF cultures and other tests for etiology. The etiology of HaNDL is hypothesized as an auto-immune mediated disorder. HaNDL syndrome is benign and rare (estimated incidence 1 per 500,000 persons per yr) but it is likely to be underdiagnosed. Men are more often involved than women (3:1). There is a peak incidence around the age of 30 yrs.

MIGRAINE/HEMICRANIA-MOVEMENT DISORDERS SYNDROMES: DIAGNOSTIC ITEMS AND ASSESSMENT

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Introduction Specific movement disorders syndromic phenotypes have been associated with cephalalgic manifestations: chronic paroxysmal hemicranial syndrome; paroxysmal dystonia-migraine inherited conditions or CACNA1A conductance mutational-related syndromes: familial hemiplegic migraine-benign paroxysmal torticollis.

Methods Valuation of patients case-samples, series and pedigrees, performing a rationalizing methodical procedure in terms of factorial grouping and development.

Results and Conclusions Functional roles of cortical spreading theories and recent brainstem/hypothalamic areas involved in migraine/trigeminal cephalalgias, are considered in developmental factors in basal ganglia-brainstem-thalamic loops in paroxysmal dyskinesias and motor hyperkinesias

A STUDY ON SERUM ZINC AND COPPER LEVEL IN MIGRAINE AND TENSION HEADACHE IN KASHAN 2003

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Backgrounds Although zinc and copper are found in a little amount in body, they have obvious structural Functional Importance and have an important role on a variety of biological processes. The aim of our study was to evaluate these element changes and diagnostic role of these in serum of patients with Migraine and Tension headache during interictal period.

Material and methods This research was done on 30 patients with Migraine and 30 patients with Tension headache who referred to neurologic ward of Beheshti hospital and private clinic in Kashan during 2003. In the interictal phase was determined serum zinc and copper level.

Findings In migraine the most causes was related to 31–45 years age group (63.3%): 18 females (60%) and 1 male (3.3%) and in the tension headache the most causes in 15–30 years age group (56%): 15 females (50%) and 2 male (6.6%) The average of serum zinc and copper level in Interictal phase of Migraine, respectively 13.18 ± 2.64 and 17.18 ± 4.36 μ mol/l; lit and in tension headache 15.75 ± 3.76 and 20.11 ± 4.08 μ mol/l; lit. These findings were significant statistical difference between this two groups (p value =0.001).

Conclusions These data indicate that serum zinc and copper level decrease in Migraine patients during Interictal period as a diagnostic or etiologic marker.

A GROUP INTERVENTION FOR YOUNG PEOPLE WITH CHRONIC HEADACHE

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Background Chronic headache is a common problem in childhood. Recent studies have indicated that children with headache usually

become adults with headache. Considering the chronicity of headaches, learning life-long skills in headache management during childhood are important. Although pharmacological approaches remain the main treatment for frequent and/or severe headaches, many families find medication alone to be inadequate. Generally, group interventions in headache management using psychological approaches have mixed results. One of the limitations of the evaluation of treatments is that the outcome measure is usually focused on the frequency of headaches. Few studies of group treatments have evaluated how the young person is affected by their headache.

Methods Eight patients (four boys and four girls; age 11–15) with a diagnosis of migraine / chronic daily headache attended six, monthly sessions. Sessions aimed at developing headache management and enhancement of quality of life. Individual sessions focused on psychoeducation about headache, relaxation, imagery, stress management and management of headaches at school. Groups lasted 90-minutes and were facilitated by a clinical psychologist. A single-group session was attended by parents. Measures relating to the affects of headaches on the patient's life were completed pre/post intervention by five patients.

Results The rating scales indicated that four of the five patients reported that they could manage their headaches better following the group and that the headaches had a lesser affect on their lives. Feedback from patients showed that they valued learning strategies to cope with headaches in addition to meeting other people with headache.

Conclusions A group intervention was designed for young people with chronic headache drawing on the broad literature in this field. The current evaluation is limited by sample size but suggests that such interventions have a positive affect on quality of life.

TWO-DAYS EDUCATIONAL PROGRAMME INCREASES DIAGNOSTIC ACCURACY IN PRIMARY HEADACHES: A PROSPECTIVE STUDY

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Headache diagnosis and treatment can be managed by general practitioners (GP) in primary care settings. The objective of this study was to investigate the effects of 2-days headache GP education programme primarily on the diagnostic accuracy. Two-days education programme included theoretical lectures and face to face practice with the patients with headache specialists. Three GPs evaluated headache patients before and after the education. Each GP planned to interview with a total of 60 (30 before, 30 after the education) patients. All patients have been evaluated by headache specialists following GP interview. A total of 189 patients included into this study. Diagnostic accuracy increased from 56.3% to 81% ($p < 0.001$). Headache education programme also significantly improved proper treatment ($p = 0.043$). It has been shown that overdiagnosis of migraine has dropped from 42.1% to 15.8%. Headache education programme showed significant improvement in diagnostic accuracy and proper treatment in primary headaches. The programme has also decreased the overdiagnosis rate of migraine. Such headache education programmes can be standardized and given to the primary care setting GPs. Local headache education programmes arranged by the local universities might have a favourable effect on the diagnosis and treatment of headache.

ID MIGRAINE TM IS A VALID SCREENING TEST FOR ADOLESCENT MIGRAINE

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IHS noted only two differences between adolescent and adult migraine; i) the lower limit of duration might be shorter (1–72 hours), ii) migraine headache might be commonly bilateral in adolescents and children. The three questions of ID Migraine™ which has been improved for adult migraineurs, do not include any questions about these two characteristics of migraine. Therefore, we suggest that ID Migraine™ can also be used in adolescents as a screening tool. The objective of this study was to investigate the validity of ID Migraine™ in a large, school based adolescent student population. The study was conducted among 1064 12–17 years-old adolescents in the secondary schools of central city of Bursa. In phase I; 17-item questionnaire was answered by all of the students. In phase II; three different investigators conducted a face to face semi-structured interview with all the students with headache and made a final diagnosis. In phase III; all recurrent headache sufferers with one or more headache during the last three months were given the Turkish version of the ID Migraine™ test. Of 1,064 students who have completed ID Migraine™, 50 were excluded due to inadequate data quality so 1,014 subjects have been analysed. ID Migraine™ revealed a sensitivity and a specificity of 62.1% and 71.1% respectively. Sensitivity was higher for migraine with aura (71.1%). Disability showed the highest sensitivity (67.2%) for migraine sufferers out of three ID Migraine™ items. The highest specificity was for nausea (80.4%) for migraine. Girls and younger adolescents had a higher sensitivity than boys and elder adolescents. Specificity of ID Migraine™ was higher for boys and elder adolescents. ID Migraine™ is a useful and valid screening tool for adolescent migraine headaches in large scale adolescent student populations and might increase the awareness, proper diagnosis and treatment of migraine during the early periods of life.

COMPARISON BETWEEN TASTE TEMPERAMENTS OF PATIENTS WITH MIGRAINE WITHOUT AURA TYPE HEADACHE WITH NORMAL HEALTHY PEOPLE: A PILOT CASE-CONTROL STUDY

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Background Taste temperaments as hypothalamic body control-and-response function giving us information about basic intrinsic or externally-imposed changes in normal living functions, could be considered as a basic parameter in classification and approach to such intricate diseases as chronic headaches.

Materials and Methods Twenty-one patients with chronic headaches already diagnosed as having migraine without aura and 22 age, gender and socioeconomic level matched, healthy, headache-free control subjects were selected for the study. A 29-item Intention-to-Use questionnaire was applied to all participants to evaluate their taste interests for sweet, bitter, salty, sour, and pepper tastes; and headache patients also instructed to complete another disease intensity questionnaire.

Results Two separated groups could be detected in control group as sweet-sour temperament with ($n=9$) and without ($n=13$) phobic behavior to some distinct tastes, while temperaments in headache patients have had different pattern as three groups detected as sweet-sour temperament with distinct phobic behavior to some tastes ($n=9$), sweet temperament without any phobias ($n=8$) and strong interest to sour taste without any phobias ($n=4$). There was no significant correlation between disease intensity scores and the latest temperament ($r=0.02$, $p=0.10$).

Conclusions Taste temperaments could give us basic assessment of idiopathic diseases like chronic headaches, but more investigations still to be needed.

CLINICAL EVOLUTION OF HYPNIC HEADACHE

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Background and aims Hypnic Headache (HH) is a primary headache, which occurs exclusively during sleep. The natural history of HH is not well known. It is assumed that it tends to be chronic unremitting, but only 25 patients have been observed for at least 2 years. To better comprehend the outcome of HH, we have prospectively followed 8 patients for a period ranging from 2 to 6 years.

Results We diagnosed 8 cases (7 females and 1 male) with HH. The mean age of the patients was 67.9 ± 7.3 years (range 53 to 76), while the mean age at onset was 62.5 ± 5.8 years (range 51 to 70). Four patients (3 females and 1 male) showed an episodic pattern, with active periods followed by complete remissions. Two of these patients were treated successfully with lithium and caffeine, remained pain free after the treatment was tapered, but relapsed afterwards. The remaining two patients presented only a single active period up to now, lasting 4 and 8 months respectively, with a subsequent spontaneous remission. The other four cases had a chronic headache from onset. In two cases the nocturnal headaches responded to lithium and caffeine at bedtime, but any attempt to discontinue the drugs resulted in the recurrence of the attacks. A patient did not respond to any treatment (lithium, caffeine, indomethacin and verapamil). In the last case verapamil and caffeine were only partially effective.

Conclusions In view of our findings we propose that HH be divided in two subtypes, chronic and episodic. We suggest that episodes of this disorder with remission periods of ~; 1 month should be denoted by the term 'episodic HH' and for those patients who have not experienced a remission over a period of at least 1 year, the disorder should be called 'chronic HH'.

NEW BETABLOCKER IN PROPHYLAXIS OF MIGRAINE - EFFICACY AND SAFETY OF NEBIVOLOL VS METOPROLOL

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Background and aims Migraine prophylactic efficacy of oral treatment with Nebivolol (5 mg/d), compared to Metoprolol (142.5 mg/d) was evaluated in a phase III, randomised, double-blind, parallel-group, monocentre study.

Methods 30 patients with migraine, with an average migraine frequency of at least 2 attacks per month within the last 3 months were included. Treatment consists of 4 weeks run-in period, 2 weeks up-titration (Metoprolol only), 14 weeks treatment on full dose, 2 weeks down-titration. Primary endpoint was the frequency of attacks within the final 4 weeks under Nebivolol in comparison to Metoprolol. Secondary endpoints were responder rate, duration and intensity of attacks, MIDAS questionnaire, CGI, incidence of adverse events.

Statistics Frequency tables were compared between both groups by using Fisher's exact test versus a generalized Fisher test. Mean values were compared between both groups by using the Wilcoxon Mann Whitney U-test.

Results Nebivolol is equally effective in the reduction of the frequency of migraine attacks as Metoprolol. Both medications reduce the number of attacks to approximately 50% of baseline. An overall increase in the responder rates for approximately 12 to 14% within the treatment period could be observed in both groups. The percentage of patients who experienced very good therapeutic efficacy after 16 weeks of treatment under full dose of medication was clearly better for the Nebivolol group than for the Metoprolol group.

Assessment of the therapeutic risk clearly shows that Nebivolol is superior to Metoprolol. A higher total number of AEs was reported for the Metoprolol group as compared to the Nebivolol group.

Conclusions Both substances applied in this clinical trial were highly effective in prophylactic treatment of migraine. Nebivolol is equally effective in the reduction of the frequency of migraine attacks as the Metoprolol. Nebivolol seems to be an effective drug for migraine prophylaxis.

MIGRAINE PATIENTS THERAPY EVALUATION OF MOSCOW CITY POPULATION IN RUSSIA

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Background Migraine is most important and widely spreading form of headache. Migraine is very actual and social disease that acts the young, work-activity people population group of people. This is the case of the great economical deficit of the whole population.

Objective Using by the original evaluation inventory to assess direct and indirect costs of migraine therapy.

Methods The value of Migraine therapy was studied by specific evaluation inventory, which consist of 4 parts: 1-social-demographically part (passport data, anamnesis, demography factors); 2- asking for medical aid (taking medications, specialists consultations); 3-migraine influence on the patients quality of life, 4-pharmacoeconomy analysis questions (direct and indirect costs).

Results Mean patients age was 38 years. Female patients consist of 80% of whole group. More than 50% patients have high education. Mean monthly income was 200 USD. Patients didn't have any tax and medical insurance refunds. Most of patients were outpatients; they didn't have free care and pay directly to their doctor 21 USD in average. Migraine patients asking for neurologist or general practitioner 6 time a year in average. Doctors prescribed medications during 1-2 months a year. Transport expenses patients paid by themselves, they consisted of 2 USD using by public transportation for one doctors consultation.

Conclusions Migraine is expensive and important social disease. Patients don't have medical insurance and paid occasionally directly by themselves for their consultations and medications. Their direct and indirect costs were consisted of 30% of full year patient's income.

DEPRESSION, ANXIETY, STRESS, INSOMNIA IN MIGRAINE

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Background and aims Migraine is a chronic process, it has an episodic course with asymptomatic phases among crisis, in which headache is the main component. Migraine is often associated other processes: depression, anxiety, panic between others. Our goal is to determine the migraine's profile in a Neurologic consultation of the University Hospital of Salamanca, and the frequency of depression, anxiety, stress and sleeping disorders in migraine.

Methods 155 patients (36 men and 119 women) were studied in an external consultation of Neurology during the year 2005, age between 15 and 75 years. We followed a diagnostic criteria according to the Headache Classification of International Headache Society, IHS, and classification of Mental Disorders, DSM IV. In statistical analysis, frequencies and means of the different parameters were calculated; and relative risks, RR, with 95% confidence intervals, CI, between some variables.

Results The mean age was 36 years (34 years in men and 37 years in women), 99 had migraña without aura and 56 with aura (visual

and sensitive symptoms, and dysphasia, basilar migraine) and retinal migraine. 50.97% of the patients had stress, dream upheavals 37.42%, depression 27.74% and anxiety 21.94% and one of them 60%. Anxiety and stress were more frequent in migraine with aura, though there were no statistically significant differences (RR 1.42, 95% CI 0.92–2.20; 1.38, 0.90–2.12 respectively), nondifferences in depression and insomnia. For gender: depression and insomnia were more frequent in women than in men, difference not statistically significant (RR 1.30, 95% CI 0.95–1.34; RR 1.131, 0.95–1.34), nevertheless anxiety and stress were similar in both genders.

Conclusions Depression, anxiety, stress and insomnia are frequently associated processes to migraine that they condition the evolution and the election of the preventive treatment.

INCREASED RISK OF MIGRAINE IN MARFAN SYNDROME

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Background and aims To study the prevalence of migraine in Marfan syndrome. **Methods.** The patients were recruited from Landsforeningen for Marfan syndrome, a patient organization. A total of 46 persons were eligible for a validated semi-structured telephone interview by a physician trained in headache diagnostics.

Results The prevalence of migraine without aura was 13% among men and 40% among women. The prevalence of migraine with aura was 44% among men and 37% among women. The overall prevalence of migraine was 63% with an equal sex ratio. This corresponds with a 3.6- and 2.0-fold significant increased risk among men and women, respectively, compared with the general population. Analysing the different migraine characteristics showed that unilateral pain location and pulsating quality were 33% less frequent in those with Marfan syndrome compared with migraineurs from the general population. Otherwise the frequencies of the different migraine characteristics were similar in the two groups. The prevalence of tension-type headache in Marfan syndrome was higher in men and lower in women than found in the general population. One man and a woman had postural headache a few days per year, and two men and three women complaint about pain in their temporomandibular joint when chewing, and one man and three women had had headache due to rhinosinusitis.

Conclusions The high prevalence and equal sex ratio of migraine is puzzling and likely to be secondary to Marfan syndrome.

A POPULATION BASED STUDY OF INFREQUENT, FREQUENT AND CHRONIC TENSION-TYPE HEADACHE IN ADOLESCENTS AND ADULTS

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Background and aims To evaluate the one-year-period prevalence of tension-type headache in a large population based sample.

Methods. The study population included 33,764 twins aged 12 to 41 years old from the population based new Danish Twin Registry. They received a posted headache questionnaire.

Results The questionnaire response rate was 83.5%. The questionnaire has previously been evaluated against a clinical interview by a physician, and Kappa was 0.74 and 0.77 for self-reported tension-type headache and frequency of tension-type headache, respectively. All twins were included since we found no significant difference between mono- and dizygotic twins or between twin A and B. The self-reported one-year-period prevalence of tension-type headache was 86.0%; 78.9% among men and 92.5% among women. The one-year-period prevalence of infrequent episodic, frequent episodic and chronic tension-type headache was 63.5%, 21.6% and 0.9%, respectively. Frequent episodic and chronic tension-type headache was significantly more frequent in women than men. The prevalence of frequent episodic tension-type headache increased slightly in men until age 39 then it declined, while it increased about 20% point in women from age 12 years to age 20–39 years old and then it declined. Congruently, the prevalence of chronic tension-type headache increased until age 39 and declined thereafter in both sexes. Chronic tension-type headache is rare in persons 12–14 years old. These effects were confirmed by age trends of the different subtypes of tension-type headache using a regression model.

Conclusions Tension-type headache is very frequent and more attentions should be directed toward management and research of this type of headache.

COMETE: A PROSPECTIVE SURVEY TO ASSESS THE RELATIONSHIP BETWEEN PREMENSTRUAL SYNDROME AND MENSTRUAL MIGRAINE

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Introduction Menstrual migraine (MM) attacks appear to be triggered by a hormonal factor. Their relationship with premenstrual syndrome (PMS) is debated. **Objective** To assess prospectively the frequency of PMS among migraineurs, and analyse its distribution according to the presence or not of menstrual migraine attacks.

Methods Prospective survey where 152 neurologists included menstruated migraineurs according to the IHS criteria. Each patient had to fill out a questionnaire during 2 consecutive menstrual cycles. PMS was defined as the association of a somatic symptom (tender breasts, bloating, general swelling) and a psychological symptom (depression, irritability and anxiety) starting during the 3 days preceding the menses and ending within 4 days after their beginning.

Results Among the 635 participating migraineurs, 404 returned a completed questionnaire. Twenty patients (5%) had a PMS, and 334 women (83%) had MM attacks; 319 participants (79%) had menstrually-related migraine (attacks both related and unrelated to menses) and 15 women (4%) had pure MM (attacks exclusively related to menses). There was no difference in the distribution of PMS among women with MM attacks (17 patients, 5%) and those without MM attacks (3 patients, 5%).

Discussion In this survey no correlation was found between PMS and menstrual migraine. These results could be explained by a lack of statistical power due to the low prevalence of PMS in our population. This low prevalence may result from the use of a strict definition and the high proportion of women under oral contraception.

Conclusions This prospective survey performed among migraineurs showed a high prevalence of MM and no relationship between premenstrual syndrome and menstrual migraine.

IS IT A RATIONAL CHOICE TO TREAT WITH LUMBAR EPIDURAL BLOOD PATCH HEADACHE BY SPONTANEOUS CERVICAL CSF LEAK?

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Objective To evaluate the spread of blood injected into the epidural space during lumbar epidural blood patch (LEBP) for treatment of spontaneous cervical CSF leakage (SCCSFL) by MRI. **Background** Spontaneous intracranial hypotension generally results from spinal spontaneous CSF leakage. Treatment is usually conservative. Sometimes an autologous EBP at the site of CSF leak may be necessary.

Materials and methods We report one case of SCCSFL [among the 32 with this condition evaluated between 1992 and the present].

Results A 45-year man presented sudden, intense, gravative fronto-occipital orthostatic headache. Neurological examination, blood routine tests, and a brain CT were normal. A brain MRI showed diffuse pachymeningeal enhancement. Gadolinium spinal MRI shows CSF epidural collection from C2 to D3 level. After one month of bed rest, orthostatic headache was still present. The pt was treated with autologous lumbar EBP (25 mL) at L2-L3 level. The blood was mixed with 0.05 mL of gadolinium. During and after injection, he remained in Trendelenburg position (TP) approximately 30° for 1 h. Spinal post-patch MRI showed gadolinium mixed with blood in the epidural space from the lumbar level to cervical level (C2-C3). He subsequently remained in TP for 22 hours. He was asymptomatic within 24 hours after LEBP. At 6 month follow-up he was asymptomatic.

Conclusions We demonstrate that EBP, even though injected at the level of lumbar spine (i.e., far from the site of CSF leak), may move upward reaching the cervical segments. This is possibly favoured by TP. So a rapid coagulation response at dural hole level stops CSF leakage. Thus, EBP at the level of the cervical spine, where the procedure is hard to be attempted, may be not necessary. This, at our knowledge, is the first report that shows the spread of blood from lumbar to cervical epidural space with LEBP.

HEADACHE, ANXIETY, DEPRESSION AND ESTROGEN DEFICIENCY IN PATIENTS WITH LEIOMYOMA OF UTERUS

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Aim of investigation Clinic of leiomyoma of uterus involves not only gynaecological but also cumulative somatic and psychical abnormalities. Very often women having leiomyoma of uterus suffer from chronic headaches. The aim of our investigation was to study mechanisms of such headache.

Methods Gynaecological examinations, hormone control and psychological testing, standardized estimation of somatic status.

Results 170 patients with leiomyoma of uterus have been investigated. The age of the patients was from 30 to 49 years old. All patients have been hysterectomy operated: the 1st group (84 patients) had radical surgery (RS); the 2nd group (86 patients) had reconstructive plastic surgery (RPS). Before surgery 46 patients (27.1%) suffered from chronic headache and had high levels of anxiety and depression. In a year repeated inspections detected that 42 patients (24.7%) had chronic headache, at that 32 patients had RS. Before operation hormone control showed hyperlevel of estrogens and reduced level of progesterone for all patients. After operations the 2nd group patients had a normal level of estrogens but 66 patients from the 1st group had estrogen deficiency. After operation

in most cases patients suffering from chronic headache belong to the 1st group, that headache is redoubled by anxiety and depression.

Conclusions The estrogen deficiency is the important part of pathogenesis of headache, anxiety and depression in patients with leiomyoma of uterus before and after surgical operations.

THE HEADACHE LEGACY OF EL ZAHRAWI OF CORDOBA

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El Zahrawi (936–1013), one of the great pioneers of surgery, was born in the district of Cordoba, and practiced as a physician in that city. He was arguably the most famous medical practitioner of his time, and his works were translated into many European languages. Through these translations he had an enormous influence in the later development of European Medicine. What is not commonly known is that El Zahrawi was the first person to describe and record the sectioning of the temporal artery for vascular headache. The next time this procedure was mentioned was 500 years later by Ambroise Pare, who sectioned his own temporal artery for migraine. Since then the procedure has been described many times between 1945 and 1989 for the treatment of vascular headache. 53 patients diagnosed with Chronic Daily Headache are presented who were treated during 2001 by section of superficial scalp vessels. A four-year review showed that 32 subjects (60%) no longer needed to use analgesics, 10 (19%) significantly reduced their analgesic intake, and 11 (21%) were unchanged.

TREATMENT OF CHRONIC TENSION-TYPE HEADACHE WITH AN INTRA-ORAL ORTHOSIS

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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 (ie, 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 intra-oral 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 a palatal speech adjusted intra-oral orthosis would be of value in the treatment of CTTH. Pre- and post-treatment quality of life scores were obtained from 38 CTTH patients, who were treated with an intra-oral orthosis. Post-treatment quality of life scores were significantly better than pre-treatment scores. It was concluded that the palatal speech adjusted intra-oral orthosis is a valuable tool in the treatment of CTTH.

COMPARISON OF MIGRAINE ACT AND MIDAS QUESTIONNAIRES IN MIGRAINE PATIENTS FOLLOWED UP FOR UP TO 3 MONTHS

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Objective To assess the Migraine Assessment of Current Therapy (MACT) responsiveness vs MIDAS in migraine patients followed up for up to 3 months.

Methods Validated Spanish versions of the MACT and MIDAS questionnaires were administered to IHS diagnosed migraine patients at baseline and at 3 months. Investigators were free to change the baseline treatment according to the initial MACT score. Patients were stratified according to baseline MACT score. Satisfaction with medication at baseline and at 3 months was measured on a 7 point scale. Validity indices (sensitivity/specificity) and AUC [95%IC] for change in treatment at baseline or improvement in patient satisfaction at 3 months vs improving the MACT (>1 point) or MIDAS (>4 points) score at 3 months were calculated by using a ROC curve analysis.

Results 3272 patients (78% female) fulfilled the inclusion criteria, signed a written consent and completed the study. Baseline mean MIDAS values (by MACT score 0–4) were: 29(0), 24(1), 21(2), 17(3) 13(4). Investigators modified baseline treatment in (by MACT score): 95%(0), 88%(1), 78%(2), 49%(3), 15%(4) of patients ($p<0.001$). Overall, baseline treatment was modified in 66% of patients. Eighty-five and 80% of patients that were changed the baseline treatment improved in their MACT and MIDAS score at 3 months, respectively. Satisfaction with therapy (% completely or very satisfied) increased from baseline (15%) to the end of the study (49%). Sensitivity, specificity and AUC for baseline treatment change vs. MACT {or MIDAS} were 85% {75%}, 72% {58%}, 0.84[0.82, 0.85] {0.7[0.68, 0.72]}; $p<0.001$. Sensitivity, specificity and AUC for improvement in patient satisfaction vs. MACT {or MIDAS} were 83% {75%}, 72% {58%}, 0.82[0.81, 0.84] {0.7[0.69, 0.73]}; $p<0.001$.

Conclusions Baseline treatment change and improvement in satisfaction at 3 months were more strongly associated with changes in MACT than with changes in MIDAS. Study funded by MSD Spain

PREDICTIVE MODEL FOR THE MIGRAINE ACT QUESTIONNAIRE IN PRIMARY CARE

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Objective To establish a predictive model for the Migraine Assessment of Current Therapy (MACT) questionnaire in a primary care setting.

Methods A validated Spanish version of the MACT questionnaire was administered to IHS diagnosed migraine patients at baseline and at 3 months. Investigators were free to change the baseline treatment according to the initial MACT score. Patients were stratified according to baseline MACT score. Odds Ratios [95%CI] for improving at least 1 point in the MACT score at 3 months for patients changing baseline treatments versus patients not changing treatment were calculated using a logistic regression model adjusted for baseline disability, sex, age, attack frequency and duration, baseline treatment change and MACT. Satisfaction with medication at baseline and at 3 months was measured on a 7 point scale.

Results 3272 patients (78% female) fulfilled the inclusion criteria, signed a written consent and completed the study. Baseline percent patients (by MACT score) were: 23%(0) 18%(1), 21%(2), 15%(3) 23%(4). Baseline treatments were analgesics (61%), metamazol (36%), NSAIDs (51%), ergots (25%) and triptans (24%; $p<0.001$

Pearson Chi-square). Investigators changed baseline treatments in (by MACT score): 95%(0), 88%(1), 78%(2), 49%(3), 15%(4) patients ($p<0.001$ Pearson Chi-square). Overall, baseline treatment was changed in 66% of patients. The adjusted likelihood of improving 1 point in the MACT score was 3.6 times greater among patients who changed treatment than those who did not (85% vs 28%; OR 3.3 [2.4–4.6] $p<0.001$). The model yielded a 86% sensitivity and 85% specificity to detect a 1 point change in MACT score at 3 months ($p<0.001$). Patient satisfaction with therapy (% completely or very satisfied) increased from baseline (15%) to the end of the study (49%).

Conclusions The MACT questionnaire is a sensitive and specific tool to detect improvements due to changes in treatment. Study funded by MSD Spain

OPHTHALMOPLAGIC MIGRAINE: REVIEW OF FRENCH CASES ACCORDING TO THE INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS II-2004

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Background Ophthalmoplegic migraine (OM) is a rare disease, recognized by the ICHD-II into the category of cranial neuralgias and central causes of facial pain. Firstly considered as a variant of migraine, ICHD-II have suggested that it could be an inflammatory and transitory cranial neuropathy considering recent MRI data.

Objective We propose to review cases identified as OM into database of the "Observatoire des Migraines et Céphalées" set up by the French Headache Society. Among more than 35000 cases of headache patients in this database, between October 2002 to December 2005, 9 cases identified as OM were retrospectively reviewed according to the diagnostic criteria proposed by the ICHD-II.

Results Nine cases were identified in 6 headache centres with a mean age of 36 years (16–74) with 7 women and 2 men. All patients suffered from migraine with or without aura and 60% have familial history of migraine. Seven patients have had more than two attacks of cranial nerve palsy and two only one. The delay between cranial palsy and headache was known in 7 cases. The third nerve was concerned in 55% of patients. Brain Ct-Scan or MRI performed in 8 cases was normal. The paralysis of the cranial nerve was reversible in all cases with or without treatment.

Conclusions This study confirms the rarity of the OM and put several questions. Two of our patients have suffered from only one attack of OM but as no other causes of cranial palsy were disclosed we classify them as OM. This possibility should be offer in ICHD-II because some patient have only one attack during several years. The ICHD-II does not recommend preferring MRI than Ct-Scan to eliminate a differential diagnosis in spite of their different interests in an anatomical way. We propose a review of the knowledge of OM in 2006.

OUTPATIENT ERGOT ALTERNATIVES WHEN PROPHYLAXIS AND/OR TRIPTANS FAIL

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Background Usage of ergot preparations has declined dramatically since the advent of triptan medications due to overwhelming evi-

dence that triptans are more effective and better tolerated than ergots. Clinical trials and anecdotal evidence, however, show that 30% of patients are triptan nonresponders.

Objective To describe the effectiveness of a combined ergot alternative (ErgoPak – TM) in the outpatient treatment of migraine headache in patients for whom standard regimens for prophylaxis and/or triptans were ineffective.

Methods A retrospective chart review was performed on 15 headache patients with definite common and classic migraine headache. The patients had failed triptan and/or prophylactic regimens. All patients were placed on an outpatient regimen of ergonovine maleate, daily; and dihydroergotamine mesylate (DHE) injectable, and DHE nasal spray, as needed. Some patients were placed on a new prophylactic regimen but none continued triptan therapy.

Results Of 15 charts reviewed, 10 patients had failed triptan therapy due to lack of efficacy and/or lack of tolerability. Twelve patients failed attempts at prophylaxis. Eight patients had failed both triptan therapy and prophylaxis. It appeared subjects reviewed also had problems with rebound headache. All 15 patients were placed on the above-mentioned regimen. Ten patients used DHE. All patients experienced at least a 50% reduction in headache frequency and severity.

Conclusions Ergonovine prophylaxis with intermittent DHE nasal spray and DHE injectable (ErgoPak – TM) is a viable outpatient approach in patients refractory to other prophylactic regimens and/or triptans.

THE IMPACT OF GENDER ON MIGRAINE

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Background The biological differences in hormonal status of males and females is the most popular explanation for higher prevalence of migraine in females. But the contribution of gender has not been adequately studied. The aim of our study was to explore the impact of gender on migraine without aura.

Methods Neurological examination, RIII reflex method, Spielberger anxiety and Beck depression scale, quality of life questionnaire were applied to 24 male and 86 female migraineurs. All patients were compared after being divided into 6 groups (feminine females, masculine females, masculine males, feminine males, androgynous (high level of masculinity and femininity) and nondifferentiated (Ndf) group (low level of masculinity and femininity) according to their femininity/masculinity index (Bem Sex Role Inventory).

Results The dominance of feminine and Ndf patients was characteristic for the investigated group. Feminine and Ndf patients more often presented prodrome and postdrome symptoms, more often experienced night attacks, fonophobia and vertigo. Pain thresholds were lower in feminine and Ndf groups. Anxiety and depression level were higher among feminine and Ndf migraineurs. Gender did not influence the total score of quality of life decrease. Although the impact of socio-cultural factors on the level of disability was specific depending on the gender characteristics. For feminine females marital dissatisfaction, decrease in ability to perform household tasks and low sexual activity brought to the highest disability rate. For masculine males professional dissatisfaction, loss of self control were also important. For androgynous patients decrease in social activity was specific.

Conclusions Feminine gender characteristic may be partly responsible for higher prevalence of migraine in females. Femininity and Ndf are associated with more pronounced clinical, neurophysiological and affective derangements in migraine. The impact of socio-cultural factors is gender specific. Thus, the gender characteristic should be taken into consideration in migraine treatment design.

EFFECT OF PARACETAMOL ON CORTICAL SPREADING DEPRESSION AND TRIGEMINAL NOCICEPTION

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Background and aims Previous studies have shown that acute administration of non-narcotic analgesics, including paracetamol can decrease the density of 5-HT₂ receptor in cerebral cortex. This receptor down-regulation may involve in the anti-nociceptive mechanism of these drugs by attenuating the cortical excitability. The present study was conducted to determine whether acute paracetamol administration can alter the development of cortical spreading depression (CSD) and CSD-evoked trigeminal nociception.

Methods Adult male Wistar rats were separated into paracetamol and control groups (10 rats each). Paracetamol (400 mg/kg body weight, intraperitoneally) was given 30 minutes before CSD induction. Saline of the same volume was given to the control rats. CSD was elicited by cortical application of 3 mg of solid potassium chloride. Electroencephalogram was continuously recorded for one hour. Trigeminal nociception was determined using number of Fos-immunoreactive (Fos-ir) cells in trigeminal nucleus caudalis as an indicator.

Results Shortly after application of potassium chloride, the cortical recording revealed a series of depolarization shift characteristics of CSD. Pretreatment with paracetamol did not alter this CSD development. The sum of area-under-curve of all CSD waves observed in one hour period in the paracetamol and control groups were 768.9 (153.1) and 809.7 (110.9) mV•minute, respectively ($p=0.653$). Despite no effect on CSD development, pretreatment with paracetamol significantly decreased the number of Fos-ir neurons in trigeminal nucleus caudalis. The numbers of Fos-ir cells in paracetamol and control groups were 18(6) and 33(6) cells per slide respectively ($p=0.002$).

Conclusions The present study showed that the mechanism by which paracetamol attenuates the CSD-evoked trigeminal nociception is unlikely to be secondary to the modulation of cortical excitability.

MODULATION OF NITRIC OXIDE MAY INVOLVE IN THE ANTI-NOCICEPTIVE MECHANISM OF PARACETAMOL

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Background and aims Nitric oxide (NO) is an important transmitter in the pain system. Activation of NO is involved in the process of neuronal sensitization in the trigeminal nucleus caudalis (TNC). This study aimed at investigating whether anti-nociceptive effect of paracetamol on cortical spreading depression (CSD)-evoked trigeminal nociception involves the modulation of the NO system.

Methods The experimental animals comprised two groups of adult male Wistar rats, namely paracetamol and control groups (12 rats each). Rats in the first group received paracetamol (400 mg/kg BW, intraperitoneally) 30 minutes before CSD induction whereas saline of the same volume was given to the control group. Three milligrams of solid potassium chloride was applied on parietal surface in order to elicit the CSD. Two hours after CSD induction, rats were killed and brainstems and cervical cords were removed for Fos and nitric oxide synthase (NOS) immunohistochemical studies. Fos- and NOS-immunoreactive cells in TNC were counted.

Results Application of potassium chloride can activate the trigeminal nociceptive system as evidenced by an increase in the number of Fos- and NOS immunoreactive cells in the TNC. The numbers of Fos- and NOS-immunoreactive cells were significantly correlated ($r=0.694$, $p=0.001$). Pretreatment with paracetamol significantly attenuated the degree of CSD-evoked trigeminal nociception. The numbers of Fos-immunoreactive cells in paracetamol and control groups were 17(5) and 34(5) cells per slide, respectively ($p=0.001$). Number of NOS-immunoreactive cells was also significantly lower in the paracetamol group compared with the control group (20(7) and 42(9) cells per slide for paracetamol and control groups, respectively, $p<0.001$).

Conclusions The present study showed that paracetamol can attenuate the CSD-evoked trigeminal nociception as well as minimise the expression of NOS in the trigeminal system. Therefore, attenuation of the NO system may involve in the anti-nociceptive effect of this drug.

TREATMENT OF HEMIPLEGIC MIGRAINE WITH TRIPTANS: A RETROSPECTIVE STUDY OF TOLERABILITY AND EFFICACY

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Background and aims The objective of this study was to investigate the efficacy and tolerability of triptans in patients who suffer familial (FHM) or sporadic (SHM) hemiplegic migraine. Triptans are contraindicated to them, because of suspicion that triptans might enhance the risk of ischemic stroke.

Methods Subjects have been selected from the Finnish Migraine Gene Project database and they fulfil the IHS criteria of FHM or SHM and have used triptans at least once as an abortive treatment in migraine attack. Subjects have fulfilled the questionnaire and systematically interviewed by telephone and headache response with triptans and treatment related adverse events were rated on a scale from 0 to 10 (no response or side effect 0, excellent response or unbearable side effects 10). Subjects were also asked to define possible side effects and cardiovascular risk factors more precisely.

Results We found 73 patients (65 females) with hemiplegic migraine who have used triptans at least once as an abortive treatment. Mean age was 43.3 (SD±11.5). 39 patients from 29 families had FHM. 37 patients (50.7%) had also basilar type migraine symptoms. Patients had used an average 260.2 (SD±452.7) times triptans. Average triptan response was 7.1 (SD±2.9) and adverse event severity 4.9 (SD±3.4). None of them had an ischemic stroke or a heart attack. One patient reported prolonged neurological symptoms (dizziness, ataxia, visual disturbances, hemiparesis) related to a single dose of rizatriptan, but there was no pathological findings in MRI and there was dramatic relief in symptoms after 3 months when acetazolamide was started.

Conclusions Triptans seem to be safe and effective treatment for most patients who suffer hemiplegic migraine. Of 73 patients only one reported a possible serious adverse event, however, the role of rizatriptan remains unclear.

THE FREQUENCY OF NEUROIMAGING REQUESTS IN HEADACHE PATIENTS APPLYING TO PRIMARY, SECONDARY AND TERTIARY LEVEL HOSPITALS

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Background and purpose Headache is the most frequent complaint in neurology outpatient clinics. We investigated the frequency of

neuroimaging requests in headache patients attending to different levels of hospitals. These units consisted of a primary care unit, an outpatient clinic in secondary level hospital and a headache outpatient clinic of a teaching hospital.

Methods A total of 500 patients with headache and a normal neurological examination were included. The medical records and cranial images were retrospectively reviewed. The patients were classified according to International Headache Society (IHS) criteria. The results of neuroimaging procedures, (computed tomography and magnetic resonance imaging) were evaluated according to the relation with headache. Multivariate analysis with a linear logistic regression technique was performed on the clinical data, which included patient age, sex, headache type, headache age and pain duration.

Results The percentage of secondary headache in primary level was 16.3%, in secondary level 12.3%, and in tertiary level 7%. Migraine and drug abuse headache was statistically significantly higher in the tertiary unit. Neuroimaging was performed in 24.3% of patients attending to primary, 30% of secondary and 62.1% of tertiary level units. Imaging results in patients presenting to secondary and tertiary units revealed statistically significant more nonspecific changes compared to results of procedures performed in primary care units. In all three level units, the percentage of imaging results explaining the headache showed no statistical difference (2.1%–3.1%).

Conclusions The total number of major pathologic findings seen in neuroimaging procedures of headache patients are quite low. A careful history supplemented by a general and neurological examination can determine the headache type, and lower the number of unnecessary neuroimaging procedures. On the other hand, suspicion of an atypical headache should always lead to neuroimaging.

ALLODYNIA IN MIGRAINE. IS UNIFORM ITS PREVALENCE?

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Background and aims The prevalence of allodynia in migraine patients has been reported as very high. All the reported series are based on specialized headache clinics. We want to report allodynia's prevalence in migraine patients attending a non-specialized centre and a Primary Health centre. We also are interested in possible differences between allodynic and non-allodynic migraineurs.

Methods We made a very extensive structured survey to all consecutive migraine patients attending our Neurology-Headache unit (NHU) and a General Practitioner unit (GPU). We instructed patients in allodynic symptoms detection and gave them a form to register them in each migraine attack during 2–3 months. Afterwards, an statistical analysis was made to seek for differences between allodynic and non-allodynic migraineurs.

Results 71 patients completed the survey: 53 in NHU and 18 in GPU. 8 without attacks. 6 had chronic migraine. 47 were Migraine without aura (MO) patients, 24 Migraine with Aura (MA). Allodynia was found in 36.96% NHU patients and in 17.65% from GPU. Prevalence in MA patients was 42.86% and just 26.19% in MO. Patient's age at the beginning of migraine was 18.15 years (vs. 20.58) in allodynic migraineurs, and duration of illness 22.95 years (vs. 18.44). A trend to relationship was found between intensity of allodynic symptoms and their localization: as greater the intensity, greater the allodynic area.

Conclusions Allodynia seems less prevalent in migraine patients as they are less selected. Allodynia is more frequent in MA patients. Migraine patients with allodynic symptoms are younger at the beginning of the illness and also suffer it for longer time. Intensity and localization of allodynia seem to be related.

PREVALENCE OF ANXIETY AND DEPRESSION IN TENSION-TYPE HEADACHE

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Background Tension-Type Headache (TTH) is the most common reason of primary headache patients in the Republic of Belarus. Anxiety and depressive disorders are frequent the comorbidity in patients with TTH.

Aim Research of correlation of various clinical forms of TTH and anxiety and depression.

Methods 48 non pregnant women without previous psychiatric symptoms had TTH and going with The International Classification of Headache Disorders (2003). The mean age of the group was 28.4 years (ED: 4.4). Duration of TTH was 2.1 years (ED: 1.5). 56.5% had episodic TTH and 43.5% had chronic daily headache. Depression and anxiety were measured according Hamilton's Anxiety Rating Scale, Beck Depression inventory and Spilberger's test.

Results The great correlation between the duration of TTH and the Symptoms of the depression has been discovered ($r=0.61$) as well as between the episodic TTH and anxiety ($r=0.56$).

Conclusions TTH is most common among women. The anxiety and depression are usually concomitant TTH. The expression of these symptoms depends on the duration of the TTH and frequency of the headache.

INHIBITORY EFFECT OF L-NAME ON CSD-INDUCED TRIGEMINAL NOCICEPTION: VASCULAR VS. NEURONAL MECHANISM

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Background Nitric oxide (NO) has long been accepted to involve in migraine pathophysiology. The inhibition of NO production by the nitric oxide synthase (NOS) inhibitor is a possible alternative for the treatment of migraine headache. However the mechanism underlying the anti-migraine effect of NOS inhibitors is still unclear.

Objective This study was conducted to clarify whether the NOS inhibitor alters the cortical spreading depression (CSD)-evoked trigeminal nociception via the vascular or neuronal mechanism.

Methods Male Wistar rats were separated into the control, CSD and CSD with NOS inhibitor groups. Application of 3 mg potassium chloride on parietal cortex was used to induce CSD. N-Nitro-L-Arginine Methyl Ester (L-NAME) was intravenously injected into the rat in the CSD with NOS inhibitor group after the second wave of the CSD. Cortical blood flow (CBF) and pial arteriolar diameter were measured using laser Doppler flowmetry and intravital videomicroscopy. Cortical activity was monitored using glass microelectrode inserted in frontal cortex. Trigeminal nociception was determined by the number of Fos-immunoreactive neurons in the trigeminal nucleus caudalis.

Results Application of KCl induced the development of series of depolarization shift characteristics for CSD. In the vascular compartment the cyclical changes of CBF and arteriolar diameter were observed. Administration of L-NAME could minimize the amplitude of the hyperemic peak as well as the maximal vasodilatation of hyperemic cycles. The numbers of Fos-IR cells on ipsilateral and contralateral sides of the trigeminal nucleus caudalis were significantly lower in the CSD with NOS inhibitor group than that in the CSD group. No significant difference was observed when amplitude and area under curve of the depolarization shift were compared.

Conclusions The findings from this study indicated that the inhibitory effect of L-NAME on CSD-induced trigeminal nociception is mediated mainly on the vascular compartment.

HEADACHE REVEALING CEREBRAL VENOUS THROMBOSIS IN A PATIENT CARRIER OF BOTH METHYLENETHETRAHYDROFOLATE REDUCTASE C677T AND THE G20210A PROTHROMBIN MUTATION

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Background Headache in cerebral venous thrombosis (CVT) is the most frequent symptom, often the inaugural one, and it may appear in isolation. Here we report a case of CVT presenting as a new daily persistent headache and associated to familiar methylenetetrahydrofolate reductase (MTHFR)-C677T and prothrombin G20210A mutation as genetic risk factors.

Methods A 36-year-old woman suffered from a three month's history of new onset daily headache, right-sided, pressing, occasionally associated with vomiting and phonophobia, unresponsive to analgesics. Neurological examination was normal, except optic disk's nasal border blurring. The patient had been taking oral contraceptives because of an endometriosis. Also she had a daughter with thrombotic thrombocytopenic purpura.

Results Brain magnetic resonance angiography allowed visualization of the interruption of blood flow in the left transverse and sigmoid sinus with involvement of the jugular vein, which were consistent with the diagnosis of CVT. The parenchyma in MRI was unremarkable. Thrombophilia screening of the patient demonstrated heterozygosity for the G20210A prothrombin genotype and MTHFR-C677T homozygosity. We genotyped up to three members of the family (two daughters and a sister), finding a daughter heterozygous for the G20210A prothrombin mutation and all the three relatives showed homozygosity for the MTHFR-C677T variant. Anticoagulation was started and oral contraceptives discontinued in the patient, obtaining headache improvement.

Conclusions In general, we must suspect in any progressive headache of recent onset a secondary headache, which becomes necessary to investigate. In our patient, the primary etiology was an uncommon association of familiar MTHFR-C677T and prothrombin G20210A mutation causing a CVT.

YAWNING AS A SYMPTOM PREVIOUS TO A MIGRAINE CRISIS

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Introduction Yawning has always been considered as a premonitory symptom to a migraine crisis. The yawning symptom is not presently considered in the International Headache Society's classification [1]. While the mechanisms of this behavior are not completely known, it is known that it originates within the key structures of the nervous system: the paraventricular nucleus of the hypothalamus and the hippocampo [2]. Presently, in a group of patients who were studied, this symptom was presented with the clinical characteristics of an aura according to the International Headache Society's criteria.

Objective To determine if yawning before a migraine crisis can be considered as an aura.

Methods Ten patients, between 21 and 45 years of age, diagnosed as having migraine with visual aura and "yawning" were studied. Nine patients were female and one patient was male. The International Headache Society (2004) criteria were applied. Patients with epilepsy, cranial cephalic trauma, and cerebral vascular disease were excluded from the study. The duration of yawning in those patients oscillated between four and sixty minutes and was associated with fatigue, depression, temporo-mandibular joint pain, panic and fear of

not being able to control it. All patients were administered EEG and MRI and were reported normal. The MIDAS test showed incapacity of moderate to severe. Laboratory exams showed no alterations.

Results It was shown that yawning preceding a migraine crisis in the patients who were studied using the characteristics of duration and incapacity could be considered as a manifestation of unusual aura.

Conclusions Increasing the study group to determine if yawning in patients can be considered as aura is necessary.

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PECULIAR DEFENCE MECHANISMS OF MIGRAINE AND TENSION TYPE HEADACHE PATIENTS

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Objective This study represents a research contribution to the discussed issue concerning the identification of psychological variables in the headaches' aetiology, having particular regard to defence mechanisms.

Methods 110 unselected adult headache patients filled in, (93 ♀, 17 ♂; mean age 33years, range 19–51 years), from S.Charles Headache Centre. The experimental sample 83 migraine (72 without aura and 11 with aura), 27 TTH (15 chronic, 12 episodic) has been compared with a control group of 128 non-pathologic adults (79 ♀, 49 ♂; mean age 35years, range 20–54years). All the 238 subjects have been submitted to these psychometric tests: SCL-90-R, DMI-short version and DSQ-40.

Results Through the analysis of variance (Anova Between Groups, $p < 0.001$), the scores of the SCL-90-R show a higher number of general symptoms in the headache patients compared to the control group. For the scores at the DMI, the migraine patients (M) use projection to a far smaller extent. This finds an explanation in the rigid educational environment from where these patients are coming, such as to prevent the external expression of aggressiveness, and cause the patients to turn such aggressiveness against themselves. At the DSQ, the M appear to use anticipation more and dissociation to a far smaller extent. Such result confirms that M are able to remove emotional tensions from a somatic standpoint, for the purpose of showing themselves as affectively more pleasant. TTH patients avail themselves more frequently of annulment and to a smaller extent of suppression compared to the control group, since they are not able to remove problems and/or retain disturbing feelings.

Conclusions It is confirmed that headache sufferers show, in addition to specific psychological characteristics, peculiar defence mechanisms, which characterize them and distinguish them from the remaining part of non-pathologic population.

LACK OF ASSOCIATION BETWEEN THE HEMOCHROMATOSIS (HFE) GENE AND MIGRAINE

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Background and aims Several recent studies suggested that iron metabolism may be involved in migraine pathophysiology. The hemochromatosis (HFE) gene is located in 6p21.3 and encodes for a HLA class I-like molecule involved in iron regulation. Missense mutations in the HFE gene are responsible for the majority of

hemochromatosis, a disease characterized by excessive absorption of dietary iron and toxic deposition of this metal in several organs. The aim of this study was to evaluate whether the presence of HFE gene mutations would modify the occurrence of migraine.

Methods 256 consecutive unrelated migraine patients (98 men, 158 women; mean age \pm SD=40,3 \pm 9.4 yrs) were involved in the study. The diagnosis of migraine was made according to the IHCD-II criteria. 225 patients fulfilled the diagnostic criteria for migraine without aura and 31 for migraine with aura. A group of 237 sex, age and geographically matched healthy subjects (95 men, 142 women, mean age \pm SD=41.5 \pm 13.3 yrs) were used as controls. The C282Y and H63D mutations of the HFE gene were assessed with a single-stage PCR-based method followed by digestion with the restriction enzymes Rsa I and Mbo I.

Results No C282Y mutation both in migraine patients and in healthy controls was found. Allelic and genotypic frequencies of the H63D mutation were nearly identical between cases and controls (AF: $c_2=4.52$; $p=0.10$; GF: $c_2=2.53$; $p=0.28$). No significant difference between migraine with aura and migraine without aura patients was found.

Conclusions In this study of an Italian population we found no evidence of a genetic association between mutations of the HFE gene and migraine. Our results suggest that it is unlikely that genetic variations within the HFE gene greatly contribute to migraine susceptibility.

EFFECTIVENESS AND PATIENT SATISFACTION OF TOPIRAMATE TREATMENT FOR MIGRAINE PROPHYLAXIS

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Objectives Topiramate (TPM) is an effective treatment for migraine prophylaxis and nowadays is the only antiepileptic drug approved in Spain for this condition. We have evaluated treatment adherence, the impact of this treatment on migraineurs, and its effectiveness and safety on a real clinical setting.

Methods A multicentric, prospective, case record evaluation of ambulatory patients of migraine patients treated with topiramate for 6 months. Systematic evaluations at baseline and at month 3 and 6 were performed. We recorded treatment compliance, number of migraine days per month, Headache Impact Test-6 (HIT-6), patient-reported satisfaction level, weight, and spontaneous adverse events.

Results We evaluated 79 patients. Range of TPM dose was 25–200 mg/day (median, 100 mg/day). Twenty percent of patients withdrawn due to adverse events, none serious, and 6% due to lack of efficacy. A reduction $\geq 50\%$ in the number of migraine days per month was observed in 57% of our sample. There was a significant reduction on HIT-6 scores in 58% of our patients, from 63.7 at baseline to 49.4 at month 6, $p=0.017$. Weight reduction $>5\%$ was observed in 14% of our patients. Satisfaction level was graded as good by 80%, fair by 11% and bad by 9% of our sample.

Conclusions Prophylactic treatment with TPM for 6 months significantly reduces migraine impact and disability. There were no serious adverse events and the most frequent cause of withdrawal was the appearance of paresthesia. Most patients treated with TPM were highly satisfied with this treatment.

EFFICACY AND SAFETY OF ORAL ELETRIPTAN FOR THE TREATMENT OF ACUTE MIGRAINE IN ADOLESCENTS

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Background and aims Eletriptan is a potent 5-HT_{1B/1D} agonist that has shown efficacy for the acute treatment of migraine in adults. This study is the first to report efficacy and safety data on eletriptan 40mg (E40) vs placebo in the acute treatment of migraine in adolescent patients (aged 12–17 years).

Methods This was a multicenter, double-blind, placebo-controlled study comparing E40 with placebo. The primary endpoints were: 2-h headache response and 2-h pain-free response. Secondary endpoints were: 2-h absence of nausea, photophobia and phonophobia, 2-h functional response, headache recurrence at 24 h and use of rescue medication at 24 h. Post-hoc analyses were: 24-h sustained headache response and 24-h sustained pain-free response.

Results E40 was well tolerated in this population, and the profile of adverse events was similar to that observed in Phase III trials in adult patients. Although high response rates on E40 were observed for 2-h headache response (57%) and 2-h pain-free response (22%), high placebo response was also observed (57% and 15%, respectively). E40, however, did show a significant reduction in headache recurrence at 24 h vs placebo (9% vs 27%, $p<0.05$), and a reduction in use of rescue medication at 24 h (32% vs 39%, $p<0.05$). Post-hoc analyses showed E40 to have a significant benefit over placebo in sustained headache response (52% vs 39%; $p=0.04$) and sustained pain-free response (22% vs 10%; $p=0.013$).

Conclusions E40 was well tolerated in this adolescent population and showed benefits over placebo for the following endpoints: headache recurrence at 24 h, rescue medication use, 24-h sustained headache response and 24-h sustained pain-free response. The high placebo response observed for the primary endpoints is in accordance with similar studies of oral triptans in adolescent patients, and suggests use of alternative endpoints may be necessary in this age group.

CAPSAICIN INHIBITS BASAL AND INTERLEUKIN-1BETA-STIMULATED PGE2 RELEASE FROM PRIMARY CULTURES OF RAT TRIGEMINAL GANGLIA NEURONS

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Introduction capsaicin (CAP), a pungent substance present in chilli pepper, is known to possess analgesics and antiinflammatory properties. Here we investigated the effects of capsaicin on prostaglandin E₂ (PGE₂) release from rat trigeminal neurons in vitro.

Methods Trigeminal ganglion neurons cultures were prepared as described in previous studies. Briefly, ganglia from 6–7 days old rats were quickly removed, were digested by collagenase and trypsin, and finally neurons were collected through Percoll spin centrifugation. Cells were seeded on 24-well tissue culture plates, coated with poly-D-lysine and laminin at a density of 130–150 × 10³ cells for well and incubated at 37°C in a humidified atmosphere containing 5% CO₂. The culture medium was changed within 24 h from seeding. Plating medium was enriched with 50 ng/mL of 2.5 S murine Nerve Growth Factor. Cytosine arabinoside 10 μM was added to arrest non-neuronal cell growth. All experiments were performed from 3 to 6 days after dissection. Immunocytochemical analysis against neurofilament 200 was performed to demonstrate purified neurons culture. PGE₂ was measured by radioimmunoassay. CAP and capsazepine (CPZ) were tested. Interleukin-1β was used as proinflammatory stimulus.

Results IL-1β induces a time-dependent increase in PGE₂ production and release. We found that 5 μM of CAP was able to reduce prostanoid release under both basal and IL-1β-stimulated conditions. We also found that the inhibitory effect of capsaicin on prostaglandin E₂ release under basal conditions was partially antagonized by 10 μM of

CPZ, a competitive antagonist to vanilloid receptor. Furthermore, capsazepine showed an intrinsic stimulatory activity. In the presence of interleukin-1β, capsazepine failed to antagonize the inhibitory effect of capsaicin on cytokine-stimulated prostaglandin E₂ release.

Conclusions These findings demonstrate the antiinflammatory action of CAP in a model of trigeminal neurons stimulation in vitro. Some of these results could be explained by TPRV1 unrelated mechanisms.

ELETRIPTAN IS MORE EFFECTIVE THAN SUMATRIPTAN IN REDUCING HEADACHE RECURRENCE IN PATIENTS AT HIGH-RISK FOR RECURRENCE

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Background and aims Eletriptan has been shown to significantly reduce recurrence rates among patients achieving a headache response within 2 h. The aims of the current study were to (i) evaluate which clinical variables influence risk of recurrence and (ii) compare the efficacy of eletriptan and sumatriptan in reducing headache recurrence in patients at high risk for recurrence.

Methods First-attack data were pooled from 10 double-blind, placebo-controlled migraine trials including the following study drugs: eletriptan 40mg (E40; n=3,340); eletriptan 80mg (E80; n=1,854); sumatriptan 100mg (S100; n=1,126) and placebo (n=1,719). Multivariate regression analyses identified significant predictors of recurrence within 24 h of initial treatment response. Two high-risk subgroups were defined. Patients qualified for inclusion in the first high-risk subgroup if they had the following 3 significant predictors of recurrence (high baseline pain severity, female, age ≥35 years); and in the second high-risk subgroup if they had the following 2 significant predictors of recurrence (female, age ≥35 years).

Results Gender, age, headache severity at baseline and baseline nausea were shown to have a significant effect on risk of recurrence (all $p<0.05$). Aura subtype, time of dosing, baseline photophobia and phonophobia, and baseline functional impairment did not have a significant effect on recurrence. Among patients qualifying for the 3-risk-factor high-risk subgroup (n=769), recurrence rates at 24 h were lower on E40 (36%) and E80 (33%) compared with both S100 (51%; $p<0.01$) and placebo (45.3%; $p=0.053$). Recurrence rates at 24 h were also lower on E40 (31.2%) and E80 (28%) compared with both S100 (43%; $p<0.0001$) and placebo (41.3%; $p<0.001$) in the 2-risk-factor high-risk subgroup (n=2,700).

Conclusions Gender, age and baseline headache severity are identified as significant independent predictors of recurrence. Eletriptan was more effective than sumatriptan in reducing the risk of headache recurrence among 2 high-risk subgroups.

ELETRIPTAN-HIGHLY EFFECTIVE AND WELL TOLERATED IN TRIPTAN-NAIVE AND TRIPTAN-EXPERIENCED PATIENTS: RESULTS OF A COMBINED ANALYSIS

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Background and aims Triptan-naïve (TN) patients (starting a triptan for the first time) represent a clinical subgroup with different

treatment needs than triptan-experienced (TE) patients. This aim of this study was to evaluate the efficacy and tolerability of eletriptan in TN and TE patients.

Methods Efficacy and tolerability data were analyzed from 10 similarly designed, randomized, parallel-group, double-blind trials in adult patients (aged 18–64 years). The primary efficacy endpoint was 2-h headache response for all but one study (where 1-h headache response was the primary endpoint). Secondary endpoints included 2-h pain-free response and 24-h sustained response.

Results The numbers of patients (TN vs TE, respectively) treated with eletriptan 20mg (E20) were N=179 vs 255, with eletriptan 40mg (E40) were N=1,381 vs 1,971, and with placebo (PBO) were N=735 vs 998). 2-h headache response rates were significantly higher in TN and TE patients, respectively, on E20 (54% and 46%) and E40 (61% and 63%) vs PBO (31% and 21%; $p < 0.0001$ for all comparisons with PBO). 2-h pain-free response rates were also significantly higher in TN and TE patients, respectively, on E20 (20% and 13%) and E40 (28% and 32%) vs PBO (8% and 4%; $p < 0.0001$ for all comparisons with PBO). Among TN patients, 24-h sustained response was significantly higher E20 (34%) and E40 (45%) vs PBO (20%; $p < 0.0001$ for all comparisons with PBO). Significantly higher responses were also seen for E20 and E40 vs PBO for 24-h sustained response in the TE group (29% and 41% vs 9%, respectively). Tolerability was similar for TN and TE patients, respectively, regardless of whether they were treated with E20 (any severe adverse event = 6.1% vs 3.9%), E40 (4.6% vs 4.5%) or placebo (5.4% vs 5.9%).

Conclusions E20 and E40 are highly effective and well-tolerated in both TN and TE patients.

ZOLMITRIPTAN ORALLY DISINTEGRATING TABLET (ODT) IS HIGHLY EFFECTIVE AND WELL TOLERATED FOR THE ACUTE TREATMENT OF MIGRAINE IN A PRIMARY CARE SETTING: RESULTS FROM AN INTERNATIONAL STUDY OF PATIENT EXPERIENCE AND PREFERENCE

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Objective To evaluate zolmitriptan ODT for the acute treatment of migraine in primary care. Background: Zolmitriptan ODT is efficacious and well tolerated in the acute treatment of migraine. However, established regulatory endpoints used in controlled clinical studies are not always meaningful in primary care, where patient experiences are important. Primary care physicians require information on patient-reported outcomes in order to provide effective treatment strategies for migraineurs.

Methods 621 patients presenting in primary care with an established migraine diagnosis were recruited in this open-label study. During the 6 month study period, patients treated 1–3 migraine attacks per month with zolmitriptan ODT 2.5 mg. Patient preferences and treatment experiences were recorded using investigator-led questionnaires. The primary outcome was the percentage of patients wishing to continue using zolmitriptan ODT at the end of the study. Secondary objectives included patient assessments of efficacy and tolerability.

Results The ITT population comprised 595 patients (7171 migraine attacks treated). In total, 75.4% of patients wished to continue using zolmitriptan ODT. The majority (56.5%) reported that zolmitriptan ODT typically started to work within 30 minutes. Furthermore, 61% stated that headache pain typically disappeared within 60 minutes, and 74.4% stated that they were able to resume usual activities within 2 hours. Zolmitriptan ODT was considered a rapidly effective, highly effective and reliable treatment by 79.3%, 76.3% and 83.7%

of patients, respectively. 90.4% of patients had either no zolmitriptan-related side effects or side effects that were of little or no concern. Only 6.4% of patients reported that side effects would prevent future use of zolmitriptan ODT.

Conclusions By using new and tangible outcome variables relevant to patients, zolmitriptan ODT was reported as rapidly effective, allowing patients to quickly resume usual activities, which may explain the high proportion of patients who wished to continue using it in primary care.

EFFICACY OF TOPIRAMATE IN PEDIATRIC MIGRAINE PROPHYLAXIS

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Background and aims Migraine is the most common type of primary headache in childhood and it often hampers the common daily routines. The aim of our study was to investigate the efficacy and safety of topiramate in the prevention of pediatric migraine.

Methods Twenty-five children (mean age 11 years, range 5–16 years; 10 females, 15 males) were recruited. In 23 children migraine without aura was diagnosed according to the International Headache Society classification (2004), while the remaining 2 children had migraine with aura.

Results Before treatment, our patients showed 8 ± 5.7 (mean \pm standard deviation) pain attacks per month, ranging from 1 to 30. The children received a mean topiramate dose of 1.3 mg/Kg/d, ranging from 0.5 to 1.8 mg/Kg/d, for a period of 3.2 ± 1.2 months. Treatment was effective (reduction in attack number $\geq 50\%$) in 19 out of 25 children (76%). In particular, 3 patients (12%) became free from migraine episodes. One patient (4%) interrupted the treatment for adverse side-effects (excessive drowsiness). Seven patients in which the initial treatment was effective underwent a worsening in migraine frequency after the topiramate interruption and needed a further treatment after 4.3 ± 2.8 months. Six patients had a reduction in pain episode frequency higher than 75%, while in one child the therapy was ineffective. Two patients had a third treatment after 3 and 4 months from the second topiramate cycle interruption, respectively. In both, the therapy was ineffective. Adverse events were observed in 6 out of 25 children (24%). They consisted in drowsiness (3 patients), anxiety (1 patient), weight loss (2 patients), behavioural disturbs (3 patients).

Conclusions Our results suggest that topiramate is useful and safe tool in pediatric migraine prophylaxis. Even low doses allowed us to control migraine in most our children, thus improving their life quality.

EFFECTIVENESS OF BOTULINUM TOXIN TYPE A IN THE PROPHYLAXIS OF SEVERE AND TREATMENT-REFRACTORY MIGRAINE

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Background and aims Both central and peripheral sensitization are probably involved in migraine pathophysiology. The purpose of the present study was to assess the effectiveness of botulinum toxin type A (BontA), which presumably acts by inhibiting the liberation of excitatory neurotransmitters, in patients total or partially refractory to both drug therapy and local anaesthetic injections.

Methods Fifteen patients (21–60 years, 11 women/4 men) experiencing at least 3 migraine attacks per 28 days after receiving both one or more prophylactic drugs and a 12-weeks treatment course with ropivacaine injections. BontA was injected in scalp trigger points at a dose of 12.5 IU in each trigger point up to a maximum of eight points (i.e. 100 IU maximum injected dosage). The injection was repeated 12 weeks later and patients followed up during 12 additional weeks. Patients' evaluation included a headache diary, the Headache Impact Test (HIT-6), the SF-36 Quality of Life Questionnaire, and a Visual Analog Scale measuring the degree of improvement experienced.

Results The frequency of migraine attacks decreased significantly at 12th and 24th weeks in the 8 patients considered as responders to treatment (VAS value >50) and non significantly in the whole sample. This decrease was mainly due to the reduction in attacks of moderate and severe intensity, without relevant changes in those of mild intensity. In the whole sample, HIT-6 scores were significantly reduced both at 12th and at 24th weeks ($p=0.008$ and $p=0.001$), and the mental component of the SF-36 was also significantly improved ($p=0.002$ and $p=0.012$). The prevalence of BontA side effects, mainly pain at injection site and postinjection rebound headache, ranged from 20–35% of the sample.

Conclusions The use of BontA can be considered as a valuable therapeutic option in patients with severe and treatment refractory migraine.

PROPHYLACTIC EFFECT OF LOCAL INFILTRATION IN PREVENTIVE-RESISTANT MIGRAINE WITH LOCAL CRANIAL OR NECK TENDER POINTS. RESULTS OF AN OBSERVATIONAL STUDY OF 21 CASES

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Background Chronic head and neck tender points could be triggers of migraine crisis. Their treatment might have a beneficial effect on migraine. AIMS: To investigate the therapeutic value of anaesthetic plus steroid infiltration of cranial or neck tender points in migraine prophylaxis.

Material and methods We performed an observational and longitudinal study. We recruited 21 migraineurs from a Headache Unit, who presented neck or cranial tender points. When preventive treatment was ineffective, local infiltration with 1 ml of mepivacaine (2%) and 1 ml of triamcinolone was performed. We tested the effect of this method in the change of frequency, intensity and duration of crisis, response to symptomatic treatment and analgesic abuse, before and after (1–3 months) infiltration.

Results 20 of 21 of patients were women (mean age 39). Mean time of symptoms onset was 123.5 months. 76.2% took Non-Steroid Anti-inflammatory Drugs with low efficacy, and 71.4% used triptans (useful in four patients). Preventive treatment had been tested in all patients (33.3% more than two types) which was effective in 40%. 69.2% of tender points were a finding in physical exam. 47.6% of patients had one tender point and 52.4% had two or more. Infiltration was effective in 60% and very effective in 22% (82% of global efficacy), but was ineffective in 18% of cases. 71.4% required just one infiltration. After treatment 52.4% reported better response to symptomatic drugs, 52.4% had a decrease in crisis duration, 33.3% reduction in crisis frequency and 47.6% had an improvement of crisis intensity. It strikes that all these parameters improved in 33.3% of patients. Similar efficacy was observed in migraineurs with and without aura. Two cases presented mild local complications (pain and haematoma).

Conclusions Local infiltration seems to be useful and safe in migraineurs resistant to preventive treatment who present cranial or neck tender points

HEADACHE REVEALING CEREBRAL VENOUS THROMBOSIS IN A PATIENT CARRIER OF BOTH METHYLENETETRAHYDROFOLATE REDUCTASE C677T AND THE G20210A PROTHROMBIN MUTATION

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Background Headache in cerebral venous thrombosis (CVT) is the most frequent symptom, often the inaugural one, and it may appear in isolation. Here we report a case of CVT presenting as a new daily persistent headache and associated to familiar methylenetetrahydrofolate reductase (MTHFR)-C677T and prothrombin G20210A mutation as genetic risk factors.

Methods A 36-year-old woman suffered from a three month's history of new onset daily headache, right-sided, pressing, occasionally associated with vomiting and phonophobia, unresponsive to analgesics. Neurological examination was normal, except optic disk's nasal border blurring. The patient had been taking oral contraceptives because of an endometriosis. Also she had a daughter with thrombotic thrombocytopenic purpura.

Results Brain magnetic resonance angiography allowed visualization of the interruption of blood flow in the left transverse and sigmoid sinus with involvement of the jugular vein, which were consistent with the diagnosis of CVT. The parenchyma in MRI was unremarkable. Thrombophilia screening of the patient demonstrated heterozygosity for the G20210A prothrombin genotype and MTHFR-C677T homozygosity. We genotyped up to three members of the family (two daughters and a sister), finding a daughter heterozygous for the G20210A prothrombin mutation and all the three relatives showed homozygosity for the MTHFR-C677T variant. Anticoagulation was started and oral contraceptives discontinued in the patient, obtaining headache improvement.

Conclusions In general, we must suspect in any progressive headache of recent onset a secondary headache, which becomes necessary to investigate. In our patient, the primary etiology was an uncommon association of familiar MTHFR-C677T and prothrombin G20210A mutation causing a CVT.



Fig. 1

AN END TO THE YOM KIPPUR (AND RAMADAN) HEADACHE: A RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED STUDY OF ROFECOXIB IN PREVENTING RITUAL FASTING HEADACHE

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Background Religious fasting is associated with headache. This has been documented as 'Yom Kippur Headache' and 'First- of - Ramadan Headache'. The Cox2 inhibitor, rofecoxib, has been reported effective in preventing perimenstrual migraine and in preventing recurrence of migraine. Its half life is a relatively long 17 hours.

Objective To determine whether 50mg rofecoxib taken just prior to the 25 hour Yom Kippur fast (nil by mouth), would be effective in preventing headache.

Methods We performed a double blind randomized trial of rofecoxib 50mg vs placebo, taken just prior to the onset of fasting, Yom Kippur 2004. Setting: Patients were recruited from the general community and hospital staff. Participants We studied a volunteer sample of 105 subjects aged 18–65 with known fasting headaches, who intended to complete the 25 hour fast. We had enrolled 170 patients 65 of which did not return the study questionnaire. No patients withdrew because of side effects.

Intervention The treatment group received 50mg of rofecoxib just prior to the fast. The control group received placebo.

Main outcome measure The incidence of headache in the two groups. Secondary outcomes were severity of headache, and general ease of fast. Results: In the treatment group (n=53), ten or 18.9% (95% CI=1–32%) vs. 34 or 65.4% (95% CI=51–78%) of the placebo group (n=52), had headache at some point during the fast ($p<0.0001$). Severity of headache in the treatment group was significantly less for the treatment group (3.45 vs 6.29 on a visual analog scale of 10 ($p=0.009$)). None of those receiving rofecoxib reported a 'more difficult than usual fast' whereas the distribution of difficult to easy fast among the placebo group was more even.

Conclusions Rofecoxib 50mg taken prior to a twenty five hour ritual fast prevents and attenuates fasting headache.

AN UNUSUAL CASE OF LOW PRESSURE HEADACHE

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This case is presented because of its unusual nature and difficulty in both diagnostic localization and treatment of CSF leak. The patient presented with typical symptoms of orthostatic headache associated with nausea and tinnitus, one day after developing neck pain while golfing. Initial head CT and MRIs of brain and cervical spine were unremarkable. Neurologic referral resulted in recommendations for treatment with caffeine and hydration, and work-up with LP and MRI plus CT myelography. Opening pressure on LP was 7.2 cm H₂O, and all CSF analyses were normal. MRI revealed subdural space thickening, but without pachymeningeal enhancement. Cervical and thoracic T2 hyperintensity in the extradural space was interpreted to represent probable CSF leak. A split-injection cervical /lumber myelogram was nondiagnostic due to insufficient contrast. At ten weeks, the patient presented to a tertiary headache center, and was referred for radioisotope cisternography. This revealed evidence of possible CSF leak through the cribiform plate. A peculiar pattern of tracer, seen only on day 1 of imaging, suggested possible tracking out the nerve roots, although there was no isotope pooling. Standard CT cisternography/myelography was recommended for further clarification. Cisternography revealed an

intact cribiform plate with no leak. CT myelography revealed contrast extravasation along the right C6 and left C6 and C7 nerve roots, indicative of a fast leak. No focal dural tear was identified. The patient was referred for neurosurgical evaluation. At surgery, it was found that at places, the dura thinned, and in some places, disappeared into meninges. In some areas, there were no meninges at all, with direct visualization of spinal cord. Direct repair did not appear possible. The abnormal area was exposed as much as possible, and was sealed with Tisseal. The patient has remained headache-free. This case illustrates and discusses the diagnostic difficulties encountered with rapid CSF leaks.

CLINICAL DATA SUGGESTING OUR PATIENT HAS OR IS AT RISK TO HAVE A CHRONIC DAILY HEADACHE. NEUROLOGISTS OPINION

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Background and aims Chronic Daily Headache (CDH) is a very common and uncomfortable illness that neurologists are used to manage, but not always with good results. The Spanish Neurological Society Headache Group wanted to know more about it, in this case, about clinical data to detect patients with CDH or at risk to suffer it.

Methods Nine meetings with a total of 97 neurologists were made all around Spain. Using metaplan method (structured brainstorming), several questions were made. In present paper we describe and analyse the answers to: Which clinical data do you think are important to notice our patients suffer or are at risk to suffer CDH? This study was supported by Menarini-Spain.

Results Up to 260 free answers were collected. 78% of the ideas are included in the 7 more repeated, which are: psychiatric comorbidity (anxiety, depression) was commented by 67% of the participating neurologists; followed by analgesic and mixtures overuse (46% of the neurologists); then pharmacological treatment failure (preventive and symptomatic) (35%); increase in attack frequency (22%); being woman, housewife and >40 years (17%); migraine transforming to tension-type features, getting chronic (12%) and patients increasing their health care seeking (10%).

Conclusions All of the listed clinical data are relatively easy to recognise and should be taken in account for CDH detection and prevention. In neurologists opinion, psychiatric comorbidity is the major characteristic leading to CDH in patients with headache. Medication overuse is felt as a very important item, and also misuse and failure of preventive and symptomatic pharmacological treatment. The knowledge of these considered important factors for CDH patients should lead to a better management of the illness.

WHAT SHALL WE DO TO PREVENT (AND TREAT) CHRONIC DAILY HEADACHE? NEUROLOGISTS OPINION

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Background and aims Neurologists must prevent and treat numerous patients with Chronic Daily Headache (CDH). Treating migraine, cluster headache and other primary headaches is easier as we have accurate information based on clinical and experimental data. All this valuable information is not always available for CDH. The Spanish Neurological Society Headache Group wanted to know the opinion of neurologists pertaining CDH management, in particular how to prevent and treat this entity.

Methods A total of 97 neurologists in 9 meetings representing the Spanish neurological society were interviewed. A metaplan method was used (structured brainstorming), to answer several questions. In the present paper we describe and analyse the answers to: How can we prevent (and treat) CDH? This study was supported by Menarini-Spain.

Results A total of 321 different answers were proposed by participants. 82% of the neurologists independently thought information to the patients was the keystone, including information about the headache, the treatment proposed, the risk of medication overuse and others. Overall 45% proposed accurate management of psychiatric comorbidity; broader use of preventive treatments was mentioned by 43% and changes in lifestyle (sleep, diet, sport) by 41%. Other proposals were: increase in patient follow-up visits (28%), adequate symptomatic treatment (22%), good relationship between neurologist and general practitioner (10%) and correct diagnosis of the headache (10%).

Conclusions Perhaps we were expecting a magical drug solution, but instead of it, talking with the patients at risk of suffering CDH is possibly the best option. An adequate relationship between the patient and the doctor is essential, and great doses of information. Of course, accompanied by an adequate management of psychiatric comorbidity, good preventive and symptomatic treatments, lifestyle changes and a long list of things we must do properly to prevent CDH or treat it when is already present.

GREAT OCCIPITAL NERVE BLOCKADE IN CHRONIC MIGRAINE WITH CERVICO-OCCIPITAL LOCALIZATION: A CLINICAL AND NEUROPHYSIOLOGICAL STUDY

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Background and aims Physiological and physiopathological data showed the convergence of trigeminal and cervical afferents on to neurons in the trigeminocervical-complex (TCC) of the brain stem. Great occipital nerve (GON) infiltration with local anesthetics and steroids was successfully used for diagnostic and therapeutic purpose in cervicogenic headache. Aim of the study was to evaluate in chronic migraine with cervico-occipital localization the efficacy of (GON) blockade in stopping pain and in incrementating efficacy of preventive therapy. Secondary endpoint was to evaluate the trigeminocervical reflex in chronic migraine patients before and after the GON blockade and comparing them with healthy subjects.

Methods We enrolled consecutively 14 healthy subjects and 10 patients affected from chronic migraine according to IHS criteria 2004. All patients suffered from cervico-occipital distribution of pain and were submitted, at T=0, to GON blockade using lidocaine 2% (5 ml) and betametasone (2 mg) and to neurophysiological studies before the injection. Follow-up visits were done at 1 (T=1), 3 (T=2) and 6 (T=3) months. Neurophysiological and clinical data, numeric pain intensity scale (NPIS) and Migraine Disability Assessment Scale (MIDAS) were collected and administered at every step.

Results at the baseline our patients showed the following characteristics: 1) headache frequency (days per month): 18 ± 3 ; 2) pain-killer assumption: 14 ± 3 ; 3) NPIS score: 8 ± 1 ; 4) MIDAS score: 55 ± 9 . At T=1 and T=3 follow-up visits we observed a significant reduction in all clinical parameters considered ($p < 0.05$).

Conclusions our results showed that GON blockade in chronic migraine with cervico-occipital localization is effective in reducing pain intensity, pain-killer assumption, disability and headache frequency up to first month after injection. Otherwise this positive effect disappear at 6 months follow-up visit. The Authors suppose that the efficacy of the GON blockade could be due to its action on TCC.

GREAT OCCIPITAL NERVE BLOCKADE FOR CLUSTER HEADACHE IN EMERGENCY DEPARTMENT: CASE REPORT

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A 44-year-old man with a past medical history of episodic cluster headache presented in emergency department with complaints of cluster headache attack with cervico-occipital distribution of pain. The neurological examination showed no abnormalities as well as brain and spine MRI. Great Occipital Nerve (GON) blockade, with Lidocaine 2% (5 ml) and betamethasone (2 mg), were performed in the right occipital region (ipsilaterally to cluster headache), during the attack. GON blockade was effective immediately for the attack and the cluster period resolved after the injection. We suppose that the action of GON blockade may involve the trigemino-cervical complex, an overlapping area between trigeminal and cervical sensory afferents projections in the central nervous system, probably in the upper cervical segments such as the trigeminal nucleus caudalis and lateral cervical nucleus, producing central desensitization of this area and, probably, altering the trigeminal autonomic reflex pathway. We moreover strongly suggest to use GON blockade in emergency departments for cluster headache as attack abortive therapy.

SELF-PROVOKED NECK CUTANEOUS LESION AND CLUSTER-MIGRAINE: RESPONSIVENESS TO TOPIRAMATE

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A 55-year-old female had stereotypic headaches sharing clinical characteristics of TACs and migraine. On the first side, the onset was when she was 43-year-old. The attacks lasted 60 to 120 min each. The patient had experienced ten 4-months periods of identical headaches in the last ten years prior to evaluation but in the last year she presented chronic daily headache. The pain was associated right-eye ptosis, bilateral lacrimation and rhinorrhea. On the other side, the pain was initially always located in the right jaw; after this the pain spread to right eye, to right anterior region of the neck, to right cervico-occipital region and then became bilateral. The pain was associated with nausea, vomiting and phono-photophobia. Interestingly, anterior neck pulsed finger-pressure was effective too in relieving pain. Continuous neck finger-pressure provoked cutaneous lesion (Fig.1). Neurological examinations and MRI/MRA study of the brain and neck imaging were normal. Treatment with indomethacin, prednisone and gabapentin were ineffective. Then we started a monotherapy with topiramate (25 mg tid). In the following three months she experienced a strong improvement in intensity and frequency (from 15 days/month to 1 day/month) of attacks. In the pathophysiology of primary headaches the trigeminocervical complex (TCC) seems to play an important role. TCC is a nociceptive structure that exerts fundamental control over inputs from cervical and trigeminal nociceptors, essential in the pathogenesis of primary headaches. However, it also receives other inputs that participate in head pain control. The parasympathetic system (vagus nerve), together with the TCC, could increase or decrease the pain signals. For the Authors, the efficacy of topiramate could be due to the action on trigeminocervical complex and the self-provoked neck cutaneous

lesion observed in this patient due to continuous pulsed finger-pressure during attacks could represent the equivalent of a vagus nerve stimulation, effective in relieving pain.

INFLUENCE OF ALLODYNIA AND THE AUTONOMIC SYSTEM ACTIVATION ON THE RESPONSE TO TRIPTANS IN MIGRAINE

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Background and Objective to test the hypothesis that the existence of allodynia and the activation of the autonomic nervous system influence the response to triptans during acute attacks of migraine without aura (MA-).

Patients and methods the presence of autonomic symptoms was carefully evaluated in 76 consecutive subjects (M/F 27/49; mean age 36.2±6.4) with history of MA- by both a structured interview and telethermographic investigation. Based on these findings, the entire group was dichotomized into a subgroup with autonomic symptoms (A+) and a subgroup without (A-). The two subgroups were comparable for demographic characteristics and other clinical variables, including pain severity. Clinical response to triptans (eletriptan 40-mg tablets) during 3 consecutive migraine attacks was recorded in each subject. End points were pain-relief and pain-free response at 1 and 2 hours.

Results Pain-relief was reported in 58.2% of migraine attacks at 1 hour and in 75.8% at 2 hours, while pain-free was observed in 27.3% at 1 hour and 28.0% at 2 hours. Response to treatment turned out to be related to the co-existence and the complexity of autonomic symptoms. In particular, the more complex the autonomic activation, the less evident the benefit of treatment.

Conclusions As the autonomic system contributes to the sensitisation of the nociceptors with consequent peripheral and central allodynia, and the progressive occurrence of allodynia is supposed to be one of the most relevant contributors to triptans inefficacy, our findings support the assumption that the activation of the autonomic nervous system plays a pathogenic role in the clinical response to these drugs in migraine. The degree of activation of the autonomic system might be used as a marker to predict the clinical outcome to triptan therapy.

EPIDURAL BLOOD PATCH TO TREAT THE HEADACHE BY SPONTANEOUS CSF LEAK

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Objective To evaluate the efficacy of epidural blood patch (EBP) in the treatment of headache by spontaneous CSF leakage (SCSFL). **Background.** Spontaneous intracranial hypotension (SIH) generally results from spontaneous spinal CSF leakage. Treatment is usually conservative but EBP has emerged as the most important nonsurgical treatment for SCSFL.

Patients and methods We observed 30 patients with SCSFL between 1992 and 2005. 11 patients (6 women and 5 men; age range 31–66 years, mean age 40) received EBP. All patches were performed in lumbar region, using 15 to 30 ml (mean 23) of autologous blood. All patients maintained a 30 degree Trendelenburg position during the procedure and for 24 hours after the procedure. Follow-up ranged from 6 months to 2 years.

Results All patients had orthostatic headaches. Other manifestations were nausea, vomiting, mild neck stiffness, tinnitus, blurred vision, diplopia and bilateral upper limb numbness. CT myelography or spinal

RMI or brain RMI or radionuclide cisternography showed CSF leakage sites in 6 out of 11 patients, 2 sites were at the cervical level, the others at the lumbar level. In 10 out of 11 patients brain RMI showed diffuse pachymeningeal gadolinium enhancement (neuroimaging of intracranial hypotension). All patients failed an initial conservative treatment which consisted of bed rest and rehydration over a period of 1 to 13 months. All treated patients became asymptomatic, 1 responded only after 3 EBP and 1 had a residual headache during the Valsalva manoeuvre for 2 months. Until now none has had a relapse.

Conclusions Our data confirm the efficacy of EBP in the SCSFL headache and suggest also the importance of a prolonged Trendelenburg position specially when the leak site is at the cervical level and we perform the autologous blood patch in the lumbar region.

TEMPORARY CONFUSION DEPENDING ON THE USE OF TRIPTAN

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Triptans are used very often in treatment of migraine attacks. Common side effects are tingling, numbness, a sensation of warmth, heaviness, and pressure or tightness in different parts of the body including the chest and neck. In addition, there are some other side effects such as agitation, aphasia, ataxia, confusion, tremor and vertigo. In this study, a case which shows a temporary confusion depending on the use of naratriptan during the migraine attack was presented. **CASE:** A woman, 45-year-old, with no specific medical history was brought to the emergency service with a complaint of acute headache. Headache was unilateral, throbbing and came with nausea and photophobia. There was no pathologic evidence in examination and the results of laboratory; so, it was diagnosed as migraine attack and common analgesics were applied. Headache was not resolved contrary increased. Then naratriptan was given. After a while, the headache stopped. However, the next day she was brought to the emergency service again because of unconsciousness and not recognizing the people around. She was confused. In her cranial MRG; hyperintense views, which does not cause signal changes in bilateral ganglions, were determined in TW2 and Flair sequences. In the second day of her stay in the clinic, she regained her conscious. Vitamin B12 level was determined as low (154 pg/ml, normal range 193–986) with further laboratory examinations. Replacement was started. The treatment of the patient was reorganized and she was monitored. Her control cranial MRG taken three months later was normal. Even though triptans are commonly used in the treatment of migraine attacks, neurological side effects should not be disregarded. Advanced biochemical examinations should be done on patients showing side effects to triptan.

HEADACHE IN GENERAL NEUROLOGICAL OUTPATIENT CLINICS

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Background and aims Headache and cranial neuralgias are one of the most common diagnostic in outpatient neurological care. The objectives of this study is to analyze the importance of headache and cranial neuralgias as cause of consultation, diagnostic group, and specific diagnostic in general neurological outpatient clinics. We want to study the request of complementary investigations and resolution capacity in headache and cranial neuralgias care.

Methods Observational, prospective and descriptive study of general neurological outpatient clinics in older than 14 years population, during 12 consecutive months in our sanitary area. The International

Classification of Headache Disorders (2nd edition) and the International Classification of Diseases (9th edition CM) were used in this study.

Results We attended 4005 programmed visits, 1278 (31.9%) complained of headache or cranial neuralgia. Of these 72% were women and average age of 41.1±17.2 years. They were the most frequent cause of consultation (33.1%). Headache was the first diagnostic group (30.1%). Migraine (36.57%) and medication-overuse headache (22.07%) were the most frequent type of headache followed by new daily-persistent headache (11.12%) and tension-type headache (9.88%). 57.5% of cerebral CT scan and 35.2% of cerebral MR were asked for headache or cranial neuralgias. 17.7% of cases were resolved at first visits and 79.8% at second visits.

Conclusions Headache and cranial neuralgias are the first cause of consultation and the most frequent diagnostic group in general neurological outpatient clinics. Migraine and medication-overuse headache are the most frequent type of headache. They are the main reason for request cerebral CT scan and MR. The great majority of cases were resolved at second visits.

PLACEBO IN MIGRAINE

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“There is not an unique definition of placebo (or placebo effect), and the most common is “any effect attributable to a pill, potion, or procedure, but not to its pharmacodynamic or specific properties” [1]. The mechanisms of placebo effect have not been definitively understood: we deal with the intriguing field of mind/ brain relationship, psychology and biology. The mechanisms of placebo are related to psychological aspects, as “desire”, “expectation”, “conditioning”. However, the placebo is not only a psychological mechanism, because it is related to the brain structures: studies evidenced that placebo has implications also in biological field: antidepressants has influence both in brain structure and functions [2].

Placebo is a significant issue in headache disorders. Noteworthy, the placebo rate is higher in headache children than in adults. Studies on triptans showed an answer to placebo from 18 to 35% in adults and from 25 to 61% in children and adolescents [3, 4]. In preventive therapy to answer to placebo has been estimated as high as 40%–50% in children [5]; in adults, the placebo effect in preventive therapy is about 50% [6].

On one hand, the high placebo response in headache trials may be an obstacle. On the other, it is an important resource both in clinical field and for the understanding of the mechanisms involved in triggering and relieving headache.

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A PROSPECTIVE STUDY OF PREMONITORY AND RESOLUTION SYMPTOMS IN 100 MIGRAINE PATIENTS

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Objective To clarify the nosology of migraine premonitory (PS) and resolution (RS) symptoms.

Methods 100 migraineurs consulting their general physician were asked to fill in, for three attacks, a PS and RS questionnaire. “True” PS/RS were those experienced the day before (or the day after) the headache had started only if they were not present in a questionnaire completed in a pain-free period.

Results True PS and RS were experienced by 84% and 80% of subjects for the first attack. The mean and range (per patient) of PS were 6.8 and 0–21 and of RS 4.7 and 0–15. Anxiety, phonophobia, irritability, unhappiness and yawning were the commonest PS, whereas asthenia, tiredness, somnolence and concentration difficulties were the most common RS. Gender, age and MIDAS scores did not influence PS and RS. Both PS and RS were more frequent in migraine with aura subjects. Patients on preventatives showed a decreased frequency for PS, and to a lesser degree for RS. Severity of headache was associated with a higher frequency of RS. Individual RS and especially PS were quite consistent after 3 attacks. Almost two-thirds of the symptoms were noticed in at least 2 out of 3 attacks, while more than a half of PS and more than a quarter of RS repeated in 3 out of 3 attacks.

Conclusions Around 80% of unselected migraineurs experience RS and PS. Migraine with aura and severe pain are risk factors for experiencing PS and RS, while preventatives were protective, especially for PS.

NONCORONARY SERIOUS ADVERSE EVENTS OF ERGOTICS

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Objective Ergotics can induce serious adverse events, usually coronary ischemic events. We show four patients with noncoronary serious adverse events related to chronic use of ergotamine or derivatives.

Methods We prospectively collected the noncoronary serious adverse events of ergotics in migraine patients in the last 10 years.

Results Four migraine patients who were overusing ergotics presented as these serious adverse events. There were two women and two men, aged between 40 and 60 years, with a history of chronic migraine who were overusing ergotics (ergotamine and/or dihydroergotamine) as symptomatic treatment. Three of them had also taken methysergide for prevention. They developed: 1) renal failure due to retroperitoneal fibrosis, which required nephrostomy; 2) ischemia in his right hand due to complete occlusion of the radial artery in a patient with no atheromatosis or embolic sources, which required thrombectomy; 3) painful erection due to fibrosis penis; and 4) cardiac insufficiency due to fibrotic destruction of mitral and tricuspid valves, which needed replacement.

Conclusions These cases show that the chronic use of ergotamine derivatives in migraine patients can induce serious noncoronary adverse events.

SYMPTOMATIC TREATMENT OF MIGRAINE IN CLINICAL PRACTICE WITH INTRANASAL ZOLMITRIPTAN

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Objective To analyse our experience with the new, 5 mg intranasal formulation of zolmitriptan in the symptomatic treatment of migraine attacks.

Patients and Methods This series includes 82 patients who had treated an average of 7 migraine attacks. Eighty patients had experience with oral triptans and 20 with subcutaneous sumatriptan. The main reasons for using nasal zolmitriptan were: poor efficacy of oral triptans (41.5% of the patients), use of subcutaneous sumatriptan (24.4%) or medical criteria (34.5%).

Results Among the 80 patients experienced with oral triptans, 50 (62.5%) preferred nasal zolmitriptan, 14 (17.5%) oral triptans and the remaining 16 (20%) did not express any preference. The main reason for this preference were shorter speed of action and better efficacy. Within those 20 patients who were using subcutaneous sumatriptan, 8 (40%) preferred subcutaneous sumatriptan, 5 (25%) nasal zolmitriptan and 7 (35%) did not express any preference. The reasons for preference of intranasal zolmitriptan over subcutaneous sumatriptan were convenience and better tolerability. A total of 55 patients noticed efficacy within 60 minutes. Half experienced at least one adverse event, always mild. The most frequent were: bad taste (n=23) or nasal irritation/itching (n=8).

Conclusions The new intranasal formulation of 5 mg zolmitriptan is a good option for the symptomatic treatment of migraine, which could be considered as an intermediate between oral triptans and the subcutaneous formulation of sumatriptan.

EXPERIENCE WITH INTRANASAL ZOLMITRIPTAN IN CLUSTER HEADACHE

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Objective To analyse our experience with the intranasal formulation of zolmitriptan 5 mg in the symptomatic treatment of cluster headache in daily clinical practice.

Patients and methods We collected a total of 20 patients with cluster headache and experience with intranasal zolmitriptan; 18 had used subcutaneous sumatriptan and 9 oral triptans. The main reasons for trying intranasal zolmitriptan were: poor tolerability in 13 patients and insufficient efficacy in 6.

Results Among the 18 patients experienced in subcutaneous sumatriptan, 12 (67%) preferred nasal zolmitriptan, 3 (17%) subcutaneous sumatriptan and 2 (11%) did not express any preference. The reasons for preferring intranasal zolmitriptan were: higher convenience (n=6), better tolerability (n=5), lower price (n=2) and higher efficacy (n=1). Seven out of the 8 patients who had taken oral triptans preferred intranasal zolmitriptan, in all cases due to higher subjective efficacy. A total of 11 patients showed efficacy within 30 minutes. Only 3 patients referred adverse events, always mild.

Conclusions The 5 mg intranasal formulation of zolmitriptan is a potential new option for the symptomatic treatment of cluster headache. This formulation should be considered in patients with poor tolerability to subcutaneous sumatriptan and in those attacks where quick access to inhaled oxygen is not possible. These results suggest that a controlled trial with intranasal zolmitriptan in this indication would be worthwhile

CONTRACTION OF THE RAT CAROTID ARTERY TO ALPHA-ADRENOCEPTOR AGONISTS AND 5-HT AFTER OVARIECTOMY AND REPLACEMENT OF FEMALE SEX HORMONES

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Background and aims The prevalence of migraine is higher in females than in men, and changes in 17beta-estradiol levels seem to affect the frequency of attacks in female migraineurs. The underlying mechanisms are not yet understood, but it is feasible that female sex hormones interact with the vascular tone of the carotid vascular bed, which is most likely involved in the headache phase of migraine. We set out to compare contractile responses to alpha-adrenoceptor agonists and 5-HT in the rat isolated carotid artery after ovariectomy and subsequent hormone replacement with 17beta-estradiol, progesterone or their combination.

Methods Female Sprague-Dawley rats were bilaterally ovariectomized and divided into five groups; sham-operated animals and ovariectomized animals treated with placebo, 17beta-estradiol, progesterone or a combination of 17beta-estradiol and progesterone. Segments of carotid artery were isolated and mounted in Mulvany myographs. Blood samples were taken to measure plasma levels of adrenaline and noradrenaline.

Results Noradrenaline induced a concentration-dependent contraction, which was exclusively mediated by alpha1-adrenoceptors, except for the ovariectomized animals treated with placebo, where alpha2-adrenoceptors were also involved. The potency of noradrenaline was significantly reduced in ovariectomized animals treated with progesterone as compared to those treated with placebo. The plasma levels of noradrenaline and adrenaline were not significantly affected by ovariectomy or subsequent replacement of 17beta-estradiol, progesterone, or the combination of these hormones. The potency of 5-HT was significantly reduced in animals having endogenous (sham-operated) or exogenous (treated with 17beta-estradiol, progesterone, or the combination of these hormones) circulating sex hormones as compared to placebo-treated ovariectomized animals.

Conclusions Taken together, our results indicate that circulating progesterone and/or 17beta-estradiol may reduce contraction of the rat carotid artery to noradrenaline or 5-HT. This may be one of the mechanisms through which female sex hormones may aggravate migraine in women.

CONTRIBUTION OF MYOFASCIAL TRIGGER POINTS TO MIGRAINE SYMPTOMS

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Background and aims Examination of cervical muscles in migraine patients often reveals myofascial trigger points (TrPs) whose target coincides with the site/s of migraine pain. This study evaluated the contribution of TrPs to typical migraine symptoms in these cases.

Methods Forty-eight patients (39 women, 9 men, 25–46 yrs) were examined, affected with frontal and/or temporal migraine and TrPs in the sternocleidomastoid, splenius cervicis or semispinalis cervicis muscles (targets located in the same sites as the migraine attacks). All underwent measurement of electrical pain thresholds in skin, subcutis and muscle at TrP and target level at baseline and after TrP infiltration with local anesthetic (on days 0, 3, 10, 30 and 60). Number and intensity (VAS scale) of migraine attacks were recorded for 60 days before and 60 days after start of treatment. All patients were free from any other pain medication during the study.

Results At baseline, pain thresholds of all three tissues at TrP and target level were significantly lower than those recorded in 20 healthy controls of comparable age, testifying hyperalgesia ($p < 0.001$). During treatment: - all thresholds increased progressively and significantly in both TrP and target (ANOVA: $p < 0.002$); - number and intensity of migraine attacks decreased significantly compared to pre-treatment ($p < 0.01$). The threshold increase correlated significantly with the reduction of migraine pain/hyperalgesia ($p < 0.02$).

Conclusions Myofascial trigger points whose targets coincide with sites of migraine contribute substantially to subjective and objective migraine symptoms. Systematic local treatment of TrPs in these cases, by improving the pain picture, can eventually allow a reduction of doses of specific migraine drugs.

THE PATHOPHYSIOLOGY OF MIGRAINE IN CHILDREN: THE CONTRIBUTION OF NEUROPHYSIOLOGY

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Although migraine represents the most common primary headache in childhood its pathophysiology is scarcely understood. In spite of the bulk of studies dealing with this problem in adults, the pathophysiological base of pediatric migraine has been only rarely investigated. As the adults, children with migraine show a reduced habituation to repetitive sensory stimuli [1, 2]. Although this characteristic neurophysiological phenomenon suggests an abnormal excitability of the cerebral cortex in this disease, whether cortical excitability in migraine is reduced or increased is still far to be demonstrated. We investigated the cerebral cortex excitability in 15 children (mean age 11.7±1.6 years, 5 males, 10 females) affected by migraine without aura (MO) and in 10 age-matched control subjects (CS) (mean age 10.9±2.1 years, 6 males, 4 females). We calculated the somatosensory evoked potential (SEP) latency and amplitude modifications after paired electrical stimuli at 5, 20 and 40 ms interstimulus intervals (ISIs), comparing it with a single stimulus condition assumed as the baseline. In MO patients, the amplitudes of the cervical N13 and of the cortical N20, P24 and N30 responses at 20 and 40 ms ISIs showed a higher recovery than in CS (two-way ANOVA, $p < 0.05$). Since the SEP recovery cycle depends on the inhibitory interneuron function, our findings suggest that a somatosensory system disinhibition takes place in migraine. This is a generalized phenomenon, not limited to the cerebral cortex, but concerning also the cervical grey matter. The shortened SEP recovery cycle in migraine children, besides showing that the somatosensory system is hyperexcitable in this disease, might represent a useful marker to control the effect of prophylactic pharmacological treatments.

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THE EFFECTIVITY OF TOPIRAMATE FOR PREVENTING MIGRAINE

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Migraine headache is a common and disabling disorder. Topiramate (TPM), a broad spectrum anticonvulsant with multiple mechanisms of action can be effective in preventing migraine headache. The objective of our study is to evaluate the efficacy and tolerability of TPM on preventing migraine headache.

Methods We report an open label 6 months study, on using TPM as preventive therapy for migraine headache. 36 patients (26 Females, 10 Males) entered the study. Mean age 38 years old (24–60). The diagnosis of migraine was made from headache disorder specialists according IHS 2003 criteria. All the patients had a migraine history >2 year with an average of >4 migraine days per month; had been resistant to previous multiple standard therapies, and were able to keep trial records. After a 14 days washout period patients meeting entry criteria was given TPM. It was titrated by 25 mg/week till 100mg per day. All the patients kept records on the severity and the duration of their headache in a standardized chart.

Results 25 patients (69.6%) experienced a significant improvement of their headache in the first month of the therapy. 5 patients had a

moderate improvement and 6 patients, did not experienced any change in their headache. The most common side effects were weight loss (7 persons), irritability (2 persons), and diarrhea (1 person).

Conclusions TPM is effective and well tolerated for migraine preventive treatment.

EFFICACY OF TOPIRAMATE IN PATIENTS WITH CHRONIC MIGRAINE

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Background One of the new features of the ICHD-2 is the addition of chronic migraine. This entity is diagnosed when the patient have migraine without aura on 15 days per month for more than 3 months in the absence of medication overuse and not attributed to another disorder. Topiramate (TPM) is an antiepileptic drug that is also effective when was used as a preventive treatment in episodic migraine.

Objective To study the efficacy and tolerability of TPM when used as adjunctive treatment for patients with chronic migraine.

Patients and methods We selected outpatients with chronic migraine according to ICHD-2. In all patients evaluated age, sex, medical and familiar history, side and severity of the pain, provoking factors, previous treatments for migraine prevention and acute medication. The starting TPM dose was 25 mg/day with slow increase by 25 mg/week to the maximum of 200 mg/day or the highest tolerated dose. They were prospectively followed-up for mean 6 months to evaluate efficacy and tolerability.

Results We included 23 patients, 5 males: 18 females. The mean age was 32±11.7 years. 90% had positive familiar history of migraine. Stress associated was common. The intensity of the pain was moderated in 80%. Unilateral (right-side) headache was frequent. Previous preventive medication has been used in 95% (β -blockers, calcium antagonist, valproic acid and antidepressant). Neuroimaging studies were normal. Acute treatment was triptans (48%), NSAIDs (18%) and both (30%). After 100 mg/day of TPM, improvement was observed in 70% (2 patients was pain free during 3 months). Fatigue was the most common adverse event.

Conclusions In our patients with chronic migraine, treatment with 100 mg per day of Topiramate showed good efficacy with minimal adverse events.

SALIVARY CORTISOL/DHEA-S RATIO AND TESTOSTERONE/CORTISOL RATIO AS MEASURE OF HYPOTHALAMO-PITUITARY-ADRENAL (HPA) AXIS ACTIVITY IN WOMEN WITH (CM) CHRONIC MIGRAINE

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Previous studies from our group and others showed that saliva allows an easy, stress-free means for monitoring changes of adrenal function in physio-pathological conditions. In the present study, the HPA axis activity was monitored in 20 women with CM, by measuring salivary cortisol, testosterone, DHEA-S levels, and their ratios. The participants were instructed how to collect saliva samples at home, which was performed twice a day. Levels of cortisol were significantly increased in CM patients with respect to controls, while DHEA-S levels were slightly reduced. No significant change in testosterone levels were found. With regard to the cortisol/DHEA-S ratio, CM

women showed significantly higher values than controls. Moreover, testosterone/cortisol ratio, the anabolic/catabolic index of physical performance, was significantly lower than controls in CM patients. This study reports that CM appears not to be associated with impairment of circadian variation of cortisol and DHEA-S: physiological rhythmicity was actually maintained in all the subjects, with morning levels significantly higher than in the evening. The cortisol to DHEA-S ratio, which has been proposed as a measure of the relative activity of the two steroids, was higher in CM women suggesting a functional hypercortisolemia in these patients: increased concentrations of cortisol have been associated with the development of different diseases; DHEA-S has been associated with neurosteroid neuroprotective properties and low levels of Dhea-s were associated with ageing processes. In this study CM patients present alterations in HPA axis function that might contribute to metabolic and psychological alterations that have also been associated with CM. Further studies are required to elucidate the possible clinical relevance of HPA axis dysfunction in CM, since migraine is often associated with different psychopathological disorders (such as distress, anxiety, mood changes), which are often highlighted as trigger factors of migraine attacks but may also appear as reaction to migraine attacks.

HIGH PREVALENCE OF CARDIAC INTERATRIAL RIGHT-TO-LEFT SHUNT IN PATIENTS WITH CLUSTER HEADACHE

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Background and object to test the hypothesis that a potential pathogenic link between cardiac interatrial patent foramen ovale (PFO) and cluster headache (CH) exists.

Patients and methods contrast enhanced transcranial Doppler examination with monitoring of the middle cerebral artery was performed in a group of consecutive patients with CH, both at rest and after Valsalva maneuver. The prevalence of patients with a right-to-left shunt was compared to that observed in the general population of the same class of age, sex, geographic area and ethnic background.

Results 38 patients with CH (M/F 23/15; mean age 43±4) were evaluated. A right-to-left shunt consistent with PFO was detected in 14 (36.8%). Such a frequency was considerably higher than that (about 20%) previously reported in the reference control group. The association was independent on sex and age. Finally, no difference was observed when the prevalence of autonomic symptoms, the intensity of pain, and the frequency of recurrences in the group of CH-PFO+ patients were compared to those in the group of CH-PFO- patients.

Conclusions our findings support the assumption of a possible pathogenic relation between PFO and CH, and suggest the hypothesis that such an association is independent on the clinical phenotype of the disease.

ASSESSMENT OF DISABILITY IN CHRONIC DAILY HEADACHES: A COMPARISON OF WHO-DAS II WITH OTHER SPECIFIC AND NON SPECIFIC DISABILITY TOOLS

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Background and aims To compare the sensitivity of the World Health Organization Disability Assessment Schedule II (WHO DAS II) for detecting disability due to chronic pain with two established

instruments, SF-36 and HIT-6, in chronic daily headache (CDH) patients with and without analgesics overuse. Methods: SF-36, HIT-6 and WHO DAS II interviews, in their validated Italian version, were administered to 40 consecutive patients affected by CDH (according to ICHD-II criteria). No patient was under prophylactic medications. Statistical analysis included partial correlation test between items of the three instruments and alfa Cronbach parameter for evaluation of WHO DAS II internal consistency.

Results We found positive correlation between all items of SF-36 and D4, D5 and D6 WHO-DAS domains, with statistically significant differences ($p<0.01$). D5 and D6 correlated positively with all HIT-6 items ($p<0.01$), D4 domain correlated with items 3,4,5,6 of HIT-6 ($p<0.01$), D1 domain with items 4,5,6 ($p<0.05$) and D2 domain with items 3 ($p<0.05$). These data showed that WHO-DAS II is comparable to SF-36 and HIT-6. No correlation were found between WHO-DAS II items and headache clinical features (disease duration or analgesics overuse duration). Some SF-36 items, instead, showed a statistically significant correlation with duration of illness, but not with the duration of analgesics overuse. To identify internal consistency between all items of WHO DAS II we used alfa Cronbach parameter. Its value was between 0.8 and 0.9 for all domains analysed indicating a high internal consistency that reflect high sensitivity of WHO-DAS II in detecting disability in headache patients.

Conclusions The WHO DAS II is at least as sensitive as other generic and specific measures for disability in patients with chronic pain and may be useful for indicating therapy effectiveness and clinical management in this patients.

HELICOBACTER PYLORI INFECTION IN PATIENTS WITH COMMON MIGRAINE

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Background and aims Helicobacter pylori infection has recently been associated with various vascular disorders and migraine. Our study investigates the correlation between Helicobacter pylori infection, as an environmental risk factor and the common form of migraine.

Methods A total number of 49 outpatients (12 men and 37 women) affected by common migraine was evaluated. Helicobacter pylori infection was diagnosed by the 13 C- urea breath test (INFAI – test). The classification concerned the family history for migraine and the correlation of the episodes with menstruation in women. The migrainous patients were classified as having a positive or negative familial history and as having a menstrual or non menstrual type of migraine.

Results The INFAI – test was found positive in the 67% of the total population of our patients, a frequency that is higher than the expected one in the general greek population (53%). The prevalence of Helicobacter pylori infection in the total group of patients was 81% in migrainous patients with negative familial history and negative correlation with menstruation, significantly higher ($p=0.001$) than the prevalence of the same infection in migrainous patients with positive familial history and/or menstrual migraine, which was only 36%. Similar findings were remarked in the subgroup of female patients, where the prevalence of Helicobacter pylori infection in patients without familial history and/or menstrual migraine was 86%, while in female patients with positive familial history and/or menstrual migraine was only 37% ($p=0.002$). We also remarked a higher prevalence of the infection in male patients with negative familial history, but the number of the subjects of this subgroup was small.

Conclusions Our results suggest that Helicobacter pylori infection is a risk or pathogenetic factor for common migraine, especially whenever there is not a positive familial history and/or a correlation with menstruation.

DIALYSIS HEADACHE

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One of the common neurological symptoms during hemodialysis is headache. Dialysis may cause severe headache because of fluid and electrolyte disbalance. In this study, a case which shows the emergence of headache during the hemodialysis sessions is presented. CASE: 41-year-old man with hypertension, diabetes mellitus and chronic renal disease related to diabetic nephropathy has been receiving hemodialysis for almost three months. He describes a headache which he has experienced after starting to receive hemodialysis and which occurs at the last 1–1.5 hour of each four hours hemodialysis sessions. He feels the headache in the generalized area of his head and also describes it as throbbing and affecting both of the eyes, but without nausea and photophobia. Neurological examination was normal except diabetic polyneuropathy. For about one year he has had vision loss related to diabetic - hypertensive retinopathy. His brain CT measured during headache was normal. Case was diagnosed as dialysis headache considering the medical history, neurological examination and laboratory findings. It is important to distinguish the dialysis headache since it might be a big problem for the patient and can be prevented by changing the parameters or methods in dialysis.

COULD WE DISTINGUISH MEDICATION-OVERUSE HEADACHE FROM CHRONIC MIGRAINE AND CHRONIC TENSION-TYPE HEADACHE BY CLINICAL PRESENTATION?

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Diagnostic criteria for chronic migraine (CM), chronic tension-type headache (CTTH) and medication-overuse headache (MOH) are well defined by revised International Headache Classification. However, the differences between these three common chronic headache disorders are not so obvious in everyday clinical practice. The aim of this study was to determine the typical clinical characteristics of patients with medication overuse headache (MOH) and to compare their clinical presentation with chronic migraine (CM) and chronic tension-type headache (CTTH). During four years period 332 patients with chronic daily headache were consequently treated in Headache Center. There were 197 MOH, 82 CM and 53 CTTH patients. Almost 70% of MOH patients had episodic migraine as previous headache diagnosis. Demographic and social characteristics, features of chronic and previous episodic headache disorder, as well as efficacy of preventive treatment were analyzed between three groups. While the headache features of three groups were sharp different for episodic headache, the same differences were not so clear for chronic headache. Also, there were fewer differences between MOH and CM groups for the features of previous episodic headache disorder and more similarities between MOH and CTTH patients for features of chronic headache disorder. Caffeine abuse, smoking and lack of recreational physical activity were more frequently seen in MOH patients. The preventive treatment were significantly more efficacious for CM (80.5%) than for MOH (56.3%) and CTTH (52.8%) patients. These clinical observations point to the fact that the sharp differences observed between episodic headache disorders become less obvious for chronic headache.

MODULATION OF CATECHOLAMINE RELEASE FROM RAT STRIATAL SLICES BY THE FIXED COMBINATION OF ASPIRIN, PARACETAMOL AND CAFFEINE

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Background and aims The fixed combination of aspirin, paracetamol (acetaminophen), and caffeine has been used successfully to treat different kinds of pain including migraine attacks. Even when this formulation has been marketed for a long time, the exact molecular mechanisms underlying its therapeutic effectiveness have not been completely elucidated. In the present investigation, we aimed to study the effects of the fixed combination of aspirin, paracetamol and caffeine (APC) on the release of dopamine and noradrenaline from rat striatal slices in an attempt to find potential new mechanisms of action of this widely used analgesic combination.

Methods Rat striatal slice were treated with the combination of APC for eight or 24 h. Dopamine and noradrenaline were extracted from the brain samples quantified using RP-HPLC under isocratic conditions and electrochemical detection.

Results We found that APC produced a significant reduction in extracellular dopamine and a dramatic increase in noradrenaline release from the slices incubated with different concentrations of APC.

Conclusions These findings suggest that the modulation of catecholaminergic neurotransmission is a new pharmacological effect of APC which could explain the mechanism of action of this formulation, considering that the independent effect of either compound alone does not explain the potent antinociceptive properties when observed in combination.

RAEDER'S SYNDROME LIKE ONLY MANIFESTATION OF BILATERAL SPONTANEOUS CAROTID ARTERY DISSECTION

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Background We present a patient with Raeder's syndrome secondary to spontaneous bilateral carotid dissection.

Methods 59 year old man presented with a sudden attack of left retroorbital pain associated to left ptosis and mild photophobia and phonophobia. The headache didn't improve with rest. On neurological examination he had left ptosis and left miosis. Analgesic treatment began to growing dose requiring finally treatment with endovenous morphine.

Results Cranial tomography was normal. Magnetic resonance imaging(MRI) showed right sided periventricular white substance ischemic infarct and MRI angiography demonstrated a bilateral internal carotid artery occlusion with decrease flow in right intracranial internal carotid artery and right middle cerebral artery. Conventional angiography confirmed sharp occlusion of initial segment of right internal carotid, and intracranial and extracranial stenosis of left internal carotid. Angiography images was no compatibles with fibromuscular dysplasia. Homocystinemia, alpha1-antitripsin, antinuclear antibodies; routine laboratory tests, echocardiography and abdominal ultrasonography were normal. Magnetic resonance angiography at 3 months demonstrated a total recanalitation of both carotid arteries.

Conclusions In this patient left Raeder's syndrome went secondary to the intracranial left carotid dissection. This syndrome can be the only symptom of carotid dissection uni or bilateral.

ANGIOTENSIN-CONVERTING ENZYME GENE INSERTION/DELETION POLYMORPHISM IN MIGRAINE PATIENTS

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Background and aims A growing amount of evidence points in the direction of the involvement of the renin-angiotensin system in

migraine pathophysiology. The human angiotensin-converting enzyme (ACE) gene consists of three possible genotypes: II, ID or DD. In migraine patients this polymorphism has been investigated in several studies, but the results are not consistent. The objective of the present study was twofold. Firstly we wanted to examine whether a clinical response of the ACE inhibitor lisinopril or the angiotensin II receptor blocker candesartan in migraine prophylaxis could be predicted using the ACE genotype. Secondly we wanted to investigate the ACE genotype and the levels of ACE as possible risk factors for migraine with and without aura.

Methods Included in the study were 190 migraine patients aged 18–65 (93 without aura (MoA), 97 with aura (MwA)) and 201 healthy non-migraine controls >40 years of age.

Results No significant difference in ACE genotype or allele frequency between migraine patients and controls were detected. Further, no difference was found between the controls and the MwA and MoA subgroups, or between responders and non-responders to lisinopril or candesartan. Within the migraine group differences in genotype could not explain age of debut of migraine, or the presence of aura or tension-type headache. Measured serum-ACE was significantly lower in the migraine group compared to the controls.

Conclusions In a Norwegian sample, there is no difference in ACE genotype or allele frequency in a migraine group compared to a control group. Findings from other studies that the DD genotype was more frequent in MoA [Paterna et al.] and MwA [Kowa et al.] or less frequent in male migraineurs [Lin et al.] are not supported by our data. ACE genotype can not be used to predict the clinical response to lisinopril or candesartan used as migraine prophylactics.

POST-ICTAL HEADACHE IN PATIENTS AT EPILEPSY CLINIC IAHULA. MERIDA – VENEZUELA

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Background The post-ictal headache (PIH) appears later to an epileptic crisis. PIH in idiopathic generalized epilepsy (EIG) and occipital focal idiopathic (EIFO) and temporal lobe epilepsy (EFLT) has been well characterized, denominating the last case as migraine-like by their clinical similarity with migraine, postulating some authors a common physiopathological substratum between both.

Objectives 1 To know the frequency and characteristics of PIH in patients with focal and generalized epilepsy. 2 To determine similarities with migraine in both groups of patients with epilepsy.

Methods All the patients, who went to the consultation of epilepsy between September - December 2005, were included; the questionnaire of the clinic of headache IAHULA was applied to characterize the PIH.

Results They were taken care of 138 patients with epilepsy, 18 (13%), presented PIH, 11 masculine and 7 feminine ones. The etario range went of 15 to 56 years. There were 9 patients with EFLT (50%), and 9 patients with generalized epilepsy (50%). Familiar antecedents: migraine 17% and epilepsy 44%. Characteristics of PIH, global location 61%, pulsating quality 68% and severe average intensity to 68% predominated. Interictal migraine in 5 patients (38.8%) and only 2 patients, migraine without aura.

Discussion Low frequency of PIH in the studied population was observed. In spite of being EFLT, there were not elements to characterize the PIH like migraine-like, since only the pulsating quality in 68% of the patients was consistent with it, which makes think that this pattern is more consistent with EIFO, and that the region of epileptic focus of epileptic discharge may have a close relation to the induction of PIH.

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AN ASSESSMENT OF SUPPORT TOOL FOR MIGRAINE TREATMENT, FAME (FORMULA ASSESSMENT FOR MIGRAINEURS)

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Background Currently, four triptans with formulation of conventional tablet, orally disintegrating tablet, nasal spray and injection are available for acute migraine treatment in Japan. However, there are not established criteria to choose the suitable formulation for patients. FAME is developed to support physicians to choose the most suitable formulation for patients according to their life style, symptoms and compliance.

Objective The aim of this study is to assess the value of FAME by assessing patients' satisfaction after changing or adding their triptan formulation.

Methods Patients taking triptans filled FAME about current treatment and symptoms to choose the most suitable formulation for them. Based on the information of FAME, if patients agreed, patients changed their triptan formulation or used different formulation of triptan on top of current treatment. The treatment satisfaction of patients would be assessed after the treatment change.

Results The majority of patients, changed their treatment by using FAME, satisfied and aspired the recommended triptan formulation. The detailed results will be presented at the conference.

Conclusions FAME is an useful tool to choose the most suitable triptan formulation although we haven't finished all of our trials yet. We expect FAME can contribute early intervention of triptan and improvement of QOL of migraine patients.

PROPHYLACTIC TREATMENT OF CLUSTER HEADACHE WITH ORIENTAL MEDICINE (TOKI-SHIGYAKU-KA-GOSHYU-SHOKYO-TO)

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Background In oriental medicine, Toki-Shigyaku-Ka-Goshuyu-Shokyo-To (TSKGST), one of the traditional oriental prescriptions, has said to have the actions as following: warming the middle-energizer, the meridians and invigorating "qi" to dispel cold, nourishing blood and promoting blood circulation. From the viewpoint of western medicine, TSKGST chiefly has the action to improve peripheral blood circulation. The author reported that TSKGST showed good prophylaxis of migraine at IHC 2005 KYOTO. Then, the author tried to use this prescription for prophylaxis of cluster headache.

Objective A 62-years-old male, a journalist. He had suffered from cluster headache for 38 years. His cluster headache had occurred frequently in winter for several months. The attack often interrupted his sleep, persisted one hour and more, and worsened with alcohol. Neurological examination and radiological studies were normal. He also had hypersensitivity to cold as well.

Methods TSKGST 5.0~7.5g/day were prescribed to him. The effectiveness was estimated by decrease of the attack frequency.

Results Follow-up period was 24 months. Although he had experienced its aura (neck stiffness) several times, but he had not experienced cluster headache attack any more. And he could even drink without anxiety. Hypersensitivity to cold was also resolved.

Conclusions TSKGST showed good prevention effect against cluster headache in this case. Further investigation is required.

TESTING CANDIDATE GENES FOR MIGRAINE WITH AURA USING 1798 FINNISH INDIVIDUALS

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Background and aims Although various association studies have been performed in migraine, only few of the positive findings have been subsequently replicated. One of these is the C677T variant of the methylenetetrahydrofolate reductase (MTHFR) gene that has been associated to migraine with aura (MA) in several populations. The aim of our study was to evaluate the contribution of several promising candidate genes in migraine susceptibility using considerably larger sample size than used in the original studies. In addition to MTHFR, genes encoding three GABA-A receptors (GABRB3, GABRA5, GABRG), endothelin-1 and two of its receptors (EDN1, EDNR1, EDNRB) as well as estrogen receptor (ESR1) were studied. **Methods** Since we wanted to study the contribution of the entire genes including 5'- and 3'-flanking areas, we covered them with SNPs by genotyping altogether 6 MTHFR, 26 ESR1, 35 GABA-receptor and 32 endothelin system polymorphisms. We compared the allele and genotype frequencies of these SNPs between 898 unrelated Finnish MA patients (69% originated from large migraine families, 31% from a population-based twin sample) and 900 unrelated Finnish migraine-free twin controls without a family-history of migraine.

Results No evidence of association with the MTHFR C677T variant was seen (p -value 0.83). Neither the GABA-receptor nor the endothelin system polymorphisms were associated with MA. The most significant p -value was reached with an ESR1 SNP rs6557170 ($p=0.007$). Taking into account multiple testing, we felt that this result most likely is a false positive. To clarify this, we genotyped further 368 control individuals. When these individuals were included in the analysis, the p -value deteriorated to 0.02.

Conclusions Our study provided no support for these genes contributing to MA susceptibility at least in the Finnish population. These results underline the importance of larger sample sizes and stringent multiple testing corrections to diminish the number of false positive associations in migraine.

ACTIVATION OF MMP-9 IN MIGRAINE: EVIDENCE OF BLOOD-BRAIN BARRIER DISRUPTION DURING MIGRAINE ATTACKS

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Background and aims Matrix metalloproteinases (MMPs) are a family of proteases involved in the remodelling of the extracellular matrix. Loss of control and increased expression and activity of MMPs have been implicated in various neurological disorders. Up regulation of MMP-9 has been observed in cortical spreading depression induced in experimental animal models. The aim of the study was to evaluate the activity of MMP-9 in migraine patients during migraine attacks and pain-free periods.

Methods We evaluated 34 migraine patients with aura (MA) and without aura (MO), according to International Headache Society cri-

teria, 2004. We established a control group with 10 cases, matched by age and sex. We analyzed the main clinical variables related to headache (frequency, intensity, duration). MMP-9 plasma levels (ELISA, P&A) were measured during migraine attacks and pain-free periods in all patients.

Results Higher plasma MMP-9 were shown in migraine patients than in controls (247.7 ± 182.2 vs 51.7 ± 19.9 ng/mL; $p<0.001$). The increase was more significant in the group of patients with MA and during migraine attack (389.6 ± 184.8 vs 159.3 ± 116.9 ng/mL in MA; $p<0.0001$; 338.5 ± 173.1 vs 118.1 ± 98.4 ng/mL in MO; $p<0.0001$). We found no correlation between high plasma MMP-9 and frequency, intensity or duration of the migraine attack.

Conclusions An increase in plasma MMP-9 during migraine attacks is shown in patients with and without aura. This fact suggests the existence of a blood-brain barrier disruption during a migraine attack.

ANALGESIC OVERUSE AMONG ADOLESCENTS WITH HEADACHE. THE HEAD-HUNT YOUTH STUDY

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Background and aims Medication overuse is a potential risk factor for chronic headache, and the prevalence of medication overuse headache (MOH) is about 1% among adults. The prevalence of MOH among adolescents is not known. The aim of the present study was to examine the association between the use of analgesics and primary headache disorders (i.e. migraine and tension-type headache) among adolescents in relation to age, gender and headache frequency.

Methods This cross-sectional population based study was conducted in Norway 1995–1997. The total study population consisted of 5471 adolescents, 13–18 years of age, who were interviewed about their headache complaints and completed a comprehensive questionnaire including use of analgesics.

Results The prevalence of daily headache associated with analgesic use was 0.5%, with a higher rate for girls (0.8%) than for boys (0.2%). There was a significant association for both genders between analgesic use and headache, though most pronounced for migraine. There was a significant linear relation between analgesic use and headache frequency. Analgesic use was more common among girls than boys and increased with age both for those with and those without headache.

Conclusions The use of analgesics is common among adolescents with headache, especially among girls. Although this study did not directly evaluate for MOH, the trend of frequent analgesic use suggests this possibility. Parents and physicians should increase their awareness of potential analgesic overuse, especially among adolescents with frequent headache.

A VALIDATION STUDY OF AN ITALIAN VERSION OF THE "ID MIGRAINE"

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Objective Migraine is a highly prevalent and disabling disease that is substantially undiagnosed in primary care [1]. Validated migraine screening tools are of potential value in addressing this important barrier for migraine treatment. Recently Lipton et al. [2] validated a brief, self-administered migraine screener, consisting of only three items, for patients with headache in the primary care setting: the ID Migraine questionnaire. This tool showed to be a valid and reliable screening instrument with high sensitivity, specificity and positive predictive value for migraine headache [3]. The aim of our study was to validate an Italian version of the ID migraine questionnaire, to be used in Italian headache population.

Methods We performed a multicentric study involving several headache centers in Sicily, evaluating 222 consecutive patients affected by various form of headache. The responses to the ID questions were compared with the diagnosis of headache made by another physician blind to the result of the questionnaire. Sensitivity, specificity, positive and negative predictive value for migraine were calculated. Test-retest reliability was also evaluated in 20 patients that repeated the questionnaire 2–5 days after, through Kappa coefficient for intraclass correlation.

Results The statistical analysis showed a very good performance of the ID Migraine with high sensitivity: 0.94 (95% CI: 0.90–0.97), specificity: 0.70 (95% CI: 0.58–0.80) and positive predictive value: 0.87 (0.81–0.92). In patients that took the questionnaire twice, ID showed a good test-retest reliability with a Kappa coefficient of 0.70.

Discussion and conclusions The results seem to confirm the ID Migraine as a valid screening instrument for migraine at least in Italian headache population referring to headache centers. A further investigation in primary care is warranted to establish “ID Migraine” as a valid screening instrument for migraine in Italian population.

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PAIN FREE INTERVAL: RELATION TO THE QUALITY OF LIFE IN MIGRAINE

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Background and objective While the impact of headache attacks on disability and quality of life (QL) of migraine subjects is well documented, the influence of general state of patients during pain free interval is insufficiently studied. Our study was aimed to determine which conditions in pain free interval have significant impact on the QL of migraine subjects.

Methods 320 patients with MO and MA (M-48, F-272, mean age-37.9) were analyzed using clinical interview, headache and autonomic dysfunction questionnaires, manual palpation of pericranial muscles, the West Haven-Yale Multidimensional Pain Inventory with Life Impact Assessment, Beck Depression and State-Trait Anxiety Inventories.

Results QL was impaired moderately or severely in 64% of patients. Comparative analysis of subjects with poor (QL decrease >40%) and good QL (<30%) has shown that during pain free intervals subjects with poor QL significantly more often had depression, anxiety, sleep disturbances, dysfunction of pericranial muscles, autonomic (hyperventilation syndrome, essential hyperhidrosis, panic attacks) and gastrointestinal disorders.

Conclusions Our results show that QL in migraine patients is closely related to pain free interval state. The conditions that are responsible for marked reduction of QL in migraine patients include

depression and anxiety, sleep disturbances, dysfunction of pericranial muscles, autonomic and gastrointestinal disorders. The comorbid essence of these conditions should be suggested.

WHICH QUALITY OF LIFE DOMAINS ARE MOST AFFECTED BY MIGRAINE?

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Background We have previously demonstrated that both migraine and cluster headache heavily affect the patients' quality of life (QOL). However, the QOL profiles of these clinically distinct disorders were surprisingly similar. This may have been caused by a relative insensitivity of the available QOL instruments, the generic SF-36 and the migraine-specific MSQ2.1 questionnaires, to the specific effects of these headache types.

Objective To further examine the effect of headaches on QOL, the present study aimed at identifying the determinants of QOL in migraine.

Methods This was a prospective pilot study on 41 migraineurs presenting at the headache centre of an academic neurology facility. Based on clinical interviews and expert opinion, we developed a 25-item QOL questionnaire that examines, among others, role functioning (professional, family and social), cognition, mood and affect, health perceptions, sleep and medication use.

Results Factors that were most severely affected by migraine (defined as a 75% or bigger reduction in more than 70% of respondents) included role performance (professional and household duties), leisure and social activities, physical functioning, energy, mood, and the use of abortive medication. The average number of items that were at least moderately (at least 50% reduction of functioning) affected by migraine was 18.48 (SD: 3.49, median: 20, range 11–24) per person.

Conclusions Migraine affects multiple QOL domains. The currently used short QOL questionnaires may not be sensitive enough to fully capture the effects of this headache type.

CGRP8-37 INHIBITS CAPSAICIN-INDUCED VASODILATION IN THE HUMAN SKIN

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Background Application of capsaicin to the skin evokes neurogenic inflammation resulting in dermal vasodilation. The aims of this study were: to assess the arm-to-arm reproducibility of this response (part I) and to identify the contribution of calcitonin-gene related peptide (CGRP), prostaglandins (PG) and nitric oxide (NO) (part II).

Methods In part I, a 2-period open label study, capsaicin (1000microg/20microL) was locally applied to the volar surface of both proximal forearms. In part II, responders (i.e. subjects showing an increase of >100% in dermal blood flow (DBF) in both arms) participated in a randomized, single-blind, 3-way, cross-over study. During capsaicin administration, CGRP8-37 (1200 ng/min/dL forearm), indomethacin (5 microg/min/dL forearm) or NG-monomethyl-L-arginine (L-NMMA, 0.2 mg/min/dL forearm) was infused in the brachial artery of the non-dominant arm. DBF was assessed by laser Doppler perfusion imaging before and at 10, 20 and 30 minutes after capsaicin application. DBF response was summarized by the percentage increase at 30 minutes (t30, %) and the area under the curve from 0 to 30 minutes (AUC0-30, % min).

Results Part I The mean difference \pm SD in response between both arms averaged 36 ± 114 % and 139 ± 1092 % min, for t30 and AUC0-30 respectively (n=22). This corresponds with an intraclass correlation coefficient of 0.72 for t30 and 0.91 for AUC0-30.

Table 1 Part II results

Response	CGRP ₈₋₃₇		L-NMMA		Indomethacin	
	IA	NIA	IA	NIA	IA	NIA
T ₃₀ (%)	217±32*	370±52	314±28	309±30	319±33	337±36
AUC ₀₋₃₀ (% min)	2721±356*	5093±348	3417±400	3717±515	3945±499	4392±702

Conclusions The capsaicin-induced increase in DBF shows a high arm-to-arm within-subject reproducibility. This response is largely inhibited by CGRP₈₋₃₇ but not by L-NMMA or indomethacin. These findings suggest that the capsaicin-induced DBF response can be used as a pharmacodynamic model to test CGRP antagonists in vivo in humans.

EFFICACY AND TOLERABILITY OF ALMOTRIPTAN VERSUS ERGOTAMINE+CAFFEINE IN MIGRAINE TREATMENT. A RANDOMISED, CROSS-OVER, DOUBLE BLIND CLINICAL TRIAL

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Background and aims Background: Migraine is a high prevalence disease in western countries (5%–7% in males and 15%–17% in females) that causes a serious disability and has repercussions on quality of life. It is necessary to find therapies to treat migraine attacks and to satisfy patients expectations and needs at the same time.

Aims To assess the efficacy and tolerability of almotriptan 12.5mg tablets versus ergotamine 2mg + caffeine 200mg tablets in two consecutive migraine attacks.

Methods design Randomised, cross-over, double-blind clinical trial.

Settings 24 neurology services in 24 Spanish hospitals.

Patients Patients aged between 18 and 65 years with migraine diagnosis following IHS criteria for at least one year, with 1 to 6 attacks per month.

Measurements The primary efficacy endpoint was pain-free at 2 hours. In addition, several secondary variables were analysed.

Results 229 patients took at least one tablet of the study medication (safety population). 182 patients fulfilled protocol requirements and had at least one pain measurement data after treatment intake for both attacks (ITT population). 86.9% of patients were female and the average (SD) age was 33.5 (9.4) years. Patients receiving each treatment sequence were homogeneous in terms of social demographic and clinical variables. (See results in Table 1)

Table 1

	Almotriptan, %	Ergotamine + caffeine, %
Pain free at 2 h*	20.9	13.7
Pain relief at 2 h**	57.7	44.5
Use of rescue medication*	38.5	48.4
Sustained pain free at 24 h*	20.3	11.5
Recurrence at 24 h	12.4	8.6
Migraine related symptoms at 2 h		
Nausea**	17.6	31.9
Photophobia	28.0	36.3
Vomiting**	1.1	8.8
Phonophobia**	23.1	34.1
Adverse events	7.4	12.2
Treatment satisfaction*	45	30

* $p < 0.05$; ** $p < 0.01$

Conclusions Almotriptan 12.5mg was more efficacious than ergotamine+caffeine 2/200mg to treat migraine attacks in terms of pain free, pain relief, use of rescue medication, sustained pain-free and migraine related symptoms. A clear tendency to better tolerability of almotriptan was also found. When treated with almotriptan patients were more satisfied than when treated with ergotamine-caffeine.

DRUG TREATMENT IS USEFUL IN CHILDREN MIGRAINE

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The management of pediatric migraine requires an individually tailored regimen of both biobehavioral measures and pharmacologic treatment which is based on individual approach using symptomatic and preventive drugs.

Acute treatment Both ibuprofen and acetaminophen have been shown to be safe and effective in controlled trials; however, 30% to 50% of paediatric migraine attacks may be refractory to simple analgesics and non steroidal anti-inflammatory drugs. In prospective controlled studies the oral triptan preparations were not consistently more effective than placebo; these unpromising results may depend on the peculiar characteristics of juvenile migraine (i.e. shorter duration of attacks, marked gastric stasis, and higher placebo response). Sumatriptan nasal spray in several open and placebo controlled trials have shown efficacy and safety in migrainous adolescents, most likely for the faster absorption.

Preventive treatment Prophylactic medication is indicated only for children with severe and frequent attacks. In published statistics, about 30% of children require daily preventive agents, because of high frequency and/or significant disability due to headaches. However there is a paucity of controlled clinical research in this field: older therapies (β -blockers, antidepressants, serotonin modulators and calcium channel blockers) have shown conflicting or insufficient data and also the more recent therapies (anti-epileptic drugs), generally well tolerated in paediatric epilepsy, are in need of multicentered, placebo controlled trials. In conclusion pharmacologic approach to juvenile migraine represent a critical area to reduce the headache burden and disability. Urgent rigorous and innovative study designs (i.e. patients recruited from primary care Centres) to ascertain safety and efficacy of old and new drugs are needed. In future trials more careful attention needs to be given to define subtypes of migraine, to tailor the best therapy in each single patient.

"MOBILE PHONE HEADACHE" IS NOT RELATED TO RADIOFREQUENCY FIELDS: A DOUBLE BLIND PROVOCATION STUDY

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Background In a Norwegian-Swedish epidemiological investigation [1], 22% reported headache or other symptoms related to mobile phone calls.

Objective To test whether the radio frequency (RF) field from a mobile phone cause headache in a highly selected group.

Methods After a thorough recruitment and screening procedure (newspaper advertisements, telephone interview, detailed questionnaire, open RF exposure trial) 17 subjects usually developing headache or discomfort during mobile phones calls were included in

a double blind RF field exposure study. Each subject was subjected to maximally 8 trials on separate days, 4 with and 4 without RF exposure in random order. In total 65 pairs of trials, each lasting 30 minutes, were conducted. Headache and other discomfort before, during and after the sessions were indicated on VAS.

Results Except from a few instances, the subjects had no symptoms before the start of the session. When headache occurred, it usually came during the exposure, and its maximum occurred during the trial or less than one hour later. Most symptoms were mild, closely resembling those experienced during real mobile phone calls. More headache occurred in connection with non-exposure sessions than RF exposure sessions (mean VAS 11.0 versus 7.9, $p=0.22$).

Conclusions RF fields did not induce headache in this highly selected group. The fact that many developed their typical "mobile phone headache", and that the situation involved no other sensory or behavioural cues normally related to mobile phone calls (sound, stress, neck/arm position) suggest that expectation may play a major role in connection with headache triggers.

Reference

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TRIPTANS FOR TREATMENT OF ACUTE PEDIATRIC MIGRAINE: AN OPEN STUDY IN ITALY

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Background The management of pediatric migraine requires behavioural and pharmacological intervention. However, 30%–50% of pediatric migraine attacks may be refractory to simple analgesics and NSAIDs. Until now, it has been difficult to demonstrate in children and adolescent the efficacy of oral triptans tablets, because the gastric stasis, that is a marked symptom in children, affects the tablets absorption and the bioavailability. In juvenile patients the most reliable studied agents for the migraine attacks are acetaminophen, ibuprofen and sumatriptan nasal spray (SNS): all these compounds have shown to be effective and safe in controlled trials. In particular the SNS is the only 5HT_{1B}-1D agonist effective for acute attacks in adolescents and 10mg has been recently licensed in Italy for use in adolescent (12–17 years). The result of open-label study in 12 selected adolescents are presented.

Methods Inclusion criteria: a) MwA and MWA (ICHD 2004), b) age 12 to 18 years, c) presence of nausea and/or vomiting.

Samples 12 Patients (7 male) were enrolled, 8 patients with MwA and 4 with MWA. Each patient treated 2 migraine attacks with 10mg SNS (total 24 attacks treated)

Results Pain relief (from pain severe/moderate to mild/none) 1h after treatment, 6/12 and 2h, 8/12 patients. Pain free after 2h, 8/12 patients. Reduction of associated symptoms 9/12 patients. Patient satisfaction: very good 9/12, sufficient 3/12, none 0/12 Recurrence (<24h) none. The only side effect registered is the bad taste (4/12 patients).

Conclusions SNS resulted to be safe and well tolerated, showing a good efficacy profile and a fast action and it's the drug of choice in the symptomatic therapy of migraine attack in adolescent patients.

CEREBRAL VENOUS SINUS THROMBOSIS, AN EXCEPTIONAL CAUSE OF THUNDERCLAP HEADACHE

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Introduction Thunderclap headache raises the suspicion of subarachnoid haemorrhage (SAH), and it is not generally recognised as

a symptom of cerebral venous sinus thrombosis (CVST). We describe a patient who presented with thunderclap headache, mimicking acute subarachnoid haemorrhage (SAH), who appeared to have CVST in acquired protein S deficiency.

Case report We report a patient, a 38-year-old man, sweeper, with a history of hypertension and alcoholism. During work he complained of severe occipital headaches and neck pain with a sudden onset, reaching maximum intensity right from the start, accompanied by photophobia, vomiting and brief disorder of consciousness in the previous five days before admission with discreet nuchal rigidity. CT scan showed SAH involving the sulci of the right frontal convexity and angiogram-CT was normal. Three days later he had vomited and made new CT scan with similar result and an angiography showed normal arterial study. The patient with "SAH" was transferred to Department of Neurology of his area. Seven days later we found a papilloedema, a MRI revealed CVST. The patient was treated with warfarin, and had a rapid clinical and radiologic improvement. Results of the etiologic workup revealed an acquired protein S deficiency.

Conclusions The characteristics of thunderclap headache are abrupt onset and very severe pain. In patients with thunderclap headache, SAH is a possible diagnosis. Cerebral venous sinus thrombosis (CVST) is generally not considered in these cases. In our patient with thunderclap headache, CVST caused headache and clinical symptoms that were clinically indistinguishable from SAH. This case highlights the fact SAH may reveal CVST, which should be considered in the diagnostic workup of SAH, especially when the basal cisterns are not involved because it will have important practical consequences.

EVALUATION OF THE RELIABILITY OF THE FRENCH AND DUTCH VERSIONS OF THE MIDAS SCORE IN MIGRAINE PATIENTS TREATED WITH ZOLMITRIPTAN – THE METZ STUDY: MIDAS EVALUATION TRIAL WITH ZOMIG INSTANT

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Migraine might have serious implications on the social and professional activities of the patient. The MIDAS questionnaire is directed to objectify this disabling effect using 5 questions, allowing the doctor to obtain a global view of the seriousness of the pathology, and to initiate more rapidly an appropriate medication. In Belgium, 79 migraine sufferers were recruited. By submitting a Dutch or French translation of the MIDAS questionnaire, the functional invalidity was evaluated at the time of inclusion, following a run-in period of 3 weeks, after 12 weeks of treatment with zolmitriptan and again following 3 more weeks of treatment for 56 patients. The reliability coefficient for the test-retest of the Belgian translations of MIDAS rated 0.76, indicating a good reliability. The internal consistency between the questions, evaluated by Cronbach's alpha coefficient, amounted to 0.68, indicating as well its acceptability. The majority of patients found the MIDAS understandable and relevant. In this study as well, zolmitriptan significantly decreased the invalidity by 34% ($p<0.0002$) after 12 weeks. It is concluded that the Dutch and French translations of MIDAS do appear as reliable as the original English version, and can be considered as valuable instruments for measuring and follow-up of migraine in day-to-day practice.

PSYCHOLOGICAL FACTORS AND PAIN IN CHILDREN AND ADOLESCENTS

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Biologic maturation influences the perception and response to pain. This assumption outlines the role of age-related physiologic features in the modulation of pain, but also the expression of pain does change with age. Sensation of pain differs from cognition of pain, such as several psychological factors (age, previous pain experiences, coping style, skills of answers from family or social setting) are implicated in communicating pain. Factors such as cognitive maturation, language development, pain memories, perceiving coping ability, self-regulation capabilities, cultural, familial and individual attributions contribute individually and together to the pain experience and development of chronic pain. The weight of each factor in modulating pain experience and expression is unknown. We apply adult categories in the understanding and analyzing children's pain. The characteristics of children's pain is always inferred by adults, and it is at best inferential. The adults' inference is more difficult with non-verbal infants, where it's necessary to look at infants' behavioral and physiological signs of distress. Bearing in mind this view, we should consider the child not being a "little adult". That means also that many individual factors run together to affect the expression and modulation of pain, resulting in always different outcomes. Beginning by considering the child as a whole of his/her development, taking into account neurobiological and psychological maturational processes, familial and social environmental factors is crucial to avoid a restraining and unilateral approach to the disease. Taking into account all these factors has a critical importance in the assessment process and for the choice of the better drug or non-drug treatment.

TRAIT COMPONENT ANALYSIS OF FINNISH MIGRAINE FAMILIES OFFERS INSIGHTS INTO THE GENETICS OF MIGRAINE

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Background and aims Most gene locus identification studies are performed using the end point diagnosis, such as migraine with aura as the phenotype. We performed a new type of genome-wide screen using the clinical traits associated with migraine. Since migraine is a complex syndrome, we set out to study if individual clinical aspects might be inherited independently. Our aim was to analyse which IHS subcomponents provide the best evidence of linkage to the 4q24 locus and whether additional susceptibility loci for trait components could be localized. The analysis was performed on a set of families that had identified the 4q24 locus with the migraine with aura diagnosis.

Methods Our study sample consisted of 430 genotyped patients within 50 Finnish independent multigenerational migraine families. The same neurologist diagnosed all subjects. The genotypes were analyzed by parametric and non-parametric two-point and multi-point linkage analyses.

Results Strongest evidence of linkage to the 4q24 locus was observed by using photophobia (two-point LOD score 4.39) and phonophobia (4.10) as the analysed trait components. Thus these two traits showed evidence of linkage to the same locus as the endpoint diagnosis. Furthermore, trait component analysis detected significant evidence of linkage to two other loci: on chromosome 17 (4.65) with the pulsation subcomponent, and on chromosome 18 (3.41) with the

entire criteria shared by migraine without aura and typical aura with migraine headaches. Additionally, when analysing the age of onset of migraine, a new locus on 4q28 was found. In summary, the analysis detected two significant and three suggestive loci.

Conclusions The finding of these new loci and that they represent different traits suggest that individual clinical features of migraine, including the age of onset, may represent individual heredity, and that trait component analysis can be used to stratify patient samples for genetic studies.

PREVALENCE OF RECURRENT AND SEVERE HEADACHE IN THE GENERAL POPULATION

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Aims To evaluate the lifetime prevalence and gender distribution of recurrent and severe headache in the general population. This study is part of a survey aimed at evaluating the lifetime prevalence of cluster headache in the general population.

Sample and methods The sample consisted of 10,071 subjects (5,311 F and 4,760 M) and comprised all the patients aged over 14 registered in the lists of seven general practitioners (GPs) in Parma. We asked the subjects to complete a previously validated questionnaire in their GP's office, or at home after receiving the questionnaire by mail or by phone.

Results A total of 7,522 people (74.7%, 3,971 F and 3,551 M, mean age 50.8±19.0 years) responded to the questionnaire. 44.5% (n=3,344, 2,032 F and 1,312 M) reported that they suffered or had suffered from headache and 1,305 (17.3% - 910 F and 395 M) answered "no" to the question "does it ever happen to you to be headache free for many months?". The prevalence rate of recurrent, severe or very severe headache was 11.9% (n=892), 16.7% (n=662) in women and 6.5% (n=230) in men. 12.1% (n=907) of the initial sample reported sporadic and mild or moderate headache. The percentage of women was significantly higher in recurrent and severe forms compared with sporadic and mild to moderate headache (74.2% vs 48.8%, p<0.000).

Comments It is reasonable to assume that, regardless of the primary or secondary nature of the disorder, a severe form of headache that occurs without symptom-free intervals and lasts many months may eventually represent a disabling condition to those who suffer from it. From our results, it appears that 11.9% of the general population suffers from recurrent and severe headache. Therefore, this condition clearly has strong social implications.

FROM CHRONIC TO EPISODIC MIGRAINE: TOPIRAMATE AND TRIPTAN THERAPY

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This is a randomized double-blind versus placebo study aimed at evaluating the efficacy of topiramate in reducing the number of days with headache and the amount of acute medication taken monthly in patients with chronic migraine with medication overuse and the efficacy of single triptans available in Italy, in interrupting headache crises during preventive treatment.

Methods The studied sample was made up of 50 subjects: 30 patients were randomized for treatment with topiramate, 100mg a day, and 20 for placebo. Subjects treated with topiramate were fur-

ther randomized in order to evaluate, in double-blind versus placebo, the efficacy of single triptans, available in Italy. The double-blind phase consisted of a titration phase (4 weeks) and of a maintenance phase (8 weeks).

Outcome measures The reduction of the number of days with headache/28 days and the reduction of the amount of acute medication taken/28 days throughout the clinical trial in the topiramate group compared to placebo; the number of patients who were pain-free at two hours after the triptan intake and the headache recurrence rate in the 22 hours following the pain-free condition in the triptan group compared to placebo; tolerability prophile.

Results The group treated with topiramate had a significant reduction in the number of days with headache ($p < 0.0001$ vs placebo) and in the mean amount of acute medication taken ($p < 0.0001$ vs placebo); all triptans were superior to placebo; there were no significant differences between different triptans; the analgesic effect of triptans increased throughout the trial.

Conclusions Topiramate proved to be well tolerated and effective in reverting chronic migraine with medication overuse to episodic migraine.

CYCLOOXYGENASE-1 INHIBITOR IS NOT ABLE TO MODULATE THE NITRIC OXIDE INDUCED NEURONAL NITRIC OXIDE SYNTHASE ENHANCEMENT IN THE RAT CAUDAL TRIGEMINAL NUCLEUS

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Nitric oxide (NO) donor, nitroglycerin (NTG) can trigger after a delay of several hours, a typical migraine attacks in migraineurs, but not in healthy persons. In rats subcutaneous administration of NTG (10 mg/kg) is able to increase significantly after 4 hours the number of neuronal nitric oxide synthase (nNOS)-immunoreactive neurons in the caudal trigeminal nucleus (TNC). This may lead to a self-amplifying process causing central sensitization in the trigeminal system, a phenomenon also present in migraine patients. Earlier data indicate that the non-selective cyclooxygenase (COX) inhibitor acetyl-salicylate is able to attenuate the NO enhanced nNOS in the TNC. The aim of our study was to investigate if SC560, a selective COX-1 inhibitor is able to suppress this effect. Rats received indomethacin or SC560 pretreatment before placebo or NTG injections. Compared to non pre-treated controls indomethacin could attenuate the nitroglycerin-induced nNOS expression in a dose dependent manner in the TNC, but the selective COX-1 inhibitor SC560 failed to do so. These findings suggest that prostanoids are crucial in the NTG-induced nNOS expression, but not the COX-1 isoform. These data could help to better understand the activation of the trigeminal system, the pathogenesis of headaches and the action of antimigraine drugs.

ISCHEMIA OF THE CLAVOTRAPEZIUS CHANGES BEHAVIORAL RESPONSE TO OROFACIAL PAIN. EVIDENCE OF TRIGEMINOCERVICAL CONVERGENCE

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In order to determine the influence of nociceptive cervical inputs on trigeminal pain. Male rats (300–390 g) were divided into six groups: Group 1 - control group (not submitted to surgery) - containing group 1A - trichotomy on same side as formalin test (n=10) - and group 1B - trichotomy on opposite side to formalin test (n=10); Group 2 - skin incision only - containing group 2A - animals submitted to surgery to open the skin over the clavotrapezius muscle on the same side as formalin test (n=10) - and group 2B - surgery on opposite side to formalin test (n=10); Group 3 - myofascial lesion - containing group 3A - animals submitted to plication of the clavotrapezius muscle on the same side as formalin test (n=10) - and group 3B - surgery on opposite side to formalin test (n=10). The surgery was carried out seven days before the formalin test. Eighty μ l of 2.5% formalin was injected into the left upper lip trigeminal territory to induce neurogenic and inflammatory phase pain behavior (0–3 and 12–30 mins, respectively). After the test, the animals were anesthetized, and a biopsy of the clavotrapezius muscle was performed in all the animals to confirm the presence of inflammation. The myofascial same-side (3A group) showed strong neurogenic ($p < 0.001$) and inflammatory ($p < 0.001$) behavioral responses compared with the opposite-side myofascial group or the control and skin same-side and opposite-side groups. The muscle biopsies showed severe inflammation in the myofascial groups compared with the control and skin groups. Our results show an interaction between the cervical and trigeminal nociceptive systems (trigemincervical convergence), and suggest that this occurs during the early and late pain phases.

HOMOCYSTEINE AND MIGRAINE

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Background Migraine with aura represents about 20 percent of all forms of migraine and is characterized by the appearance, before pain, of transient visual, sensory and/or speech disturbances. The similarity between some manifestations of aura and some kind of transient ischemic attacks has raised the hypothesis of a similar pathophysiology. Hyperhomocysteinemia, a known causal agent of vascular disorders, does not seem to be a relevant condition in patients with migraine of any type (with and without aura) [1]; on the other hand, genetic alterations in MTHFR gene, involved in homocysteine metabolism, seem to predispose to migraine [2]. No data are available about a possible difference in homocysteine status between patients with and without aura.

Objective To determine comparatively the homocysteine levels in sera from patients affected by migraine with and without aura and tension-type headache.

Methods Total serum homocysteine was measured in 70 patients affected by migraine without aura (MWOA), 24 with migraine with aura (MWA) and 14 with tension-type headache (TTH) diagnosed according to IHS criteria.

Results Mean homocysteine levels (micromoles/L) were 8.6 ± 2.6 in TTH patients, 9.8 ± 4.2 in MWA and 9.0 ± 6.0 in MWOA patients, no significant difference being evident between groups by t-test analysis ($P = NS$). The occurrence of hyperhomocysteinemia, defined as a concentration above the upper normal limit of 15 micromol/L, was significantly higher in MWA patients compared to MWOA (MWA: 5/24, 20.8%; MWOA: 4/70, 5.7%; $p = 0.03$ by chi-square).

Discussion The higher frequency of hyperhomocysteinemia in MWA raises the hypothesis of an involvement of vascular mechanisms (endothelial hyperactivation) in the genesis of phenomena related to aura.

References

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ACETYLCHOLINESTERASE INHIBITORS FOR TRIGEMINAL PAIN CONTROL: RANDOMIZED EXPERIMENTAL CONTROLLED TRIAL USING PLACEBO, RIVASTIGMINE, DONEZEPIL, GALANTAMINE AND NEOSTIGMINE

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Objective To determine the effect of acetylcholinesterase inhibitors on trigeminal pain behaviour.

Background The spinal cholinergic system and muscarinic receptors are important for regulation of nociception. Intrathecal muscarinic receptor agonists or acetylcholinesterase inhibitors produce antinociception in both animals and humans.

Methods Male rats were divided into five groups: 1) Control group (n=18, 1ml ISS 0.9% 1ml/Kg); 2) Rivastigmine group (RIVA) (n=12, 1mg/kg); 3) Donezepil group (DONE) (n=12, 1mg/kg); 4) Galantamine group (GALA) (n=12, 1mg/kg); and 5) Neostigmine group (NEO) (n=8, 1mg/kg). Drugs were administered intraperitoneally to all the groups for three days before the day of the test and 30 minutes (RIVA, GALA, NEO) or two and a half hours (DONE) before the formalin test. Forty µl of 2.5% formalin was injected into the left upper lip trigeminal territory to induce neurogenic and inflammatory phase pain behaviour (0–3 and 12–30 mins, respectively).

Results The RIVA, GALA and NEO groups showed similar behaviour to that of the control group during the neurogenic phase ($p=0.4$, $p=0.1$ and $p=0.2$, respectively). The DONE group, however, showed lower values ($p<0.001$). In the inflammatory phase, the results for the GALA group were similar to those for the control group ($p=0.2$), those for the NEO and RIVA groups were lower ($p<0.001$ and $p<0.01$, respectively); and those for the DONE group were higher ($p<0.001$).

Conclusions The evidence from this study suggests that acetylcholinesterase inhibitors reduced trigeminal neurogenic pain behaviour in the DONE group and inflammatory pain behaviour in the RIVA and NEO groups. Inflammatory pain behaviour in the DONE group, however, increased. Rivastigmine and neostigmine can thus be considered candidates for treating inflammatory pain and donezepil can be considered a candidate for neurogenic pain.

POTENTIALIZATION OF THE ANALGESIC EFFECT OF ACETYLCHOLINESTERASE INHIBITOR BY A 5HT1B-1D AGONIST IN A DOUBLE-BLIND STUDY USING AN OROFACIAL MODEL OF PAIN

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Objective To determine the analgesic effect of 5HT1B-1D agonist sumatriptan, acetylcholinesterase inhibitor rivastigmine, and acetylcholinesterase inhibitor rivastigmine plus 5HT1B-1D agonist sumatriptan in the orofacial formalin-induced pain model.

Methods Male rats were divided into four groups: 1) Saline Solution Group (SSG) (n=6, 1 ml 0.9% 1 ml/kg); 2) Sumatriptan Group (SG) (n=6, 3 mg/kg); 3) Saline Solution (1 ml ISS 0.9% 1 ml/kg) plus Rivastigmine Group (SSRG) (1 mg/kg) (n=6); and 4) Sumatriptan plus Rivastigmine Group (SRG) (n=6, sumatriptan 3mg/kg and rivastigmine 1mg/kg). All groups received the drugs intraperitoneally 30 minutes before the formalin test. Forty µl of 2.5% formalin was

injected into the left upper lip trigeminal territory to induce neurogenic phase (0–3 min) and inflammatory phase (12–30 min) pain behaviour.

Results The neurogenic phase lasted 66.83+18.60 seconds for the SSG, 67.33+29.39 seconds ($p=0.723$) for the SG, 40.33+21.63 seconds for the SSRG and 4.83+9.10 seconds ($p<0.0001$) for the SRG. The inflammatory phase lasted 240.83+23.85 seconds for the SSG, 263.16+29.16 seconds ($p=0.53$) for the SG, 118.66+15.43 seconds for the SSRG and 9.33+2.84 seconds ($p<0.0001$) for the SRG. The statistical significance of the relationship between SSG and SSRG was $p=0.056$ for the neurogenic phase and $p<0.021$ for the inflammatory phase.

Conclusions The 5HT1B-1D agonist sumatriptan did not have an analgesic effect on the formalin-induced neurogenic and inflammatory pain model. Acetylcholinesterase inhibitor rivastigmine reduced inflammatory phase behaviour, and when we used 5HT1B-1D agonist sumatriptan plus rivastigmine, the analgesic effect of the acetylcholinesterase inhibitor was substantially increased for both the neurogenic and inflammatory phases.

SUBCLINICAL VESTIBULOCEREBELLAR DYSFUNCTION IN MIGRAINE WITH AND WITHOUT AURA, FAMILIAL HEMIPLEGIC MIGRAINE TYPE 2, AND EPISODIC ATAXIA TYPE 2

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Patients with common types of migraine present variable abnormalities in electronystagmography (ENG) and recently, subclinical vestibulocerebellar dysfunction. Familial hemiplegic migraine (FHM) is a rare, genetically defined subtype of migraine with aura. By definition, the aura includes motor weakness and at least one first- or second-degree relative with similar symptoms. FHM1-patients show a wide variety of ocular motor disturbances, but no studies on FHM2 neurology has been reported. Genetic basis and chronic cerebellar ataxia in part unite FHM1 and episodic ataxia type 2 (EA2), with considerable overlap also in their clinical phenotype. EA2-patients display ataxia episodes with permanent cerebellar signs later in life in some patients. Here, ocular motor studies show clinical as well as subclinical vestibulocerebellar dysfunction. We compared neurotologic findings of these patients to sharpen the phenotype of these diseases. We used video-oculography (VOG), ENG, caloric testing, static posturography, and audiometry to study differences in vestibular function in migraine with (MA, N=12) and without aura (MO, N=24), FHM2 (N=9), EA2 (N=12), and healthy controls (N=16). FHM2 and EA2 families were genetically defined. FHM2-patients did not present cerebellar signs whereas three EA2-patients had mild to severe ataxia. The accuracy in 20 degree saccades was significantly decreased in MO-patients when compared to that of FHM2-patients ($p=0.01$), however, EA2 patients showed more dysmetria than MO-patients did ($p=0.03$). In VOG, EA2-patients presented more nystagmus than MO-patients did. No significant differences appeared between the groups in posturography, audiometry, or caloric testing. Overall, EA2-patients showed the most abnormal results when compared to MA-, MO-, or FHM2-patients. The results show that EA2-patients exhibit more dysmetria and nystagmus than migraine patients without CACNA1A mutations. In addition, migraineurs showed in general more signs of vestibular dysfunction than the controls.

FAMILY-BASED ASSOCIATION ANALYSIS OF FUNCTIONAL VNTR POLYMORPHISMS IN THE DOPAMINE TRANSPORTER GENE IN MIGRAINE WITH AND WITHOUT AURA

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Background and aims Genetic epidemiological twin studies demonstrated a significant heritability for migraine, with >60% of liability to migraine coming from additive genetic factors. Because of the role of dopamine in the pathophysiology of migraine and the action of anti-migraine drugs on the dopamine system, genes of the dopamine system are candidates for involvement in migraine. Previous studies usually examined just one polymorphism per gene, and in most cases the studies were underpowered for analysis of a complex genetic disorder such as migraine. In the present study, we examined three VNTR polymorphisms in the dopamine transporter, the 5' UTR VNTR, the intron 8 VNTR and the intron 14 VNTR.

Methods We investigated a sample of 250 family trios each with a proband with childhood migraine differentiating migraine with and without aura according to ICHD-II. We used the transmission disequilibrium test (TDT) with the program TDTPHASE to examine the transmission of the three markers and their haplotypes to offsprings affected by migraine.

Results We found no significant transmission distortion of any marker, with the common allele of the intron 8 VNTR transmitted 247 times and not transmitted 248 times, the common allele of the 3' UTR VNTR transmitted 135 times and not transmitted 124 times, and the common allele of the intron 14 VNTR transmitted 232 and not transmitted 234 times. Likewise haplotypes of the three markers did not show significant association with migraine. Finally we examined migraine with and without aura, and likewise found no association between dopamine transporter VNTRs or their haplotypes and either migraine subtype.

Conclusions Applying TDT analyses we found no evidence for a functional genetic variation in the dopamine transporter acting as a risk factor for migraine.

"VASCULAR STEAL" PHENOMENON AS A MECHANISM OF PERSISTING VISUAL AURA. A CLUE TO UNDERSTANDING MIGRAINE AURA?

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Background Migraine aura is still a poorly understood phenomenon. Multiple mechanisms have been proposed: cortical spreading depression, neurochemical and neurovascular changes. Hypoperfusion is founded initially, followed by an hyperperfusion phase which seems involved in pain.

Case report A 23 years old woman was admitted to our institution presenting a pulsatile right hemispheric pain and a persistent (>24h) visual field defect. The symptoms were related with a long sunlight exposure. Firstly, the patient referred "light flashes" in left visual field and a few minutes later, left upper quadrantopia and headache began. The patient had a history of right hemispheric headaches and left visual fields defects always provoked by intense light stimuli exposure. The MRI showed a subcortical right occipital vascular malformation with mild hyperintense signal around it in DWI sequences. We performed a transcranial Doppler (TCD) and recorded basal blood flow velocities (BFV) in both posterior cerebral arteries (PCA) and during light stimulus with an

electric lamp placed at 30 cm from our patient eyes. BFV increased significantly in right PCA and decreased in left PCA during the light exposure.

Conclusions Our TCD findings suggest that a "vascular steal" mechanism may be involved in the pathophysiology of our case. We can't confirm if it is just subcortical due to the malformation or affects all the occipital lobe including cortical neurons and then explaining the prolonged aura phenomenon. Perhaps, the MRI hypoperfusion observed around the vascular lesion may explain the prolonged visual field defect referred by our patient.

PATIENT SATISFACTION WITH ELETRIPTAN IN THE ACUTE TREATMENT OF MIGRAINE IN PRIMARY CARE

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Introduction and aims Relatively few clinical trials have evaluated the effectiveness of triptans for the acute treatment of migraine in the primary care setting (where they are most commonly prescribed) using patient-centered outcomes such as treatment satisfaction, and impact of treatment on migraine-impaired quality of life and functioning. The objective of this open-label, primary care study was to evaluate the anti-migraine effectiveness of eletriptan versus previous migraine therapy using a patient-weighted, multi-dimensional treatment satisfaction scale as the a priori primary outcome.

Methods Patients were eligible (N=437) if they met International Headache Society criteria for migraine, with a frequency of 1-6 migraine attacks per month. Patients treated one attack with eletriptan 40mg. Prior to treatment, patients were asked to rate the importance of various clinical outcomes. Treatment effectiveness was evaluated using a 6-item Medication Satisfaction Questionnaire (MSQ), which rated treatment satisfaction on a 5-point scale. MSQ item scores were weighted, based on importance score ratings, to yield individualized satisfaction scores.

Results The mean (\pm SD) total satisfaction score on the MSQ (averaged across all items) was significantly higher for eletriptan 40mg than for previous migraine therapy (2.2 \pm 3.0 vs 0.6 \pm 2.4; p <0.001). For the total sample, the proportion of patients reporting treatment satisfaction as "good-to-excellent" was significantly higher on eletriptan 40 mg compared with previous migraine therapy on all 6 MSQ treatment satisfaction domains. Approximately one-third of patients reported "fair-to-very poor" satisfaction with previous migraine therapy across each of the MSQ domains. Treatment with eletriptan 40 mg resulted in a high level (62%-70%) of "good-to-excellent" satisfaction on each of the MSQ domains in this subgroup that reported poor satisfaction on their previous migraine therapy.

Conclusions Eletriptan is an efficacious treatment option for patients who are dissatisfied with their response to previous migraine therapy.

HEADACHE ATTRIBUTED TO LISTERIA SYSTEMIC INFECTION SHOULD BE RULED OUT TO DIAGNOSE NEW DAILY PERSISTENT HEADACHE (NDPH): REPORT OF A CASE

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The new headache classification (ICHD II) of 2004, gives diagnostic criteria of a new entity among chronic headaches: the NDPH. Secondary headaches must be ruled out, such as low or

raised CSF pressure or infectious diseases, mostly viral such as Epstein-Barr. We report the case of a young, previously healthy woman, who had probable NPDH but was found to have *Listeria* systemic infection.

Case description In December 1995, a 19-year-old female student was admitted because of continuous headache for the last two months. At the beginning her headache was temporal and bilateral, of pounding quality with jobs, but over the last days it spread all over the head and neck. Accompanying symptoms were absent, the pain was present at awakening, persisted during the whole day and nighttime, causing insomnia and reduced school performance. One month prior to hospital admission MRI was negative, HIV, EBV and hepatitis serodiagnosis were normal. At admission, neurological examination revealed contraction of neck muscles with no signs of meningitis or focal neurological deficit. A number of exams were performed including *Listeria* and Lyme serodiagnosis and a temporary diagnosis of chronic tension-type headache was made. On January 11th she was readmitted because of high *Listeria* titres and was found to have meningitis. Treated with intravenous ceftriaxone and ampicillin, she recovered in 10 days, but developed chronic post-bacterial meningitis headache that lasted for more than 2 years.

Conclusions The ICHD II is useful to differentiate primary NDPH from secondary headaches, in fact, the duration of persistent headache, in our patient, was less than 3 months and accompanying symptoms were absent. *Listeria* serodiagnosis should be added to diagnose patients with persistent headache.

SOME ARGUMENTS ON MULTIPLE EPIDEMIOLOGICAL SURVEYS ON RECURRENT HEADACHE AND ABDOMINAL PAIN EXPERIENCES IN CHILDREN

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Introduction In order to calculate caseloads for primary headaches and functional abdominal pain in childhood reliable epidemiological data are needed. The aim of our cross sectional and longitudinal epidemiological strategy is to examine children of an unselected population based sample once per annum from preschool time up to the end of primary school and in puberty (2004–2011). Actually the data have been collected twice (for preschoolers and for firstgraders). Arising methodological questions shall be discussed.

Methods Children and their parents were asked by the questionnaire FSEKB, assessing simultaneously medically defined symptoms of “primary headaches” and “functional abdominal pain” in childhood in context with sociodemographic variables and health related life-quality measures. The distribution of the children to the pain-groups will be reported here on the basis of the annual participation rates.

Results 885 (2004) vs. 832 (2005) children were announced officially, 555 vs. 350 participated. 38.1% of the preschoolers and 57.9% of the firstgraders were not allowed to or did not participate. While in the first year 14.4% of the participating preschoolers had never experienced the studied pain, this ratio reduced in 2005 for the firstgraders up to 6.9%. A rise about 20% in the frequency of children experiencing “headache in combination with abdominal pain” after school-entry (48.8% vs. 68.0%) can be stated. While children experiencing “abdominal pain” exclusively reduced from 31.9% to 18.3%, children with single or recurrent primary headache events nearly doubled from 3.6% to 6.9%.

Conclusions The presented frequencies are based on the particular participation rates of the year, not on the basis of the officially announced children for this school-year. Are we overestimating the pain problems by referring to participation rates only? How to compare resulting incidences and prevalences of the annually assessed subgroups? By which means participation rates could be raised?

OBSERVATIONAL PROSPECTIVE STUDY OF HOMEOPATHIC TREATMENT IN PATIENTS WITH MIGRAINE, ATTENDING THE HEADACHE CLINIC OF NEUROLOGY DEPT. “G. GENNIMATAS” ATHENS GENERAL HOSPITAL

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Background and aims Homeopathy trials of migraine prevention have yielded inconclusive results, partly due to different practice among various schools. We performed an observational prospective study of classical homeopathy in patients attending the Headache Clinic.

Methods Forty-two consecutive migraine patients who attended the clinic while one of the authors was available were assigned to receive homeopathic treatment, according to the principles recommended by the I.A.C.H. and G.Vithoulkas. Additional evaluation by a neurologist was performed at baseline, 6 and 12 months. Primary and secondary measures of migraine severity and impact on quality of life were recorded and analyzed.

Results Thirty-six patients opted only for homeopathic treatment until the completion of the study, aged (mean±SD) 34±12 years, with a baseline HIT-6 score of 65±4. Significant improvement was recorded at 6 months (HIT-6 score 48±8, $p<0.001$ vs baseline, Wilcoxon signed ranks test), which was further established at 12 months (HIT-6 score 41.2±7, $p<0.001$ vs 6 months). Eighteen patients had been previously administered TCAs or antiepileptics for sufficient time without remarkable improvement. A difference in HIT-6 score between those ‘resistant’ to previous therapy and ‘new’ patients was found at six months (51.5±7 vs 44.5±7, respectively, $p<0.01$, Mann-Whitney test), but not at baseline (66±3.8 vs 64±4, respectively) or at 12 months (41.6±8 vs 40.6±5.3, respectively). Migraine severity (VAS) decreased by 72% and frequency by 81% at 12 months ($p<0.0001$ for both comparisons vs baseline). Mood was consistently higher at 12 months (Verbal Analogue Scale, $p<0.001$). Observed potential adverse effects on all 42 patients were an initial ‘aggravation’ of migraine symptoms in 69%, recurrence of past medical diseases (e.g. infections, eczema) in 33%, temporary emotional instability in 59% of the patients.

Conclusions These results compare favourably with other modalities of migraine treatment. Therefore, homeopathy as applied in this context, warrants further research with appropriately designed RCTs.

A COMPARISON OF GENDER DIFFERENCES BETWEEN “HEALTHY CHILDREN” AND “CHILDREN WITH RECURRENT HEADACHE AND ABDOMINAL PAIN EXPERIENCES”

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Background The perception-organisation of healthy children (HE) and children with recurrent headaches (RH) and abdominal pain (RHAP) were examined in the first year of primary school. The children (n=43) identified by their parents as ‘recurrent pain experienced’ were recruited in 2004 from an unselected population based sample of preschool-children (n=555) shortly before school-entry. Sander et al. Reported [1] a worse perception-organisation for “children with recurrent headaches and abdominal pain” than for “healthy children”. It is hypothesized that there are no gender differences in “healthy children” and “children with recurrent pain experiences” concerning their perception-organisation.

Methods n=24 (12 boys / 12 girls) "healthy children" and n=43 (15 boys / 28 girls) "children with recurrent headaches and abdominal pain experiences" are analysed here. The level of development and the achievement of the perception-organisation are determined by the mosaic test (mosaic-test, HAWIK III, 2001). The group comparisons are computed by t-tests (SPSS).

Results The age adjusted standard range for perception-organisation lies between 7 and 13 (min=1, max=19). "Healthy boys" (HE-B: mean=13.54) and "healthy girls" (HE-G: mean=11.16) as well as "pain experienced boys" (RP-B: mean=9.8) and "pain experienced girls" (RP-G: mean=10.03) are within the normal range. Significant gender differences can be found in "healthy children" (HE-B>HE-G; t-value=2.173; $p=0.041$; confidence interval =95%; df=21) and between "healthy boys" and "boys with recurrent pain experiences" (HE-B: mean=13.54>RP-B: mean=9.8; t-value=2.12; $p0.040$; confidence interval =95%; df=15).

Conclusions The results imply the suggestion that boys of this age show more vulnerability to interference of cognitive functions through recurrent pain experiences.

Reference

1. Sander et al (2005)

AN INTEGRATED PHARMACOLOGICAL AND BRIEF ANALYTIC PSYCHOTHERAPEUTIC APPROACH FOR THE TREATMENT OF MEDICATION OVERUSE HEADACHE

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Background and aims Chronic migraine (CM) with medication overuse headache (MOH) is a very disabling condition, frequently associated with psychiatric comorbidity. At present clear guidelines for the withdrawal of the overused drug and detoxification are lacking. In this regard, a role for a psychological support has been hypothesized. We studied the efficacy of an integrated pharmacological and brief analytic psychotherapeutic approach in these patients.

Methods We enrolled patients affected by probable CM and MOH (ICHD II). They underwent a standardized neurological and psychiatric evaluation before and 6-months after medication withdrawal. Patients were randomly assigned to pharmacological treatment alone (group A), or associated with a brief analytic psychotherapy (group B). We applied the technique of Gillieron (1989), based on the principles of brief psychodynamic psychotherapy and mainly oriented toward assisting the patient with clarification and understanding of his/her disorder.

Results Twenty-one consecutive patients (1/20 m/f, mean age 46±10 years) with probable CM and MOH were included. Headache frequency was 27.9±5.4 days/month, with a mean drug intake of 60.3±35.2 tablets/month (25.5% triptans, 13.1% ergotamine, 2.2% codeine, 32.4% NSAIDs, 26.9% combined analgesics). All the patients presented with psychiatric comorbidity, in particular anxiety and depressive disturbances. To date, 15 patients had completed the 6-months follow-up (6/9, A/B), showing a clinical improvement (headache frequency 16.7±11.4 days/month, drug intake 12.9±11.0 tablets/month). With respect to baseline, patients treated with the integrated approach showed a greater decrease of headache frequency (days/month: -48% vs -32%) and drug intake (tablets/month: -87% vs -68%, $p<0.04$) than those only treated pharmacologically.

Conclusions The integrated approach improved treatment efficacy in MOH patients, particularly decreasing drugs abuse. This practical form of brief psychological support is effective and may help the patients in a shorter time and at a lower cost than long-term treatments.

ON SEARCHING FOR POSSIBLE CRANIOVASCULAR HEADACHE CENTERS IN THE BRAIN: PROJECTIONS FROM SUPERFICIAL LAYERS OF THE UPPER CERVICAL SPINAL CORD TO THE BRAINSTEM AND THALAMUS

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Primary headaches are related with the dysfunction of cranial vasculatures. The sensory cranial vascular nerves project to the ventrolateral part of upper cervical spinal cord dorsal horns and the caudal spinal trigeminal nucleus with a focus in the second cervical segment. The aim of this study is to trace where the primary vascular center projection to the upper level of the brain and thereby extend our knowledge of the neuroanatomical pathways of the cranial vessels. In this study, biotinylated dextran amine was injected by iontophoresis into laminae I and II in the ventrolateral part of the C1 and C2 spinal dorsal horn in anaesthetized rats. After one to two weeks the animals were sacrificed by perfusion. The upper part of the cervical spinal cord, the brainstem and the thalamus were removed and sections from these tissues were processed histochemically to reveal the injection sites and the anterogradely labelled terminals. Preliminary results indicate that the major termination sites from the ventrolateral C1 and C2 superficial dorsal horns include the medial and lateral parabrachial nuclei (MPB and LPB) and the cuneiform nucleus (Cnf) bilaterally in the pons; the intermediat gray layer of superior colliculus (InG) and the periaqueductal gray (PAG) bilaterally in the midbrain; the posterior nuclear group (PO) and ventroposteromedial nucleus (VPM) contralaterally in the thalamus. Sparse anterograde labeling were also detected in some other nuclei in the brainstem and the thalamus. The present results indicated that several nuclei in the brainstem and the thalamus including MPB, LPB, Cnf, InG, PAG, PO and VPM receive projections from the superficial layers of the upper cervical spinal cord and may thus be involved in the central processing of noxious signal of craniovascular origin.

NOT JUST CHEESE AND CHOCOLATE! IDENTIFICATION OF MIGRAINE TRIGGER FACTORS – AN EDUCATIONAL STUDY

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Background and aims Migraine remains a significant health issue within the Irish Health System, affecting approximately 400,000 people. Frequent or severe attacks impinge greatly on an individual's quality of life. Identifying trigger factors plays an important role when taking a nursing history and in the development of a migraine management plan. This study was developed to analyse the most commonly reported trigger factors in a sample of Irish patients who have migraine with and without aura.

Methods The study was conducted through the Migraine/Headache Clinic at Beaumont Hospital, Dublin and in conjunction with the Migraine Association of Ireland. Patients with a diagnosis of migraine with or without aura (under criteria established by the International Headache Society) completed a questionnaire. The questionnaire examined potential factors, previously associated with the onset of migraine attacks. Data was compiled from patient information collected under the following headings: Stress, Sleep, Hormonal, Alcohol, Dietary.

Results 503 patients completed the questionnaire. Stress was reported as a trigger factor by 76% of respondents. Work-related stress was identified in 45% of cases. Withdrawal from stress was cited as a trigger factor by 65% of patients. Sleep-related trigger factors were identified by 73% of respondents. 71% of women reported at least one hormonally related trigger factor with menstruation most com-

mon (55%). Alcohol was identified by 64% of patients. Dietary triggers were implicated for 59% of respondents. Chocolate was the most commonly identified dietary trigger factor (41%), followed by cheese (33%) and citrus fruits (20%).

Conclusions The study identifies key trigger-related areas when advising in the development of a patient treatment plan. Many migraine patients find difficulty in identifying a trigger factor or factors that can precipitate their attacks. The study also dispels the patient myth that dietary factors are the most prevalent triggers.

HEADACHE AND UNILATERAL TEMPORAL MUSCLE HYPERTROPHY

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Background and aims Temporal muscle hypertrophy can be indolent or a rare cause of headache. Most cases of temporal muscle hypertrophy are bilateral symmetrical or asymmetrical, but in rare cases can be unilateral. Enlargement of temporal muscles can be a reactive hypertrophy, the more common form, and nonreactive enlargements (myositic, genetic, myopathic, idiopathic or neoplastic). Dental disorders or psychogenic muscle hyperactivity are the more frequent causes. The aim is to report a case of this unusual cause of recurrent headaches.

Methods A 49-year-old woman presented with a 4-years history of left temporal persistent mild headache and a local temporal mass on the left side of her head with recurrent headache worsening and mass enlargement during weeks or months. No changes in her headache were related to jaw movements. Neurologic and systemic examination was normal. Left temporal palpation revealed a moderate diffuse enlargement of the left temporal muscle with mild tenderness. The patient used nocturnal oral splint appliances to protect teeth from damage.

Results Laboratory investigations were unremarkable, including erythrocyte sedimentation rate, complete blood count and serum protein electrophoresis. Computed tomography (CT) and magnetic resonance imaging demonstrated a homogeneous enlargement of the temporal left muscle. An old CT showed the same findings four years ago. The patient was treated with nonsteroidal anti-inflammatory drugs and muscle relaxants with clinical headache improvement, and local therapy with botulinum toxin, the alternative treatment, was unnecessary.

Conclusions We should be aware of this unusual cause of headache, the temporal muscle hypertrophy, sometimes unilateral. In this case the medical history of dental disorder was the suspected etiology, but in some cases of unilateral enlargement, if there is not a medical history or examination suggestive of bruxism or masticatory hyperfunction, the possibility of more serious etiologies must be evaluated and temporal muscle biopsy considered.

CHRONIC DAILY HEADACHE IN A SPECIALISED HEADACHE CENTER. ONE-YEAR FOLLOW-UP STUDY

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Aims To analyze the prevalence and demography of chronic daily headache (CDH) in a specialised headache center and to describe their clinical evolution at one year.

Methods We determine the percentage of patients with CDH in a specialised headache center coming from the neurological units in our area. We establish the prevalence, the classification and the rate of analgesic overuse of the patients visited with chronic daily

headache (CDH). We also collected data about the age, gender, psychiatric comorbidity and the treatment administered. Patients were reevaluated within two months and one year, considering any improvement in their personal opinion and regarding the presence of analgesic overuse.

Results In our study we finally included 77 CDH patients over a period of 18 months representing a prevalence of 32%. 81.2% were women and 18.8% men, mean age: 44 years. 42.7% fulfilled criteria for CDH with analgesic overuse. Migraine was diagnosed in 44.7% of patients, chronic tension-type headache in 25% and cervicogenic headache in 11.8%. Those patients with migraine and cervicogenic headache had a better prognosis. The rate of analgesic overuse was 13% after one year (relative reduction of 71%). The presence of analgesic overuse was associated with poor outcome at follow-up. After one-year, 82% of patients considered that they were better or much better than when they first visited the neurologist

Conclusions The prevalence of CDH in our center is lower than in other areas. The most frequent type of CDH was migraine, patients with migraine or cervicogenic headache had a better prognosis. CDH with analgesic overuse associated with a poor prognosis; analgesic overuse was reduced in 71% after one year. The majority of the patients (82%) described a beneficial impact after the assessment in a specialised headache center.

THE EFFECT OF SODIUM VALPROATE ON CHRONIC DAILY HEADACHE

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Aims To assess the efficacy and safety of sodium valproate (VPA) in the treatment of chronic daily headache (CDH) in a prospective, double-blind, randomized, placebo-controlled trial.

Background CDH is a type of intractable headache that is seen frequently. Retrospective trials of VPA have previously demonstrated its efficacy and safety in the treatment of migraine and CDH. Seventy patients, who fulfilled the criteria of chronic daily headache, included in this study. The patients have been separated into chronic migraine (CM) and chronic tension-type headache (CTTH) subgroups. Research follow-up was continued for 12 weeks for each patient. VPA was applied in 40 patients and placebo was applied in 30 patients. Visual analog scale (VAS) for pain level has been used to measure the efficiency of treatment. Some follow-up parameters like general pain VAS level (GnVAS), maximum pain VAS level (MaxVAS) and pain frequency (PF) have been evaluated.

Findings There was a statistically significant decrease in MaxVAS levels and PF in VPA given group according to placebo group in the end of first and third months (p values; 0.020 and 0.028 for MaxVAS, 0.00 and 0.00 for PF). However, there was no change in GnVAS parameter. In patients with CM, there was a statistically significant difference in MaxVAS, GnVAS and PF parameters ($p=0.01$, $p=0.0$ and $p=0.000$, respectively). In patients with CTTH, there was no statistically significant difference in GnVAS and in MaxVAS, But the reduce in PF was statistically significant ($p=0.000$). There was no severe side effect.

Conclusions Sodium valproate has significantly positive effect on MaxVAS levels and PF in CDH patients. It was more effective in CM than in CTTH. In this study group, VPA was well tolerated.

TOPIRAMATE VERSUS AMITRIPTYLINE IN THE PREVENTIVE TREATMENT OF CHRONIC PRIMARY HEADACHE

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Background and aims The diagnostic debate about chronic headache has delayed the development of therapeutical guidelines. The revised edition of the international headache classification (ICHD-II) seem to have solved most of diagnostic problems: migraine is considered chronic if attacks occur at least 15 days a month since 3 months (as well as already stated for tension type headache before). Amitriptyline has been extensively studied as preventive drug. In the last years topiramate has begun to be used in headache therapy. The aim of this study was to compare amitriptyline and topiramate in the therapy of chronic headache.

Methods A sample of 98 adult patients consecutively referred to Headache Disorder Centre, Department of Neurological and Psychiatric Sciences, University of Bari were enrolled. All of them were affected by a form of chronic migraine or tension-type headache according to ICHD-II. The Symptom Check List 90R was administered to all of them to point out possible psychopathological disorders. Patients were randomly assigned to amitriptyline, 20 mg or topiramate 50 mg, therapy. No significant differences were found between the groups both in demographic data and in attacks frequency. Drug efficacy and tolerability were assessed after a three months therapy period.

Results A decrease >75% in attack frequency was shown in 63.15% of cases after topiramate and in 65.71% after amitriptyline treatment, without significant difference between drugs. Both drugs were well tolerated. Patients with anxiety and depressive symptoms showed a higher improvement when treated with amitriptyline.

Discussion and conclusions These results suggest that topiramate can be effective and well tolerated in chronic headache as well as amitriptyline. This drugs might modulate the nociceptive system preventing both peripheral and central sensitization which predispose to attack recurrence. Amitriptyline should be the first choice drug in the case of headache comorbidity with psychopathological symptoms.

PROGNOSTIC SIGNIFICANCE OF PERSONALITY PROFILE IN PATIENTS WITH MIGRAINE WITHOUT AURA

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The aim of this study was to assess whether the psychological profile may have prognostic significance in migraine patients. The Minnesota Multiphasic Personality Inventory (MMPI)-2 was used for the psychological assessment of patients with migraine without aura to explore personality traits. Patients with psychiatric disease and medication overuse were excluded. One hundred and two patients completed the study. Migraine-related disability was measured using the Migraine Disability Assessment (MIDAS) questionnaire at baseline (T0) and again after 2 years (T1), during which patients received prophylactic treatment for migraine. At T1 patients were classified into those exhibiting significant improvement (group 1: MIDAS scores reduced by at least 50%) and those with unsatisfactory changes in headache-related disability (group 2: scores reduced by less than 50%). At T1 49 patients were in group 1 and 53 in group 2; at T0, group 1 patients had significantly lower MMPI-2 scores in the neurotic (hypochondriasis: $p < 0.01$; depression: $p < 0.001$; hysteria: $p < 0.01$) and schizophrenia ($p < 0.01$) scales. None of the other variables studied, i.e. age, sex, age at migraine onset, number of years from migraine onset, T0 MIDAS score, T0 headache frequency and severity differed significantly between the groups. When the analysis was performed on the two subgroups with the best (MIDAS score reduction of at least 75%: $n = 20$) and the worst outcome (MIDAS score reduction $\leq 25\%$: $n = 14$), results were substantially unchanged even though their mean group scores exhibited greater differences. Findings suggest that psychological factors can influence the clinical course of migraine and that psychological evaluation with MMPI-2 may be a reliable approach to

obtain prognostic data and information for therapy planning in patients with migraine.

UNILATERALISM AS A PREDICTOR OF RESPONSE IN TREATMENT OF CHRONIC HEADACHE PATIENTS WITH BOTULINUM TOXIN

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Background Botulinum toxin type A has showed efficacy in treating some chronic patients with headache in clinical practice and some clinical trials. At present we don't know if some clinical pattern could predict a good response to this treatment. This is very important in order to select adequately the patients for this treatment.

Objective To know the factors that can predict the therapeutic response in patients with chronic headache treated with botulinum toxin type A.

Methods This is an open and prospective study. Inclusion criteria: headache during more than 15 days per month for more than 3 months, no response to at least two preventive treatments and follow-up in our unit for at least 6 months. We used the 'follow-the-pain' technique.

Results We included 35 patients (26 women and 6 men). Mean age: 36 years (24–50). Time with chronic headache: 14 months (7–36). 22 patients presented migraine and tension-type, 6 chronic migraine, 4 cervicogenic headache and 3 chronic cluster headache. 29 patients were overusing acute treatments. Range of dose administered: 50–100 units; number of times injected: 2.5 (1–6). In 15 cases, we obtained very good response (reduction >75%), in 9 good (between 50%–75%), in 5 moderate (between 25%–50%) and in 6 poor (less than 25%). In all cases with very good response the headache was almost exclusively unilateral and in 5 of the 6 cases with poor response it was bilateral. The response was not related with the overuse of acute treatment.

Conclusions The botulinum toxin type A could be a good alternative in some patients with chronic headache who do not respond to usual therapies. Our data suggest that the unilateralism of the pain is a very good predictor in order to obtain a clinical response. These data also suggest that the action mechanism should be essentially peripheral.

CHRONIC DAILY HEADACHE. PSYCHOLOGICAL PROFILE AND RELATIONSHIP TO RESPONSE TO TREATMENT

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Background Psychological data differentiates chronic headache patients and people without headache. Psychological differences between distinct types of chronic headache and relationship to treatment are incompletely known.

Objectives To study the psychological profile of chronic daily headache (CDH) patients and whether the psychological profile influences pharmacological treatment response.

Methods We studied 212 CDH patients (180 women) evolved from 62 chronic migraine (CM) (48 women) and 150 tension type headache (TTH) (132 women). Psychological evaluation was performed with: anxiety scale (STAI), Beck depression inventory, Maudsley obsessions inventory and Minnesota Multiphasic Personality inventory (MMPI); 87 patients were also studied with SCL-90-R. Patients received treatment with antidepressants (60%), adrenergic-blockers (10%), calcium antagonists (3%), botulinum

toxin (9%) or combinations (15%). Favourable response (<50% CDH reduction) was present at six months in 109 patients (51.4%); 18% were lost to follow-up. Logistic regression and T-test when appropriated were used for statistical analysis.

Results Hypochondria score was higher in TTH than CM patients ($p=0.01$). No psychological differences were observed between responders and non-responders. Age showed a trend to be higher in patients with response to treatment (50.1 sd.15; 45.7 sd.15) ($p0.07$).

Conclusions In the present large sample the psychological profile or CDH patients was similar in TTH and CM. Only hypochondria was higher in chronic tension type headache. We did not find psychological differences between patients who respond or not to pharmacological treatment suggesting that improvement is not related to psychological profile.

THE IMPACT OF RECURRENT HEADACHE AND ABDOMINAL PAIN ON THE INFORMATION PROCESSING SPEED OF BOYS AND GIRLS IN THE FIRST YEAR OF PRIMARY SCHOOL

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Introduction In the framework of an experimental study it is analysed whether there are gender differences concerning the impact of recurrent headache and abdominal pain experiences on the information processing speed of firstgraders. The pain experienced children were traced by their parents' judgements and recruited from an unselected population based sample of preschool children. It is suggested that boys and girls with recurrent pain experiences will differ concerning their information processing speed.

Methods The sample consists of N=38 children (N=10 recurrent headache (RH) <3♂; vs. 7♀>; N=17 recurrent abdominal pain (AP) <4♂; and 13♀>; N=11 recurrent headache and abdominal pain (RHAP) <5♂ and 6♀> and the control group consisting of N=23 healthy children (HE) <10♂ vs.13♀>. The performance of the information processing speed is determined by the number-symbol-test (ZS, of HAWIK III). The means of the groups were compared by the t-test (SPSS).

Results The standard range for information processing speed lies between 7 and 13 (on a scale from 1 to 19). The performance of the pain experienced boys and girls (mean ♂ 10.7, SD 3.87; mean ♀ 11.7, SD 3.91) is characterized by a broad observed variability differing from 2 – 19. The performance of the healthy children (mean ♂ 12.4, SD 3.24; mean ♀ 12.9, SD 3.29) varies from 7 to 18. The results show no significant sex differences, neither for the whole nor for the pain related groups ($t= -0.729$, $p=0.474$, confidence interval =95%, $df=21,69$). But there is a tendency towards better performance of girls than boys with recurrent pain experiences (means RHAP 11,36<AP11,54<RH12,5<HE12,9).

Conclusions There are no gender differences in the impact of recurrent pain experiences on the quality of the information processing speed for children visiting the first year of primary school.

GLOBAL CAMPAIGN AGAINST HEADACHE. A SPANISH POPULATION STUDY

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Background WHO, IHS, EHF and AHS have launched a campaign to reduce the burden of headache in the world.

Objective To know the attitudes of Spanish population in relation to headaches before the start of the campaign in Spain.

Methods We performed a population telephone survey to know the prevalence of headache, consultation rates, satisfaction with the health system, consequences of headache over personal life and pattern of treatments used.

Results 1201 people were interviewed. Prevalence of headache in the last year was 51% (62% in women). 21% referred headaches as severe. 3.5% presented daily or near daily headaches and 12% used analgesics more than two times a week. 84% thought that the health system should increase the awareness about headache. Only 35% had a medical diagnosis (65% in severe cases), only 42% used prescribed medication and 7% received preventive treatment. 25% reduced activity during migraine.

Conclusions Even severe headaches still remain undiagnosed and undertreated in Spain and most of the people think that the health system should change its attitude in relation with this problem. We hope that the situation will improve with the campaign in the next 2 years.

EFFICACY AND TOLERANCE OF TOPIRAMATE IN INITIAL DOSES OF 15 MG VS. 25 MG IN THE PREVENTION OF MIGRAINE

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Introduction Many studies have proved the effectiveness of topiramate in preventing migraine and chronic daily headache.

Objectives To measure the effectiveness and the best tolerability of topiramate in initial doses of 15 mgrs vs 25 mgrs in patients who are refractory to other prophylactic treatments.

Materials and methods A prospective study with patients diagnosed of migraine or transformed migraine according to HIS criteria with more than six months history and treatment with topiramate was performed. It included a total of 30 patients, 22 women and 8 men, with ages ranging between 18–60 years. Two groups (A and B) were established with the same number of patients after randomized distribution. Group A began treatment with dispersable doses of 15 mgrs and group B began with doses of 25 mgrs. Weekly increments were made in both groups, until to reach a total dose of 100 mgrs/day.

Results The effectiveness was measured by the frequency of attacks and tolerance was measured by the appearance of adverse events. The treatment was effective in both groups by reducing the number of attacks in more than 50% in 60% of the patients; 25%–50% in 30% of patients with 10% did not have any headaches. Adverse events were more frequent in group B; the most common were cognitive impairment, paresthesias and weight loss.

Conclusions A preventive treatment for migraine with topiramate, with initial doses of 15 mgrs and weekly increments up to 100 mgrs per day, is as efficient as initiating with 25 mgrs. It has presents better tolerance and less adverse events, thus implying fewer treatment withdrawal.

GASTRIC STASIS IN MIGRAINE: MORE THAN JUST A PAROXYSMAL ABNORMALITY DURING A MIGRAINE ATTACK

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Objective To evaluate gastric motility and emptying in the ictal and interictal period in migraine.

Background Nausea is a predominant symptom of migraine and the basis of it is thought to be gastric stasis. Objective methods to establish this are however lacking. We utilized gastric scintigraphy studies to determine gastric motility in the ictal and interictal period of migraine.

Methods Ten migraine subjects were compared to equal number of age and sex matched controls. Gastric scintigraphy using a standard meal was performed in all control subjects once and in all ten migraine subjects in the interictal period and nine studies were performed in the ictal period migraine.

Results The time to half emptying was delayed in migraine ictally (78%) and interictal period (80%) using normative data at this institution. Gastric stasis was less pronounced ictally (149.9 minutes) compared to interictal period (188.8 minutes). There was a significant delay compared to non-migrainous controls (migraine 188.8 minutes vs normal controls 111.8 minutes; $p < 0.05$). These data were replicated in percentage of radioactive material remaining in the stomach at 2 hours.

Conclusions Contrary to previous belief, this study has demonstrated that migraineurs suffer from gastric stasis both during and outside an acute migraine attack. This may suggest that migraineurs may have an abnormal autonomic function compared to non-migrainous controls. The potential role of this in pathophysiology of migraine is discussed and avenues for further investigations are explored.

ANATOMICAL VARIATIONS FORMATION OF NEUROVASCULAR BUNDLES AND MYELINATED NERVE FIBERS ANALYSIS IN THE HUMAN DURA MATER

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Background The purpose of this study was to investigate in greater detail the nerve fibers trajectories within the human dura mater, as well as the myelinated fiber analysis.

Methods Variations in origin and topography of meningeal vessels and nerves in the human dura mater were investigated on 57 adult cadavers using Shubich M.G. and Hodos I.B. method and its improved modifications. Samples of neurovascular bundles from the dura mater of the anterior, middle and posterior cranial fossae were studied using the method by Krutsay. Morphometric analysis was performed by examining nerve images quantitatively.

Results Visualization of neurovascular bundles by Shubich M.G. and Hodos I.B. method in dural wholemounts revealed two separate systems of nerve fibers in the human dura mater that could be distinguished by the orientation of their trajectories: one that runs parallel to the meningeal vessels and another with a more or less orthogonal orientation that runs rostromedially. The transverse area of nerve fibers was average 652 microns² in the neurovascular bundles of the anterior cranial fossa, average 3 490 microns² in the middle cranial fossa and average 2 479 microns² in the posterior cranial fossa. The total number of myelinated axons was average 30 in the neurovascular bundles of the anterior cranial fossa, average 429 microns² in the middle cranial fossa and average 71 microns² in the posterior cranial fossa. The histograms of fiber diameter had a unimodal distribution.

Conclusions These findings may be important for the analysis of clinical and neurological sings.

VALIDITY OF THE MIGRAINE-SCREEN-Q (MS-Q) QUESTIONNAIRE FOR MIGRAINE SCREENING IN PRIMARY CARE PRACTICE (PCP) SETTINGS

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Background Migraine is a highly prevalent illness that remains undiagnosed in PCP. The validity and reliability of MS-Q has been demonstrated in neurological clinics and in occupational medicine.

Aim To assess the validity and reliability of MS-Q as a migraine screening tool in PCP settings.

Methods A cross-sectional, multicenter study in PCP settings was implemented in patients ≥ 18 years of age attending a health center for any reason, and able to complete the MS-Q questionnaire. Migraine was diagnosed using IHS criteria. A scoring ≥ 4 in MS-Q was considered as possible migraine. Statistical methods included kappa coefficient, and determination of sensitivity, specificity, and positive and negative predictive values.

Results 9,670 patients [48.9 \pm 17.2 years (mean \pm SD); 61.9% females] were enrolled by 410 PC physicians. Migraine was presented in 24.7% of participants according to IHS criteria and in 20.4% according to MS-Q. Kappa coefficient ranged from 0.70 to 0.84 ($p < 0.001$). Sensitivity was 0.82 (95% CI, 0.81 to 0.84), specificity; 0.97 (95% CI, 0.97 to 0.97), positive predictive value; 0.90 (95% CI, 0.89 to 0.91), and negative predictive value; 0.94 (95% CI, 0.94 to 0.95).

Conclusions The MS-Q was found to be a valid screening tool for migraine headaches at the PCP level. Given the very high specificity shown by the MS-Q, it may be particularly useful for screening underdiagnosed migraine patients at the PCP level.

CARDIOVASCULAR RISK FACTORS IN YOUNG MIGRAINEURS

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Background and aims Migraine is a risk factor for ischaemic stroke, particularly in young women. The underlying mechanisms are unknown, but may in part be due to migraineurs having an increased risk profile for cardiovascular disease. A previous study has shown that migraineurs are more likely to have classical cardiovascular risk factors. The aim of this study was to compare novel cardiovascular risk markers between young adult migraineurs and nonmigraineurs.

Methods A total of 51 migraineurs (63% with aura, 37% without aura) and 51 matched controls without lifetime or family history of migraine were recruited from the general population. Measurements included aortic augmentation index (AIx) and pulse wave velocity (PWV), markers of arterial stiffness; carotid intima-media thickness (IMT), a marker of generalized atherosclerosis; flow-mediated dilation (FMD) of the brachial artery, a measure of endothelial function and serum C-reactive protein (CRP), an inflammatory biomarker. These markers are independent predictors of cardiovascular disease, including stroke.

Results Mean (SD) age was comparable between migraineurs (24.6 4.0; range 19–35 years) and controls (24.7 4.0; range 20–35 years). Gender distribution (78% female) and smoking status (14% current smokers) were comparable in both populations. Among migraineurs, mean (SE) aortic AIx and PWV were increased by 5.2% (95% CI, 1 to 10; $p = 0.02$) and 0.3 0.1 m/s (95% CI, 0.1 to 0.5; $p = 0.009$), respectively, as compared to controls. The difference in FMD, normalized for the magnitude of the stimulus, was decreased in migraineurs (mean difference 7.3 10–3.%; 95% CI: 1–13; $p = 0.01$). The median C-reactive protein level was 1.42 mg/L (interquartile range, 0.59 to 2.48) in migraineurs, as compared to 0.90 mg/L (0.36 to 1.79) in controls ($p = 0.03$). After adjustment for possible confounders, the difference in PWV did not remain significant ($p = 0.15$). No difference was observed in IMT.

Conclusions Young adult migraineurs have a higher cardiovascular risk profile than individuals without migraine. These results need confirmation in larger studies.

MOTOR CORTEX EXCITABILITY CHANGES IN UNILATERAL MIGRAINE PATIENTS: A FOCAL TRANSCRANIAL MAGNETIC STIMULATION (TMS) STUDY

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Background and aims Focal Transcranial Magnetic Stimulation (TMS) was employed to assess motor cortex excitability changes in 17 patients (37.8±10 years) with unilateral migraine with and/or without aura according to the ICHD-II criteria (frequency attacks 2.8±1.8/month).

Methods TMS was performed at least 2 days after the last migraine attack and the Motor Evoked Potentials (MEPs) were recorded from the ADM muscle of both sides. Eight patients had a headache within 24 hours following the TMS ('attack') whereas 9 patients did not ('no-attack'). The following TMS parameters were analysed and compared between the two subgroups of patients: a) resting motor threshold; b) cortical silent period duration at threshold (100%) and following increasing values of TMS intensity (from 110 to 180% of threshold); c) short- (S-ICI=1–3 ms) and long- (L-ICI=80 ms) intracortical inhibition to paired-TMS.

Results The excitability threshold and the ICI were not significantly different between the two subgroups of patients and no inter-hemispheric asymmetries were found. In the 'attack' subgroup, the silent period duration at threshold was lengthened and increased linearly from 110 to 180% threshold intensity. Conversely, in the 'no-attack' subgroup, the silent period duration was not linearly related to stimulus intensity and reached a plateau following TMS of 140% above threshold values.

Conclusions The analysis of the cortical silent period duration revealed that in unilateral migraine patients the motor cortex was 'hyperexcitable' interictally, whereas it was 'hypoexcitable' in close temporal proximity to the headache attack.

DIAGNOSING MIGRAINE AT PRIMARY CARE PRACTICE (PCP) SETTINGS: AN UNMET NEED

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Background Migraine is a highly prevalent illness that still remains undiagnosed in PCP.

Aims To determine the level of undiagnosed migraine at the Primary Care level.

Methods This was a cross-sectional, multicenter study in PCP settings. Patients were male and female 18 years of age and older, attending the health center for any reason, and able to understand health care questionnaires. Diagnosis of migraine was established by IHS criteria and by means of a 5-question migraine-screening questionnaire (MS-Q). New diagnosis cases of migraine were defined using both IHS Criteria and MS-Q score (≥4) among patients with no previous history of migraine. Misdiagnosis cases of migraine were defined using both IHS Criteria and MS-Q score (<4) among patients with previous history of migraine.

Results 9,670 patients [48.9±17.2 years (mean±SD); 61.9% females] were enrolled by 410 PC physicians. According to IHS criteria, migraine was presented in 24.7% of all participants compared with 20.4% using MS-Q. New diagnosis of migraine based upon IHS-criteria and using MS-Q was presented in 6.1% and 5.7%, respectively,

among patients with no previous migraine. Misdiagnosis of migraine based upon IHS-criteria and using MS-Q was presented in 3.5% and 5.4%, respectively, among patients with previous migraine.

Conclusions There is a portion of migraine patients without adequate diagnosis at the PCP level. MS-Q may be a valid and easy screen tool for screening new migraine patients at this level, although migraine diagnosis should be confirmed according to IHS criteria.

MIGRAINE AND FUNCTIONAL DYSPEPSIA: A NEUROGASTROENTEROLOGY RESEARCH

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Introduction Several patients with headache often present functional dyspepsia. At now, no data are available on the pathophysiological mechanisms responsible for this association.

Objectives The aim of this study was to verify whether an alteration of post-prandial gastric tone or sensitivity may explain this association.

Material and methods 35 patients (22 F, 13 M, mean age 32±8 yrs) affected by functional dyspepsia with (18 patients) and without (17 patients) migraine without aura (ICHD-II), took part in the study. Diagnosis of functional dyspepsia was made according to Rome II criteria. As control group, 14 age-/sex-matched healthy volunteers (HV) were enrolled. All subjects underwent gastric tone measurement in fasting condition and after the administration of 200 ml liquid meal by barostat (computer-controlled system connected to a double-lumen extrusion and an anelastic balloon placed at its distal end, which is introduced into the stomach). After minimal distending pressure (MDP) determination, which represents the pressure applied against the balloon by abdominal content, pressure was set at MDP+2 mmHg and gastric volume (GV) was measured for 30' during fasting and for 60' post-prandially. At fasting and after the end of the GV measurement an evaluation of perception of discomfort thresholds (DTh) was performed by sequential ramp distensions in stepwise increments starting from MDP (2 mmHg, 2' duration). At the end of each distension, the subject scored the sensation on a 0–6 scale (1= perception threshold, PTh; 5= DTh). Gastric volume and accommodation were calculated as difference between mean post-prandial and mean fasting volume.

Results Mean post-prandial GV increase and fasting PTh and DTh were similar among the 3 groups. DTh after meal was lower in dyspeptic-migraine patients than in HV and dyspeptic without migraine.

Conclusions Patients with migraine and functional dyspepsia may be characterized by meal-induced hypersensitivity of the stomach.

SYMPTOMATIC TRIGEMINAL NEURALGIA IN A TEENAGER

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Background and aims Trigeminal neuralgia is the most frequent cranial neuralgia, the incidence is about 1 per 100000 persons per year. It presents with stabbing pain often in the distribution of the mandibular and maxillary division of the trigeminal nerve. The disorder is more common in women than in men and rarely affects anyone younger than 50.

Methods A nineteen-year-old woman with 6 months of left sided trigeminal neuralgia and deafness is described.

Results Cranial MRI and cerebral angiography demonstrated an ipsilateral cavernous angioma of the pons involving the trigeminal roots. As the pain was refractory for most treatments, surgical excision was made.

Conclusions Cavernous malformations can affect the trigeminal nerve and cause trigeminal neuralgia.

MIGRAINE IN THE ELDERLY IN MATARO AREA, SPAIN

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Objectives Descriptive analysis of a patients group older than 65 years recently diagnosed of migraine in Mataro area.

Methods Prospective and descriptive study of outpatients older than 65 years, evaluated in our Hospital who fulfilled the diagnostic criteria for migraine of the International Headache Society (IHS).

Results The last ten years, 2149 outpatients were evaluated for headache symptom. 135 were older than 65 years. Among these 49 (46.3%) fulfilling IHS criteria for migraine. This group represents the 2.3% of the total number of patients evaluated. 67% of elderly migrainous patients were women. Median age was 72 years (65 to 89 yrs), 55% of them with familial history of migraine. Twenty patients had begun their symptoms after the age of 65 yrs (41%), and 29% the year previous to the diagnosis. In 7 patients, tension-type headache was associated. 43% had migraine without aura, 20% with aura and 37% probable migraine. 20% treated their migraine with paracetamol, 10% with non esteroidal antiinflammatory drugs and 8% with ergot preparations.

Conclusions Almost a half of elderly patients diagnosed of migraine begin their symptoms during the previous year and a half of them after the age of 65 yrs.

CLINICAL PATTERN AND AUTONOMIC PROFILE IN CLUSTER HEADACHE

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Objectives The goal of the study was the analysis of clinical pattern and autonomic profile of patients with episodic cluster headache (CH).

Methods 17 patients with episodic CH accordingly to the criteria of IHS (2004) were included in the study, with the age range 19–57 years, 11 men and 6 women, duration of the disease -2–7 years. Assessments of autonomic cardio-vascular tests (active orthostatic test 30/15, test with slow and deep respiration, Valsalva maneuver) with a questionnaire for estimation of suprasegmentary autonomic disturbances [1] were performed.

Results All the patients presented with attacks of severe unilateral headache, localized in the orbital, supraorbital or / and temporal region, with the frequency range 2–6 /day, average duration of 40 min, associated with one or more ipsilateral autonomic signs. Fifteen patients with CH (88.2%) have showed pathologic values in autonomic parasympathic cardiovascular tests. Autonomic cranial signs and pain intensity were more pronounced in patients who presented more than one pathologic autonomic tests. Suprasegmentary vegetative profile of the patients was characterised by polymorph disturbances.

Conclusions Cardiovascular autonomic tests denote the presence of a peripheral autonomic failure in patients with CH, the pathogenesis of which remains to be elucidated, with the supposition for the existence of common mechanisms with ipsilateral cranial signs. Suprasegmentary autonomic disturbances associated with CH attacks may have a pathogenic value, being influenced by headache mechanisms, together with reduced threshold for the autonomic perception and pain.

Reference

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CHARACTERIZING THE TIME COURSE OF ADVERSE EVENTS ASSOCIATED WITH THE USE OF TOPIRAMATE FOR MIGRAINE PREVENTION

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Background Topiramate 100mg/d is an effective, safe, and generally well-tolerated migraine preventive therapy, as demonstrated in 3 pivotal trials. The most common topiramate-associated AEs occurred more frequently during titration to target dose.

Aims To characterize the time course of topiramate-associated adverse events (AEs) from 3 pivotal, randomized, double-blind, 26-week, topiramate migraine trials.

Methods The pooled safety population consisted of all subjects who took ≥ 1 dose of topiramate during the double-blind phase (n=386, mean age=39.9 yrs, 86% female). Double-blind phase consisted of a 4-week titration (25 mg/week increases to 100mg/d or maximum-tolerated dose, whichever was lower) and a 22-week maintenance period. Incidence, time of onset (Kaplan-Meier analyses), and duration of 5 most common topiramate-associated AEs (paresthesia, fatigue, anorexia, nausea, and any cognitive symptoms (including confusion, difficulty with concentration/attention, and difficulty with memory)) were assessed.

Results Incidence of paresthesia was 50.5%; cumulative incidence of paresthesia was 22.2% by day (d) 14 of double-blind treatment, 42.5% (d28), and 49.5% (d42). For fatigue, these percentages were 15.0% (total), 6.8% (d14), 11.3% (d28), and 14.3% (d42). For anorexia, these percentages were 14.5% (total), and 5.0% (d14), 12.3% (d28), and 13.8% (d42). For nausea, these percentages were 13.2% (total), and 4.7% (d14), 8.7% (d28), and 10.5% (d42). For cognitive symptoms, these percentages were 21.3% (total), and 9.4% (d14), 15.8% (d28), and 18.5% (d42). Mean duration of any AE in patients on topiramate 100mg/d was 119.1 \pm 65.5 days. Mean duration of paresthesia was 114.0 \pm 60.9 days. One study limitation was multiple occurrences of an AE were assumed to contribute to overall duration of that AE. AEs caused 25% of topiramate-treated subjects to prematurely discontinue therapy.

Conclusions Onset of the most common topiramate-associated AEs tended to occur within the titration period of the 6-month double-blind phase. These AEs had an average duration of approximately 4 months.

EFFICACY OF TOPIRAMATE FOR THE PREVENTION OF MIGRAINE IN PATIENTS WHO USED OTHER MIGRAINE PREVENTIVE MEDICATIONS PRIOR TO ENROLLMENT IN 3 PIVOTAL PLACEBO-CONTROLLED TRIALS

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Background Topiramate is approved for the prophylaxis (prevention) of migraine headache in adults. Based on efficacy/tolerability, topiramate 100mg/d (50mg BID) is the target dose for most patients with migraine. The most common adverse events in pivotal trials included paresthesia, fatigue, cognitive deficit, anorexia, and taste alteration.

Aims Characterize the efficacy of topiramate for migraine prevention in subjects who used other migraine preventive medications prior to enrollment in 3 pivotal, randomized, double-blind, placebo-controlled, 26-week trials.

Methods Post-hoc sub-analyses of pooled study data performed to determine the change in mean monthly migraine frequency from baseline to endpoint (LOCF) in intent-to-treat patients who had used

migraine preventive medications (tricyclic antidepressants, beta-blockers, or neurostabilizers other than topiramate) within approximately 8 months prior to trial enrollment. Prior to entering the baseline phase, patients completed a washout period (≤ 14 d) to taper from these medications. Between-group differences assessed using ANCOVA. p -values were not adjusted for multiplicity.

Results Cohort of randomized patients who received migraine preventive medication other than topiramate prior to pivotal trial enrollment showed similar baseline characteristics when subdivided into pooled topiramate groups (50, 100, or 200 mg/d $n=129$, 89.9% female, mean age=38.8 years) and the placebo group, ($n=55$, 81.8% female, mean age=39.8 yrs). Topiramate 100 mg/d and 200 mg/d significantly reduced mean monthly migraine frequency by 1.8 ± 2.9 (baseline= 5.6 ± 2.5 migraines) and 1.9 ± 3.0 (baseline= 5.4 ± 2.1 migraines) at endpoint, respectively, compared with the placebo reduction of 0.5 ± 2.2 (baseline= 5.3 ± 2.5 migraines, $p \leq 0.01$). Significantly greater percentages of patients on topiramate 100 mg/d (38.9%), and 200 mg/d (36.7%) exhibited $\geq 50\%$ reductions in monthly migraine frequency ($p < 0.05$ vs placebo [18.2%]).

Conclusions When the cohort of patients who had previously taken other migraine preventives was analyzed, topiramate 100 mg/d and 200 mg/d groups showed apparent significant effects on mean monthly migraine frequency similar to those previously seen in the entire study population that received these doses.

TOPIRAMATE PROPHYLACTIC TREATMENT IN INFANTILE AND YOUTHFUL MIGRAINE

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Background Headache are one of the most important causes for consultation in primary attention and Neuropediatrics C.E. as well. There are cases where, in order to decrease migraine frequency and intensity, working on triggering factor elimination is not enough and implementation of preventive treatment is needed.

Patients and methods 166 patients (87 women and 79 men) between 6 and 18 years old with diagnosed migraine were traced. Prophylactic treatment with Topiramate (average 2.65 mg/kg/day) during a 4 to 6 months time frame was developed. Out of that total, 34 (20.6%) were diagnosed as migraine with aura patients, 128 (77%) were diagnosed as migraine without aura patients, and 4 (2.4%) were diagnosed as mixed migrained patients.

Results • 14(8.5%) cases classified as abandoned treatment (non effective or secondary effects arousal) • 62 (37.3) patients were symptom free, and • 90 (54.2%) patients showed evident improvement.

Conclusions 1. Where other treatment failed, Topiramate proved itself as a valid migraine prophylaxis alternative. 2. It proved effective even at low dosing 3. In rare occasions secondary effects were registered. 4. It admits sole night dosing possibility. 5. It is an efficient migraine prophylactic treatment.

CHANGE OF BRAIN METABOLISM IN ANTINOCICEPTIVE CIRCUITS IN CLUSTER HEADACHE

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Background and aims Previous neuroimaging studies have shown hypothalamic activation in cluster headache attacks and brainstem activation in migraine attacks. Although hypothalamic activation is thought to be relatively specific for cluster headache and related disorders, it is unclear which changes in brain metabolism accompany the shift between the 'in bout' to the 'out of bout' period.

Methods 12 patients with episodic cluster headache were subjected to FDG-PET twice (CTI ECAT EXACT HR+ Scanner). One scan was acquired during the 'bout' period (but without pain during scanning) and the other 'out of bout'. Additionally, 11 healthy volunteers were scanned once. After attenuation correction and reconstruction, images were transformed into standard stereotactic space using NEUROSTAT. After smoothing (6 mm FWHM), group comparisons (paired t-test) of 'in bout' and 'out of bout' scans were conducted with SPM2. To analyse small brain structures, an additional analysis without smoothing was performed. For comparison of patients versus volunteers ('in bout' versus volunteers and 'out of bout' vs. volunteers), voxelwise unpaired t-tests were performed.

Results In patients, 'in bout' scans revealed significant increases of metabolism in the perigenual anterior cingulate cortex (ACC), prefrontal cortex, insula, thalamus and temporal cortex, as compared to 'out of bout'. Without smoothing, increased metabolism was also detected in the PAG. Decreases were observed in the cerebellum and cerebellopontine area. Compared to volunteers, the FDG signal in patients was lower in perigenual ACC, prefrontal cortex, insula, and caudate nucleus.

Conclusions Sequential FDG-PET in cluster headache patients revealed 'in bout' activation of brain structures known to be involved in descending pain control. Interestingly, compared to healthy controls brain metabolism in most of these structures was decreased in patients - irrespective of the bout. This may point to a deficient top-down modulation of pain leading to an increased susceptibility for the generation of cluster headache.

ASSESSING THE EFFICACY AND SAFETY OF TOPIRAMATE FOR THE PREVENTION OF CHRONIC MIGRAINE

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Background Chronic migraine is the most common form of seriously disabling headache. Preventive treatments are essential to its management, yet there is little or no controlled data regarding the treatment of these patients.

Aims To determine whether topiramate is effective for the preventive treatment of chronic migraine.

Methods A 16-week double-blind, randomized, placebo-controlled study (TOPMAT-MIG-201: TOPiramate in CHRONic MigraineE-TOP-CHROME) was performed in patients with chronic migraine (≥ 15 migraine days/4 weeks). Topiramate (or matching placebo) was given BID and titrated with weekly 25 mg/d increments to a target dose (100 mg/d). Adjustments were allowed for tolerability/efficacy reasons, with the final dose being kept between 50–200 mg/d. Existing migraine preventive treatments, except for antiepileptic drugs, were continued throughout the trial. The primary efficacy parameter was change in migraine days. Quality of life was evaluated with the questionnaires MSQ-14, HIT-6, and MIDAS, and tolerability by adverse event reports and early trial terminations.

Results Eighty-two patients were screened, 59 were randomized to topiramate or placebo (32/27), and 46 had medication overuse. Baseline means were 15.5 and 16.4 migraine days/4weeks for topiramate and placebo, with mean changes from baseline in the last 4

treatment weeks of -3.5 and +0.2 days/4weeks, respectively ($p=0.020$). No significant intergroup differences were found for MSQ-14 and HIT-6. MIDAS showed improvement with topiramate ($p=0.042$ versus placebo). Adverse events were reported by 75% of patients on topiramate and 37% on placebo. The most common adverse events, paraesthesia, vomiting, dizziness and nausea, were reported by 59%, 16%, 13%, and 9% of patients on topiramate versus 7%, 4%, 0%, and 0% on placebo, respectively. Of those treated with topiramate, 75% completed the study (52% on placebo).

Conclusions Topiramate produced a significant and clinically relevant reduction in migraine days in a population of chronic migraine sufferers, many of whom had medication overuse.

HEADACHE IN UNIVERSITY STUDENTS

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Background Headache is one of the most common complaints in medical practice. Studies in well defined populations are useful in identifying factors that influence frequency and severity of headache and in understanding its impact on people.

Aim To perform a descriptive study of headache in university students based on mutual interview, physical and neurological examination.

Methods Two hundred and one randomly selected students from different faculties were included in the study. Subjects having headache complaint in the last one year were invited. Diagnosis was established according to 2004 headache classification with detailed history and neurological examination. Migraine Disability Assessment Scale (MIDAS) questionnaire was evaluated on subjects with migraine for its impact on performance.

Results One hundred one (50.2%) of the students were female and 100 (49.8%) were male. Mean age was 23.0 (17–29). A positive family history of headache was found in 71.6%, especially in the first degree relatives (39.8%). Migraine was found in 44.3% and tension type headache was found in 51.7% of the students. One hundred eightyseven (93%) subjects had no previous physician referral and one hundred eightyfive students reported frequent analgesic use, ranging from once a week to daily. MIDAS was found to be >3 in 30 students.

Conclusions This study reveals that headache is not often taken into consideration in university students although it causes drug abuse/overuse without prescribed medication and significant loss of daily performance.

PAIN SENSITIVITY IN PRIMARY HEADACHES. A POPULATION STUDY

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Background Increased pain sensitivity may play a role in the pathophysiology of primary headaches, it has however mainly been evaluated in highly selected patients.

Aims To evaluate pain sensitivity in primary headaches in a large sample of the general population.

Methods 1175 residents, aged 25–76 years, representing a random sample of the population in Denmark were invited to participate. Information about headache was obtained by clinical interview and classified according to ICHD. Tenderness was recorded by manual palpation. Pressure pain threshold (PPT) was measured using an algometer at the temporal muscle. The examiner was blinded for the headache diagnosis.

Results 523 (253 men, 270 women) participated. In women tenderness was increased in chronic and frequent episodic tension-type headache compared to women without headache ($p<0.001$). There was no significant differences in PPT among the headache disorders. A trend towards a lower PPT in chronic tension-type headache was seen. No difference in PPT between migraine and subjects with no headache or infrequent episodic tension-type headache was detected (women: $p=0.9$; men: $p=0.73$).

Conclusions In agreement with previous clinical studies tenderness was increased in chronic and frequent episodic tension-type headache. In migraine pain sensitivity, detected by pressure pain threshold, was normal between attacks.

MEDICATION OVERUSE HEADACHE: COMPARATIVE RESULTS BETWEEN IN- AND OUT-PATIENT MANAGEMENT

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Objective The aim of this study was to compare the efficacy of a detoxification scheme in two populations consisting of 10 patients each: one group was hospitalized while the second group was admitted to Day Hospital daily.

Methods We studied two groups, each of 10 patients, affected by Medication Overuse Headache (MOH), without psychiatric comorbidity or opioid/barbiturate overuse. Patients underwent a 10-day treatment scheme consisting in: withdrawal of the overused drugs and administration of dexamethasone and amitriptyline. Subsequently, drugs were tapered and a prophylactic treatment commenced. Patients kept diaries of pain and medication use. Primary end-points were: Headache days/month Index (number of days with headache/30 days), at 1 and 3 months, and analgesic intake in the 3 months following detoxification. Secondary end-points were: responder rate (more than 50% reduction in headache frequency) and successful detoxification rate (monthly intake of less than 10 triptans/combination drugs or less than 15 NSAIDs). Finally, treatment tolerability was evaluated.

Results Headache index and analgesic intake was significantly lower at follow up compared to the month before treatment. The responder rate in two groups was of 70% at 1 month and of 85% at 3 months. Medication overuse was no longer an issue at the 3-month follow-up in 75% of patients. There were no significant differences regarding all evaluated parameters between the two groups.

Conclusions Although the sample is small, our results suggest that an out-patient management of Medication Overuse Headache, in the absence of conditions requiring hospitalization, is a valid therapeutic option. This treatment protocol was well tolerated and yielded a high degree of efficacy in both groups of patients, demonstrating that out-patient management can be effective in achieving analgesic withdrawal and can reduce management costs.

BILATERAL HYPOTHALAMIC ACTIVATION IN SUNCT: A SECOND CASE

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The primary headache syndrome of short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is often refractory to treatment. Regarding its pathophysiology, only two cases of functional magnetic resonance imaging (fMRI) have been reported, with hypothalamic activation ipsilateral to the pain in

one patient [1] and bilateral hypothalamic activation in a second case [2]. We describe the case, including fMRI data, of a 36 year old otherwise healthy woman, suffering from SUNCT without remission for more than 4 years. She experiences on average 15 right-sided SUNCT attacks per day (range 10–20) lasting 45 seconds on average (range 10–80) with an average pain score of 7/10 on a verbal rating scale (range 3–9). The patient has been completely refractory to medical treatment, including lamotrigine (up to 400 mg/day), gabapentin, topiramate and carbamazepine. She had a negative intramuscular indomethacin test (100 mg). Intravenous lidocaine was ineffective but could not be increased above 3 mg/min due to psychiatric side-effects. She underwent several unsuccessful invasive procedures, including a right-sided Jannetta operation and implantation of a left motor cortex stimulator. She underwent an exhaustive search for secondary causes, including MRI of the brain and cervical spine, lumbar puncture as well as cerebral digital subtraction angiography. While on a fentanyl patch, she underwent a BOLD fMRI study at 3 Tesla, during which she recorded 4 habitual SUNCT attacks. Condition-specific effects (pain state versus pain-free state) were estimated using SPM2. Significant BOLD-signal increases during the pain-state were detected bilaterally in the hypothalamus as well as in several brain regions involved in central pain processing. The fMRI data in this patient thus strengthen the observation of bilateral [2], rather than unilateral [1], activation of the hypothalamus during SUNCT attacks.

References

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COMPUTER ASSISTED PROGRAMME FOR THE USE OF ICHD-II: A SOFTWARE FOR THE GENERAL PRACTITIONERS

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The diagnosis of migraine is based on an accurate medical history centered on the clinical characteristics of headache, along with the exclusion of a possible secondary origin through the physical and neurological examinations; and supported, if needed, by neuroimaging and laboratory tests. The work load of general practitioners (GPs) may oblige to an inadequately quick approach to the migraine sufferer, in turn possibly preventing a proper diagnosis and/or limiting the quality of the therapeutic choices. We developed a computerized program designed for use in the office of a GP, which completely revisits a previous version: the system provides an assisted diagnosis according to ICHD-II criteria for the principal forms of primary headaches (migraine, tension-type headache, cluster headache), and highlights the red flags of a possibly secondary headache. A relevant feature is that criteria for the selection of a particular diagnosis are listed at the end of the process. Furthermore, the characteristics of the patient's headache, which were previously inserted in the program by the physician, are summarized, allowing to critically evaluate the suggested diagnosis. The diagnostic workup is enriched by an additional system of windows, containing informative notes and explanations on the terminology used. If the presenting clinical picture bears anomalies or is unusual, the program advises the interviewer to request an in-depth visit by a specialist. In conclusion, this program provides the GP with a valuable time-saving support; it is not intended as a passive diagnostic instrument, but aims for educational growth, promoting the learning of the ICHD-II criteria and a critical attitude.

ABNORMALITIES IN HEAD-NECK STATIC POSTURE AND MOTION TESTING IN MIGRAINE PATIENTS

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Background and aims Migraine attacks may be accompanied by tension headache-like symptoms, such as neck and shoulder pain. Headache due to cervical dystonia has been recently recognised. The aim of this study was to assess static head-neck posture and range of head-neck motion in migraine patients without any disorders of cervical spine or soft tissues of the neck.

Methods In 32 headache-free migraine patients and 32 controls we assessed static head-neck posture and range of head-neck motion (neck rotation, flexion and extension and sidebending, while in the sitting position). We used a specific computerized device. The results were expressed in degrees.

Results Head-neck static posture was abnormal in 32% of the migraine patients and 6% of the controls. In motion testing, statistically significant differences between right versus left side neck rotation ($p < 0.001$) and flexion versus extension ($p < 0.01$) were found in migraine patients, but not in controls.

Conclusions The results of this study suggest that in migraine patients head-neck static posture and motility may be abnormal. It is possible that in certain patients muscle tenderness and contraction, secondarily involved, were responsible of these abnormalities. Alternatively, central pain and/or sensitisation mechanisms may be evoked in the interpretation of our results.

MIGRAINE, STROKE AND INTERATRIAL SEPTAL ABNORMALITIES

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Introduction Patent foramen ovale (PFO) is more frequent in migraine with aura and it has been postulated as a possible cause for emboli among patients under 55 years old. Our goal is to study the association between PFO and migraine in ischemic stroke patients in this group of age

Methods Observational study with inclusion of consecutive stroke patients admitted to our Stroke Unit from January 1995 to January 2005. We selected patients under 55 years of age with first-ever acute cerebral infarction. Gender, vascular risk factors, subtype of stroke, the performance of transesophageal (TE) or transthoracic (TT) echocardiography and the presence of PFO or atrial septal aneurysm (ASA) were analysed according to previous history of migraine.

Results 334 patients, 211 males and 123 females. Mean age 44.4 ± 9.4 years. The 14.6% of women and the 1.9% of men had previous history of symptomatic migraine ($p < 0.001$). Migraine patients were younger than no migraine ones (40.14 vs 48 years, $p = 0.003$) and had more infarcts of unusual cause (27.3% vs 11.5%, $p = 0.044$). TE±TT echocardiography was performed in 72.7% of migraine patients and 59.6% of no migraine patients ($p = 0.224$). Previous history of migraine was not significantly associated to FOP (31.2% vs 16.1%, $p = 0.162$). However, migraine patients had FOP plus ASA more frequently than no migraine ones (25% vs 4.3%, $p = 0.009$; Odds Ratio: 7.417; 95% CI, 1.952 to 28.184).

Conclusions Previous migraine is more frequently associated to double interatrial septal abnormality- PFO plus ASA- and not to isolate FOP in cerebral infarct patients under 55. Echocardiography is recommended in this group of patients.

ALTERED GROWTH HORMONE SECRETION IN CLUSTER HEADACHE REMISSION

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Background and aims Hypothalamic dysfunction has been proposed to be closely related to the pathogenesis of cluster headache (CH). We have previously shown decreased, nocturnal lipolysis in both phases of CH. Lipolysis is stimulated by catecholamines, growth hormone (GH) and cortisol, and inhibited by insulin, hormones which are directly or indirectly regulated by hypothalamus. Our aim was to investigate the nocturnal secretion of noradrenalin, GH, cortisol and insulin in CH patients in remission and healthy controls.

Methods Ten CH patients in remission and ten healthy controls participated. Venous blood samples were collected between 23.00 and 07.00 hours, in hourly intervals for analysis of noradrenalin, insulin and cortisol and in thirty minute intervals for analysis of GH. ANOVA for repeated measurements were used for statistical analyses. Time, group were used as fixed factors in the model and BMI was used as a covariate to control for unbalance between groups. The GH values were log (ln) transformed.

Results GH varied over time and showed different patterns between groups ($p < 0.05$). The interaction effect revealed a more distinct peak in controls, but the time to the max peak or the nocturnal concentrations did not differ. Cortisol concentrations increased significantly during the night ($p < 0.00001$), but the temporal pattern did not differ between groups. Nocturnal concentrations and time to the max peak for cortisol, noradrenalin and insulin as well as the temporal pattern for noradrenalin and insulin did not differ between CH patients in remission and controls.

Discussion The results do not show any differences in hormone concentrations but indicate a different temporal pattern of GH secretion during CH remission. GH stimulates lipolysis mainly by increasing the sensitivity for catecholamine activity in adipose tissue. The results may indicate a desynchronized interaction between GH and catecholamines that might explain the altered nocturnal lipolysis in CH remission.

EVALUATION OF AUTONOMIC NERVOUS SYSTEM FUNCTION OF MIGRAINE PATIENTS: CAROTID BAROREFLEX AND ITS DYNAMICS DURING STATIC MUSCULAR EFFORT IN HEADACHE-FREE PERIOD

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Aims The aim of the study was to assess carotid baroreflex-mediated heart rate (HR) and mean arterial pressure (MAP) reactions in migraine patients in comparison with healthy controls during headache-free period.

Materials and methods On 18 migraine patients (in headache-free phase, mean age 31 ± 1.8 yrs) and 30 controls (gender and age matched) beat-to-beat HR and finger mean arterial pressure were monitored non-invasively with Physiograph UT-8506 elaborated in Tartu University. Bradycardic and hypotensive reactions to carotid baroreceptors activation were evaluated by Ekberg's neck suction method (-60 mmHg, for 5 s) at rest, during static muscular exercise (handgrip) for 60 s, with force 50% of maximal voluntary contraction and postexercise arterial occlusion in loaded upper arm for 1 min. Values are expressed as mean values \pm standard error.

Results At rest HR (74 ± 2 vs 70 ± 3 bpm) was insignificantly increased, bradycardic reaction to baroreflex activation (6.0 ± 0.3 vs 10 ± 0.6 bpm; $p < 0.05$) was decreased but finger MAP and hypotensive reaction to carotid baroreflex activation didn't differ significantly in patients comparing to controls. At handgrip exercise cessation moment the amplitude of pressor reaction (26 ± 2 vs 30 ± 4 mmHg; $p < 0.05$) and HR acceleration amplitude (22.2 ± 2 vs 28 ± 2 bpm; $p < 0.05$) were decreased and trajectory of HR dynamics during handgrip was changed in patients comparing to controls. As well as smaller part of pressor reaction amplitude was supported by post exercise arterial occlusion ($36\% \pm 8\%$ vs $57\% \pm 3\%$; $p < 0.05$).

Conclusions modified carotid baroreceptor reflex at rest, as well as during pressor reaction, and changed heart rate trajectory dynamics during handgrip are related with autonomic dysfunction in migraine patients, mainly the part of baroreflex-mediated cardiovascular responses

PSYCHIATRIC COMORBIDITY AND BEHAVIOR IN CHILDREN AND ADOLESCENTS WITH MIGRAINE WITHOUT AURA, MIGRAINE WITH AURA AND TENSION-TYPE HEADACHE

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Background and aims The association between migraine/tension-type headache (TTH) and psychiatric comorbidity has been well defined in adult patients, but there are only few studies in children and adolescents. Therefore, we were interested to examine psychiatric comorbidity and behavioural problems in young patients with primary headaches using a validated psychiatric scale and strict criteria for headache diagnosis.

Methods We examined 305 children and adolescents. One hundred sixty-four patients had migraine without aura (MO), 56 had migraine with aura (MA), 30 had TTH and 55 were headache-free controls. Patients with probable migraine or probable tension-type headache as well as patients with medication overuse were excluded. All patients were seen consecutively at our headache outpatient clinic. The controls were recruited at schools. The headache diagnoses were based on the criteria of ICHD-II. For assessing psychiatric symptoms and behavior we used the Child Behavior Checklist (CBCL). The CBCL is a questionnaire for parents with 113 behavior items, each scored from 0 to 2. For statistical analyses, we used Kruskal-Wallis tests and Mann-Whitney U-test, respectively.

Results Comparing the four groups all CBCL scores were lowest in controls. The differences were statistically significant for the total scores ($p < 0.001$), the internalizing scores ($p < 0.001$), and the subscores of somatic complaints ($p < 0.001$), thought problems ($p = 0.001$), and social problems ($p = 0.007$). The anxious/depressed subscores ($p = 0.016$) and subscores of attention problems ($p = 0.045$) failed statistical significance after Bonferroni-Holm correction. Comparing the four groups with each other revealed marked differences between MO and controls as well as between MA and controls, less marked differences between TTH and controls and almost no differences between the three headache-types.

Conclusions Children and adolescents presenting to a headache center for MO, MA or TTH have more often psychiatric symptoms and behavioral problems than headache-free controls. Our findings stress the importance of assessing psychiatric comorbidity systematically.

BURNING MOUTH SYNDROME AS AN INITIAL SYMPTOM OF THE NEUROSARCOIDOSIS

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Background Burning Mouth Syndrome (BMS) is characterized by a burning sensation in one or several oral structures, the pathogenesis may be divided in to local, systemic and psychological etiologies. The many reasons systemic for BMS are described as candidiasis, carcinoma, stomatitis, diabetes, and AIDS. Sarcoidosis is a multi-system glaucomatous disorder of unknown etiology, with multiples manifestations, neurosarcoidosis (NSD) occurs in 5%–10%, the sites of clinical involvement are meningeal (cranial nerves and involvement hypofisis), peripheral nerve, muscle, and parenchymal regions (brain and spinal cord).

Methods A 42-years-old woman with a 2 years history of a continuous glosodynia. She had pain exacerbations with the odors and foods. Both general physical and neurological examinations were normal. MRI, CT scan, were normal, the patient had used non-steroidal anti-inflammatory drugs, benzodiazepines, tricyclic antidepressants and topiramate without response; CSF was abnormal with increased mononuclear cells and elevated total proteins concentration, and hypercalcemia and elevated serum angiotensin-converting enzyme were reported. Others causes were excluded. The patient received treatment with Prednisolone 0.5 mg/kg/d, five days after use of the Prednisolone, the glosodynia disappeared and after four weeks CSF, Calcium, and angiotensin-converting enzyme were normal.

Conclusions BMS may be as an initial symptom of the Sarcoidosis and emphasize absolute need to exclude this cause.

CHRONIC PAROXYSMAL HEMICRANIA (CPH) RELIEF WITH LAMOTRIGINE: A CASE REPORT

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Objective Report a case of CPH refractory to Indomethacin but with an excellent response to Lamotrigine.

Background Indomethacin is the only proven drug that consistently provides completed and sustained relief of symptoms of CPH. Although the IHS classification requires Indomethacin as a diagnostic criterion, others agents also have been reported to be of some benefit. Lamotrigine (LMT), an inhibitor of veratrine- aspartate induced glutamate release, has been suggested as possibly effective for preventing aura associated with migraine, as well as, others primary chronic daily headaches.

Methods A 34-years-old woman with a 6 years history of continuous right side headache, located always in the orbito-temporal region of the same side, lasting 20 minutes. She had pain exacerbations accompanying symptoms of right eye ptosis, conjunctival injection, lacrimation, nasal congestion and rhinorea ipsilateral. Both general physical and neurological examinations were normal. MRI, CT scan, and cerebrospinal fluid examination were normal. During initial treatment Indomethacin was prescribed 25mg tid for five days without response, incremented a 50 mg tid for 10 days without response and finally increased a 75 mg tid x 10 days with partial response and appearance of gastrointestinal symptoms, so the drug was discontinued and reappeared the pain. LMT was begun at 50 mg /day and increased as tolerated at 150 mg/day. Three days after use of the LMT 50 mg tid, there was pain relief.

Conclusions LMT may be efficacious for patients with CPH refractory to Indomethacin.

SUMATRIPTAN NASAL SPRAY SAFETY AND EFFECTIVENESS IN MIGRAINE WITH AURA ADOLESCENTS

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Background and aims Migraine is a common cause of headache among late childhood and adolescence and is the most common cause of severe, recurrent headaches up in 15–19 ys, with a great impairment on quality of life, sociality and school performances. In 2004, Italian Health Ministry rules triptans use in adolescent age.

Aims study is assessing safety and effectiveness of Sumatriptan nasal spray in Migraine with Aura adolescent.

Methods According to IHS 2004 criteria, 24 migraine with Aura (MA) patients (M/F 13/11) aged 12–17 ys (mean 13.4 SD±1.48), were selected in Headache Centre of Child and Adolescents Neuropsychiatry Department in Naples, between February 2003 and September 2004. Monthly frequency migraine attacks were 3 to 7. All patients were non responders at analgesics and NSAIDs.

Standard neurological and clinical laboratory tests, EEG wake and sleep recordings, electrocardiograms, and nasal examinations were performed at first clinic visit. Patients presented visual aura in 42.85%, limbs paresthesia 28.57%, and arms hyposthenia 28.57%. Before and after treatment of each migraine, patients scored pain on a four-point scale (0=none; 1=mild; 2=moderate; 3=severe).

Results The success of individual Sumatriptan clinical administration appears related to time to treatment, with resolution pain time in 10 minutes for 64.58% and in 30 minutes for 35.42%. Overall, triptan tolerability in adolescents is similar to that reported in adults. The most common specific drug-related adverse event was unpleasant taste, which was reported in 37.58% of patients and epistaxis in 12.52%. Mean scored value pain after treatment with Sumatriptan was 0.75 (SD±0.8) vs 2.89 (SD±1.24) ($p=0.000$).

Conclusions Triptans (selective 5-hydroxytryptamine_{1B/1D} serotonin agonists) are a new class of agents used in the treatment of migraine. Study results suggest that Sumatriptan nasal spray may effectively alleviate migraine in adolescents MA patients.

EPISTAXIS: A SYMPTOM OF INCREASED PARASYMPATHETIC ACTIVITY IN PATIENTS OF MIGRAINE?

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Objective To describe the Epistaxis as a symptom of the increased parasympathetic activity in patients with migraine attacks

Background Migraine is an episodic syndrome consisting of a variety of clinical features that result from dysfunction of the parasympathetic nervous system, because increased parasympathetic outflow to the cranial cavity induces vasodilatation of cerebral and meningeal blood vessels, it can enhance plasma protein extravasation and the release of proinflammatory mediators that activate perivascular nociceptors. Parasympathetic stimulation causes release ACH, VIP, NO around meningeal vasculature, these substances can induce mast cells degranulation, and release of the Histamine and others inflammatory mediators. Symptoms such as lacrimation and nasal congestions may be explicated for the parasympathetic system activity. Many patients with migraine exhibit Epistaxis (EP) associated with migraine attacks.

Methods A total of the 545 patients with Chronic Migraine (CM) were interviewed with two single questions. 23 (4.2%) patients had EP associated with migraine attacks, of them 9 (39%) had relief of the pain with EP and 23 (100%) had rhinorea and nasal congestions with migraine attacks. The mean age of the patients with CM and EP was 39.2 years. Others causes of EP were to excluded. Nasal bleeding usually responds to first-aid measures such as compression.

Conclusions EP may be a symptom of the parasympathetic activity increased in patients with migraine attacks.

EFFECTIVENESS AND TOLERABILITY OF TOPIRAMATE AND FLUNARIZINE FOR MIGRAINE PROPHYLAXIS: COMPARATIVE CASE-SERIES STUDY

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Introduction Flunarizine and topiramate have shown to be effective in the prophylaxis of migraine. Aim of the Study. To compare two independent groups with similar characteristics who were treated with either flunarizine or topiramate as initial prophylactic for migraine.

Patients and methods All patients reported more than four episodes per month or transformed migraine, according to Silberstein's criteria, and had never received prophylactic treatment. In both groups

was determined: mean number of migraines, number of migraine days, and responder rate in the previous month and at the fourth month of treatment.

Results 125 patients were included in each group for intention-to-treat analysis. There was significant decrease ($p=0.0001$) in mean number of attacks at the fourth month, but with no significant difference between groups: topiramate (5.88 ± 3.7 to 2.1 ± 2.5 attacks), flunarizine (5.24 ± 3.2 to 2.3 ± 2.7 attacks). The mean percentual reduction in number of migraines at the fourth month: topiramate $58.2\%\pm 38.2\%$, flunarizine $55.4\%\pm 37.5\%$.

Responder rates Topiramate 71%, flunarizine 67%. There was also significant decrease ($p=0.0001$) in mean number of days with headaches in the fourth month, but with no significant difference between groups: topiramate (16.2 ± 7.2 to 6.7 ± 8.3 days), flunarizine (16.2 ± 6.8 to 5.9 ± 7.7 days). The mean percentual reduction in number of days with headaches was: topiramate $54.7\%\pm 42.1\%$, flunarizine $61.8\%\pm 39.7\%$.

Side effects Topiramate 69 patients, flunarizine 53 patients ($p=0.0427$).

Dropouts Topiramate (28%), flunarizine (11%) ($p=0.0013$).

Conclusions Both drugs showed a high degree of effectiveness when used as the initial drug in the prophylactic treatment of migraine. Topiramate offered better results preferentially in migraine. Patients treated with topiramate experienced more side effects, none of which were serious. Topiramate could be considered as a first-line treatment for migraine prophylaxis.

MEASURING THE SEVERITY OF HEADACHE, A PILOT STUDY

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Background and aims Different approaches exist for the management of headache complaints. Patients are mostly treated by their general practitioner or neurologist. For some headache types, non-invasive treatments like physio- and manual therapy can be beneficial. Apart from the headache diagnosis a description of the patients complaint will help to select the appropriate treatment. This headache description should also include the severity of the headache containing behavioural aspects. Our aim was to study the use of a grading system proposed by Sjaastad et al 2002. Our research question was: to what extent differs the headache severity among headache sufferers who seek no treatment for their headache from the severity from those who are in treatment from either their GP, neurologist or physiotherapist.

Methods Subjects with headache (n: 87) since at least 2 months and at least twice a month were asked to complete the severity list [1], the Headache Disability Inventory [2] and a VAS scale. Differences between groups were analysed using Kruskal Wallis Anova and consequent Mann-Whitney tests.

Results The vast majority (n: 41) was not in treatment, 12 were treated by their GP, 9 by a neurologist, 25 by a physiotherapist. The severity score was higher in the GP and neurologist group ($p=0.000$). No significant differences were found for the HDI and VAS between the groups.

Conclusions This grading system appears to be a useful tool to objectivate the severity of headache. It can be used in daily practice as well as in scientific work. Apart from the headache diagnosis this can document the headache complaint that is being studied. Further research is necessary to indicate whether this tool can be helpful in the referral of patients.

References

1. Sjaastad et al (2002)
2. Jacobson et al (1994)

EFFECT OF NITROGLYCERIN ON TEMPORAL SUMMATION THRESHOLD OF NOCICEPTIVE FLEXION REFLEX IN MIGRAINE PATIENTS

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Background and aims In migraineurs nitroglycerin (NTG) induces severe delayed headache, resembling spontaneous migraine attacks. The temporal summation threshold (TST) of the nociceptive flexion reflex (NFR) is considered an objective method that offers the potential to examine the central nervous system pain processing. The aim of the present study was to evaluate the NFR-TST during nitroglycerin-induced migraine.

Methods Twenty-two patients (16 female and 6 male, mean age 35.6 ± 8.25 , range 18–55 years), suffering by migraine without aura (1.1 IHS, 2004) were selected. Headache was induced by sublingual administration of 0.9 mg of NTG. NFR-TST and the subjective painful sensation were measured before and 30, 60, 120 and 240 min after drug administration.

Results All patients exhibited a significant ($p<0.01$) reduction of the NFR-TST 120 min after drug administration. In particular a subgroup of patients experiencing severe attack showed a significant ($p<0.01$) reduction of NFR-TST at both 60 and 120 minutes.

Conclusions NTG appeared to support a reliable experimental model of migraine, based on the neuronal effects on the integrative-nociceptive structures. The NFR-TST facilitation during NTG-induced attack reflects an extracephalic generalized hypersensitivity of pain pathways during migraine attack that could provide the susceptibility for triggering migraine attack and probably its persistence.

CAN HIGH-FREQUENCY RTMS RESTORE NORMAL INTRACORTICAL EXCITABILITY IN MIGRAINE WITH AURA? EFFECTS OF PRIMING STIMULATION ON 1 HZ RTMS OF MOTOR CORTEX

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Objective We showed that motor intracortical inhibition (ICI) is reduced in migraine with aura (MWA) patients and that 1 Hz rTMS induced paradoxical effects increasing motor intracortical facilitation (ICF) in these patients (Exp Brain Res. 2005;161:34–8). In conditions of enhanced excitability due to a reduced inhibition, high frequency rTMS acts potentiating intracortical inhibition (J Physiol 2005; 565.2 : 659–6652–3; Neurosci Lett 2000; 284: 147–150.)

Methods ICI and ICF were assessed by paired-pulse TMS (pp-TMS) in baseline and after rTMS (over the hot-spot of the right abductor pollicis brevis muscle) in MWA patients and in six controls. 1.pp-TMS: a conditioning stimulus (CS) at 80% Motor threshold (MT) intensity followed by a test stimulus (TS) at 120% MT, with two interstimulus intervals: 2 msec for ICI and 10 msec for ICF 2.rTMS: priming-rTMS (900 stimuli, 10 Hz frequency, in trains of 50 stimuli separated by 45 s intervals) was followed by a 900 stimuli train at 1 Hz rTMS. rTMS was delivered at 90% of MT intensity. Motor evoked potential (MEP) amplitude of TS post-rTMS was expressed as percentage of baseline MEP. MEPs amplitude at 2 and 10 ms ISIs recorded before and after rTMS were expressed as percentage of change from the respective mean TS alone.

Results In baseline, ICI was significantly lower in migraineurs with respect to controls. In healthy controls MEP amplitude and ICF were significantly reduced by priming-1 Hz treatment with respect to baseline values. Differently, priming stimulation significantly increased ICI in migraineurs, leaving quite unchanged MEP amplitude and ICF values with respect to baseline.

Conclusions in migraineurs rTMS-priming potentiates intracortical inhibition and revert the paradoxical increase in ICF observed with 1 Hz rTMS. These findings strengthen the hypothesis of reduced inhibition in migraine with aura and might open perspective for new treatment strategies.

ASSESSMENT OF FUNCTIONAL DISABILITY DUE TO EPISODIC CLUSTER HEADACHE

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Objective To assess disability in different activity domains in a sample of episodic cluster headache (ECH) patients during the active phase of their illness, using the MIDAS questionnaire.

Methods The 12 consecutive patients (10 men, 2 women), with an IHS diagnosis of episodic ECH, mean age of 32 years (range 18–45), and mean illness duration 3,6 years (range 1–12) completed the translated form of MIDAS questionnaire, specific tool designed to assess headache-related disability. Patients completed the form, not less than 2 days after the onset of a cluster period and not more than 7 days after the end of their cluster period.

Results The mean MIDAS score was rather high: mean score 52.9 (95% CI 18.63–87.16). The individual MIDAS item scores indicated that all daily activities were affected by the headaches: 75% (95% CI 46.8%–91.1%) were forced to miss family/social or leisure activities, 58.3% (95% CI 32%–80.7%) had to stop work and 50% (95% CI 25.4%–74.6%) had their productivity reduced by more than 50%. Household work was also impaired.

Conclusions Patients with episodic cluster headache have marked functional disability. The activities most affected by their headaches are social, family and leisure commitments, but paid work and household work are markedly impaired in a high proportion of patients.

DAILY PERSISTENT HEADACHE AFTER REPEATED USE OF COCAINE

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Background Cocaine-induced headache is a frequent complication in people with acute or chronic use of this substance. The mechanism of this headache is unknown but it may be related to the sympathomimetic or vasoconstrictive effects of cocaine. By definition, the headache develops after one hour of cocaine use and resolves within 72 hours.

Objective to present a case with persistent headache related with use of cocaine.

Case description A 26 year old healthy man, with sporadic use of inhaled cocaine, develops a bilateral frontotemporal and pulsatile headache immediately after use of cocaine during two years. The symptoms improve within 24 hours after intake without any therapy administrated. Headaches were always episodic during this time and fulfilled the criteria for cocaine-induced headache. 18 months ago, after one of this episodes related with inhalation of cocaine, the patient develop his usual headache but, in this occasion, the headache remain until now. In spite of withdrawal of the substance, our patient remain with a chronic persistent daily headache (similar to the new daily persistent headache) without any

response to multiple therapeutical approaches. MRI and neurophysiological examinations were normal.

Conclusions We speculate that cocaine can produce not only acute headache. It could be possible that the repeated use could origine a daily persistent headache.

A PROSPECTIVE, MULTICENTRE, RANDOMISED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE EFFICACY OF PATENT FORAMEN OVALE (PFO) CLOSURE WITH THE STARFLEX SEPTAL REPAIR IMPLANT TO PREVENT REFRACTORY MIGRAINE HEADACHES: THE MIST TRIAL

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Background and aims Observational studies demonstrated that PFO closure in stroke and decompression sickness patients led to the resolution of migraine in 65%–90% of patients. The MIST (Migraine Intervention with STARFlex® Technology) Trial is the first trial to investigate these observations with a prospective, double blind, placebo-controlled design.

Methods Patients aged 18–60 years with migraine with aura (International Headache Society 1988 classification), refractory to two or more classes of prophylactic medications and with a minimum of 5 migraine headache days and 7 headache-free days per month were recruited. Transthoracic contrast echocardiography was used to detect right-to-left shunts and to semi-quantitatively assess their size. Patients with a moderate or large PFO were randomised to PFO closure with the STARFlex® septal repair implant or to a sham procedure. Daily headache diaries were completed during baseline evaluation and follow up periods. Patients and their headache specialists remained blind to randomisation during the 180-day follow-up period.

Results 432 patients were recruited and screened for shunts. 260 (60.2%) had a shunt of which 163 (37.7% of total and 62.7% of those with shunts) had a moderate or large PFO. Of these, 16 withdrew or were withdrawn for medical reasons before randomisation. 73 patients were randomised to the sham procedure and 74 to the closure procedure with STARFlex®. Unblinding will be completed in January 2006.

Conclusions The results from the diagnostic phase of the trial confirm that moderate or large right-to-left shunts (mostly PFOs) are very common in migraine with aura patients. The prevalence of these is about 6-fold greater in the trial population than in the general population. The MIST Trial will provide clinical evidence on the efficacy of PFO closure for patients with severe migraine. The final results from the trial will be available for presentation at the 8th EHF Congress.

MIGRAINE AND RIGHT-TO-LEFT SHUNT IN NEUROLOGICAL PATIENTS

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Introduction Patent foramen ovale (PFO) is more frequent in migraine with aura patients. Our goal is to describe this association in suspected ischemic stroke patient hospitalized in a Neurology department.

Methods Observational study with inclusion of consecutive neurological patients admitted to our Neurology department from January 1997 to December 2005. We selected suspected ischemic stroke patients who had previous history of migraine and a right-to-left shunt by the Transcranial Doppler (TCD) with IV injection of agitated saline. Demographic characteristics, neurological disease, vascular risk factors, affected hemisphere and the performance of transesophageal (TE) and/or transthoracic (TT) echocardiography were analysed.

Results 17 patients had previous migraine from a total of 60 right-to-left shunt patients (10.2%). 10 females and 7 males, mean age 33.76 years (range 15–57). Nine (52.94%) had previous history of migraine with aura and 8 (47.60%) migraine without aura. The most frequent risk factors in migraine patients were: arterial hypertension (1 patient), diabetes mellitus (1), hyperlipemia (2), current smoking (10), acute myocardial infarction (1). Right hemisphere was affected in 9 patients and left one in 8. The in-hospital diagnoses were: transient ischemic attack (8 patients), episode of migraine with aura (3), aura without headache (1), brain infarction (3), cerebral venous thrombosis (1), ischemic optic neuropathy (1).

Conclusions Migraine frequency is similar to the general Spanish population in this group of in-hospital patients with right-to-left shunt. Smoking is the most important vascular risk factor associated to migraine and right-to-left shunt.

CHILD MIGRAINE AS A FAMILY INHERITED SYNDROME

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The migraine syndrome can be understood as being a heterogeneous state, consisting of some more, still not found, hereditary disposition factors which altogether, interacting with other surrounding factors, give the recognizable clinical picture. The aim of this research is to determine heredity of the migraine syndrome. The presence of headaches similar to those tested was compared among all the members of the family within three generations. Heredity of the migraine syndrome was investigated among 24,828 families of children aged 3 to 16 years, in Vojvodina, during the period of 16 years. Positive family anamnesis of the recurrent headaches was detected among 98.6% children with migraine headaches, 64.7% among children with headaches of different etiology, and 32.4% among children without recurrent headaches. The family as a whole is the most significant for heritability of the migraine syndrome, with the correlation quotient of 0.9653, and determination quotient of 93.17%. The highest heritability of the migraine syndrome comes from a mother, grandfather from the father's side, grandfather from the mothers side, grandmother from the father's side, grandmother from the mother's side, female second cousin from the mothers brother, aunt from the fathers side, and a female second cousin from the fathers sister. The relation among the members of the nuclear family is significantly stronger than the relation to the members of wider family. Child migraine is a family inherited syndrome. The probability of a child having the migraine headache, in case that someone from the family members has it is 0.664 for a mother, 0.644 for a father, 0.411 for a grandmother from the fathers side, 0.175 for a grandmother from the mothers side, 0.165 for a grandfather from the mothers side, and 0.102 for a grandfather from the fathers side.

Keywords Headache, Migraine, Heredity, Heritability

EPIDEMIOLOGY, CHARACTERISTICS AND DISPOSITION FACTORS

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The aim of this investigation was to identify the specific features of migraine headaches (epidemiology, clinical and disposition which would provide easy and precise diagnosis of migraine syndrome in children. Investigations were carried out in the period from 1988 to 2004, on 30,636 children (50.38% boys, and 49.62% girls), in nine towns of south part of Serbia & Montenegro - the territory of Vojvodina. Migraine syndrome was found with 8.63% children aged 3 to 17 years (8.0% male and 9.6% female). Migraine with aura makes 25.55%, migraine without aura 67.21% and other migraine syndromes 7.23% of the migraine syndromes with children of the same population. Migraine attacks often follow identical patterns (94.9%). Symptoms associated with migraine attacks in children, dominate the clinical picture of migraine attack itself. Migraine episodes accompanied by symptoms specific for migraine syndrome include: nausea, vomiting, pallor, photophobia, phonophobia, dark circles under and around the eyes, vertigo and abdominal pain. Apart from a direct heredity, as disposition factors of the migraine syndrome the following factors should also be accepted: the order of birth, the length of breast-feeding period, exact age when the ready-made industrial food was introduced as well as the age when the child was introduced to a whole-day basis stay particularities in the pattern of behavior, material status of the family, atmosphere within the family, previous record of paroxysmal torticollis, episodic vertigo of unknown etiology and recurrent abdominal pain, kinetosis and insufficient dominance of the hemisphere.

EFFICACY OF TOPIRAMATE IN PROPHYLACTIC TREATMENT OF MIGRAINE

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Objective To evaluate the efficacy and safety of topiramate (TPM) in migraine prophylaxis.

Methods 58 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 present more than 6 months with 2 and more attacks per month. Primary efficacy measures included frequency of migrainous attack per month, number of days with migraine per month and migraine severity at scale 0 to 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 TPM 100 mg BID or 200mg BID.

Results 7 patients were excluded from the study due to TPM adverse effects (twice very mild), 21 patients had mild adverse effects of TPM during titration phase. TPM was administered at dose 100 mg/day (50 patients) or 200mg/day (8 patients). Number of migrainous attack/patients/month improved from 5.9 to 2.3. Average of MIDAS improved from 3.6 before treatment of TPM to 1.7 after treatment of TPM.

Conclusions This study demonstrated that TPM was effective in the prophylaxis treatment of migraine.

HEADACHES AND MULTIPLE SCLEROSIS (MS)

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Background Multiple sclerosis (MS) can frequently manifest different symptomatology at on-set. Quite often, the initial symptom can be strong headaches or migraines. In this abstract we are reporting on the prevalent clinical manifestation and neuroradiological findings of headaches in MS.

Methods In 1258 patients with a clinically and radiologically diagnosed MS, we picked 9 male and 16 female patients, aged 18–42

years and with average disease duration 12+5.3 years, who had experienced heavy headaches as first signs of the disease. The patients were separated in three groups and were re-examined two years after having completed a treatment preferably with mitoxandrone.

Results 12 out of 25 patients showed a chronic progressive MS, 8 a chronic relapsing remitting MS and 7 an acute progressive MS. After treatment they presented a significant improvement to a complete elimination of the headaches. 8 of them partially improved and 2 still had them. Before treatment, the encephalogram was 18 times pathological and only in 6 steady pathological signs was found. The MRI was performed in all patients and showed pathological lesions at different points. There was a correlation to the clinical symptoms 8 times. It was repeated in 18 patients after completing treatment and in 4 of them there were less focuses found.

Conclusions 1) Headache, as initial symptom of MS rises about to 2%. 2) After treatment there is significant improvement in 80% of all patients. 3) We have to consider MS as differential diagnosis in chronic headaches.

THE ASSOCIATION BETWEEN POOR WELL-BEING AND MIGRAINE IS RELATED TO COEXISTING TENSION-TYPE HEADACHE

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Objective Psychiatric comorbidity in migraine is well established, but possible coexisting tension-type headache (TTH) is seldom incorporated in the analyses. The aim is to assess the association between migraine, TTH and psychiatric comorbidity in a general population.

Methods A survey of the general population in 2001. 848 persons (73.5%) aged 25–76 years participated. Medical doctors conducted all diagnostic interviews based on ICDH-I and II. Migraine and TTH was assessed in all subjects. Migraine was defined as at least one attack within the last year. Frequent TTH is defined as frequent episodic TTH or chronic TTH.

Results When analysed in univariate regression analyses, migraine was associated with lower self-rated health ($p=0.02$), higher depression scores ($p=0.01$), higher Eysenck neuroticism scores ($p=0.03$) and lower Quality of Life ($p=0.005$). When coexisting TTH was included in the analyses, migraine was not associated with psychiatric comorbidity. Instead, frequent TTH was significant related to lower self-rated health ($p=0.0001$), higher depression scores ($p=0.0001$), higher Eysenck neuroticism scores ($p=0.0001$) and lower Quality of Life ($p=0.0001$).

Conclusions In this population study, the association between migraine and psychiatric comorbidity disappeared when adjusted for frequent TTH. This necessitates that coexisting TTH is included in future analyses of migraine and psychiatric comorbidity.

NO CHANGE IN MEDICATION PATTERN AND WORK ABSENCE FOR PRIMARY HEADACHES DESPITE INCREASED CONSULTATION RATES

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Objective Knowledge about changes in consultations, medication and work absence for primary headaches is important clinically and in a public health perspective. The aim is to assess changes in consultations, medication and work absence for migraine and tension-type headache (TTH) in Denmark.

Methods Cross-sectional surveys in 1989 and 2001 of the general population. Medical doctors conducted all diagnostic interviews based on ICDH-I and II. Participation was 75.6% (740) in 1989 and 73.5% (711) in 2001. Headache status was categorized as pure migraine, frequent TTH (frequent episodic or chronic TTH), coexisting migraine and frequent TTH, or no headache (infrequent TTH or no headache).

Results Headache consultations increased for all headache groups ($p=0.008$). Prescription medication ($p=0.45$) and work absences ($p=0.70$) due to headache were largely unchanged. All cause consultations and absences were unchanged but individuals with headache had higher rates ($p=0.02$), most markedly for those with coexisting migraine and TTH.

Conclusions Many headache sufferers still do not seek medical care and do not receive adequate treatment. Despite increased headache consultation rates, only moderate changes in medication and no improvement in work absences were observed. The impact as measured by consultations, medication and absence was highest for individuals with coexisting migraine and TTH.

PROGNOSIS OF MIGRAINE IN A GENERAL POPULATION

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Objective Knowledge of the prognosis of migraine in general populations is limited due to the few population-based follow-up studies. The aim is to analyse long-term prognosis of migraine and to identify prognostic factors.

Methods Of 740 persons (aged 25–64 years) examined in a 1989 Danish cross-sectional headache study (baseline), 673 were eligible in 2001 (follow-up). All interviews were conducted by medical doctors and based on ICDH-I and II. 81.6% (549) participated. Poor outcome of migraine was defined as migraine frequency >14 days at follow-up.

Results Of 64 migraineurs in 1989, 54 had low frequency migraine (1–14 days/year) and 10 had high frequency migraine (>14 days/year). At follow-up, 27 migraineurs (42%) experienced remission (0 days/year), 24 (38%) had low frequency migraine, while 13 (20%) experienced poor outcome (>14 days/year). Poor outcome was observed in 13% (7) of subjects with low frequency and 60% (6) with high frequency at baseline. Prognostic factors for poor outcome of migraine were high baseline migraine frequency and age at onset before 20 years.

Conclusions Clinical assessment of headache status at baseline and follow-up ensured high validity. Generally, the prognosis of migraine is favourable but increased focus should be directed towards the minority at risk for progression.

PROGNOSIS OF TENSION-TYPE HEADACHE IN A GENERAL POPULATION

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Objective Knowledge of the course of tension-type headache (TTH) in general populations is limited due to lack of population-based follow-up studies. The aim is to analyse long-term prognosis of TTH and to identify prognostic factors.

Methods Of 740 persons (aged 25–64 years) examined in a 1989 Danish cross-sectional headache study (baseline), 673 were eligible in 2001 (follow-up). All interviews were conducted by medical doc-

tors and based on ICDH-I and II. 81.6% (549) participated. Outcome was assessed for individuals with chronic TTH (CTTH) or frequent episodic THH (fETTH) at baseline. Poor outcome was defined as CTTH at follow-up.

Results In total, among 146 subjects with fETTH and 15 with CTTH at baseline, 72 (45%) experienced infrequent or no TTH, 64 (40%) had fETTH, and 25 (16%) experienced CTTH (poor outcome) at follow-up. Poor outcome was observed in 17 (12%) with fETTH at baseline and 8 (53%) with CTTH at baseline. Prognostic factors for poor outcome were baseline CTTH, coexisting migraine, not being married and sleeping problems.

Conclusions Clinical assessment of headache status at baseline and follow-up ensured high validity. Generally, the prognosis of CTTH is acceptable and only a small proportion of subjects with fETTH is at risk of progression.

PREVENTION BY CORRECTION-TREATMENT OF THE PLATELET HYPER-AGGREGABILITY ON MIGRAINE ACCOMPANYING SCINTILLATING SCOTOMA, AND ON MIGRAINE EVALUATED BY MIDAS SCALE

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Background and aims To investigate the preventive effect of correction-treatment of the platelet hyper-aggregability on severe migraine.

Methods As for the platelet aggregability test, an aggregation area analyzing method with 9 classes display using "the double ADP method", low and high concentrations of reagent; ADP and collagen, is utilized. The method is exact and easy to know the level of platelet aggregability. Correction means to make the platelet hyper-aggregability (class 9 and 8) to normal aggregability (class 5). Subjects were consecutive 9 patients for part 1), and 13 patients for part 2), who showed both severe migraine and platelet hyper-aggregability.

Results Excellent preventive effects on migraines were obtained in all cases. After the correction-treatment, part 1); migraine attacks did not appear completely in all cases for many years. In addition, the scintillating scotoma itself disappeared completely except 2 cases. In one of two cases that were using Triptans, it became not necessary. Part 2); number of MIDAS scale showed remarkable and significant decrease. Days of miss-work from 18.7 to 1.8 ($p=0.0015$), days of migraine from 14.2 to 2.5 ($p=0.0015$), and severity of migraine from 7.7 to 3.2 ($p=0.0042$) on average.

Conclusions Based on these results, the author proposes that the fundamental cause of migraine is the long-standing platelet hyper-aggregability. The effect gained by correcting the platelet hyper-aggregability must be elicited by stabilizing the Serotonin metabolism, and through the recovery from reduced cerebral blood flow. If the platelet hyper-aggregability is not corrected, white matter lesion will develop and rapidly progress [1], and finally it becomes to Binswanger's dementia. Thus, this must be the best preventive treatment-method for migraine and dementia. The author strongly recommends apply this method.

Reference

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TREATMENT OF CHRONIC CLUSTER HEADACHE WITH GAMMA KNIFE STEREOTACTIC SURGERY: REPORT ON SEVEN CASES

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Introduction Cluster headache is well defined in the classification and diagnostic criteria of the International Headache Society (IHS). Some cases (about 10%) evolve towards chronicity. Refractory chronic cluster headache (RCCH) raises a real therapeutic challenge. Although questions remain about the choice of the target, radiosurgery on the trigeminal nerve has been proposed in these difficult cases.

Method Between September 2003 and February 2005, seven patients (6 male, 1 female) underwent gamma knife stereotactic radiosurgery (GKS) for RCCH. The target was the cisternal portion of the trigeminal nerve on which a dose of 90 Gy at the 100% isodose was delivered. Duration of chronicity was higher than 3 years and mean follow-up is 16 months.

Results Three patients experienced excellent outcome (pain free and no medication), one patient had a good result (75% improvement, occasional medication), no improvement was observed in three patients. The delay of relief was within 1 to 2 months. One patient presented a recurrence two years after GKS, after a head trauma. Only two patients reported slight sensory disturbance in the face (paresthesias or hypesthesia without any neuropathic pain).

Conclusions Our observations confirm that GKS contributes to the treatment of RCCH with no major side effect. The rate of success is about 50%–60%. Considering the chronicity of the patients we have operated on, and the failure of the multiple treatments they had followed before, it is improbable that this result would simply reflect the natural evolution of the disease.

17B ESTRADIOL POTENTIATES CGRP-MEDIATED RELAXATIONS IN CAUDAL AND MESENTERIC ARTERIES IN OVARIECTOMISED RATS

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The prevalence of migraine is 2–3 times higher in females than in males, and is intricately related to levels of female sex steroids. These might interact with calcitonin gene-related peptide (CGRP), a potent vasodilator implicated in the pathogenesis of migraine. We investigated the effects of treatment with 17estradiol, progesterone or their combination on vasodilatation to CGRP and acetylcholine in mesenteric, caudal and basilar arteries obtained from ovariectomised rats. Female Sprague Dawley rats were bilaterally ovariectomised and divided into five groups; sham operated animals and ovariectomised animals treated with placebo, 17b estradiol, progesterone or their combination. Segments of mesenteric, caudal and basilar arteries were isolated and mounted in Mulvany myographs. Both CGRP and acetylcholine induced concentration-dependent relaxations in all arteries studied. The potency of CGRP in caudal and mesenteric arteries was significantly increased in ovariectomised animals treated with 17b estradiol (pEC_{50} : 8.71 ± 0.15 and 10.84 ± 0.34 , respectively) as compared to those treated with placebo (pEC_{50} : 8.23 ± 0.06 and 9.76 ± 0.20 , respectively), while no differences in E_{max} were observed. Animals treated with progesterone or the combination of hormones did not differ from the placebo-treated animals. In basilar arteries, relaxations to ? CGRP were not different between the various groups. Neither the potency, nor the E_{max} of acetylcholine differed between the groups in any of the arteries studied. Our results demonstrate that 17b estradiol increases the potency of CGRP in caudal and mesenteric arteries, without having a similar effect on acetylcholine-mediated responses. Although we did not observe a potentiation of CGRP responses in basilar arteries, such a mechanism may well be present in cranial arteries involved in the pathogenesis of migraine, such as the meningeal arteries, which are too small to study in vitro. This potentiation of CGRP-mediated vasodilatation by 17 b estradiol may be of one the mechanisms through which female sex hormones exacerbate migraine attacks.

SECONDARY MIGRAINE HEADACHE AS A SIGN OF CEREBRAL AVM IN A TEN YEARS OLD GIRL – A CASE REPORT

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Introduction Brain arteriovenous malformations (AVMs) include several types of vascular malformations from small criptic lesions to huge anomalies. The clinical symptoms are headache, vomiting, transient motor deficit, epilepsy or stroke. AVMs are always detectable by CT, MRI and angiography. Recently, Transcranial Color Doppler ultrasonography (TCCD) showed abnormal complex of cerebral vessels with pathological spectral velocity waveform. Embolisation is indicated for malformations fed by arteries large enough to be accessible to catheterisation permitting selective occlusion.

Materials, methods and results We report a ten years old girl, who was admitted because of the first migrena-like headache. She had no neurological dysabillities. EEG showed slow waves, fundoscopic examination and laboratory tests were normal. TCCD showed a complex of cerebral vessels at the region of the left anterior cerebral artery (ACA) with very high velocities in both systole and dyastole, and with abnormal spectral velocity waveform in both ACAs, suspected on AVM. Magnetic resonance imaging (MRI) showed an area of serpiginous multiple loss of signal at the left frontal region, which corresponded to a vascular structures. Magnetic resonance angiography (MRA) and digital subtraction cerebral angiography showed arteriovenous malformation in the area of mediocortical part of the left side upper frontal gyrus. Two embolisations of AVM were performed in a six months interval. Now, the girl has no headaches, parestesias or motoric disturbances. Control TCCD shows normal morfological findings of great cerebral arteries, but with high velocities in left MCA and ACA yet.

Conclusions Migrena-like headache could be secondary due to brain AVM. Embolisation is an optimal method for treatment of this type of AVM, where feeding arteries are large enough to be accessible to catheterisation permitting selective occlusion. TCCD is a very sensitive noninvasive method for the diagnosis and monitoring of brain circulation changes in children with AVMs.

FROVATRIPTAN FOR THE PREVENTION OF POST-DURAL PUNCTURE HEADACHE

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Objective Post-dural puncture headache (PDPH) occurs in approximately 40% of cases of diagnostic lumbar puncture (DLP). This study assesses the efficacy of frovatriptan (F) as a prophylactic treatment of PDPH.

Methods 21 patients (39±12 years) submitted to DLP with a 20-gauge needle were treated with F 2.5 mg orally od, according to a non-randomized, open label design. Treatment was administered for 5 days following DLP. Previous treatments were withdrawn one month prior to study inclusion. PDPH was diagnosed according to ICHD-II. Occurrence, intensity and duration of PDPH and related symptoms were assessed during the 5-day in-hospital period following DLP.

Results DLP caused a mild PDPH in 4 (19%) patients ($p < 0.01$). 5 days of PDPH out of 105 days of treatment ($p < 0.01$) were recorded: 2 patients had PDPH for 1 day, 1 patient for 2 consecutive days, 1 patient on the last day of treatment. No symptoms except headache were reported. In the 5 patients with a previous DLP, 3 had PDPH on that occasion vs. 1 after the new DLP ($p = NS$).

Conclusions though based on a non-randomized, open label study, results of our study support the hypothesis that prophylaxis with Frovatriptan may successfully reduce the risk of PDPH.

TRIGEMINAL TRACT DEMYELINATION PRESENTING AS MIGRAINE-LIKE HEADACHE

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There's increasing evidence of the role of the brain stem in the pathophysiology of migraine. It is well known that the activity in nociceptive pathways is modulated by structures in the brain stem. There are some reports showing casual relation between trigeminal and pontine lesions and migraine-like headache. A 46-year-old woman without familiar or personal history of primary headache developed a progressive headache. The headaches was throbbing, moderate-severe in intensity and left hemicranial and eventually associate photofobia and phonofobia, but she denied nausea or vomiting. Two weeks after the headache onset the patient complaint about left forehead and hemifacial numbness. Neurological and neuroophthalmological examination were normal including corneal reflex. Brain-MRI showed in T2-weighted images three high signal intensity lesions located in left anterolateral pontine, left-frontal white and frontal periventricular white matter (Fig. 1) suggestive of demyelinating plaque. Other studies were normal. Functional studies have shown activated areas in dorsal midbrain and pontine tegmentum in patients suffering migraine. These evidence probably only show participation and no generation of the symptoms.. Lesions in the midbrain close to the periaqueductal grey matter are associated with an increased prevalence of headache. This could explain according to the role of the PAG in the descending system of pain modulation. Nevertheless, the implication of pontine lesions and its laterality could provoke controversy about the pathophysiology of the migraine. This case provides further information for the involvement of the brain-stem and trigeminal nerve in the initiation of migraine and strengthens the debate over the laterality of the headache.

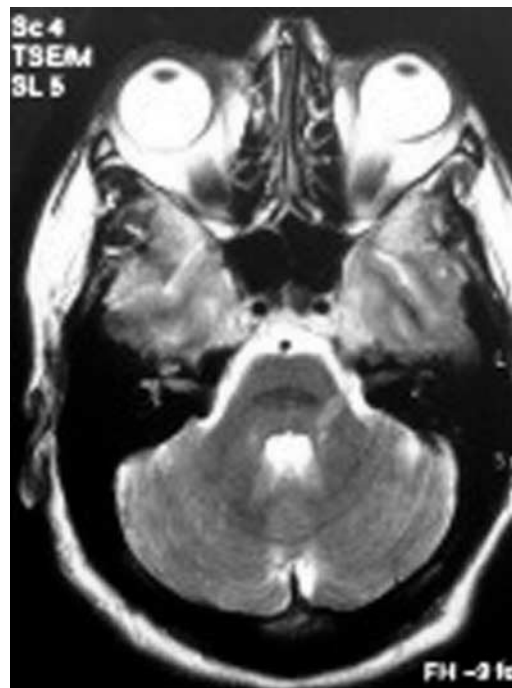


Fig. 1

SUCCESSFUL TREATMENT OF HYPNIC HEADACHE SYNDROME WITH FLUNARIZINE

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Hypnic headache (HH) is primary headache described by Raskin in 1988 and characterized by recurrent nocturnal episodes of headache that periodically wake the sleeping patient. The pathophysiology of HH is still unknown. It has been postulated that HH is a spectrum disorder overlapping with other primary headaches. We describe eight patients (4 women and 4 men) with hypnic headache according to the HIS-II classification and initially treated with flunarizine. Structural lesion has been ruled out performing brain MRI in all cases. The dose was variable between 2.5 to 10 mg. We report eight patients fulfilling the diagnostic criteria HIS-II for HH treated with flunarizine. In the literature different drugs have been used in HH treatment, lithium is the most frequently used and also showed the best average efficacy. However, flunarizine, caffeine and indomethacin could obtain similar ratios, and they have a better adverse effect profile. In our opinion flunarizine is a very good alternative in the prophylactic treatment of HH. The efficacy of flunarizine was moderate only in one of our patients. According to our patients' evolution we think that flunarizine is a good therapeutic option for HH, and the low doses (2.5 mg night) could be enough.

HEADACHE AND RECURRENT ABDOMINAL PAIN IN CHILDREN AND ADOLESCENTS: A CONTROLLED STUDY BY CHILDREN BEHAVIOR CHECKLIST (CBCL)

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Introduction Recurrent Abdominal Pain (RAP) and primary headache are the most common disorders that occur during early years of life. Two disorders show similarities on different fields: high familial recurrence and epidemiology, psychological trigger factors, limiting of daily activities and so on. Very few studies have been carried out comparing directly the two disorders. Our aim is analyzing the psychological profile of RAP and headache patients.

Material and method The Children Behavior Checklist 4–18 (CBCL) (parent version) had been administered to the mothers of 70 Headache patients (m.a.12,4), 70 RAP patients (m.a. 9) and 70 controls (m.a. 11,7). Headache patients (24 MO, 7 MA, 16 ETTH and 13 CTTH) were enrolled from the Child and Adolescent Headache Center of University of Rome "La Sapienza"; RAP sample (38 Functional Abdominal Pain and 32 Irritable Bowel Syndrome (IBS)) was recruited from Department of Pediatric Gastroenterology of the University of Rome "La Sapienza". The control group sample had been recruited from different schools in Rome. Headache diagnoses were made according to ICHD-II criteria (2004); RAP diagnoses fulfil Rome II criteria. ANOVA was used to compare CBCL scales and subscales of the three groups.

Results Both headache and RAP samples showed a similar trend vs control in Internalizing Scale ($p=0.001$ and $p=0.004$, respectively) and Somatic Complaints Subscale ($p=0.000$); moreover, we found a significant difference in Internalizing Scale for TTH and IBS, and in Somatic Complaints for all sub-samples. No significant differences were found in Externalizing Scale. MA patients had significantly higher scores in Attention Problems Subscale.

Discussions There is a very similar trend in DAR and headache patients for the association with Internalizing Disorders; both groups showed a similar psychopathological liability.

Conclusions The psychological profile of children with headache and RAP shows similarities needing debate for the implication for therapy and underlying mechanisms.

RECURRENT CAROTYDINIA WITH RESPONSE TO FLUNARIZINE

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The term carotidynia was first used by Fay in 1927 when he called attention to the presence of tenderness to pressure in the neck in patients with atypical facial neuralgia. Since the description there has been postulated several pathogenetic hypotheses. We present two cases of recurrent carotidynia with response to flunarizine. CASE-1: A 29-years old man consults because a history of a recurrent (four to five episodes per month) intense lateral neck pain which has appear 7 years earlier. The pain was intense and increase with neck palpation. He also complains of phonophobia, photophobia and nausea during the episodes, but there were not definitive previous history of migraine. There was no nasal congestion, carotid bruit, lacrimation, or Horner's sign. The neurological and general examinations were absolutely normal. Non-contrast brain CT and brain and neck MR were normal. Simplex lateral cranium and neck RX didn't show any calcification. We put the patient on flunarizine 2.5 mg per day with an asymptomatic 6 month period. CASE-2: A 52-years old woman complaint of a recurrent laterocervical pain that increases with the palpation of sternocleidomastoideus area. She suffer about 3–6 pain crisis per month. She did not complain of phonophobia, photophobia, aura, nausea or vomiting. There were no trigger points or manoeuvres. Cranial and neck MRI was normal. She didn't answer to naproxen or ibuprofen. We put the patient on flunarizine 2.5 mg per day with a remarkable clinical improvement. Carotidynia is not an entity but a syndrome encompassing many varieties of pain in the carotid region. Some types of recurrent carotidynia should be considered as a "topographic-pain distribution" of a migraine-like headache. Flunarizine could be a therapeutic option in these patients.

SUBCUTANEOUS HISTAMINE VERSUS TOPIRAMATE IN MIGRAINE PROPHYLAXIS: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND STUDY

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Background Histamine has a selective affinity for H3 receptors and it may specifically inhibit the neurogenic edema response involved in migraine pathophysiology, topiramate is an effective migraine preventive therapy in adults.

Objective To evaluate the therapeutic potential of the subcutaneous administration of histamine in migraine prophylaxis, compared to topiramate by undertaking a clinical trial.

Methods Ninety patients (90) with migraine with or without aura were selected under criteria established by the International Headache Society and enrolled in a 12-week double-blind controlled clinical trial to evaluate the efficacy of subcutaneous administration of histamine (1 to 10 ng twice a week) $n=45$ compared to oral administration of topiramate (100 mg daily dose) $n=45$. The variables studied were: headache intensity, frequency, duration, MIDAS and analgesic intake. A Friedman Repeated Measures ANOVA on Ranks Test was used to evaluate the statistical significance of differences between basal values and values found.

Results The data collected during the 4th, 8th and 12th week of treatment revealed that histamine caused a significantly ($p < 0.01$) greater reduction in intensity and duration of migraine attacks as well as a reduction in analgesic intake. No difference was detected in the frequency of attacks and MIDAS. Histamine was well tolerated. Four patients treated with topiramate experienced adverse events.

Conclusions The present study provides evidence of the superior efficacy of histamine applied subcutaneously in migraine prophylaxis when compared to topiramate. Histamine applied subcutaneously may represent a novel and effective therapeutic alternative in resistant migraine patients.

RELATED FACTORS OF INDUCING INTRACRANIAL ANEURYSMS TO RUPTURE

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Objective To analyze the related factors of affecting intracranial aneurysms to rupture.

Methods Eighty patients with unruptured intracranial aneurysm in this study were divided into two groups. 26 patients without subarachnoid hemorrhage (Group I) had not been interfered by operation, while 36 patients operated for hemorrhage or aneurysms with syndromes were in Group II. Eighty patients were followed-up by letters and telephone from March to September, 2002.

Results Among 53 patients followed up, a ratio of male to female were 13:13 in Group I. Presently, their age ranged from 8.17 to 76.17 years with a mean age of 46.06. The mean period of follow-up was 4.02 persons year since discharging. Twenty-seven followed-up cases were in Group II with 7 males and 20 females. Their present age ranged from 14.83 to 73.25 years with a mean age of 51.74. The mean period of follow-up was 6.61 persons year since discharging. Five patients of Group I died of the rupture of aneurysms 1.22 years after discharging on the average. The annual rupture rate was 4.79 per 100 persons. A vertebral aneurysm enlarged from 27 to 34 mm in one patient of group I in 2.25 years after discharging. The annual rate of aneurysm enlarging was 1.30 per 100 persons year. None of Group II died of the rupture of aneurysms or cerebral hemorrhage in other sites. A new basilar aneurysm developed in one patient of group II in 2.42 years after discharging. The annual rate of aneurysm developing was 0.56 per 100 persons year.

Conclusions The factors that have effect on the rupture of intracranial aneurysms include age, gender, symptoms of patients, sizes and locations of aneurysms.

PRODROME, AURA, POSTDROME AND THE MIGRAINE ATTACK: HOW ARE THEY RELATED?

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This study probes the relationship of prodrome, aura, and postdrome (PAP) to one another and to the acute migraine attack. 1025 ICHD-2 (1.1–1.2 and 1.5.1) patients were evaluated retrospectively using a detailed database. The presence and characteristics of prodrome, aura, and postdrome as well as migraine duration in years and migraine family history were recorded. Headache triggers, characteristics, associated symptoms, acute and chronic disability, and sleep habits were graded (0–3). 85.6% of the migraineurs were females, mean age was 38.2 (SD 12.2), mean lifetime duration of headache was 14.9 years, and mean headache frequency 12.7 headaches per month. Prodrome occurred in 35.9%, aura in 35.6%, and postdrome in 69.6%. All three occurred in 13.0% of patients; none in 17.5%; prodrome alone in 5.7%; aura alone in 4.8%; postdrome alone in 26.5%; prodrome and aura in 3.1%; prodrome and postdrome in 14.4%; aura and postdrome in 14.9%. Patients with all 3 of PAP com-

pared to patients having none of PAP had significantly ($p < 0.05$ to < 0.001) more triggers as a whole and individual triggers, more of all associated features of migraine, more head pain with movement, more acute and chronic disability, worse sleep, and more family history of migraine. Few differences were seen between each of prodrome, aura, and postdrome occurring alone. Unlike aura or prodrome, postdrome alone or any combination with postdrome (postdrome with prodrome, postdrome with aura) showed greater intensity of associated symptoms and headache features than in patients with no component of PAP. The postdrome with prodrome combination showed higher grades of triggers compared to none of PAP. Conclusion: Patients with all components of PAP have the most intense expression of the acute attack. Few differences are seen between each of PAP alone. Patients with postdrome appear to be unique, having many similarities to patients with all of PAP.

ACUTE SUMATRIPTAN REDUCES HEAD PAIN CONCURRENTLY WITH BRAIN SEROTONIN SYNTHESIS DURING SPONTANEOUS MIGRAINE ATTACKS AS MEASURED BY POSITRON EMISSION TOMOGRAPHY (PET)

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Background and aims Migraine is a highly disabling brain disorder. Triptans efficacy in migraine has been ascribed to cerebrovascular 5-HT_{1B} and/or 5-HT_{1D/1F} receptors on trigeminovascular afferents. However, triptans access brain parenchyma and central 5-HT receptors. We thus investigated if brain 5-HT synthesis was altered by sumatriptan in patients with migraine headache.

Methods Six patients (5 female; 1 male, 39.3±5.4 years; migraine without aura- IHS diagnostic criteria) had three scans: Scan-1: within 6 hrs of migraine onset; scan-2 fifteen min after sumatriptan injection (Imitrex, 6 mg, s.c.); scan-3: migraine-free within one month. Head pain was rated at arrival, before scan-1, and every 15 min after sumatriptan injection. Seventy minutes dynamic PET scans (about 15 mCi of α -MTrp) were taken with venous blood sampling. Images of the brain trapping constant (K^*) were colocalized with individual MRI in 3-D. Twenty-two regions of interest were selected including periaqueductal gray, limbic, frontal, parietal, visual and sensorimotor cortices. Two-way RMANOVA (Fisher LSD post-hoc) correction; $p < 0.05$ was taken as significant.

Results Plasma tryptophan levels were similar for all scans. The mean (\pm SEM) values of K^* were 5.96±0.64 (scan-1), 4.07±0.39 (scan-2) and 5.15±0.33 (scan-3) μ L/g/min. SCAN*REGION interaction was significant. 5-HT synthesis in scan-2 was significantly lower than that of scan-1; and scan-3 showed significantly lower synthesis as compared to scan-1; while that in scan-2 was lower than scan-3. The pain (1–5 scale) was 2.6±0.4 (scan-1), 1.0±1.2 (scan-2), and 0 (scan-3) and differences were significant. A significant linear relationship was found between 5-HT synthesis and pain severity in scan-1.

Conclusions (1) 5-HT synthesis is greater during attacks than in between attacks, (2) sumatriptan lowers synthesis below that in migraine-free conditions. These data indicate an increased serotonergic tone at the time of a migraine attack, negatively modulated by sumatriptan. Supported by a research grant from GlaxoSmithKline.

FAMILIAL HEMIPLEGIC MIGRAINE TYPE2, TOWARDS THE ANIMAL MODEL

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Familial hemiplegic migraine (FHM) is a rare and severe form of migraine with aura. It affects about 1/10,000 to 1/50,000 individu-

als and is transmitted as an autosomal dominant trait. This disorder is usually associated with hemiparesis and can be accompanied with clinical features ranging from ataxia to epileptic seizures. Familial Hemiplegic Migraine type 2 is due to mutations of the ATP1A2 gene encoding the $\alpha 2$ subunit of a Na⁺,K⁺ pump. Cellular models suggest a loss-of-function effect for FHM2 mutations. This suggests a decrease of the resting potential, an increased probability of neuronal depolarization and hyperexcitability through a rise of [K⁺]_e facilitating cortical spreading depression (CSD); and a parallel increase of [Na⁺]_i and [Ca²⁺]_i and finally neurotransmitter release. These effects resemble those caused by the Ca²⁺ channel mutations responsible for FHM1 (CACNA1A). In order to elucidate the effect of ATP1A2 mutations, we are generating two mouse models to dissect the pathogenetic role of the FHM2 mutations: an Atp1a2 knock-in mouse carrying the FHM2 W887R mutation and an Atp1a2 conditional knock-out mouse. The latter is being generated by introducing two loxP sequences in a targeting construct. Recombination is ensured by crossing homozygous and/or heterozygous Atp1a2 loxP mice with transgenic mice expressing the Cre recombinase driven by different tissue-specific promoters. The knock-in mouse model will be central to explore the role of the ATP1A2 mutation in the pathological mechanisms underlying the migraine aura. The knock-out conditional mouse will allow investigating the consequence of the absence of the $\alpha 2$ Na⁺/K⁺ ATPase in different neuronal cell types and the relative effects on the pathogenesis of this form of migraine.

THE NEUROIMMUNOLOGICAL APPROACH TO THE PATHOGENESIS OF THE TENSION TYPE HEADACHE

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Background The immunologic studies that investigate pathogenesis of tension type headache are going on. Although the studies about interleukines, TNF- α , IgG, complemans and NO were reported, the parameters like MIP-1 α , RANTES, eotaxin and endotelin-1 (ET-1) haven't been studied yet.

Objectives The aim of our study was investigated the role of TNF- α , IL-6, NO and MIP-1 α , RANTES, eotaxin and ET-1 at the pathogenesis of tension type headache and compared these parameters with migraine patients.

Material and methods The level of these parameters were measured during headache period and headache free period at 72 patients with tension type headache (32 of them episodic and 40 of them chronic type), 58 patients with migraine (30 of them with aura and 28 of them without aura) and 30 healthy patients.

Results It was founded that TNF- α , IL-6, NO, MIP-1 α , RANTES, eotaxin and ET-1 levels were increased at the patients with tension type headache and migraine during the headache period when was compared with control group and the patients in headache free period.

Conclusions These results can be thought that they are similarity in neuroimmunologic reactions between tension type and and MIP-1 α , RANTES, eotaxin and ET-1 could be have a role in pathogenesis of tension type headache.

CHRONIC DAILY HEADACHE (CDH): RISK FACTORS FOR TRANSFORMATION FROM EPISODIC TO CHRONIC HEADACHE

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Background and aims The pathogenesis of CDH, a group of daily or nearly daily headaches, is unknown. The aim of our study was to identify risk factors underling the evolution of episodic headaches into CDH.

Methods All patients visited at our tertiary referral centre in a period of 6 months were screened. Patients with CDH were assessed using a semistructured interview. The first consecutive 54 patients were evaluated by mean of Mini International Neuropsychiatric Interview.

Results Of the 546 patients visited, 107 patients (19.6%) had CDH. 88 patients ended the study: 71 female (mean age 50 \pm 14 years) and 17 male (mean age 47 \pm 14 years). 67 patients (76%) had migraine without aura before developing CDH, 13 patients (14%) had episodic tension-type headache and 6 patients had migraine with aura. 2 patients (2.2%) had CDH at onset. According to ICHD-II classification, 42 patients (47.7%) had probable chronic migraine (CM) with probable medication-overuse headache (MOH), 26 (29.5%) had probable chronic tension-type headache (CTTH) with probable MOH, 4 (4.5%) had CM and 16 (18.2%) had CTTH. Mean pre-CDH frequency was 4.7 days/month. 51 patients (58%) had "low" headache frequency, 26 (29.6%) "intermediate", 5 (5.7%) "critical" headache frequency. 46 patients (52%) reported a life event correlated to the transformation from episodic to CDH. The following sleep disturbances were reported: insomnia 58 (66%), daytime sleepiness 32 (36%), snoring and/or sleep apnea 44 (50%), parasomnia 61 (70%). 18 patients (20%) reported familiarity for substance's abuse and 40 (46%) familiarity for psychiatric disorders. Psychiatric comorbidity was found in 29 patients (54%). Familiarity for substance's abuse and for psychiatric disorders was higher in patients with psychiatric diagnosis.

Conclusions Our data showed that stressful events, medication overuse, sleep disturbances, familiarity for psychiatric disturbances and substances abuse play an important role in the transformation of episodic headache into CDH.

MIGRAINE AND ENVIRONMENT IN GROWING UP AGE

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Introduction The incidence of migraine (M) in growing up age has recently increased due to the worsening of children's environment: i.e. both parents working, high number of separations or divorces, etc. However, sudden changes in weather conditions and pollution may also affect M. In this study we have tried to estimate how much the above factors could have influenced a young migraine suffering population from 1995 to 2005.

Methods 120 patients, 20 for each year, have been evaluated (62f.58m, MwoA 109 MwA 11, age range 5-17 years). For these patients the headache triggering factors have been reevaluated (Table 1).

Table 1

	Triggering factors, %						
	1995	1997	1999	2001	2003	2005	Tot
Emotional stress	90	90	80	90	100	70	83
Physical stress	50	30	30	40	60	30	40
Environment stress	70	80	90	50	90	60	73
Lights	50	40	60	30	70	40	48
Smell	40	20	40	60	30	40	33
Smoke	20	40	20	40	10	20	25
Food	20	20	20	10	00	10	15
Weather variations	40	50	60	60	70	80	60
Solar exposure	10	20	40	60	90	70	48

Results Stress situations appear to be the triggering causes of headache, however they do not seem to change in the course of time, whilst sensitivity to weather changes is on the increase, in particular solar exposure. This gives us an indication that climatic modifications may affect migraine in a considerable manner. Of course, these are just preliminary data, but if they are supported by other works and indications of precise climatic changes, they may provide a more accurate picture for greater attention to these variables.

Conclusions As Migraine patient is sensitive to variations, recent climatic changes and different solar activity may be an important cause of migraine increase.

CONSULTATIONS FOR MIGRAINE WITH AURA, MIGRAINE WITHOUT AURA AND CHRONIC DAILY HEADACHE: A MULTI-NATIONAL SURVEY

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Background and aims Little is known about consultation differences between countries. This study compared consultation rates of headache sufferers in 4 countries (UK, Netherlands, France and Belgium).

Methods A postal survey was carried out with members of Headache Patient Societies, aged between 18 and 65 years, suffering from IHS migraine without aura (MO), IHS migraine with aura (MA) or chronic daily headache (CDH). Data was analysed by logistic regression.

Results The sample included 1313 headache sufferers. Significant differences were found for the general practitioner; neurologist; the nurse; pharmacist; the psychologist; acupuncturist; chiropractor, homeopath and osteopath.

Conclusions The findings show that consultation rates vary according to country and types of headache. The difference between migraine and CDH may be explained by a difference in treatment need by CDH sufferers. The country differences may be explained through differences in health care systems, culture or headache societies. Further studies are needed to establish which explanations account predominantly for the country differences.

TEMPORAL PROFILE OF VASCULAR CHANGES INDUCED BY SYSTEMIC NITROGLYCERIN IN THE MENINGEAL AND CORTICAL DISTRICTS

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Nitric oxide (NO) has been indicated as a key molecule in the pathogenesis of vascular headaches. Migraine headache is essentially due to sensitization and activation of meningeal afferents and pain-sensitive intracranial structures. Nitroglycerin, a NO donor, provokes headaches in migraine sufferers but not in normal subjects. Clinical studies indicated that this NO donor causes regional changes in cerebral blood flow (CBF), similar to those reported in spontaneous migraine. In this study we have examined the effects of Nitroglycerin (10 mg/Kg i.p.) on the CBF at the cortical and meningeal levels, in anesthetized rats. Regional CBF was monitored continuously using Laser Doppler flowmetry before and after nitroglycerin/vehicle administration for a period of 150 minutes. Additionally, we evaluated the effect on CBF of L-NAME – a nonspecific NO synthase inhibitor. Nitroglycerin caused a significant increase in cerebral blood flow with a dual temporal pattern in the two districts under

evaluation: cortical blood flow significantly increased 90 minutes after the NO donor administration, while the blood flow increase at the meningeal level was observed at later times (+120 and 150 minutes). Pre-treatment with L-NAME (50 mg/Kg i.p.) significantly inhibited nitroglycerin-induced increases in blood flow in both compartments. This study shows that nitroglycerin induces changes in the meninges and in the cortex with a differentiated temporal profile. In both compartments, however, the effect is mediated by NO synthesis.

BILATERAL CLUSTER HEADACHE: CLINICAL FEATURES AND SUGGESTIONS FOR PATHOPHYSIOLOGY

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Cluster Headache (CH) is characterized by pain attacks recurring on the same side. In few cases the pain spontaneously switch side. In episodic CH, a side switch may occur both during separate bouts (11%–18%) or in the same active period (5%–14%). Aim of this study was to give a full description of bilateral CH patients and to compare them to a group of CH patients with no side shift. A group of 50 patients suffering from bilateral CH (42M-8F; mean age 39±12 (17–70); 39 episodic, 11 chronic, mean illness duration 13.6 years) was studied. They were compared to an age- and sex-matched group of 50 unilateral (never experienced side shift) CH patients (43M, 7F; mean age 38 (17–72); 43 episodic and 7 chronic CH; mean illness duration 12.3 years). History and headache characteristics were collected by means of a detailed interview. In bilateral CH patients, clinical features on one side were compared with those on the opposite side; bilateral CH patients were then compared to the unilateral CH patients' group. Both attacks and cluster period duration were shorter in bilateral vs unilateral CH (75.5 min vs 82.1 and 41.7 dys vs 75.9 respectively). No significant difference was found by comparing occurrence of autonomic features in bilateral vs unilateral CH even if bilateral CH showed a trend for a greater frequency of all autonomic features but not for conjunctival injection. Three pts (7.7%) presented side-shift within the same bout, while the other 36 on different bout. In our bilateral CH patients, an elevated concordance for the majority of headache characteristics and associated autonomic phenomena was observed by comparing attacks on opposite side. These data suggest that bilateral CH has an unique origin, probably in the CNS. Complex mechanisms are at work in inducing side shift in CH.

SOCIODEMOGRAPHIC FEATURES OF 188 PRIMARY HEADACHE PATIENTS IN A TURKISH HEADACHE POLI-CLINIC

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Background and aims Headache is one of the most common complaints in general population. International Headache Society's (IHS) classification has been used in epidemiologic studies since its first publication in 1988. New criteria have been published in 2004 by the same organization. This study's aim is to collect and compare sociodemographic data from primary headache patients by 2004 IHS criteria who were referred to the Headache Polyclinic of the Neurology Department of GMMA Haydarpaşa Training Hospital.

Method This is a retrospective survey of patients records. One hundred eighty-eight patients were screened in face-to-face interviews, and data collected using a standard questionnaire for headache during a period of three years. All patients were divided into 3 categories; migraine, tension headache and other primary headache disorders including cluster headache.

Results • Most of the patients in our Headache Outpatient Polyclinic were women (79.3%) and approximately 30 percent of them were between the ages 30 and 40. • Migraine without aura (31.3%), frequent episodic tension type headache (18.0%) and probable migraine (14.3%) were the most frequent diagnoses according to the IHS 2004 headache criteria. • When the education levels and occupational features of the patients with a diagnosis of migraine and tension type headache were evaluated, it was found that most of the patients were housewives; who were unemployed (61.5%), uneducated or had lower educational levels. However, patients in the cluster headache group were in working position (66.6%) and majority of them being of a higher educational level. • Examining the marital status, it was found that majority (75.8%) were married.

Conclusions Migraine is a common cause of consultations to the specific headache clinics. The results from this study show the profile of patients who attended a specific headache polyclinic in Turkey from 2002 to 2005.

MEDICATION OVERUSE HEADACHE – THE EFFECT OF A TWO MONTHS DRUG FREE PERIOD

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Background Based on the assumption that medication overuse by itself transforms and aggravates primary headache, ICHD-II introduced specific diagnostic criteria for medication-overuse headache. Data are needed to elucidate this assumption.

Objective To describe the emerging profile of headache frequency following a two months drug free period in patients with medication overuse.

Methods All patients treated and discharged from Danish Headache Center in 2002 and 2003 had prospectively filled out a diagnostic headache diary on a daily basis. For patients with probable medication-overuse headache (pMOH) we determined headache frequencies before and after medication withdrawal from these prospective recordings.

Results Among 1326 patients, 337 had pMOH. Eligible were 216 who stayed medication free for two months. Overall, 45% of the patients improved, 48% had no change and 7% had more headaches. Median age was 48 years, male/female ratio 1:2.7. The relative reduction in headache frequency varied considerably with a 67% median reduction in migraine, 0% in tension-type headache (TTH) and 37% in patients with both migraine and TTH (MT). Comparing the diagnostic groups, the relative reduction in frequency differed significantly between migraine and TTH ($p < 0.001$) and between MT and TTH ($p < 0.01$). Triptan/ergot-overusers improved the most ($p < 0.0001$). The difference between MT and TTH remained significant controlling for triptan/ergot-overuse ($p < 0.05$).

Conclusions These data demonstrate the benefit of withdrawal in already established medication overuse. They also strongly support the existence of medication-overuse headache as a clinical entity.

DEPRESSION AND DISABILITY IN HEADACHE ATTRIBUTED TO DISORDERS OF THE NECK

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Background Previously we found that disability is an important determinant of the severity of depression symptoms in primary headaches but not in low back pain [1]. In the present study we compared the depression-disability relationship in patients with

headache attributed to disorders of the neck (“cervicogenic headache”) to those with low back pain.

Patients and methods During a 2-year period 298 consecutive patients with the clinical diagnosis of cervicogenic headache (n=182) or low back pain (n=116) filled in a questionnaire on pain characteristics, the MIDAS questionnaire reflecting the number of days with lost or decreased work, household and social activities, and the Beck Depression Inventory (BDI). Non-parametric tests and multiple general regression were used for statistical analysis.

Results Pain intensity and frequency and the Beck score did not differ between the two groups, but the MIDAS score was significantly higher in the low back pain than in the headache group ($p = 0.017$). In multivariate analyses, age and gender had no independent effect on depression and disability. Disability was related to pain frequency and pain intensity in low back pain, and to pain frequency and the severity of depressive symptoms in cervicogenic headache. On the other hand, the severity of depression was associated with pain intensity and severity in both groups.

Conclusions Disability, but not the severity of depressive symptoms is affected by the location of pain caused by the disease of the spine. Disability and depressive symptoms are interrelated in cervicogenic headache but not in low back pain. Determinants of depression severity in cervicogenic headache are a combination of those found to be significant in primary headaches and in low back pain.

Reference

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SUBCUTANEOUS SUMATRIPTAN 3MG+RECTAL INDOMETHACIN 50MG FOR SEVERE REFRACTORY MIGRAINE ATTACKS: AN OPEN PILOT STUDY

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Background and objectives Severe migraine attacks may be refractory to oral drugs. Some patients obtain relief with injectable or rectal preparations even when oral preparations failed. The aim of this study was to evaluate the efficacy and tolerability of the combination 3 mg subcutaneous sumatriptan and 50 mg rectal indomethacin for severe refractory migraine attacks.

Patients and methods Twenty consecutive patients with migraine were instructed to treat two severe consecutive attacks with different combinations of an oral triptan plus an anti-inflammatory. At 4 hours, those not pain free had to use 3 mg-sumatriptan (subcutaneous) plus 50 mg-indomethacin (rectal). Information on the severity of the attack at the time of intake and after 1 and 2 hours was collected. Adverse events were also evaluated.

Results Fifteen patients (12 women, 3 men, ages 25 to 52, mean 38,7) completed the study. Three patients didn't present attacks refractory to their oral medications. One patient was lost to follow up and 1 patient broke the protocol. The oral medications used before the study drugs were rizatriptan plus rofecoxib (7 patients), sumatriptan plus naproxen sodium (5 patients) and sumatriptan plus lysine clonixinate (3 patients). None presented vomiting after taking the oral treatments. A total of 26 refractory attacks were treated (4 patients had 1 attack treated with the study medications). At 2 hours, nine patients (17 attacks, 65.4%) were pain free. The remaining 9 attacks in 6 patients were still moderate or severe after 2 hours. Adverse events were reported by 6 patients and included dizziness, diarrhea, chest pressure and heartburn.

Conclusions The combination of subcutaneous sumatriptan and rectal indomethacin seems to be effective and well tolerated for the migraine attack already severe and refractory to oral preparations. Further controlled studies are necessary to confirm these observations.

PREVALENCE OF HEADACHE IN A JAIL MASCULINE POPULATION OF BRAZIL

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Background and objective A Jail in Brazil is characterized by over population and humiliating conditions. Psychological disturbances and worsening of pre-existing conditions may develop. The aim of this study was to evaluate the prevalence of headache in the inmate's male population of a Brazilian Jail.

Methods Barbacena City Jail has 88 male inmates. Seventy one were studied through a questionnaire to identify the presence of headache, its frequency, circumstances of onset and clinical characteristics. The questionnaires were conducted by an inmate graduated as doctor (GP) and considered psychiatrically healthy, who was convicted for the murder of his ex-wife. Seventeen patients were excluded since they were extremely dangerous not allowing the proximity of other inmates.

Results Among the 71 subjects, the prevalence of headache was 49.3% (35 inmates, ages 19–58 years, mean 32.6). Twenty four inmates (33.8% of the whole population studied and 68.6% of those suffering from headache), aged between 23 and 46, claimed to have started suffering from headache after detention. Those presenting daily or near-daily headache accounted for 37.1% (13 inmates) of the sample. Headache with at least 4 characteristics of migraine (severe, pulsating, with nausea and photophobia) had a prevalence of 8.6% (3 inmates) and headache with moderate severity, pressure-type and diffuse location accounted for 91.4% (32 inmates).

Comments The prevalence of daily or near-daily headache was higher than in previous studies with populations other than clinic-based. The psychological pressure may have a role. In addition, nearly a third of the studied population (approx. two thirds of those with headache) claimed to have started suffering after detention, suggesting that jail conditions may have worked as a trigger mechanism. Prevalence of headache with features suggesting migraine and TTH is coincident with previous epidemiological studies. Further studies are necessary to confirm these observations.

PREVALENCE OF FIBROMYALGIA AND MIOFASCIAL PAIN SYNDROME IN PATIENTS WITH TRANSFORMED MIGRAINE. COMPARATIVE STUDY WITH CONTROLS AND PATIENTS WITHOUT MIGRAINE

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Background Fibromyalgia (FM), Miofascial Pain Syndrome (MPS) and Transformed Migraine (TM) are common chronic pain disorders. Previous studies found a high prevalence of FM in TM patients, suggesting that they could be co-morbid disorders. Chronic regional pain due to miofascial origin is also highly prevalent affecting 20% of the general population.

Objectives To evaluate the prevalence of FM and MPS in patients with Migraine Transformed when compared with controls and subjects without migraine.

Patients and methods We enrolled 30 consecutive patients (25 women, 5 men) with TM seen at a tertiary center. In addition, 30 subjects without migraine and 30 controls matching age and sex were also enrolled. MT was diagnosed according to the Silberstein et al criteria (1996). FM was diagnosed according to the American College of Rheumatology diagnostic criteria (1990). MPS was diagnosed according to the Andrew Fisher criteria (2003). To select patients without migraine we applied Lipton et al ID migraine test (1997).

Results The 90 patients had between 18 and 74 years (mean 33.1). FM was diagnosed in 20 (22.2%) of the subjects. Among these patients, 12 (40%) of the TM group, 2 patients (6.6%) of the group without migraine and 5 (16%) controls. MPS was diagnosed in 3 of the 90 patients (3.3%), 100% of these had TM. In patients with MPS, trigger points were encountered in medium gluteus, elevator of escapula and suboccipital muscles.

Conclusions We found a higher prevalence of FM in patients with TM (40%) when compared to patients without migraine (6.6%) and controls (16%) ($p < 0.0001$). Moreover, MPS was present only in patients with MT (NS). Further studies are necessary to clarify the relationship between TM, FM and MPS.

PROGRAM TO ASSESS HEADACHE TREATMENT STRATEGIES: BASELINE AND PRELIMINARY RESULTS FROM AN OBSERVATIONAL STUDY OF BOTULINUM TOXIN TYPE A PROPHYLACTIC HEADACHE TREATMENT

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Background and aims Results from several trials suggest that botulinum toxin type A (BoNTA; BOTOX®: Allergan Inc., Irvine, CA, USA) may be effective headache prophylaxis in some populations. The aim of this study was to assess the safety and effectiveness of BoNTA in usual clinical practice.

Methods This was an observational epidemiologic analysis of data prospectively collected from eligible BoNTA-treated patients in 10 Headache Treatment Centers including demographics; the ICHD headache diagnosis for which BoNTA was used; headache characteristics; previous and current headache treatment use and responses; assessment of response to BoNTA; MIDAS questionnaire; and report of adverse events. Patients maintained a daily headache diary and were evaluated at each routine follow up visit.

Results 703 patients were enrolled (mean age: 42.7 ± 13.36 ; range: 13 to 82 years; 78.5% female, 95.4% Caucasian). Approximately 2/3 (461/703) of patients met criteria for chronic migraine. The average headache-related disability and average headache severity were rated as moderate to severe by 79% and 95.4% of patients, respectively. Over 90% of patients (634/702) failed at least 1 prophylactic headache trial, and for 73.1% (513/702) of these patients, this was the most common reason for BoNTA use. Improvement of headache symptoms after BoNTA treatment was reported by 62.9% of patients (307/488) and 65.8% of physicians (321/488). After 3 months MIDAS total scores declined by a mean of 31.7 points from baseline (71.1); the number of headache days per 3 months declined by a mean of 20.3 days from baseline (58.1 days). Only 3/703 patients (0.4%) discontinued treatment due to adverse events.

Conclusions BoNTA was shown to be an effective and well tolerated prophylactic headache treatment in a severely disabled, treatment-refractory population of patients with chronic migraine.

CLINICAL RECOGNITION OF ALLODYNIA AS A PROGNOSTIC FACTOR IN MIGRAINE THERAPY

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Objective To describe the frequency and study the therapeutic implications of allodynia in migraine.

Background and methods Allodynia is not routinely evaluated during clinical interviews, even though many recent studies have pointed out its therapeutic implications. In this study we tried to

assess the frequency and clinical manifestations of allodynia in our clinic-based migraine population.

Results 60% of our migraine patients reported allodynia. 80% of the allodynic patients had cephalic allodynia, 23% had both cephalic and extracephalic allodynia and 8.7% reported pure extracephalic allodynia. In terms of therapeutic assessment, triptan therapy was effective in 65.2% of the migraineurs but only in 53.1% of allodynic patients.

Conclusions Allodynia is a very frequent manifestation of migraine, indicating central sensitization within the migraine process. The clinical recognition of allodynia is important, since its presence seems to be a prognostic factor of the outcome of certain therapeutic approaches.

PREVALENCE AND CHARACTERISTICS OF HEADACHE IN A HEALTH CLUB POPULATION

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Background Chronic headache promotes disability. Regular physical exercise may reduce headache frequency.

Objectives The aim of this study is to evaluate the prevalence and characteristics of headache in a health club population.

Methods One hundred consecutive attendees of a health club were interviewed. They all had to be regular attendees for at least 12 months practicing aerobic exercises no less than 3 times a week. A detailed headache questionnaire was used with all subjects who answered Yes to the question: Did you have a headache during the last 12 months? For those who answered No, another question arguing about the occurrence of a headache attack in special circumstances was used.

Results Fifty seven men and 43 women (ages 29.7±9 years) were included. Eighty subjects (40 women and 40 men), answered yes to the first question. The headache was present for longer than 3 years in 25% of the subjects. In 63% of the sufferers, the headache was pulsatile and the fronto-temporal location was the most frequent affecting 42% of the subjects. Moderate or severe headache was referred by 54% and photophobia frequently occurred in 59% of the sufferers. Resting was the best attitudes for 70% while less than one attack each 10 days was informed by 73% of the sample. MIDAS was lower than 4 days in 83% of the subjects.

Comments Although retrospective and based on recall, this study demonstrated that a regular exercise practitioner has a high prevalence of infrequent headache. However, the most presented clinical characteristics suggest migraine. It is uncertain whether the regular practice of physical exercise have a role in reducing the headache frequency and impact on quality of life or those suffering less are the ones who practice exercise. Further studies are necessary to clarify these observations.

IMPACT OF WEIGHT INCREASE ON HEADACHE PREVALENCE. THE HEAD-HUNT STUDY

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Background and aims Previous evidence suggest a possible association between headache and obesity. The aim of the present study was to evaluate the association between headache and weight increase among individuals not likely to suffer from headache at baseline.

Methods Two consecutive public health surveys within the county of Nord-Trøndelag, Norway, were conducted in 1984–86 (HUNT-1) and 1995–97 (HUNT-2). The impact of weight gain was assessed among 22,685 adults not using analgesics, therefore likely to have

relatively little headache at baseline (HUNT 1) and who responded to headache questions at follow-up eleven years later (HUNT 2).

Results Using multiple logistic regression, there was an increased prevalence RR for headache (RR=1.4, 95% CI:1.3–1.6), among those with a weight gain of >10 kg compared to those without. This was also found for non-migrainous headache (RR=1.4, 95% CI:1.2–1.6), for migraine (RR=1.3, 95% CI:1.1–1.6) and for chronic headache (RR=2.0, 95% CI:1.2–3.3). There was a significant linear trend between prevalence of headache and increased weight gain, most pronounced for non-migrainous headache ($p<0.0001$).

Conclusions Weight gain is a risk factor for headache, especially for chronic headache.

HEADACHE IN SAUDI POPULATION

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Headache is a common neurological practice. Incidence and prevalence figures have varied considerably in different studies. There are little and incomplete data on headache in the Kingdom of Saudi Arabia. Previous studies have shown that tension headache is frequent. We conducted a clinical study in OPD neurology clinic over more than 200 cases of chronic/recurrent headache. The preliminary and most important results indicate a high frequency of psychogenic headache in the group of 'non migraine headache'. Other results will be available. It seem from this study that tension headache had been over estimated and psychogenic headache underestimated. Further more headache appeared as a main if not the only manifestation of a depressive illness with significant improvement on antidepressive medication.

COMBINED ORAL HORMONAL CONTRACEPTIVES POSSIBLE CAUSE OF PERSISTENT AURA WITHOUT INFARCTION

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Background Persistent aura without infarction (PAoI) symptoms are rare. Provocative factors and reliably effective treatment is not known.

Objective To describe the patient whose PAoI symptoms were prevented when she stopped to use combined oral hormonal contraceptives (COHC).

Methods Case report: A 32 year old woman with a history of Migraine with aura (MA) described as typical aura consisting of visual, sensory, speech symptoms and dizziness with gradual development duration, complete reversibility associated with a headache fulfilling Migraine without aura criteria. Attacks started at 12 years age, disappeared at 17 years age and again begun 1 year ago when the patient began to use COHS (Logest).

Results The patient reported persistent typical aura consisting of visual, sensory, speech symptoms and dizziness repeated every day during 12 days. This was a third similar attack during 1 year period when the MA attacks restarted again. Neurological examination, MRI and Transcranial Dopler sonography not revealed any pathological findings. The patient was treated with analgetics and Pentoxifylline 9 days until aura symptoms disappeared. The using of COHC was taken away. The MA attacks became very rare and there were no PAoI symptoms during the next 2 years.

Conclusions COHC may provoke not only worsening MA but be cause of PAoI.

DISABILITY DUE TO HEADACHE AS MEASURED USING WHODAS II, THE WORLD HEALTH ORGANISATION DISABILITY ASSESSMENT SCALE

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Background WHO identifies migraine among the world's top 20 causes of disability, with an impact that extends to the family and community.

Objective To measure disability due to different headache types in the multicultural population of Luxembourg using the WHODAS II scale and compare it to the reference population assessed by the WHO.

Methods A self administered questionnaire (BURMIG), including WHODAS II was used with headache sufferers. The disability lies between 0 (no disability) and 100 (maximum disability). A multiple logistic and a cumulative logistic models were used for statistical evaluation.

Results In our sample of 2117 headache sufferers (41±12 years, 77% female, 68% economic workers) 75% reported a headache frequency of 1–9 days/month, 61% were identified as having migraine (MIG) and 10% as having chronic daily headache (CDH, >15 d/month). Ninety-five % of our population were disabled, compared to only 50% in the WHO reference population. Further, the number of the 10% most severely disabled headache sufferers had a WHO-DAS score >40, compared to >15 in the reference population. The distribution of the overall health is not significantly different between non migrainous (NMIG) and MIG whereas NMIG and CDH ($p=0.0039$) are: CDH sufferers rate their overall health as worse than other headache sufferers (Bad overall health: NMIG=4%, MIG=6% and CDH=24%). NMIG and CDH sufferers seem to be equally emotionally affected ($p=0.86$) rather than MIG sufferers who are more numerous in the moderate, severe and extreme categories. For all other questions, NMIG seems to be less bothering than MIG and CDH ($p<0.05$).

Conclusions Headache, including NMIG, MIG and CDH, are certainly the main reason for intermediate disability in this studied population. CDH are shown to have the most bothering impact on the professional, social and private daily life.

FACTORS RELATED TO THE IMPACT OF DIFFERENT HEADACHE TYPES. THE LUXEMBOURG BURDEN OF MIGRAINE (BURMIG) STUDY

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Migraine, a common disabling neurobiological disorder is under-recognized, under-treated and commonly mismanaged. We investigated the impact of non migrainous headaches (NMIG), migraine (MIG) and chronic headaches (CH, >15 d/month) in Luxembourg.

Objective To present results on the key factors affecting the impact of NMIG, MIG and CH in a multicultural population.

Method BURMIG a validated questionnaire containing measures of headache, disability and quality of life, was administered following a national survey of headache prevalence.

Results Out of 3535 participants, 732 headache sufferers (41±12 years, 69% female, 64% economic workers) responded the BURMIG questionnaire. 78% had a frequency of 1–9 days/month. 46% were identified as having MIG, 7% CH. There were more women with MIG than with NMIG or CH ($p=0.02$). People with CH were older at onset of headache than people with NMIG and MIG ($p<0.001$). The mean number of missed days at work/school was larger ($p<0.0001$) in CH (7.8±18.4) than in NMIG (1.5±5.8) and MIG (0.4±2.0). 35% of CH had a major depressive disorder compared with 11% in MIG and 6% in NMIG ($p<0.001$). During 3 months, 44% CH had taken medications for at least 15 days but only in 2% in NMIG and 5% in

MIG ($p<0.001$). 29% CH had tried more than 7 different acute drugs compared to 2% in NMIG and 4% in MIG ($p<0.001$). Headaches had a negative impact on professional situation: 21% in the NMIG, 38% in the MIG and 56% in the CH groups ($p<0.001$) as on familial situation (NMIG=23%; MIG=53%; CH=63%; $p<0.001$) and on social life (NMIG=10%; MIG=24%; CH=40%; $p<0.001$).

Conclusions Headaches have a major impact on professional, social and private life. The impact is considerable in people having migraine and even more severe in chronic headache sufferers.

BOTULINUM TOXIN TYPE A PROPHYLAXIS OF CHRONIC DAILY HEADACHE USING A SIMPLIFIED SUBCUTANEOUS INJECTION TECHNIQUE

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Background and aims Botulinum toxin type A (BoNTA) seems to inhibit the release of neuropeptides/neurotransmitters (substance P, glutamate, CGRP, etc) sensitive neurons. Considering the trigemino-vascular origin of headaches, BoNTA subcutaneous injections at limited sites should be sufficient to produce a headache prophylaxis. The objectives of this study are (1) to determine the preventive efficacy and (2) to show the quickness, easiness, and tolerability of this BoNTA simplified injection technique in CDH prophylaxis.

Methods A total of 534 CDH patients were previously washed (prophylaxis medication and excessive analgesic use) and then treated with 100 U of BoNTA (BOTOX®) injected subcutaneously at three points per hemicranium (total 6 sites), at 3 month intervals minimum. Evaluations and/or pre and postinjection comparisons performed: (a) headache evolution time (chronicity); (b) monthly acute medication use, (c) MIDAS score, (d) BoNTA latency, (e) BoNTA duration of effect, (f) % subjective improvement after injection, and (g) injection sessions per patient.

Results Transformed migraine or rather "mixed headache" was predominant (50%). Subcutaneous BoNTA produced a statistically significant reduction ($p<0.001$) in frequency, intensity, headache duration, and mean total monthly acute medication at three months. Overall improvement was statistically significantly greater ($p<0.001$) in chronic migraine than in chronic tension type headaches. There were only 5 secondary effects and none was serious. Mean time needed for injections was 5–7 minutes. The only three patients without a response were presented a psicogenic component and needed psychiatrist evaluation. To date, no tachyphylaxis has been observed.

Conclusions This BoNTA subcutaneous simplified injection technique for CDH prophylaxis is much more comfortable, fast, safe and efficacious than the until now used intramuscular techniques (more than 30 injections). The excellent results indicate the immediate need for placebo-controlled studies using this technique.

MIGRANOUS STROKE. RESULTS OF A COLLABORATIVE PROSPECTIVE STUDY

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Introduction Migranous stroke (MS) is an infrequent complication of migraine patients. Actually, only the migraine with aura is admitted as cause of MS. The majority of studies on MS are retrospective and without clear information about the headache characteristics and the treatment of the stroke related attack.

Objective To know the clinical characteristics of migraine and the preventive or acute treatments that could be related with the appearance of MS.

Material and methods We are conducting a cooperative prospective study in a series of Spanish hospitals to include all the patients with MS. We applied the former IHS criteria for definitive diagnosis of MS, but we also include patients with migraine without aura that present a stroke following a migraine attack. All patients are studied with the same exhaustive protocol to exclude other causes of stroke.

Results We present the results of the first 34 patients recruited. The mean age was 35.9 years (21–60), distribution by sex was 29 women and 5 men, MRI was positive in 25 cases, 24 patients were affected by migraine with aura and 10 by migraine without aura, the attacks were moderate-severe in all patients with a mean duration of 16 hours (4–60). Only five patients were receiving preventive treatment and five were the patients who received vasoactive drugs in the stroke related attack.

Conclusions We find no relationship between the clinical characteristics of the attacks or the use of preventive or acute medication and the appearance of MS. It is necessary to define the role of migraine in the patients that present a stroke following an attack of migraine without aura. Some of the patients showed no ischemic lesion in MRI but focal signs persisting after a week; we agree with actual IHS criteria that these represent a different subgroup of patients

BLINK REFLEX IN MIGRANOUS PATIENTS

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Background and aims Migraine attack is known to be the result of functional brainstem anomaly and brainstem pathways involved in the blink reflex maybe activated in the premonitory phase of migraine attacks. Our aim was to study the possible changes of blink reflex (BR) latencies with standard techniques in migranous patients in treatment and non-treatment groups and to represent new evidences for the trigemino-vascular hypothesis of migraine.

Methods 30 patients (27 female, 3 male) ranged between 20–56 years and 20 control (15 female, 5 male) between 18–55 were included. Patients were diagnosed according to the clinical criteria of International Headache Society Classification. Br measures were made with four channels EMG device. Unilateral R1 and bilateral R2 blink reflex latencies were investigated with electrical stimulation of the supraorbital nerve from both sides in all patients. Statistical analysis was with t test and f anova test.

Results Patients had significantly higher short latencies for LR1(L) and higher long latencies for RR1(R), LR(L), LR2(L) and RR2(L) compared with the control group ($p < 0.05$). Long LR1 latencies were significantly longer in patients who had an attack at the time of investigations. Mean value of 12.44 in these patients and 10.91 in patients who had an attack at least 3 days and 10.59 in patients who had an attack longer than 3 days. Patients older than 40 years old had longer short latencies for RR2(L) with a mean value of 27.05 whereas patients under 40 years old had a mean value of 24.8. Similarly, patients older than 40 years old had significantly higher values for LR1 (L) ($p < 0.05$).

Conclusions BR seems to be reliable investigation for hypothesis of trigemino-vascular system which is the milestone of migraine pathogenesis and can be used in monitorization for migraine therapy in the future.

TWO MIGRAINE TALES

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Background he migraine with aura is an entity usual in the general population. The female preponderance is a general observation and represents more or less 4% of all primary migraines. The aura is a sign in some cases of migraine. According our observation should be different in a common pathway. Perhaps the emotional behavior of the people, the environmental and the age play a role in the particular features of a clinical picture. Like examples, we show two histories around the Middle Age and the magic think in kids.

Case material Our scientific works start in the Middle Age; in then the medicine received, the influence of the Greek culture in the Galeno was a very important reference and the roman medicine that follow the general rules marked for these precedent. In the Middle Age the Medicine was a dark period in then the sanitations across the suggestion, the magic environmental framework and some substances derivates of the plants were the therapeutic model in the ill people. Hildegard was a very interesting woman. She born in 1098 in Mayence and died in 1179 dc She lives in Disidodenberg convent and San Rupert monastery in she was an abides. His skills in the Medicine, Botanic, Music results in sanitations in then the angels and God were the invocation that currently used and was a very hard union between the auras and the way to describe his therapeutic method. Like the suggestion, the magic and the science were the tools that she develops in not only a Medicine as in his seven books, the descriptions of twenty-seven plants and a Gregorian chants in then she based her knowledge. The other history is Wonderland Alice Adventure a medical clinical picture in the the patients are the children's, and the features are based in the Carroll Lewis book. We describe two cases in this way and the common pathway between both histories is the magic environmental in one hand and the description and the magic thinking of the kids in the second hand.

Conclusions We show in an imaginary trip across the history two histories in then the aura should be an influence of the environmental in a case of Hildegard of Von Bingen and the magic think in kids in a case of the clinical picture called Alice Wonderland Adventures.

EXCITABILITY OF VISUAL AND MOTOR CORTEX IN MIGRAINE PATIENTS WITH AND WITHOUT AURA

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Introduction The pathophysiological mechanisms of migraine with (MA) and without aura (MO) are still unknown. Migraine aura is predominantly visual that is why the hyperexcitability of the occipital cortex has been the focus of investigations. The aim of this study was to assess the difference of visual cortex (VC) excitability in MA and MO patients. The perception of phosphenes induced by transcranial magnetic stimulation (TMS) applied over the VC was used as an index of cortical excitability.

Methods 42 migraine patients underwent TMS: 10 with MA (2 male and 8 female; 32 ± 6 y.o.) and 32 patients with MO (5 male and 27 female; 38 ± 8 y.o.). The migraine frequency and intensity were analyzed with patients headache diaries and 10-points VAS. The phosphenes threshold (PT) and m.abductor poll. brevis motor evoked potentials threshold (MEPT) were tested. The VC and motor cortex were activated by a single magnetic pulse through a 125-mm circular MagLite coil (Medtronic, Danmark).

Results In MA/MO patients: migraine attacks per month were $2.9 \pm 0.6/8.2 \pm 1.8$ ($p < 0.05$); migraine intensity were $5.1 \pm 2.1/8.2 \pm 0.9$ points ($p < 0.05$); migraine days per month ? $3.1 \pm 0.5/11.0 \pm 2.5$ ($p < 0.05$); PT levels were $50.9\% \pm 2.6\%/57.6\% \pm 12.0\%$ ($p < 0.05$); at the same time MEPT were $41.4\% \pm 2.9\%/44.3\% \pm 7.4\%$ ($p > 0.05$). The described phosphenes in MA patients were polymorphous, reproducible, more bright, distinct and clear in comparison with the MO patients. The increased of magnetic stimulus (PT+10%) enhanced subjective intensity of the phosphene in MA subjects.

Conclusions The MA is characterized by the hyperexcitability of the VC and by the more pronounced subjective visual perception. The motor cortex thresholds in MA and MO patients are equal and close to normal. Future drug discovery should focus on the changes of the PT level in migraine patients.

TOPIRAMATE FOR MIGRAINE PREVENTION IN CHINESE POPULATION

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Introduction Randomised placebo controlled trials (MIGR-001 and MIGR-002) and comparative trial (MIGR-003) showed that Topiramate is effective as preventive therapy for migraine with similar efficacy as Propranolol. We would like to explore the efficacy and safety of Topiramate in this aspect of our local population.

Methods A 12-week prospective observational study. Patient with episodic migraine, with or without aura, according to International headache classification were recruited. Topiramate was titrated by 25 mg/week to a maximum of 200 mg daily or as tolerated. Those with migraine <2/month were excluded. Efficacy was assessed under intention to treat analysis (ITT) by a reduction in mean monthly migraine frequency and migraine intensity which was measured by a visual analogue scale (VAS).

Results 52 patients were enrolled. 18 of them withdrew during the study period because of patient's decision, adverse effect, lack of efficacy and loss to follow up. The baseline age, migraine frequency/month and VAS were 41.8±9.1, 8.5±7.8 and 76.5±19.2 respectively. The mean migraine frequency/month decreased from 8.5 to 6.4 ($p<0.001$) and VAS decreased from 76.5 to 58.0 ($p<0.001$) at the end of the study. The responder rate (? 50% reduction in monthly migraine frequency) was 52.9%. There was no statistically significant difference in baseline migraine frequency or in VAS between responders and non-responders. Among all the patients enrolled, the most common adverse effect was parasthesia (46.2%). Others including somnolence (11.5%), short term memo-

ry impairment (11.5%) and worsening of migraine (11.5%). Among those patients presented with the aforementioned adverse effect, only 16.7% of them withdrew from the study. The mean daily dosage of Topiramate in last 4 weeks before endpoint was 79.3 mg daily (SD=35.6).

Conclusions Topiramate is an effective agent for migraine prevention. The responder rate in our local population was similar to MIG-001 and MIG-002, which is 54% and 49% respectively.

EPIDEMIOLOGICAL STUDY OF MIGRAINE AND MIGRAINE PROPHYLAXIS IN NEUROLOGY UNITS IN SPAIN

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Objective To evaluate migraine incidence in Neurology Units and characteristics of those patients that initiate a prophylactic treatment for migraine prevention.

Methods Observational, multi-centre, epidemiological study. During 5 days of consultation (ambulatory, hospital out-patient, headache clinic) data of the number of patients that were referred or followed-up because headache were recorded. Of those patients with migraine and who were going to be prescribed a prophylactic drug, specific data about migraine characteristics, impact assessed by Migraine Disability Assessment Scale (MIDAS) and demographical data were also recorded.

Results A total of 117 neurologist participated in the study with 8,890 patients seen (58% in general neurology clinics). A total of 1332 (15%) patients suffered from migraine and 40% of them had been treated or were still taking a prophylactic drug. The majority (72.5%) presented migraine without aura. Mean age for initiating a prophylactic treatment was 37.6 years-old. The main cause for prescribing a prophylactic drug was the presence of two or more attacks per month with disability during three or more days. The impact of migraine in these patients were high, nearly half of them had lost a work-day in the previous month and considered the maximal intensity of the pain graded to 8/10 score.

Conclusions Migraine is a major health issue generating more than 15% of consultations to neurologists. Mean age of initiation of prophylactic treatment is coincidental with greater personal, social and work activities.