PRESIDENTIAL SYMPOSIUM

PS-1
Pharmacogenetics/genomics: basic concepts and clinical relevance
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The term pharmacogenetics was coined about 45 years ago to denote the science about how inheritance influences drug actions. The study of single genes for drug metabolizing enzymes has been an area of particular interest to pharmacogenetics. Pharmacogenomics is the study of not just single genes on drug action, but rather the functions and actions of all genes in the genome on drug action. Pharmacogenomics has a broader and somewhat more ambitious reach than just pharmacogenetics, as it includes also the use of genomics and proteomics in the identification of new drug targets. Atypical plasma choline esterase and N-acetylation polymorphism are classical pharmacogenetic entities discovered in the 1950s. During the last 25 years, the study of genetic polymorphism in drug oxidation via the cytochrome P450 (CYP) enzyme system has been the focus of interest. In humans there are 57 CYP genes and 33 pseudogenes arranged into 18 families and 42 subfamilies. Foreign chemicals including drugs are metabolized by CYP enzymes from families 1, 2 and 3. Genetic polymorphisms are well established for CYP2C9, CYP2C19 and CYP2D6. In recent years important progress in the understanding of the Pharmacogenetics/genomics of drug targets including the serotonin transporter has been made.

PS-2
The pharmacogenetics of the serotonin system
Serretti Alessandro
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The pharmacogenetics of the serotonin system has been studied in mood disorders and schizophrenia. The functional polymorphism in the upstream regulatory region of the serotonin transporter gene (5-HTTLPR), the A218C gene variant on the tryptophan hydroxylase gene (TPH) and the 102TC variant in the 5HT2A receptor were independently associated with short-term SSRI’s antidepressant efficacy. Lithium long-term prophylactic efficacy in mood disorders has been asso-

ociated with SERTPR and TPH, though in unreplicated studies. A number of further candidate genes were analysed but revealed no association. Data from antipsychotic drug studies revealed no association. Data from antipsychotic drug studies associated with SERTPR and TPH, though in unreplicated studies. A number of further candidate genes were analysed but revealed no association. Data from antipsychotic drug studies associated with SERTPR and TPH, though in unreplicated studies. A number of further candidate genes were analysed but revealed no association. Data from antipsychotic drug studies associated with SERTPR and TPH, though in unreplicated studies. A number of further candidate genes were analysed but revealed no association. Data from antipsychotic drug studies associated with SERTPR and TPH, though in unreplicated studies. A number of further candidate genes were analysed but revealed no association. Data from antipsychotic drug studies

variables, such as age, baseline severity levels, concurrent medical conditions, dosage of the drugs and plasma levels. Some other studies analysed samples undertaking different treatments, or small samples, with no control for placebo effect. The measurements of outcome are often not consistent, and some authors measure the response rate, while others focus on the final outcome, often with different scales. Despite all these limitations, pharmacogenetics is a relatively new field of investigation in psychiatry and it holds great potential for refining and optimizing psychopharmacology.

PS-3
Ethnic differences in pharmacogenomics and therapeutic implications
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Pharmacogenetic (interchangeably used as pharmacogenomic herein) entities extensively studied and showing an interethnic difference in the drug-metabolizing enzyme activity include N-acetyltransferase 2 and cytochrome P450 (CYP) 2C (i.e. CYP2C9 and 2C19) and CYP2D6. In the CYP pharmacogenetic-ics individuals are classified into the extensive and poor metabolizer (EM and PM, respectively) groups. Because the frequencies of the CYP-related PMs differ interethnically, a drug that is metabolized via a pharmacogenetically determined enzyme (e.g. codeine via CYP2D6 to morphine) should show, on a theoretical basis, an interethnic difference in the therapeutic consequences (e.g. drug effectiveness and/or adverse drug reaction) of that drug. However, this theoretical consideration has not been proven, because (1) no prospective parallel study using the same research protocol has been conducted in the different ethnic groups and (2) pharmacogenomic-oriented studies have been performed within the same ethnic groups. Some drugs used for headache treatment (e.g. codeine, sumatriptane, rizatriptane) are metabolized via pharmacogenetically determined enzymes (e.g. for rizatriptane by monoamine oxidase). However, whether and to what extent the enzyme(s) involved in the metabolism of these drugs would be related to their therapeutic effectiveness remain obscure. I will discuss the given topics in light of (1) interethnic differences in the frequencies of PMs of CYP2C9, CYP2C19 and CYP2D6 and (2) therapeutic importance of the interethnestic differences in the genetically determined drug-metabolizing activity for the future perspectives of the worldwide therapeutics benefits. Ethnic differences in pharmacokinetics and pharmacodynamics attributed to those in pharmacogenetics or pharmacogenomics appear not to be therapeutically applied to the relevant ethnically different patients.
Drug development aims at documenting the safety and efficacy of pharmaceutical agents for subsequent regulatory review. For practical purposes these studies are restricted in number of trial subjects and time. Thus, some effects of drugs may be uncovered only after use in larger populations and for extended times. Technological advances in genomics, proteomics and metabolomics have raised hopes that we will be equipped with new tools to predict long-term effects of drugs based on the limited datasets generated in regulatory trials. Still, few benefits have come out of these technologies despite large investments. A limiting factor is the uncertainty among companies and regulators how to interpret the novel data generated by, for instance, genomic analyses. Only through a concerted action including regulators, healthcare providers and industry will this goal be achieved. Recently the FDA published a proposal for stimulating pharmacogenomic analyses to evaluate drug effects in preclinical and clinical settings (http://www.fda.gov/cder/guidance/6400fnl.htm). In addition, cross functional research initiatives involving industry and academic medicine have been initiated to increase our knowledge about the benefits and limitations of biomarker technologies. Thus, patients may eventually benefit from one of the most significant recent technology advancements in clinical research.
THE IHS LECTURE

SL

Placebo and headache
Hans-Christoph Diener

It has been known for a long time that almost any treatment or procedure used in headache patients will lead to an improvement. This is true for the treatment of headache attacks and the prevention of headache. The concept of controlled randomized trials revealed that placebos have a profound effect in headache patients. The consequence was that most modern trials in the treatment of headache use placebo groups. The responder rate to placebo depends on the endpoint and is around 20–30% for improvement of headache in trials treating acute headache events and around 30% in prevention trials. Originally it was assumed that the placebo effect would decrease over time. Long-term studies with topiramate or botulinum toxin, however, showed that the effect of placebo lasts over 6 or 9 months. Subcutaneous placebo is more effective than oral placebo. In the USA and in southern Europe the placebo response is higher than in northern Europe. Children and adolescents have a much higher placebo response than adults. Expectation will play a major role, when the randomization ratio between placebo and verum is known. The quality of a trial has no influence on the placebo responder rate. Placebos can lead to side-effects. In trials treating anxiety placebo resulted in headache in 20% of the patients. Information about possible weight gain in a migraine prevention trial resulted in profound increase in body weight in the placebo run-in phase. Placebo might have a similar mode of action as ‘real’ drugs. PET and functional MRI studies indicate that placebo will activate similar brain structures as opioids.
Migraine as an ion-transporter disorder
Michel D. Ferrari MD, PhD
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Migraine is a common, episodic, multifactorial, neurovascular disorder with high socio-economic and personal impact. Although much is known about the underlying mechanisms of the headache (activation of the trigeminal vascular system) and aura (CSD: cortical spreading depression), little is understood of how and why attacks begin. Both genetic and environmental non-genetic factors seem to set and modulate the trigger threshold for migraine attacks. Familial hemiplegic migraine (FHM) is an autosomal dominantly inherited subtype of migraine associated with hemiparesis during attacks. Genes for FHM are candidate genes for the common types of migraine and studying the functional consequences of FHM gene mutations may help to elucidate common pathways for triggering migraine attacks.

FHM1 is caused by missense mutations in the CACNA1A gene on chromosome 19p13. The gene encodes the main α1A subunit of neuronal P/Q type calcium channels that modulate the release of neurotransmitters including monoamines, acetylcholine, glutamate, and calcitonin gene-related peptide (CGRP). Different CACNA1A mutations have been associated with a wide spectrum of brain disorders. These range from pure episodic disorders without interictal abnormalities such as FHM, episodic ataxia type 2 and epilepsy, via combinations of these disorders, to severe progressive ataxia and excessive, mild head trauma-triggered, fatal cerebral oedema. Genetic studies support the involvement of the CACNA1A gene in the common types of migraine. Two transgenic knock-in mice models, harbouring human FHM mutations (one associated with pure FHM, the other with FHM and fatal cerebral oedema), have recently been constructed. Intensive functional characterization is underway to unravel the in vivo consequences of these mutations. The first results point to an increased release of neurotransmitters and a reduced threshold for CSD.

FHM2 is caused by mutations in the Na+, K+ ATPase pump α1 subunit gene ATP1A2 on chromosome 1q23. The gene is primarily expressed in glial cells. ATP1A2 mutations can also cause epilepsy and alternating hemiplegia of childhood (AHC). Transgenic knock-in mice models are underway. It is predicted that FHM2 mutations will result in reduced glial cell re-uptake of glutamate and K+ from the synaptic cleft, leading to increased levels of glutamate and K+. This, in turn, should facilitate the initiation and propagation of CSD as was found for FHM1 mutations.

Recently, missense mutations in the SCN1A gene on chromosome 2q24 were found to cause FHM3. This gene encodes the α1 subunit of neuronal voltage-gated sodium (Na+,1.1) channels that are critical for the generation and propagation of action potentials in cortical neurons, and mutations of which have previously been associated with epilepsy. FHM3 mutations were found to induce a two- to four-fold accelerated recovery from fast neuronal inactivation and are thus predicted to allow for higher neuronal firing rates and enhanced neuronal excitability. This should also lead to a greater propensity to CSD, again pointing at a pivotal role for CSD in FHM and possibly also normal migraine.

Several other loci and genes have been associated with migraine as well. These include loci on chromosome 1q, 3p21 (likely to harbour a neurovascular gene responsible for a combination of vascular retinopathy, Raynaud’s syndrome, and migraine), 4q21–24 (linked to migraine in patients from Finnish and Icelandic genetic isolates), 6p12–21, 11q24, 14q21–22, 15q11–13, Xq24–28 (in Australian families) and the Notch3 CADASIL gene (in migraine with white matter abnormalities). Other possibly involved migraine genes encode for a 5-HT transporter and MTHF reductase, as well as for insulin, endothelin type A and dopamine D2 receptors.

Unraveling the genetic basis of migraine and studying the functional consequences of the genes involved will improve our understanding of the mechanisms involved in the onset of migraine attacks and the interaction with migraine trigger factors. This may ultimately lead to specific, more effective and well-tolerated migraine prophylactic drugs. Because of the many clinical and pathophysiological similarities, other episodic disorders such as ataxia, epilepsy, AHC, and trauma-triggered cerebral oedema may also profit from these exciting developments.

Migraine: what is the link between spreading depression and head pain?
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This presentation will review the evidence emphasizing the importance of cortical spreading depression (CSD) to migraine aura, headache, and review new data showing that five prophylactic drugs suppress CSD evoked in an experimental model. CSD has been implicated in migraine aura for many years based on the clinical description of a slowly propagating wave of excitation followed by inhibition. Imaging studies confirmed this relationship and particularly studies using high-resolution functional BOLD brain imaging, for example Hadjikhani et al. 2002, Cao et al. 1999. Regarding the aura as a noxious event, Bolay (2001) and colleagues confirmed experimental work by Moskowitz and colleagues (1994) showing that CSD increases the expression of the early
immediate gene c-fos within trigeminal nucleus caudalis. This increase was blocked by trigeminal nerve sectioning, suggesting its expression was dependent upon peripheral inputs from the trigeminal nerve. Bolay and colleagues also showed that CSD evoked a trigemino-parasympathetic reflex and this reflex was also dependent upon an intact trigeminal nerve as well as intact parasympathetic efferents. Both findings implied that CSD was sufficient to activate the trigeminal nucleus caudalis, that these inputs were noxious and probably sufficient to generate the headache of migraine. More recent work on CSD showed that valproic acid, topiramate, DL propranolol (but not D propranolol), amitriptyline, and methysergide suppressed CSDs evoked by topical KCl or by electrical stimulation and suggests a coherent target for pharmacologically distinct drugs. These findings raise fundamental issues regarding the importance of CSD to migraine phenotypes in addition to those anticipated by aura.

SS2-I2
Migraine and epilepsy: a clinical evaluation of the interface
Frederick Andermann MD, FRCP (C)
Professor of Neurology and Pediatrics, McGill University

Though migraine and epilepsy are both paroxysmal disorders of the nervous system, they are genetically distinct. There are, however, a number of conditions in which these disorders coexist and where a causal relationship is apparent or suspected.

Some patients who have migraine with aura develop major seizures intercalated between the aura and the headache. Spreading depression, exceptionally crossing the central sulcus to involve the precentral gyrus, is a possible explanation for this rare but well-described entity. It occurs in about 3% of patients with migraine and aura according to Ehrenberg.

Migraine and a family history of migraine are features of children with benign rolandic epilepsy and also of those with benign occipital epilepsy.

Pre-ictal, peri-ictal and postictal headache with migraine characteristics occurs with varying frequency in patients with temporal and extratemporal intractable seizures. Migraine is a feature of patients with MELAS, where it is often associated with intractable focal status epilepticus. A family history of migraine with or without aura is almost invariably present in children with alternating hemiplegia of infancy. Not all paediatric neurologists are convinced that this is a significant association. In children with benign alternating hemiplegia of childhood with onset during sleep, migraine appears to be a major factor.

These relationships cannot be explained by chance association of these common disorders.

SS3-I1
Cyclic vomiting syndrome: a migraine variant triggered by corticotrophin-releasing factor?
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Cyclic vomiting syndrome (CVS) is characterized by recurrent, severe (6 ×/h), stereotypic (99%) vomiting episodes that punctuate periods of normal health (1). Recent studies indicate that CVS affects 1.9% of school-aged children (2) and causes substantial medical (58% require IVs) and academic (20 missed school day absences annually) morbidity (3). Concomitant symptoms include pallor (91%), lethargy (93%), anorexia (81%), nausea (82%), abdominal pain (42%), photophobia (38%) and phonophobia (30%). The differential diagnosis includes serious GI, urological, neurological and psychiatric disorders (8%, e.g. malrotation) and metabolic disorders (5%, e.g. fatty acid oxidation disorder). Current treatment includes avoiding known triggers, using both prophylactic (e.g. tricyclic antidepressants) and abortive medication (e.g. triptans), and providing supportive care (e.g. ondansetron, lorazepam).

CVS has been considered to be a migraine variant that exists along a paediatric ‘periodic’ spectrum of CVS, abdominal migraine and migraine headaches. All share on-off temporal patterns, associated symptoms, family histories of migraine and positive responses to antinausea treatment. Recent studies suggest that mitochondrial DNA mutations, perhaps through deficits in cellular energy, may increase susceptibility to attacks (4). Current studies examine the role of corticotrophin-releasing factor in initiating GI and autonomic symptoms (5). Further studies of CVS may provide insight into migraine itself.

References
Synthesis and actions of steroids in the brain: implications for headache research

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Fluctuating ovarian steroids function as trigger for migraine, but the underlying mechanisms are unknown. There is evidence that falling levels of oestrogen are a precipitating factor, and that oestrogen treatment allows postponement of migraine attacks. The role of progesterone is controversial, and there is no clear evidence for a role of this hormone in menstrual migraine. Over the past few years there have been major advances in our understanding of steroid effects on the brain, which may spur new investigations into the association between steroid hormones and certain forms of headache, in particular migraine. When examining the role of steroids in disturbed brain functions, several findings need to be taken into account: (1) estradiol and progesterone can be formed within the brain. Thus, their circulating levels do not necessarily reflect levels to which neural cells are exposed; (2) oestrogens and progestins exert pleiotropic effects throughout the nervous system and regulate vital glial and neuronal functions; (3) the effects of steroids on the brain involve a large variety of mechanisms. It is also important to be aware of the fact that all oestrogens and progestins are not the same, and that they have different pharmacological and biological properties.

Imaging cellular mechanisms of migraine

Andrew Charles
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Intercellular calcium waves in astrocytes, spreading depression, the spreading oligemia of migraine, and the clinical phenomena of migraine aura all propagate with similar temporal and spatial patterns. However, many details of the relationship between these phenomena remain uncertain. We have used video imaging of intracellular calcium concentration and in vivo imaging of cortical spreading depression (CSD) and migraine. Increases in astrocyte calcium concentration can be communicated as intercellular waves over long distances. It is now clear that these astrocyte calcium waves are mediated by regenerative release of ATP and stimulation of purinergic receptors. Extracellular ATP release by astrocytes is metabolized to adenosine. Both ATP and adenosine released in association with astrocyte calcium waves could play a role in the neuronal and vascular phenomena of spreading depression. OIS imaging of cortical spreading depression reveals complex multiphasic wavefronts associated with sequential vasodilation and vasoconstriction. CSD can be modulated by conditions that modulate astrocyte Ca2+ waves and ATP release. These findings will be discussed in the context of previously reported PET imaging studies of migraine.

Current therapy of trigeminal autonomic cephalalgias (TACs)

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The trigeminal autonomic cephalalgias (TACs) are a group of primary headaches classified together in the second edition of the International Classification of Headache Disorders (1). The group includes cluster headache, paroxysmal hemicrania and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT). These syndromes have had a reputation for being difficult to manage and certainly they seem generally better managed by headache specialists. I will discuss medical management, as surgical management is covered elsewhere in the meeting.

Cluster headache may be treated with either acute attack treatments or preventive approaches. Acute attack treatments include triptans, sumatriptan nasal spray and injection and zolmitriptan nasal spray, and inhaled oxygen. Preventive treatments include verapamil, corticosteroids, lithium, methysergide, topiramate, gabapentin and greater occipital nerve injections.

Paroxysmal hemicrania is treated with indomethacin, when it is tolerated, and otherwise it can be most challenging to manage. SUNCT may be treated with lamotrigine, topiramate or gabapentin. Sub-acutely it may be settled with intravenous lidocaine by infusion (2).

References


Terminating migraine with alldynia and ongoing central sensitization using parenteral administration of COX1/COX2 inhibitors

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Objective To determine whether delayed infusion of COX1/COX2 inhibitors (ketorolac, indomethacin) will stop migraine in alldynic patients, and suppress ongoing sensitization in central trigeminovascular neurons in the rat.

Background The majority of migraineurs seeking secondary or tertiary medical care develop cutaneous alldynia during the course of migraine, a sensory abnormality mediated by sensitization of central trigeminovascular neurons in the spinal trigeminal nucleus. Triptan therapy can render alldynic migraineurs pain-free within a narrow window of time.
(20–120 min) that opens with the onset of pain and closes with the establishment of central sensitization. Can drugs that tackle ongoing central sensitization render allodynic migraineurs pain-free after the window for triptan therapy has expired?

**Methods**

Patients exhibiting migraine with allodynia were divided into two groups ($n = 14$, each): group 1 received delayed sumatriptan injection (6 mg) 4 h after onset of attack—which failed to render them pain-free—and ketorolac infusion (two 15-mg boluses) 2 h later; group 2 received delayed ketorolac monotherapy 4 h after onset of attack. Pain intensity (visual analogue scale) and skin sensitivity (quantitative sensory testing) were measured when the patients were migraine-free (baseline); 4 h after onset of migraine (just before treatment); 2 h after sumatriptan; 1 h after ketorolac. In the rat, we tested whether infusion of ketorolac (0.4 mg/kg) or indomethacin (1 mg/kg) will block ongoing sensitization in peripheral and central trigeminovascular neurons. The induction of sensitization (using topical application of inflammatory soup on the dura) and its suppression by COX1/COX2 inhibitors were assessed by monitoring changes in spontaneous activity and responses to mechanical and thermal stimuli.

**Results**

Patients had normal skin sensitivity in the absence of migraine, and presented cutaneous allodynia 4 h after onset of migraine. In group 1, all patients continued to exhibit allodynia 2 h after sumatriptan treatment, and none of them became pain-free. However, 71% and 64% of the patients in groups 1 and 2, respectively, were rendered free of pain and allodynia within 60 min of ketorolac infusion. Non-responders from both groups, in contrast to the responders, had had a history of opioid treatment. In the rat, infusion of COX1/COX2 inhibitors blocked sensitization in meningeal nociceptors and suppressed ongoing sensitization in spinal trigeminovascular neurons. This inhibitory action was reflected by normalization of neuronal firing rate and attenuation of neuronal responsiveness to mechanical stimulation of the skin.

**Conclusions**

The termination of migraine with ongoing allodynia using COX1/COX2 inhibitors is achieved through the suppression of central sensitization. Although parenteral administration of COX1/COX2 inhibitors is impractical as routine migraine therapy, it should be the rescue therapy of choice for patients seeking emergency care for migraine. These patients should never be treated with opioids, particularly if they have had no prior opioid exposure.

**Keywords:** headache, nociception, trigeminal, hyperalgesia, triptans, inflammation, pain

**Acknowledgements**

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**SS7-I1**

**Spreading depression (SD) and its possible role in migraine and in neuron damage**

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SD is a transient slow wave of suppression of neuron activity that propagates slowly in forebrain grey matter even if synapses are blocked. Electrical silence is often preceded by a high-frequency impulse shower which can influence neurons at distant sites. Within white matter SD is not observed. Underlying SD is a self-regenerating process in which neurons depolarize, swell, lose K$, and gain Na$, Ca$ and water. Ions redistribute through several slowly inactivating ion channels which are opened by depolarization that is mediated by ion shifts and/or inappropriate transmitter release (reviewed in 1, 2). SD probably causes migraine aura, and it may trigger the process causing migraine headache (3). Severe hypoxia of forebrain grey matter induces an SD-like process but, unlike normoxic SD which is self-limiting, hypoxic SD lasts as long as the shortage of O$. In normal tissue SD causes no irreversible injury, but in conditions of metabolic impairment repeated waves of SD cause neuron damage, e.g. in the penumbra zone adjacent to an ischaemic infarct, or sites injured by trauma. Depolarization-induced neuron injury is calcium dependent. Fainting due to concussion can perhaps also be caused by SD.

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LS1
Headache clinics
Jensen Rigmor
The Danish Headache Centre, Department of Neurology, Glostrup Hospital, University of Copenhagen, Denmark

Headache clinics have been increasingly popular over recent decades, first, because the need for specialized care for severely affected headache patients has been recognized by the medical society and second, because more patients demand such specific care. Most headache clinics have been initiated by one or two headache specialists and gradually expanded to offer a multidisciplinary treatment programme. However, should headache clinics be organized like pain clinics or is there a specific need for other treatment modalities in headache clinics? What are the clinical characteristics of the patients, can we offer an optimal treatment strategy for specific headache groups as medication overuse headache and what diagnostic procedures can we offer to the complicated patient? The literature about organization and treatment results in specialized headache clinics is actually very limited, and most of the applied strategies are based on clinical experience. This lunch seminar will focus on the cost-effectiveness of specialized headache clinics, discuss the various models of organization and present the treatment results from the Danish Headache Centre. A lively and fruitful discussion with the audience is of utmost importance as your clinical experience is very valuable in the further development of this new era of clinical headache research.

Keywords: headache clinics, organization, multidisciplinary treatment, cost-effectiveness, treatment programme

LS2
Surgical treatment of trigeminal neuralgia
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The strategy to treat drug-refractory trigeminal neuralgia includes several surgical procedures, including radiosurgery. In our Institute the choice between different procedures has been guided mainly by the age of patients. Moreover, during the last 20 years the introduction of new methodologies has considerably modified the original criteria. Percutaneous procedures include radiofrequency selective thermorizotomy (TRZ) and balloon compression (PMC) of the trigeminal ganglion within the Meckel cistern. More than 2000 patients underwent percutaneous procedures in our department and this has been the choice treatment since 1990 when the introduction of microvascular decompression (MVD) of the trigeminal root in the posterior fossa reduced considerably the indications for TRZ and PMC. Percutaneous procedures were affected by certain side-effects concerning particularly the development of sensory deficits and, in a few cases, anaesthesia dolorosa (1.5%). MVD replaced percutaneous procedures in patients younger than 70 years and our experience in more than 500 patients allows to confirm the high success rate (80%) but also to focus on side-effects and complications. Recently radiosurgery has been introduced to treat older patients and recurrences of TRZ, PMC and MVD. The last introduced methodology is deep brain stimulation (DBS), reserved for patients with pain paroxysms confined to the first division of the trigeminal nerve.

LS3
Oriental approach to headache
Moderators: Fred Sheltell MD & Kenji Nakashima MD
1Director and Founder, New England Center for Headache, Stamford, CT, USA, and 2Professor and Chairman, Department of Neurology, Institute of Neurological Sciences, Tottori University, Faculty of Medicine, Japan

The practice of Oriental medicine has always been fascinating, albeit somewhat mysterious in terms of its philosophy and mechanisms, especially to practitioners of traditional ‘western’ medicine. Nonetheless, there are a growing number of practitioners of Oriental medicine in the west as well as the east. Controversies continue to surround the validity of the practice of Oriental medicine in spite of the fact that these techniques have been employed successfully for centuries.

Philosophically, practitioners of Oriental medicine view overall health as being related to a balance of positive and negative energies, with acupuncture and herbal techniques targeting restoration of balance and consequently function.

This workshop will begin with the story of the origin and treatment of Emperor Goshirakawa’s (1127–1192) headaches, whose symptoms may have been an early description of allodynia. This introduction will be followed by descriptions and rationales for the practice of acupuncture and herbal medicine by two of its expert practitioners, from Korea and Japan. Finally, recent double-blinded placebo-controlled studies of Oriental medicine techniques will be reviewed by a prominent practitioner of western medicine.

As Ramsay (Chair, NIH Panel on acupuncture) has stated, ‘The challenge in studying acupuncture is to integrate the theory of Chinese medicine into the conventional research model and into the conventional health care arena’.

LS4
The neck and headache
Nikolai Bogduk
University of Newcastle, Department of Clinical Research, Royal Newcastle Hospital, Newcastle, Australia

Pain from the neck can be referred to the head, where it is perceived as headache. The anatomical basis for this phenomenon is convergence in the trigemino-cervical nucleus.
Convergence has been demonstrated both in animal studies and in clinical studies using normal volunteers and patients. The most likely sources of pain are the upper cervical synovial joints.

Cervicogenic headache remains contentious because of conflicting approaches to its diagnosis and management. Some specialists believe that cervicogenic headache can be diagnosed clinically. Most of the proposed criteria, however, lack reliability, and none has been shown to be valid. Pain specialists advocate diagnostic blocks of cervical nerves or upper cervical joints. A suitable compromise is that possible and probable cervicogenic headache can be diagnosed on the basis of history and examination, but a definitive diagnosis requires diagnostic blocks.

Few treatments have been tested, let alone proven. No drugs have been shown to be effective. For probable cervicogenic headache, manual therapy or exercises are more effective than usual care with analgesics. For headaches stemming from the C2–3 zygapophysial joints intra-articular injection of steroids can be palliative. Radiofrequency, third occipital neuromy is the only treatment shown to be able consistently to abolish pain completely.

LS5

Genetic association studies in migraine: guidelines and pitfalls

G. M. Terwindt
Neurologist, LUMC Leiden, the Netherlands

Migraine is a multifactorial disorder, which means that multiple genes and environmental factors are involved. In contrast to Mendelian diseases, complex traits are relatively common and are presumably due to multiple interacting genes, thus making genetic analysis more difficult. Because the inheritance pattern is not understood, non-parametric methods such as association studies, which assess the association between DNA variants and a common disorder, are being used to identify regions of the genome and candidate genes that contribute to this disorder.

In migraine, multiple association studies have been performed, many of them without replication of results. This may lead to doubt about the utility of this approach for a common condition like migraine. With the discovery of massive numbers of genetic markers and the development of better tools for genotyping, association studies will inevitably proliferate. Now is the time to consider critically the design of such studies, to avoid the mistakes of the past and to maximize their potential to characterize the genetic basis of migraine.

LS6

Issues arising from botulinum toxin treatment

Co-Leaders Ryuji Kaji & Ninan T. Mathew MD

• Introduction: Ryuji Kaji
• Basic mechanisms of action of botulinum toxin in headache: Roger Aoki
• Clinical and preclinical data on botulinum toxin—role in episodic migraine: Rami Burstein
• Botulinum toxin type a (botox) in chronic daily headache/transformed migraine—recent data: Ninan T. Mathew
• How can we improve clinical trials in chronic daily headache? What are the appropriate endpoints? David Dodick
• Questions and answers: Faculty

LS6-1

Issues arising from use of botulinum toxin in headache

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The biochemical mechanism of action of botulinum neurotoxin is to inhibit SNARE-mediated release of neurotransmitters, especially at the neuromuscular junction. Recent evidence suggests that this same mechanism is applicable to nociceptive neurons and may be involved in the reduction of chronic pain perception. Dr Aoki will summarize preclinical results and propose a hypothesis for the antinociceptive mechanism for botulinum neurotoxin type A.

Dr Burstein will present preclinical data describing the interactions between peripheral nociceptors (A-delta and C-fibres) and Botox. The clinical data will propose a way to differentiate between Botox responders and Botox non-responders.

Recently published data on the efficacy of botulinum toxin type A (Botox) in patients with more than 15 days a month (mostly transferred migraine) will be presented by Dr Mathew. In addition, clinical characteristics of responders will be discussed based on observations on a large series of patients.

Dr Dodick will discuss the inherent problems in designing prophylactic studies, in a chronic headache population. The need for selecting appropriate endpoints will be emphasized.

LS6-2

Issues arising from botulinum toxin treatment

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Botulinum toxin injection is becoming a powerful treatment of migraine for its capability of reducing the number of attacks. Although promising results in clinical trials have been published, the following issues must be addressed before its full usage: 1. What are the best sites of injection for migraine prevention? 2. Who are the best candidates for injection? It is known that botulinum toxin disrupts SNARE complex-mediated exocytosis, and that capsaicin (vanilloid) receptor turnover depends upon this exocytosis. However, it is unknown whether this receptor ever plays a role in the pathomechanism of migraine. In this seminar, I will discuss these matters in the light of the possible mechanism of action of the botulinum toxin for shutting down a vicious cycle that generates migraine.
Management of headache in pregnancy

Elizabeth Loder MD
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This seminar will review the management of primary headache disorders in pregnancy. Many of the common forms of primary headache are likely to improve during pregnancy, so that some women will be able to manage their headaches with reassurance and non-pharmacological treatments, including rest, ice or heat, or relaxation strategies. Women whose troublesome headaches persist should be offered more specific treatment. In general, the same treatments that are helpful in non-pregnant patients are used, with exceptions for drugs known or suspected to have harmful effects in pregnancy. Non-pharmacological therapy should be emphasized. Pregnancy risk ratings, information from teratogen information services and other ratings can be used to identify drug treatments for headache that pose the lowest possible risk during pregnancy and lactation. Some dangerous secondary causes of headache are more likely to occur during pregnancy or the postpartum period, and vigilance for these must be maintained. These include cerebral venous thrombosis, pre-eclampsia and eclampsia, intracranial haemorrhage and low volume headache syndromes related to the use of neuraxial blockade for anaesthesia during delivery.

LS8

Neurostimulation in refractory headaches

Organizers: Jean Schoenen, University of Liège, Belgium, and P. J. Goadsby, UK

Various primary headache disorders may become refractory to drug treatment and cause distressing disability. For many years destructive lesioning methods have been used in such cases, with equivocal results. More recently, neurostimulation has been introduced as an alternative treatment which has in theory the advantage of not producing any nervous lesion. Although it is still only an emerging therapy for which it is too early to draw definitive conclusions, first encouraging results have been published and time seems ripe for an interim analysis.

This seminar will critically examine the results obtained with hypothalamic stimulation in refractory chronic cluster headache (J.S.) and with occipital nerve stimulations in refractory chronic migraine (P.G.). We will also discuss the potentials of vagal nerve stimulation in headaches. Every clinician is confronted with disabled headache patients who do not respond to the classical treatments and the question ‘to stimulate or not’ may come into his mind, now or in the near future.

LS9

Issues arising from the new IHS classification

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Following the publication of ICHD-II, a number of issues have been raised. A revised version of the criteria for MoA has already been published in Cephalalgia. Recently, epidemiological data demonstrated that most patients with migraine with aura have a mixture of subtypes of migraine with aura. The use of ‘probable’ in two different meanings in relation to chronic migraine and medication overuse headache means that medication overuse headache cannot be diagnosed until it is over. Only very few patients fit into chronic migraine criteria and loosening criteria has been suggested. In the secondary headaches, the probable diagnosis is used when the causal relationship is uncertain, which is different from probable in the primary headaches. It is problematic that a treatment response must be demonstrated before a secondary headache can be regarded as definite and, in many cases, a diagnosis cannot be made until the headache has disappeared. A last issue relates to the word ‘chronic’. Chronic actually means long lasting but almost all headaches are episodic. Chronic in migraine and in tension-type headache is used synonymously with frequency, while chronic in cluster headache means no clusters. An alternative terminology has been discussed by the committee but no satisfactory terminology has been found.

LS10

Patent foramen ovale (PFO) and migraine

Peter Wilmshurst
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The seminar will consider the relationship of patent foramen ovale (PFO) to aetiology of migraine. Dr Peter Wilmshurst will review the literature linking PFO and migraine. Dr Andrew Dowson (King’s College Hospital, London) will describe the design and report initial findings in the MIST (Migraine Intervention with STARFlex® Technology) Trial. The MIST Trial is a prospective, randomized, multicentre, double-blind, placebo-controlled trial to evaluate the effectiveness of PFO closure with the STARFlex® septal repair implant to prevent migraine headache. Dr Simon Nightingale (The Royal Shrewsbury Hospital) will describe an hypothesis on the mechanism linking PFO and migraine. Open discussion will follow.

LS11

Trigeminal autonomic cephalalgias

Juan A. Pareja
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Trigeminal autonomic cephalalgias (TACs) include cluster headache (CH), paroxysmal hemicrania (PH) and SUNCT.
Although localization and autonomic accompaniments are similar, TACs essentially differ in several clinical variables:

**Mean duration of attacks.** objective measurements (range): SUNCT 49 s (5–250 s); PH 13 min (3–46 min); CH 38 min (8–238 min).

**Temporal distribution of attacks.** SUNCT attacks predominate during daytime whereas CH and PH are characterized by a considerable number of nocturnal attacks.

**Precipitating mechanisms.** In SUNCT, multiple mechanical precipitating factors within the trigeminal and extratrigeminal areas have been recognized. Refractory periods seem to be lacking after SUNCT attacks. PH may rarely be precipitated by spontaneous or provoked neck movements. In CH, attacks can be precipitated only by vasoactive substances such as alcohol and nitroglycerine.

**The absolute response to indomethacin** is a diagnostic criterion for PH.

TACs are believed to depend essentially on the activation of the trigeminal system, with pain felt in the area supplied by the V-1 nerve, together with a disinhibition of a trigemino-facial (parasympathetic) reflex responsible for the oculofacial autonomic accompaniments. Differences in the source of the pain generator and/or modulation of the pain and reflex development may give rise to the various clinical phenotypes.

LS12

**Neuro-ophthalmology and headache**

Robert B. Daroff MD

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The relationship between the eye and headache is multifactorial.

1. Eye disease may cause eye pain or headache.
2. The eye and periocular area are often the epicentre of pain in primary (migraine, cluster, tension-type), and secondary headaches (trigeminal neuralgia, carotid disease, etc.).
3. Photophobia is a frequent concomitant of primary and secondary headaches. Bright lights lower pain thresholds in migraineurs between headaches, but not non-migraineurs.
4. Subconjunctival and periocular haemorrhage can occur in migraine.
5. The most common migraine auras are visual, arising from the occipital cortex. Retinal (anterior visual) migraine is another, but rare, visual phenomenon.
6. Ophthalmoplegia and headaches have a large differential diagnosis, including Tolosa–Hunt syndrome and ophthalmoplegic migraine.
7. Pupillary disturbances are common in both primary and secondary headaches. Raeder’s syndrome (ipsilateral headache and Horner’s) may be a manifestation of cluster or carotid disease. Episodic mydriasis is an unusual, benign migraine accompaniment.
Scientific session 1: Genetics

SS1-1

Transgenic knock-in mouse model expressing the CACNA1A mutation S218L causing familial hemiplegic migraine and fatal excessive cerebral oedema after minor head trauma

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Background Mutations in CACNA1A, encoding the Ca,2.1 subunit of P/Q-type calcium channels, cause a spectrum of diseases, including familial hemiplegic migraine type-1 (FHM1). CACNA1A S218L mutation causes FHM and fatal excessive cerebral oedema after minor head trauma. P/Q-type calcium channels are widely expressed in the brain and the neuromuscular junction (NMJ), and mediate neurotransmitter release.

Objective To generate a knock-in (KI) mouse model by introducing the S218L mutation in the endogenous Cacna1a gene by gene targeting and study its in vivo consequences.

Methods Generation of transgenic S218L KI and analysis of neurotransmission at NMJs.

Results Homozygous S218L KI mice show mild ataxia and increased lethality in line with the severe phenotype in patients with the S218L mutation. S218L KI NMJs showed a ∼12-fold increase in spontaneous acetylcholine (ACh) release. Low-rate (0.3 Hz) evoked release in low (0.2 mM) extracellular Ca2+ was ∼150% higher in S218L KI. Our data support the hypothesis that CACNA1A mutations lead to synaptic function defects, likely contributing to symptoms of FHM1, but in S218L KI mice even more dramatically than in R192Q KI mice (van den Maagdenberg et al. Neurone 2004; 41: 701).

Conclusion S218L knock-in mice will be valuable tools to study migraine and trauma-related events.

Keywords: FHM, transgenic, knock-in, neurotransmission

SS1-2

The association of migraine with aura with the methylenetetrahydrofolate reductase (MTHFR) C677T variant and the homocysteine metabolic pathway in the general population

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Background Migraine is associated with increased risk of stroke. The C677T variant in the MTHFR gene results in elevated homocysteine, a risk factor for stroke, and has been reported to increase the risk for migraine in selected clinical samples.

Objective To estimate the association of the MTHFR C677T variant with migraine and to consider whether the association is mediated by cardiovascular risk factors and metabolic markers of genotype status.

Methods Participants are adults (n = 1632; 52% female) aged 20–65 from the population-based GEM study. Migraine cases without aura (MoA, n = 226) and with aura (MA, n = 187) were compared with non-migraineurs (n = 1212). We measured MTHFR C677T genotypes, metabolic markers (homocysteine, folate, and vitamin B12), and traditional cardiovascular risk factors.

Results The homozygote (T/T) genotype was more common in MA compared with non-migraineurs (16% vs. 10%, P < 0.02). Compared with the wild-type genotype, the T/T genotype was associated with increased odds of MA [OR = 2.04 (1.2, 3.4), P < 0.006], with a trend with increasing numbers of T alleles [OR = 1.40 (1.1, 1.8), P = 0.007]. ORs were slightly attenuated after adjusting for homocysteine but not by folate or vitamin B12.

Conclusions Risk for MA is associated with MTHFR C677T homozygosity, independent of cardiovascular risk factors and general markers of homocysteine metabolism.

Keywords: migraine, aura, MTHFR, homocysteine, folate

Some of these results were presented at the American Neurological Association annual meeting 2004.
SS1-3

Trait component analyses of genome-wide scan data in migraine families reveal new susceptibility loci

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Background Migraine is the most common cause of chronic episodic severe headache. We performed a trait component linkage analysis on migraine families that had previously revealed linkage to chromosome 4q24 in a genome-wide scan, using the endpoint diagnosis ‘migraine with aura’ as phenotype.

Objective Our aim was to analyse which IHS subcomponents provide best evidence for linkage to the 4q24 locus and whether additional susceptibility loci for trait components could be localized.

Methods Our study sample consisted of 430 genotyped patients within 50 Finnish independent multigenerational families. The same neurologist diagnosed all subjects. The genotypes were analysed by two-point parametric linkage analysis.

Results Strongest evidence for linkage to the 4q24 locus was achieved by using unilaterality (LOD 4.20), photophobia (3.73) and phonophobia (3.52) as trait components. Thus three IHS trait components revealed the same locus as the endpoint diagnosis. Furthermore, trait component analysis detected significant linkage to two loci: chromosome 17 (parametric two-point LOD 4.65) with the pulsation subcomponent, and chromosome 18 (parametric two-point LOD 3.27) with IHS C-criteria (pulsation, aggravation, intensity, unilaterality) was detected.

Conclusion Finding of these new loci and that they represent different traits suggest new means to study the genetic susceptibility to migraine.

Keywords: migraine, migraine with aura, linkage analysis, trait component analysis, genetics

SS1-4

Epidemiology of hemiplegic migraine in Japan: an interim report of the nationwide survey

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Background The prevalence of migraine in Japan is 8.4% in a nationwide survey. A door-to-door survey of migraine in a Japanese town (Daisen study) demonstrated details of Japanese migraineurs; however, the prevalence and details of hemiplegic migraine (HM) in Japan had remained to be clarified.

Objective To determine prevalence and characteristics of HM in Japan.

Methods We inquired of the members of Japanese Headache Society, Japanese Society of Neurology, Japan Neurosurgical Society, and Japanese Society of Anaesthesiologists concerning HM. Questionnaires asking the experience of patients with HM and patients details had been sent to 6780 specialists in nationwide Japan.

Results 1367 specialists (20.2%) have responded. The 6.8% specialists had patient(s) with HM. There were 140 cases of HM. Twenty-three were familial HM and 57 were sporadic HM in accordance with ICHD-II. Twelve cases were uncertain about family history and the other 48 cases were possible HM. As a preliminary result of this survey, the crude prevalence of HM in Japan was one per million population (0.0001%). Additional surveys are going on and the details will be reported at the conference.

Keywords: epidemiology, FHM, hemiplegic migraine, nationwide survey

(Supported by Health and Labour Sciences Research Grants, Psychiatric and Neurological Diseases and Mental Health, Government of Japan)

SS1-5

Genomic profiles in patients with chronic migraine: responders vs. non-responders

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Background Migraine and chronic migraine (CM) have a strong genetic basis with distinct genomic expression patterns. Response to treatment in CM can be variable. Gene expression changes can be used to detect these differences.

Objective To present distinct genomic expression patterns in CM patients that respond (R) compared with those that do not respond (NR).

Methods Blood samples from patients were obtained during CM and at subsequent follow-up evaluation (51.7 ± 17.0 days). Responders were patients that improved greater than the mean for the entire group. RNA from blood was processed on Affymetrix U95A microarrays and analysed using GeneSpring and SAM.

Results Mean initial frequency was 30 headache days per month and at first follow-up was 20.5 ± 10.4 (R = 11.8 ± 6.4; NR = 30.0 ± 0.0). 65 genes’ expression patterns differed between R and NR at initial and follow-up. 40 genes had decreased expression for R from initial to follow-up, while there were no changes for NR.

Conclusion Distinct genomic profiles in CM patients that respond to treatment compared with non-responders suggest different underlying pathophysiology. Future studies will
determine if it is possible to predict which patients will respond to therapy based upon their blood genomic profiles.

**Keywords:** genetics, genomics, migraine, pathophysiology, prophylactic therapy

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**Scientific session 2: Neurobiology of headache**

**SS2-1**

**Changes in arterial diameter can precede cortical spreading depression**

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**Background** Changes in vascular calibre accompany cortical spreading depression (CSD). The mechanisms of these changes remain poorly understood.

**Objective** To observe vascular changes during CSD using optical intrinsic signal imaging (OIS).

**Methods** CSD induced via controlled localized application of KCl was visualized by OIS in exposed cortex (rats) or through thinned skull (mice) with simultaneous EEG recording. Images recorded at a rate of 1–4 Hz were analysed using ImageJ software.

**Results** OIS revealed a characteristic 4-phase CSD waveform whose front coincided with EEG amplitude attenuation. Rat cortical arteries transiently dilated, then showed a prolonged constriction (53 ± 12%; 64 ± 14%) in association with the CSD waveform. Mouse cortical arteries showed constriction (98 ± 9%) followed by a return to baseline diameter. These changes were observed in both large and small vessels. No corresponding changes in venous calibre were noted. In both rats (16/23; 69.6%) and mice (7/14; 50%), changes in arterial calibre were observed to precede the CSD wavefront.

**Conclusion** OIS reveals marked changes in cortical arterial but not venous diameter associated with CSD. The observation that arterial dilation or constriction may occur ahead of the CSD wavefront suggests distinct mechanisms for propagation of vascular vs. parenchymal phenomena associated with CSD.

**Keywords:** cortical spreading depression, artery, migraine

**SS2-2**

**Segmental contraction of intraparenchymal arterioles following the onset of K+-induced cortical spreading depression in gyrencephalic feline brain**

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Cortical spreading depression (CSD) is implicated in the pathology of migraine. Cerebral vasoconstriction and subseqtent local asphyxia preceding CSD (vascular theory of aura) were reported by Van Harreveld and Ochs (AJP 1957; 189: 159), but such initial vasoconstriction has not been confirmed by subsequent investigators. Here, we examine intraparenchymal arteriolar changes in association with K+-induced CSD in six α-chloralose-urethane-anesthetized cats employing an epi- and trans-illumination (optical fibre) technique. Microinjection of K+ into the cortex induced repetitive wave-ring spread of local CBV decrease/increase unrelated to vascular arborization, as previously observed in rats (J CBFM 2005, in press). Along with the spreading wave of oligaemia, we found that arterioles of 20–60 μm exhibited transient, spatiotemporally varying, segmental contraction with the appearance of sausage strings, lasting 1.5 s to several minutes, followed by prolonged marked dilatation. The segmental contraction/dilatation was seen in all six cats. Such a sausage-shaped appearance has never been observed by us in other series of experiments employing the same technique. Subtraction images revealed that large pial vessels remained unchanged during the early arteriolar contraction phase. The time sequence of events appeared to be neuronal depolarization, tissue oligaemia, arteriolar segmental contraction, marked dilation of cerebral vessels and tissue hyperaemia.

**Keywords:** spreading depression, migraine, sausage string formation, intraparenchymal arteriole, optical method

**SS2-3**

**Nociceptin modulates the release of CGRP and nitric oxide in an in vitro model of trigeminal neuron activation**

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**Background** Nitric oxide (NO) and calcitonin gene-related peptide (CGRP) are important mediators of vasodilation of blood vessels and are also algogenic substances. Both these mediators are released from trigeminal ganglion neurons; recently, NO has been indicated as one of the molecules most involved in sensitization and so in chronic headache. Nociceptin is a relatively novel peptide which interacts with ORL1 receptor, but does not bind classical opioid receptors; nociceptin produces in vivo analgesic effects and is involved in antagonism of allodynia and hyperalgesia of noxious stimuli.

**Objective** The aim of our study is to investigate which mechanisms are involved in NO-CGRP release, using as a model trigeminal ganglion neuron culture and how nociceptin could modulate this secretion.

**Methods** Trigeminal ganglion neuron cultures were prepared as described in previous studies. Briefly, ganglia from 6- to 7-day-old rats were quickly removed, digested by collagenase and trypsin, and finally neurons were collected through Percoll spin centrifugation. For plating we used from 120 × 10^3 to 150 × 10^3 cells per dish. IL-1β was used as proinflammatory stimulus at 1 ng/ml concentration. Immunocytochemical analysis against neurofilament 200 was performed to demonstrate purified neuron culture.
Results At 24–48 h, NO and CGRP release induced by IL-1 reaches maximal expression. Nociceptin modulates the release of NO.

Conclusion Nociceptin modulates the secretion of inflammatory mediators in an in vitro model of trigeminal neuron activation.

Keywords: nitric oxide (NO), IL-1β, trigeminal ganglia neurons, CGRP, nociceptin

SS2-4
Trigeminal nociception and vascular responses in two animal migraine models—cortical spreading depression vs. nitric oxide exposure

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Background Induction of cortical spreading depression (CSD) and exposure to nitric oxide (NO) donor have been used as models for migraine research. The difference between the two models in term of trigeminovascular activation has not been reported.

Objective To compare the effects on vascular compartment and trigeminal nociception between CSD and nitroglycerin models

Methods CSD was induced in rat brain by applying 3 mg of KCl on parietal cortex. Nitroglycerin was infused in the NO donor group. Changes in ultrastructure of cerebral microvessels were used as an indicator of vascular response. Trigeminal nociception was determined by the number of Fos-immunoreactive cells in trigeminal nucleus caudalis (TNC).

Results The results showed that both models can induce Fos expression in TNC. However, the number of Fos-immunoreactive cells in the CSD group was significantly greater than that of the NO model (53 ± 7 and 30 ± 8 cells per slide, respectively, P < 0.05). In contrast, vascular changes were more intense in the NO model. Such changes included increased endothelial pinocytosis, increased microvilli formation and swelling of astrocytic footplates.

Conclusion Our findings indicated that the CSD model is more effective than the NO model in terms of trigeminal nociceptive activation, but less effective in terms of induction of vascular response.

Keywords: migraine, model, cortical spreading depression, nitric oxide

SS2-5
Noxious input regulates the contribution of the 5-HT1D receptor to triptan analgesia in inflammatory pain

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Background The 5-HT1D triptan receptor subtype is predominantly expressed in ‘pain’ responsive neurons of the trigeminal and dorsal root ganglia. At the central terminals of these afferents, the receptor is sequestered within peptidergic dense core vesicles, rather than at the plasma membrane, where it would be accessible to exogenous triptan administration. This may explain why triptans are not analgesic in acute pain.

Objective To test the hypothesis that injury/pain influences 5-HT1D receptor localization and thus the ability of triptans to regulate inflammatory pain.

Methods We used immunocytochemistry to study 5-HT1D receptor distribution primary afferent terminals in the dorsal horn of the rat spinal cord in models of persistent pain and after electrical stimulation of the sciatic nerve. We also studied the effects of systemic or intrathecal injection of sumatriptan in models of acute and inflammatory pain in the mouse.

Results Persistent injury is associated with a significant up-regulation of 5-HT1D receptor expression. Neither systemic nor intrathecal injection of sumatriptan altered baseline nociceptive responses, but intrathecal injection profoundly inhibited experimentally induced hypersensitivity in inflammatory models of somatic pain.

Conclusion Depending on the route and timing of its administration, sumatriptan may regulate non-cranial pain conditions via an action on central 5-HT1D receptors.

Keywords: sumatriptan, migraine, pain, serotonin receptor, analgesia

Scientific session 3: Paediatrics

SS3-1
Familial hemiplegic migraine is linked to the FHM2 locus in an Irish pedigree

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Background Familial hemiplegic migraine (FHM) is a subtype of migraine with aura which includes motor weakness. Three loci for FHM have been described: FHM1 (chromosome 1p31), FHM2 (chromosome 1q23) and FHM3 (chromosome 1q31).

Objective To map the locus and identify the gene responsible for FHM in an Irish family.

Methods 38 participants (17 with FHM) were recruited and venous blood samples were collected with informed consent. Genomic DNA was extracted using the phenol-chloroform method and amplified by polymerase chain reaction using primer pairs for microsatellite markers in the chromosomal regions of interest. Genotyping was performed by capillary gel electrophoresis (ABI 310) and analysed using GENESCAN software. Linkage analysis was performed using the FASTLINK program. The family was examined for linkage to FHM1 and FHM2.

Results Examination of six microsatellite markers allowed exclusion of linkage to the entire FHM1 locus on chromosome 19p13 (most significant LOD score = −16.2 for D19S221; θ = 0). Evidence of linkage to chromosome 1q23 (FHM2) was established with positive LOD scores for the three studied microsatellite markers (maximum LOD score = +5.6 for D1S2705; θ = 0).

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Conclusion Familial hemiplegic migraine in this Irish pedigree is linked to the FH2 locus on chromosome 1q23. Future work will focus on screening family members for mutations in the ATPIA2 gene.

Keywords: familial hemiplegic migraine, chromosome 1q23

SS3-2
Migraine with vomiting and 5-HTT polymorphisms.
Contribution of serotonin transporter gene polymorphisms to paediatric migraine
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Objective One of the most relevant candidates in genetic studies in migraine is the serotonin transporter gene.

Methods Two functional polymorphisms of the serotonin transporter (5-HTTLPR and STin2) were analysed in 86 Hungarian paediatric migraineurs and 464 controls to assess whether these variants are associated with paediatric migraine. Patients were interviewed regarding the frequency of vomiting and abdominal pain during their attacks.

Results There was no difference between genotype or allele distribution of 5-HTTLPR and STin2 polymorphisms in the entire group of migraineurs and controls. Analysis of subgroups resulted in an association between STin2 and migraine with aura showing an excess of genotypes not containing the 10-repeat allele (P = 0.039). Furthermore, similar allele- (P = 0.037) and genotype-wise (P = 0.011) differences were found in cases with the severe vomiting and abdominal pain positive phenotype.

Conclusions These results confirm and extend the association between 5-HTT polymorphisms and migraine with aura using paediatric probands. Our data also suggest a special phenotype for paediatric migraine characterized by excessive vomiting and abdominal pain during the attack.

Keywords: serotonin transporter gene, 5-HTTLPR, STin2, migraine with aura, migraine with severe vomiting and abdominal pain

SS3-3
Basilar-type migraine: clinical, epidemiological and genetic features
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Objective To analyse the prevalence, symptomatology and genotype of basilar-type migraine (BM).

Methods From a clinic population diagnosed by a physician (ICHD-1 criteria) we recruited 105 families comprising 362 patients with non-hemiplegic migraine with aura (MA). Among these patients, 38 patients from 29 families had BM. We sequenced all exons of the CACNA1A and ATP1A2 genes in 12 BM families with an apparently autosomal dominant mode of inheritance of MA.

Results BM occurred in 10% (38/362) of MA patients. The BM patients were equally distributed among the 105 MA families (P = 0.37). The median age at onset of BM was 17 years. The basilar-type aura comprised vertigo 61%, dysarthria 53%, tinnitus 45%, diplopia 45%, bilateral visual symptoms 40%, bilateral parestesias 24%, decreased level of consciousness 21%, tinnitus 21% and ataxia 5%. In patients with vertigo, the vertigo was positional in 22%, was characterized by head motion intolerance in 65% and had a median duration of 60 min. Additional attacks of vertigo without headache occurred in 24% of BM patients. No causative mutations were identified.

Conclusion BM is common in MA patients, vertigo being the most frequent basilar-type symptom. The CACNA1A and ATP1A2 genes are unlikely to be involved in BM.

Keywords: basilar-type migraine, symptomatology, prevalence, genetics

SS3-4
Primary chronic daily headache among adolescents: a population-based study
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Objective The first survey to examine the prevalence and impact of adolescents’ primary chronic daily headache (CDH) in a large non-referral population.

Methods We conducted a two-phase CDH survey among students aged 12–14 in five selected middle schools in Taiwan. Subjects with CDH in the past year were identified and interviewed by neurologists. CDH was defined as headache occurring at a frequency of ≥15 days/month, average ≥2 h/day, for >3 months, and its subtypes were classified based on the Silberstein–Lipton criteria with modifications.

Results Of the 7900 participants, 122 (1.5%) fulfilled the criteria for primary CDH in the past year. Girls had a higher prevalence (2.4%) than boys (0.8%) (P < 0.001). Of the CDH subjects, transformed migraine was the most common subtype (56%), followed by chronic tension-type headache (34%). Six subjects (5%) overused medication. Most CDH subjects (65%) did not take any sick leave for headaches in the past semester. Only 5% consulted neurologists and only one subject was on headache prophylactic agents.

Conclusions Our study showed CDH was not uncommon in a large non-referred adolescent sample. Medication overuse was not an important underlying mechanism. This disabling
headache syndrome is generally under-recognized and under-treated in adolescents.

Keywords: adolescents, chronic daily headache, chronic tension-type headache, prevalence, medication overuse

SS3-5

Epidemiology of headache of junior high-school children in Japan: questionnaire study

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Background There have been no available epidemiological data on headache in Japan.

Objective To collect and analyse epidemiological data on headache in junior high school children in Japan.

Design Questionnaire study.

Setting Fourteen junior high schools in Kasugai City, Aichi, Japan.

Participants Six thousand four hundred and seventy-four junior high-school students aged between 13 and 15 years (3346 males, 3126 females) replied to the questionnaire survey.

Response rate was 94.2%.

Results 1478 out of 6472 students (22.8%; male 20.0%, female 25.8%) had complained of headache except for an infection-related one. Diagnostic criteria of migraine included: (1) headache frequency was at least once in a few months, (2) headache lasting more than 4 h, (3) unilateral location, (4) pulsating quality, (5) headache accompanied by at least one of the following: nausea or vomiting, photophobia, phonophobia. The prevalence of migraine was 2.3% (1.4% in males, and 3.4% in females).

Conclusion 22.8% of students have headache. The prevalence of migraine using the strict criteria in females (3.4%) was higher than in males (1.4%) in children aged between 13 and 15 years in Japan.

Keywords: child, headache, migraine, epidemiology

SS3-6

Unilateral phonophobia and photophobia: a helpful symptom for the diagnosis of trigeminal autonomic cephalgias (TACs) and hemicrania continua (HC)

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Background Patients with TACs and HC report unilateral phonophobia and photophobia on the painful side, whereas migraine patients usually report bilateral symptoms.

Objective To compare the presence of self-reported unilateral phonophobia or photophobia, or both, during attacks comparing patients with TACs or HC, and other headache types.

Methods Prospective study in patients attending a referral clinic over 5 months and those admitted for indomethacin-test.

Results Two-hundred and thirty-nine patients were studied. Thirty-six were excluded for lack of information. In episodic migraine patients two of 53 (4%) reported unilateral photophobia or phonophobia. In chronic migraine patients six of 48 (13%) complained of unilateral symptoms, with no patients with medication overuse reporting unilateral symptoms, although these patients all had underlying migraine biology. In chronic cluster headache 10/21 (48%) had unilateral photophobia or phonophobia, and this symptom appeared in 4/5 patients (80%) with episodic CH. Unilateral symptoms were reported by 6/10 patients (55%) with HC, 5/9 (56%) with SUNCT, and 4/6 (67%) with CPH.

Conclusion Unilateral phonophobia and photophobia is more common in TACs and HC than in migraine. The presence of unilateral symptoms may be clinically useful in the differential diagnosis of primary headaches.

Keywords: photophobia, phonophobia, trigeminal autonomic cephalgia

Scientific session 4: Hormones and headache

SS4-1

Effect of female sex steroids on CGRP-mediated vasodilation in rats

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Background 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.

Objective To investigate the effects of 17β-estradiol and progesterone on vasodilatation to α-CGRP in rat mesenteric arteries.

Methods Female Sprague-Dawley rats were ovariectomized and implanted with 21-day release pellets of placebo, 17β-estradiol or progesterone. After 18–20 days, rats were sacrificed and second order mesenteric arteries were mounted in Mulvaney myographs. The arteries were preconstricted with U46619 and cumulative concentration response curves to rat α-CGRP were constructed.

Results The potency of α-CGRP was higher in rats treated with 17β-estradiol (pEC50: 10.73 ± 0.46) compared with rats treated with progesterone (pEC50: 9.66 ± 0.25) or placebo pellets (pEC50: 9.94 ± 0.24). The Emax of α-CGRP did not differ between the groups (95 ± 3%, 88 ± 6% and 92 ± 2% of contrac tion to U46619, respectively).

Conclusion Our data demonstrate that the vasodilator potency of CGRP in the rat mesenteric artery is enhanced by treatment with 17β-estradiol. If a similar mechanism is present in the cranial vasculature, this may be one of the factors explaining the higher incidence of migraine in women.

Keywords: migraine, CGRP, 17β-estradiol, progesterone, rat
Genetic risk profiling in migraine: hormonal and vascular genotypes and susceptibility to migraine

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Background It is likely that multiple susceptibility genes play a moderate yet significant role in migraine. Objective Our study analysed two hormonal and two vascular gene variants, with a view to providing preliminary data on genetic risk profiling in migraine.

Methods The ESR1 1 gene 594 A variant and PGR gene PRO-GINS insert, along with the MTHFR gene 677 T/T variant, and the ACE gene ID/DD variant were analysed in a large Australian cohort. Susceptibility risk profiles were created and analysed using $\chi^2$ analysis and odds ratios.

Results Each hormonal variant showed significant results between the migraine and control groups and together as interacting determinants of migraine susceptibility. We are currently undertaking functional analyses to support these findings. Analysis of the vascular variants also suggested a role in migraine, both individually and in combination. Results of our initial profiling analysis revealed that individuals possessing a risk profile for either the vascular or hormonal variants are ∼5 times more likely to suffer migraine than individuals who possess a no risk genotype profile ($P = 0.0003$), with 84% of migraineurs possessing the ‘risk’ profile compared with 53% of controls.

Conclusion We have provided interesting preliminary data on genetic risk profiling in migraine.

Keywords: migraine, hormonal, vascular, genotype, risk

Hypothalamic neuropeptides orexin A and B modulation of central and peripheral pathways in the pathophysiology of migraine

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Objectives To examine the role of orexin A and B in the modulation of neurogenic dural vasodilation and dural nociceptive input to the trigeminal nucleus caudalis (TNC).

Methods Rats were anaesthetized with pentobarbitone and cannulated for measurement of blood pressure and administration of supplementary anaesthesia. The diameter of a branch of the middle meningeal artery was measured with a video dimension analyser in vivo and orexin A and B given intravenously. Orexin A and B were also microinjected into the ventrolateral periaqueductal grey and the effects on neurons in the TNC in response to dural stimulation were examined using electrophysiological techniques.

Results Neurogenic but not CGRP-induced dural vasodilation was inhibited by intravenous orexin A. This response was reversed by the selective orexin 1 receptor antagonist SB-334867. Orexin A decreased the spontaneous activity and a-

fibre-mediated responses of TNC neurons to dural electrical stimulation, an effect reversed by SB-334867. Orexin B facilitated the A- and C-fibre-mediated TNC responses to dural electrical stimulation and increased the responses to mechanical but not thermal stimulation of the cutaneous receptive field.

Conclusions Orexin A can inhibit both central and peripheral activation of the trigeminovascular system, whereas orexin B facilitates central transmission and certain receptive field properties.

Keywords: orexin, neurogenic dural vasodilation, electrophysiology

Changes in cutaneous receptor field size of trigeminal nucleus caudalis neurons after dural activation during different stages of the rat oestrous cycle

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Background No previous studies have determined if the response characteristics of the trigeminal nucleus caudalis (TNC) differ during different stages of the rat oestrous cycle after dural activation.

Objectives To ascertain if the cutaneous receptor field size of TNC neurons change during different stages of the rat oestrous cycle after dural stimulation.

Methods Twenty-three Sprague-Dawley rats (16 females, seven males) were anaesthetized and a recording electrode was placed within the TNC. A 7-mm portion of the skull was removed that was centred over the sagittal sinus. Saline and capsaicin were applied sequentially to the dura for 20 min duration. Facial receptive field sizes (RFS) were mapped after placement of saline and capsaicin in male controls and female rats during the prooestrous and diestrous stages. RFS was compared between groups using analysis of variance.

Results There was no difference in RFS after placement of saline between the groups ($P > 0.05$). A greater RFS was observed after application of capsaicin in female rats during prooestrous than those during diestrous and male rats ($P < 0.001$).

Conclusions Neurophysiological testing revealed a greater enlargement of facial RFS during the prooestrous stage compared with the diestrous stage of the rat oestrous cycle after dural activation.

Keywords: oestrous cycle, oestrogen, trigeminal nucleus caudalis, receptor field size, migraine
Prevalence of chronic frequent headache and associated factors: a population-based cross-sectional study


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**Objective** To study the prevalence of chronic frequent headache in the general population and identify associated factors.

**Methods** Questionnaires were sent to all subjects (n=21,440), aged 25–55 years, registered at 16 General Practices in the Netherlands. Headache frequency and the presence of putative risk factors were recorded. The General Health Questionnaire-28 was used to screen for psychopathology. Subjects with chronic frequent headache (>14 days/month, for at least 3 months) (n=177) were compared with subjects with infrequent headache (1–4 days/month) (n=141).

**Results** The prevalence of chronic frequent headache was 3.7% (95% CI 3.4, 4.0). Risk factors associated with chronic frequent headache were overuse of acute headache medication, mainly analgesics (OR=38.4, 95% CI 13.8, 106.9), sleeping problems (OR=8.1, 95% CI 3.6, 18.1), low educational level (OR=4.3, 95% CI 2.3, 7.8), a history of head/neck trauma (OR=4.0, 95% CI 2.2, 7.1), smoking (OR=3.1, 95% CI 1.9, 5.3), and the presence of psychopathology (OR=2.7, 95% CI 1.3, 3.6). Female sex was a risk factor for headache, not for the chronification of headache.

**Conclusions** Chronic frequent headache is common and strongly associated with overuse of analgesics. Other associated factors are low educational level, smoking, sleeping problems, a history of head or neck trauma and psychiatric comorbidity.

**Keywords:** chronic frequent headache, prevalence, risk factors, medication overuse

Scientific session 5: Imaging

Hypothalamic activation in spontaneous migraine attacks: a PET study

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**Background** On the basis of functional imaging, primary headaches have distinct activation patterns, migraine being characterized by brainstem activations and cluster headache by a hypothalamic activation. However, many migraine patients experience prodromic symptoms suggesting a primary hypothalamic dysfunction.

**Objective** The aim of this study was to record cerebral activations with positron emission tomography (PET), during spontaneous migraine without aura (MoA) attacks, before and after pain relief with sumatriptan.

**Methods** We used H 15O PET to investigate seven patients (six females, one male) with MoA (code IHS 1.1), in three situations: during the headache phase, after headache relief following sumatriptan injection, and during an attack-free interval. Statistical analysis was performed with SPM2.

**Results** Within 6 h after the attack onset we found significant activations not only in the midbrain and pons but also in the hypothalamus, all persisting after headache relief by sumatriptan.

**Conclusion** In this study, a hypothalamic implication long suspected by clinical and experimental arguments is demonstrated for the first time during spontaneous attacks of MoA. Internal clocks responsible for biological rhythms or external triggers may initiate the migraine attack via the hypothalamus and its downstream connections with midbrain and brainstem nuclei.

**Keywords:** PET, hypothalamus, migraine without aura, spontaneous attacks

In vivo measurement of human middle meningeal artery using magnetic resonance angiography: implications for the study of migraine

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**Introduction** Dilation of the middle meningeal artery (MMA) has been implicated in the pathophysiology of migraine headache. Methods to monitor in vivo diameter changes of the human MMA are, however, lacking. Here we will describe a novel method to study MMA diameter changes non-invasively in humans.

**Methods** The diameter of the MMA (extracranial part) was measured in 19 healthy volunteers using magnetic resonance angiography (MRA) in combination with a 47-mm microscopy coil before and after administration of a vasodilator (nitroglycerin 1.2 mg sublingual). A semiautomatic contour detection program was used to measure the diameter.

**Results** The in vivo diameter of the MMA was 1.5 mm (±0.26 mm) before and 1.79 mm (±0.30 mm; p<0.001) after NTG administration. This increase was 20.1% (CI 12.9, 27.3). The mean MMA diameter increase in subjects with post-NTG headache (n=11) was 0.34 mm (±0.19 mm) compared with 0.22 mm (±0.20 mm) in the eight subjects without headache (p=0.188).

**Conclusion** MRA in combination with a 47-mm microscopy coil is a novel, non-invasive method to measure diameter changes of human meningeal vessels.

**Keywords:** migraine, nitroglycerin, middle meningeal artery, magnetic resonance angiography, trigeminalvascular system
SS5-3
Posterior cortical hypoperfusion during spontaneous attacks of migraine without aura: a PET study
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Background Migraine with aura (MA) attacks are characterized by a posterior cortical hypoperfusion, not seen in migraine without aura (MoA), raising the question of two different entities.

Objective The aim of this study was to record cerebral activations with positron emission tomography (PET), during spontaneous MoA attacks, before and after pain relief with sumatriptan.

Methods We used H215O PET to investigate seven patients (six females, one male) with MoA (code IHS 1.1), in three situations: during the headache phase, after headache relief following sumatriptan injection, and during an attack-free interval. Statistical analysis was performed with SPM2.

Results Within 6 h after the attack onset a significant bilateral posterior cortical hypoperfusion was found and persisted after headache relief following sumatriptan injection (adjusted rCBF decrease: 10.34% and 12.32% before and after sumatriptan compared with headache-free period). Concomitantly activations were seen in the midbrain and pons, also persisting after sumatriptan injection.

Conclusion A posterior cortical hypoperfusion demonstrated in MoA is in favour of a common pathogenesis in MA and MoA. The concomitance of the brainstem activation and the cortical hypoperfusion, their persistence after headache relief suggest that the hypoperfusion is a vascular phenomenon triggered by the activation of vasomotor brainstem nuclei.

Keywords: PET, cortical hypoperfusion, migraine without aura, spontaneous attacks

SS5-4
Posterior hypothalamic activation in paroxysmal hemicrania using PET
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Background Paroxysmal hemicrania (PH) is a severe unilateral headache lasting 2–30 min, occurring more than five times daily, associated with trigeminal autonomic symptoms, and responsive to indomethacin.

Methods Seven PH patients were studied using positron emission tomography (PET). Each patient was scanned in three states: (1) acute PH attack—off indomethacin; (2) pain-free—off indomethacin; and (3) pain-free following administration of intramuscular indomethacin 100 mg. The scan images were processed and analysed using SPM99.

Results The study showed no significant activations during state 1 compared with state 2 but there was relative activation of the pain neuromatrix in both states 1 and 2 compared with state 3. This suggests that there is persistent activation of the pain neuromatrix during the acute PH attacks and the interictal pain-free state when off indomethacin, which is deactivated by the administration of indomethacin. In addition, there was significant activation of the contralateral posterior hypothalamus in association with the headache of PH. The study also demonstrated significant activation of the contralateral ventral midbrain, which extended over the red nucleus and the substantia nigra.

Conclusion The subcortical structures activated during the headache of PH may play a pivotal role in the pathophysiology of this syndrome.

SS5-5
Recurrent thunderclap headaches revealing reversible angiopathy of the central nervous system
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Objectives To evaluate the frequency of reversible angiopathy of the central nervous system (RACNS) in a prospective series of patients with thunderclap headaches (TCH) and to describe the features of TCH during RACNS.

Methods TCH was defined as any headache reaching a very severe maximal intensity in <1 min. All 113 patients (61 women) admitted for TCH in our departments during 2004 were prospectively investigated. Diagnoses were made according to the IHS classification. In addition, we reviewed the files of 34 patients (22 women) recruited from 2001 to 2005 who had RACNS and TCH.

Results TCH revealed intracranial disorders in 61 of the 113 patients including vascular disorders in 50 with RACNS in 21 and subarachnoid haemorrhage (SAH) in 14. In the series of 34 patients with RACNS, six took inhibitors of serotonin recapture, four vasoconstrictors and eight cannabis. In two women, onset was postpartum. All had TCH, that were recurrent in 32 over a mean period of 8 days. Sexual intercourse was a frequent trigger. A mild SAH was found in four cases and was associated with symptomatic strokes in two women.

Conclusion Recurrent TCH should prompt the search for a RACNS.

Keywords: thunderclap headache, reversible angiopathy of the central nervous system, secondary headaches, sexual headaches, subarachnoid haemorrhage

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Scientific session 6: Therapeutic advances in acute headache

SS6-1
Increased activity of rat spinal trigeminal neurons caused by nitric oxide is reversed by the CGRP receptor antagonist BIBN4096BS

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Background Nitric oxide (NO) donors and calcitonin gene-related peptide (CGRP) can provoke headaches in migraineurs. Both are elevated in venous plasma during migraine attacks, suggesting a functional link between these mediators.

Objective In an animal headache model the effect of a slow continuous infusion of the NO-donor sodium nitroprusside (SNP) and the non-peptide CGRP receptor antagonist BIBN4096BS (Boehringer Ingelheim) on spinal trigeminal neuronal activity was studied.

Methods Extracellular activity was recorded from neurons in the spinal trigeminal nucleus (STN) that received afferent input from the exposed dura mater. SNP (50 μg/kg) was infused continuously i.v. over a period of 90 min. BIBN4096BS (900 μg/kg) was injected i.v. 60 min after starting the SNP infusion.

Results Infusion of SNP was accompanied by a slow continuous elevation of the spontaneous discharge activity of STN neurons reaching a maximum after about 1 h. Intravenous injection of BIBN4096BS reversed the increase in activity within some minutes. No significant change in systemic arterial pressure was observed.

Conclusion The increase in neuronal activity in the STN provoked by NO is at least partially mediated by CGRP. Blockade of CGRP receptors may be promising in migraine therapy even after the onset of an attack.

Keywords: headache, migraine, CGRP, NO, trigeminal activity

SS6-2
Therapeutic clinical benefits of a new single-tablet formulation of sumatriptan formulated with RT Technology™ and naproxen sodium

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Background Pharmacotherapy that concurrently targets pain and inflammatory components of migraine may improve outcomes over traditional monotherapy.

Objective Evaluate efficacy and tolerability of sumatriptan formulated with RT Technology™ (SumaRT) 85 mg and naproxen sodium 500 mg (NAP), a unique fixed-dose, single-tablet formulation (SumaRT/Nap) vs. components.

Methods Two identical randomized, double-blind, placebo-controlled, parallel group, single attack (moderate/severe) multicentre studies of adult migraineurs: SumaRT/Nap, sumatriptan 85 mg RT (sumaRT), naproxen sodium 500 mg (NAP), or placebo. Therapeutic gain (TG) was calculated (placebo-subtracted proportion) for early and late endpoints (2 h pain free and 2–24 h sustained pain free).

Results Study 1 (n = 1470): at 2 h, SumaRT/Nap was more effective compared with placebo as measured by pain-free and pain-relief rates (P < 0.001). SumaRT/Nap was more effective than sumaRT, NAP, and placebo treatment groups in achieving sustained pain-free responses (P < 0.001). Sustained pain-free TG was highest for SumaRT/Nap (16.4%), followed by sumaRT (7.6%); and NAP (3.7%). All treatment groups were well tolerated and adverse events were similar. Study 2 (n = 1441): analyses are ongoing; data will be available at the time of the presentation.

Conclusion SumaRT/Nap offers improved 24-h benefits over monotherapy. The sustained pain-free TG suggests there may be a potential synergistic clinical benefit with SumaRT/Nap.

Keywords: sumatriptan, naproxen, sustained pain free, therapeutic gain, synergistic

SS6-3
Symptoms of cutaneous sensitivity pretreatment and post-treatment: results from the rizatriptan TAME study

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Background Symptoms of cutaneous sensitivity (SCS) appear during migraine. Like other associated symptoms, they may be eradicated with effective treatment. The presence of these symptoms, as surrogates for cutaneous allodynia, may predict response to acute therapy.

Methods This was a randomized double-blind study in which migraineurs were treated with rizatriptan or placebo within 1 h of headache onset. The primary endpoint was pain freedom at 2 h. Patients recorded pain severity and the presence of SCS at baseline and 2 h post-treatment. The percentage of patients with SCS was compared between groups at 2 h after treatment using logistic regression analysis.

Results Pain freedom at 2 h was greater with rizatriptan (57.3% vs. 31.1%, P < 0.001). SCS were present pretreatment in 29.2% (103/353) of rizatriptan patients and 28.8% (51/177) of placebo patients. At 2 h, the percentage of patients with SCS was significantly decreased with rizatriptan (13.4% vs. 22.0%, P < 0.001). SCS were present pretreatment in 29.2% (103/353) of rizatriptan patients and 28.8% (51/177) of placebo patients. At 2 h, the percentage of patients with SCS was significantly decreased with rizatriptan (13.4% vs. 22.0%, P < 0.001), but presence of SCS pretreatment was not predictive of response to treatment (OR = 1.25, 95% CI 0.81, 1.93; P = 0.307).

Conclusion Early treatment with rizatriptan significantly reduced the percentage of patients with symptoms of cutaneous sensitivity (SCS) at 2 h. The presence of SCS, as surrogates for cutaneous allodynia, did not predict response to acute therapy.
SS6-4

Retrospective nested case–control study for estimating a risk of triptan use in Japanese patients with chronic headache

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Background It was reported by a few investigators that migraine become a risk for cerebral infarction a couple of years ago.

Objective We commenced conducting a retrospective nested case–control study to demonstrate a relationship between risk of triptan use and multicerebral infarction (MCI).

Methods Of patients with migraine consulting our institution, 120 subjects (60 subjects in each of triptan use and non-use groups) were randomly selected for enrolment into the study on the basis of inclusion/exclusion criteria set beforehand. Observation was performed for 1 year. Clinical features (e.g. demographics, diagnosis by IHS criteria, triptan use, MCI identified by MRI and CT, other risk factors expected) were taken from medical records held our institution. The ethics aspect had been considered beforehand.

Results Patients suffering from chronic headache (CH) were statistically at risk for incidence of MCI at young generation with comparison with the general population (P < 0.001). Prevalence in CH may be much higher than that in the general population. By Cox hazard regression, we identified the statistical difference in incidence of MCI between triptan use and non-use (P = 0.023), after adjusting data for confounders.

Conclusion We suspected that CH sufferers might be at risk for incidence of MCI and triptan use probably impacted on its incidence.

Keywords: cerebral infarction, cluster headache, migraine, triptan

SS6-5

Serotonin depletion potentiates the development of cortical spreading depression and enhances the expression of VR1 receptor in trigeminal ganglia

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Background Low level of serotonin (5-HT) has been reported to coincide with the attack of headache. The mechanism explaining this relationship is still unknown.

Objectives To study the effects of 5-HT depletion on the development of cortical spreading depression (CSD) and trigeminal nociception.

Methods Wistar rats were separated into low 5-HT and control groups (eight rats each). 5-HT synthesis was inhibited by para-chlorophenylalanine. CSD was induced by cortical KCl application. Cortical activity was monitored. Changes in the trigeminal nociceptive system were determined by number of Fos immunoreactive neurons in trigeminal nucleus caudalis and VR1 immunoreactive cells in trigeminal ganglia.

Results 5-HT depletion led to an enhancement of CSD and trigeminal nociception. The area under the curve of the CSD wave was greater in the low 5-HT group compared with the control (73.1 ± 11.4 and 58.9 ± 10.0 mV/s, respectively, P = 0.02). The higher number of CSD waves was observed in the CSD group (14 ± 2 and 11 ± 1 waves, P = 0.001). The numbers of Fos- and VR-1 immunoreactive cells were also greater in the low 5-HT rats.

Conclusion Our findings indicate that 5-HT depletion enhances CSD and facilitates the trigeminal nociception. These findings may explain the relationship between low 5-HT and clinical headache.

Keywords: serotonin, headache, CSD, trigeminal nociception

SS7-1

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 doctors 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 eight (53%) with CTTH at baseline. Prognostic factors for poor outcome were baseline CTTH, coexisting migraine, not being married and sleeping problems.

Conclusion 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.

Keywords: tension-type headache, prognosis, follow-up studies, epidemiology
SS7-2
Altered pain perception is related to headache frequency. A population study
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Objective To evaluate pain sensitivity in primary headaches in the general population.
Background Pain sensitivity in migraine and tension-type headache (TTH) has been evaluated mainly in highly selected patients and longitudinal epidemiological studies are sparse.
Methods In 2001, a population-based study of headache epidemiology and pain perception was conducted in Denmark. It included both a new cross-sectional study (investigation of the stimulus–response function for pressure vs. pain) and a 12-year follow-up study (measurement of pressure pain threshold and tenderness) of a cohort from 1989. Information about headache was obtained by interview and classified according to ICHD.
Results 523 subjects participated in the cross-sectional study. A clear relation between steeper and more leftward-shifted stimulus–response functions with increasing headache frequency was seen. 388 subjects participated in the follow-up study. Pressure pain threshold decreased significantly only in those patients who developed chronic tension-type headache in the follow-up period (P = 0.04).
Conclusion This study demonstrates, for the first time in a population-based study, that increased pain sensitivity is closely related to headache frequency and may be a consequence of chronicification.
Keywords: general population, primary headaches, pain sensitivity

SS7-3
Dopamine inhibits trigeminovascular transmission in the rat
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Background Clinical observations, particularly of the premonitory phase of migraine, suggest an involvement of dopamine in the pathophysiology of the disorder. Symptoms such as food cravings, depression, lethargy, yawning, mood changes, happen before, during and after the attack.
Objectives To investigate the role of dopamine in trigeminocervical neurotransmission.
Methods Rats (n = 13) were anaesthetized (Pentobarbitone 60 mg/kg then Propofol 20–30 mg/kg/h). Extracellular electrophysiological recording was performed on neurons in the trigeminal nucleus caudalis (Vc) activated by electrical stimulation of the middle meningeal artery and on spontaneously firing units. Dopamine was administered either intravenously or via microiontophoresis directly in the Vc.
Results (i) Dopamine given intravenously did not modify Vc cell firing (P = 0.71). (ii) Cell firing was strongly and reversibly inhibited by microiontophoretic application of dopamine in a dose (current)-dependent manner: P < 0.0001 at 20–40 nA with a maximum effect 5 min after the ejection (P = 0.005).
Conclusion Dopamine strongly inhibits activation of trigemino-cervical neurons in response to MMA stimulation in vivo. This effect is only seen with microiontophoretic application and not after intravenous administration, consistent with the known poor penetration of dopamine across the blood–brain barrier. Central dopamine-containing neurons may play a role in migraine.
Keywords: migraine, dopamine, trigeminal nucleus caudalis, intravenous, microiontophoresis

SS7-4
ATP injection into neck muscles induces sustained sensorimotor facilitation via P2X receptors on TTX-sensitive muscle afferents in mice
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Background Noxious input from neck muscles probably plays a key role in the pathophysiology of tension-type headache.
Objective The electrophysiological study addressed the neuronal impact of ATP-induced noxious input from semispinal neck muscles in anaesthetized mice.
Methods Noxious stimulation of semispinal neck muscles was performed by bilateral injection of ATP (100 nM, 20 μl) in anaesthetized mice (n = 69). The impact of neck muscle noxious input on orofacial sensorimotor processing was tested by the jaw-opening reflex (JOR) elicited via electric tongue stimulation.
Results Within 2 h after ATP administration the JOR integral significantly increased by 112%. In order to investigate the role of P2X receptors and TTX-sensitive fibres in ATP-induced JOR facilitation, PPADS (P2X receptor antagonist; 3–100 nM; 20 μl) or TTX (30–100 nM; 20 μl), respectively, were intramuscularly applied 15 min before ATP injection. PPADS and TTX suppressed the ATP effect in a dose-dependent manner. PPADS and TTX also induced a recovery of facilitated JOR to baseline values when substances were applied 30 min after ATP injection.
Conclusion Thus, ATP induced and maintained strong long-term facilitation of orofacial nociceptive processing via P2X receptors on TTX-sensitive neck muscle afferents. This study may be a step towards a model of tension-type headache.
Keywords: brainstem, tension-type headache, muscle, neck, nociception

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Poster Presentations

Genetics

A001
Gene expression profiling of migraine with aura during an attack-free period
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Purpose It is also known that serotonin and neuropeptides have an important role in the pathophysiology of migraine. However, little is known about the genetic background of migraine. Therefore, we investigate the gene expression patterns associated with migraine employing gene array analysis.

Methods Data were collected from seven patients with migraine with aura (MA) and seven age-matched healthy controls. Lymphoblasts were obtained from peripheral blood. Then, we established Epstein–Barr virus-immortalized lymphoblast cell lines. Total RNAs were extracted from these cell lines and, by using them, complementary RNAs were made. These cRNAs were subjected to differential cRNA microarray analysis. Moreover, gene expression results were validated by real-time polymerase chain reaction (PCR).

Results Gene expression profiling identified 15 genes as differentially expressed in lymphoblasts of MA. One-fifth of these genes were associated with cytoskeletal proteins. The expression of seven genes significantly increased 50% more than controls, while the expression of eight genes significantly decreased 50% less than controls.

Conclusion We detected 15 human genes whose expression is significantly different from normal healthy controls. It is likely that detailed analysis of the molecular events pertinent to these gene products would lead to a better understanding of the pathophysiological mechanism of migraine.

Keywords: migraine, microarray, cytoskeletal protein, gene expression

A002
Expanding the clinical spectrum and functional consequences associated with mutations in the Na+, K+-ATPase pump gene ATP1A2
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Background Familial hemiplegic migraine (FHM) is a rare autosomal dominant subtype of migraine with aura, associated with hemiparesis. Recently the second migraine ATP1A2 gene (FHM2) was identified, encoding the α2-subunit of Na,K-pumps.

Objective To identify novel mutations in ATP1A2 and perform analysis of functional consequences of the mutations in cell survival assays.

Methods Direct sequencing of ATP1A2 and analysis of mutant Na,K-pumps in transfected HeLa cells.

Results Three novel missense mutations, G615R, V628M and R593W, were identified in the ATP1A2 gene. The G615R mutation was identified in a young girl with trauma-triggered episodes that included transient cortical blindness, hemiplegia and seizures. Family members suffered from hemiplegic migraine. Mutations V628M and R593W are the first de novo mutations and were identified in families with pure FHM. All three mutations are present in conserved, important regions of the α2-subunit. Functional cell survival assays for the G615R mutant, as shown before for other ATP1A2 mutations, revealed a complete loss of ability of transfected mutant α2-subunits to compensate for inactivated endogenous Na,K-pumps. The other two mutations show unprecedented partial compensation indicating that residual pump activity can exist with FHM2 mutations.

Conclusion Identification of three novel ATP1A2 mutations, including the first de novo mutations.

Keywords: FHM2, ATP1A2, mutations

A003
MTHFR C677T polymorphism and susceptibility to migraine with aura
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Background Several studies suggested that the C677T polymorphism of the 5,10-methylenetetrahydrofolate reductase
(MTHFR) gene is more prevalent in migraine, chiefly in migraine with aura (1-4).

**Objective** The aim of our undergoing study is to test this hypothesis on non-selected migraine patients consulting our Headache Clinic.

**Methods** We genotyped up to 131 patients: 56 with migraine with aura (MA), 75 without aura (MoA) (ICHD-II criteria) using PCR (technique see (5)). Female/male ratios were 62 : 13 for MoA and 40 : 16 for MA.

**Results** The prevalence of TT homozygosis did not significantly differ between MoA (13.3%) and MA (5.4%) ($P = 0.15$). Nor was there a significant difference in MTHFR T allele frequency between MoA (37%) and MA (30%) ($P = 0.23$).

**Conclusion** These preliminary results do not confirm the higher prevalence of MTHFR TT homozygosis in MA, in which prevalence even tends to be lower. Although our prevalence rates in migraineurs are within the range of those published in controls, a definitive conclusion has to await the results from the ongoing MTHFR genotyping of our control group.

**Keywords:** genetics, 5,10-methylenetetrahydrofolate reductase (MTHFR) polymorphism, migraine with aura, folate metabolism, homocystein

**References**


**A004**

Search for a correlation between MTHFR C677T polymorphism and efficacy of riboflavin in migraine prophylaxis

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**Background** 5,10-methylenetetrahydrofolate reductase (MTHFR) may be less active in migraine because of a higher prevalence of the C677T polymorphism in its coding gene (1-4). Riboflavin is effective in migraine prophylaxis (5, 6) and it is known to enhance MTHFR activity (7).

**Objective** The aim of this study was to search for a correlation between the presence of the MTHFR C677T polymorphism and efficacy of migraine prophylaxis with riboflavin.

**Methods** Thirty-three migraineurs [22 without aura (MoA), 11 with aura (MA), ICHD-III] were genotyped and treated for 2-19 months with riboflavin 400 mg/day. Efficacy of the prophylactic treatment was evaluated by migraine diaries.

**Results** Eighteen patients (54.5%) were heterozygous for the MTHFR C677T polymorphism CT, two (6.1%) were homoygous. The change in mean monthly attack frequency before and after Riboflavin was not significantly different between the three groups, and no correlation was found between T allele prevalence and response to treatment ($P = 0.3$). However, there was a significant effect of Riboflavin in MoA patients ($P = 0.01$) without any polymorphism correlation ($P = 0.9$).

**Conclusion** These preliminary results suggest that MTHFR C677T polymorphism does not influence the therapeutic response to riboflavin in migraine.

**Keywords:** genetics, mitochondrial metabolism, 5,10-methylenetetrahydrofolate reductase (MTHFR) polymorphism, migraine prophylaxis, Riboflavin

**References**


**A005**

A genotype-phenotype correlation study in migraine between the MTHFR C677T polymorphism and habituation of pattern-reversal visual evoked potentials

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**Background** Interictally migraineurs have on average a reduction in habituation of pattern-reversal visual evoked potentials (PR-VEP) (1) and in mitochondrial energy reserve (2). 5,10-methylenetetrahydrofolate reductase (MTHFR) is involved in folate metabolism and its C677T polymorphism may be more prevalent in migraine.
Objective To search in migraineurs for a correlation between the MTHFR C677T polymorphism and PR-VEP habituation deficit.

Methods We genotyped (3) and recorded PR-VEP in 44 migraine patients: 20 without aura (MoA), 24 with aura (MA) (IChD-II); mean age 31.5 ± 14.5 years; 34 females, 10 males.

Results Twenty patients (45.5%) had the MTHFR CC genotype, 18 (40.9%) were heterozygous CT and six (13.6%) homozygous TT. PR-VEP habituation was not significantly different between these three groups (P = 0.3), nor between MoA and MA patients. We found no correlation between habituation and T allele either (P = 0.2). Mean PR-VEP N1-P1 amplitude was significantly lower in CT (4.82 μV ± 2.0, P = 0.05) compared with CC (6.60 μV ± 3.44). This was not the case in the small TT group.

Conclusion The lack of PR-VEP habituation in migraine does not seem to be related to the MTHFR C677T polymorphism. It remains to be confirmed if this polymorphism may favor the low amplitude of evoked potentials, possibly via an impairment of brain energy metabolism.

Keywords: genetics, electrophysiology, visual evoked potentials, habituation, MTHFR C677T polymorphism

References

A006

A rare report of thrombophilic derangements associated with migraine aura in monozygous twins

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Recent evidence indicates that migraine may be involved as a risk factor for cerebral infarction in young women, thus indicating an indisputable connection between migraine and cerebral ischaemia. In the present study, we have evaluated the possible relationship between migraine and prothrombotic genetic risk factors.

M.N. and M.M. (males, 52 years), monozygous twins, as well as M.A. (female, 27 years, daughter of M.M.) have suffered from migraine aura from 15 years of age, with a familial history of cardio-cerebral vascular disease. M.N. is affected by angina pectoris and M.M. by myocardial infarction and transient ischaemic attack. Data of laboratory examinations for screening of the prothrombotic state revealed: M.N. factor XIc 128.2% (range 70–120), factor XIIc 150.4% (range 70–120), activated protein C-resistance (APC) 0.6 (range > 0.7), plasma homocysteine 29 μmol/l (range 5–15), MTHFR gene (TT/CC); M.A. factor XIIc 138.6% (range 70–120), APC-resistance 0.6 (range > 0.7), plasma homocysteine 40.2 μmol/l (range 5–15), MTHFR gene (TT/CC); M.A. factor XIIc 132.2% (range 70–120), APC-resistance 0.5 (range > 0.7), plasma homocysteine 30.6 μmol/l (range 5–15), MTHFR gene (TT/CC), PAI-1 4G/5G. Our data seem to demonstrate a strict association between migraine with aura history, cardio-cerebral vascular disease and prothrombotic genetic risk factors.

A007

Use of the Norfolk Island genetic isolate for migraine gene mapping

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Background Geographical isolation and limited environmental variation make genetic isolates powerful tools for gene mapping. Additionally, these populations generally arise from a small number of founding members, possibly from quite diverse cultural background, therefore introducing admixture effects.

Objectives Our research is aimed at identifying the genes that play a role in migraine.

Methods The Norfolk Island community is primarily descended from 18th century English (Bounty) sailors and Polynesian women. It has strong family groupings and well-documented family histories and presents interesting and unique characteristics for a genome investigation into complex disease. We have recruited individuals from this isolate, to investigate the genes involved in migraine. DNA samples from two-thirds of the Islands’ adult permanent population have been prepared for these studies.

Results 602 individuals (159 affected) have been collected with information relating to migraine, e.g. age of onset, severity, triggers and medication response obtained, and affected individuals diagnosed as MA or MoA using IHS guidelines. Most of these individuals fit within a single large, 12-generation (~ 6500 individuals) pedigree extending back to the original founders.

Conclusion This pedigree should provide a unique and powerful resource for migraine gene mapping and we are currently investigating implicated loci in this genetic isolate.

Keywords: migraine, mapping, genetic isolate, Norfolk Island

A008

Migraine, depression, dysmotility and mitochondrial inheritance

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Objective To support the hypothesis that mitochondrial dysfunction results in the high coincidences of migraine,
depression and bowel dysmotility by demonstrating high prevalence of these conditions among the matrilineal relatives of patients with maternally inherited mitochondrial disease from presumed mitochondrial DNA (mtDNA) sequence variants.

Methods Families were invited to participate in an on-line questionnaire if at least one member was diagnosed with mitochondrial disease. Based upon the reported family histories, families were assigned by the investigators to either the probable maternal inheritance (PMI) group (55 families) or the probable non-maternal inheritance (PnMI) group (111 families).

Results Migraine, depression and bowel disorders were reported at very high prevalence in the PMI mothers (54%, 51% and 60%, respectively), but were present at significantly lower prevalence rates among the PnMI mothers (26%, 12% and 16%; \( P < 0.0001 \) for each) and the fathers of both groups (range 9–16%; \( P < 2 \times 10^{-6} \) for each). Similar data were obtained comparing the prevalence rates among maternal vs. paternal grandparents, aunts and uncles.

Conclusions Migraine, depression and bowel dysmotility were the most common manifestations associated with presumed mtDNA sequence-related mitochondrial dysfunction, which supports our hypothesis that mitochondrial dysfunction is a major common factor underlying the reported association of these three conditions.

A009

Dominantly inherited migraine with aura: no mutation found in the CACNA1A or ATP1A2 genes

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Objective To investigate if the CACNA1A or ATP1A2 genes are involved in migraine with non-hemiplegic aura (MA). The autosomal dominantly inherited familial hemiplegic migraine is often caused by mutations in the CACNA1A or ATP1A2 genes. Could these genes be involved in apparently autosomal dominantly inherited MA?

Methods From a clinic population diagnosed by a physician (ICHD-1 criteria) we recruited 34 extended families (comprising 175 MA patients) with an apparently autosomal dominant mode of inheritance of MA. We performed a linkage analysis of 156 of 175 MA patients and 80 unaffected relatives using a framework marker set of 44 markers for chromosome 1 and 22 markers for chromosome 19. Additionally, at least two patients from each family plus 92 healthy, unrelated controls were selected for a sequence analysis. We sequenced the 48 exons of CACNA1A and the 23 exons of ATP1A2, including promoter and flanking intron sequences.

Results We identified no linkage to chromosome 1 or 19 and no causative mutations in CACNA1A or ATP1A2 genes.

Conclusion Our study definitively rules that MA is caused by mutations in coding regions of the CACNA1A or ATP1A2 genes and our study does not support other susceptibility loci on chromosome 1 or 19.

Keywords: Migraine with aura, CACNA1A, ATP1A2, linkage analysis, mutation screen

A010

CADASIL and headache

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a rare hereditary disease characterized by recurrent transient ischaemic attacks, strokes and vascular dementia. Various mutations in the Notch3 gene cause the disease, whereas the mechanism whereby they cause the disorder remains unknown. Migraine with or without aura is one of the characteristic symptoms of CADASIL. We here report CADASIL families with Notch3 mutations (two known and one novel mutation) in Japanese pedigrees. Headache was observed in approximately 35% of all the patients, but classical migraine (migraine with aura) was rare. We also compared Japanese and caucasian CADASIL cases and found that typical migraine (migraine with aura) was rare. We also compared Japanese and caucasian CADASIL cases and found that typical migraine (migraine with aura) was rare. We also compared Japanese and caucasian CADASIL cases and found that typical migraine (migraine with aura) was rare. We also compared Japanese and caucasian CADASIL cases and found that typical migraine (migraine with aura) was rare. We also compared Japanese and caucasian CADASIL cases and found that typical migraine (migraine with aura) was rare.

Keywords: CADASIL, Notch3, Mutation, Japan

A011

Prevalence of migraine in Noonan syndrome patients

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Objective This study investigated the prevalence of migraine in patients with Noonan syndrome (NS).

Methods Twenty-two patients with NS were recruited in outpatient clinics from the endocrine paediatric unit. For the control group we used 22 normal individuals. The NS group consisted of 11 males, 19.55 ± 6.11 years old, and 11 females, 18.81 ± 5.47 years old. The control group consisted of 11 males, 19.55 ± 6.6 years old, and 11 females, 18.81 ± 5.37 years old.

Results From NS 17 referred headache 77.27%, eight males (72.2%) and nine females (81.81%). Migraine without aura (MoA) occurred in four men and three women, probable MA (PMA) occurred in one man and two women. If computed MA and PMA we found 45.45% of migraine prevalence in NS, only MA (31.81%). For the control group we found two patients with MA (9.09%). The statistical comparison between groups showed that the prevalence of SN was more high than in the control group (\( P < 0.005 \)).

Conclusion We propose an association between SN and migraine. In the future, if this association is confirmed the 12 chromosome may be a candidate for genetic study in migraine.
A012

Investigation of a clock gene polymorphism in cluster headache (CH)

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Background Diurnal and seasonal periodicity in CH suggests that circadian/infradian rhythms regulate CH attacks. Polymorphisms in the CLOCK gene influence the circadian phase in humans.

Objective To evaluate whether a CLOCK gene polymorphism is related to CH susceptibility.

Methods 101 unrelated CH patients, 87 with circadian rhythmicity of attacks, and 100 controls underwent analysis of the T3111C single nucleotide polymorphism in the 3’ flanking region of the CLOCK gene. The polymorphism was detected by enzymatic digestion with SduI (Fermentas). Allelic and genotypic frequencies were compared by means of the Fisher’s exact test.

Results There were no significant differences in allelic frequencies between total CH and control group (χ² = 1.261, P = 0.261) also when considering the CH patients with circadian rhythmicity. Alleles were in Hardy–Weinberg equilibrium in both controls and patients.

Conclusion Our study did not support the hypothesis that the T3111C CLOCK gene polymorphism is associated with CH. Our analysis also resulted in non-significant differences when the CH patients with attack periodicity were considered.

Keywords: cluster headache, genetic, polymorphism, circadian rhythm, clock

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A013

Homozgyote deletion genotype of the angiotensin converting enzyme gene may confer protection against migraine headaches in males

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Objective Studies have shown that migraine headache has a major genetic component. Meanwhile, angiotensin converting enzyme gene (ACE) has been suggested as a genetic susceptibility factor for migraine. We investigated the role of ACE in the pathogenesis of migraines in Chinese living in Taiwan.

Methods We designed a case–control study to investigate the association of the deletion/insertion (D/I) polymorphism of the ACE between 240 patients with migraine and 200 healthy controls, matched by age and sex. The D/I polymorphism of the ACE was identified by conventional polymerase chain reaction.

Results There was no significant difference in allelic frequency (I and D) and genotype polymorphism (DD, DI and II) of the ACE between migraine patients and the controls. Analysis of the difference in the ACE polymorphism stratified by gender revealed that male migraine patients with the homozygote DD genotype (ACE-DD) were significantly fewer than were male controls (OR = 0.331, P = 0.045). There was no difference in frequency or duration of headache in each subgroup of migraine patients stratified by the ACE genotype.

Conclusion Results of our study show that ACE-DD may be a slightly protective factor for migraine patients in Chinese males living in Taiwan.

Keywords: angiotensin converting enzyme gene, association study, genetic polymorphism, migraine

A014

The C677T mutation of methylenetetrahydrofolate reductase gene and plasma homocysteine levels in Japanese patients with migraine

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Background The pathophysiology of migraine is not yet fully understood but may involve painful vasodilation of cerebral blood vessels. Recently, several case–control studies demonstrated that C677T transition in methylenetetrahydrofolate reductase (MTHFR) gene, which is supposed to increase plasma homocysteine levels, was one of the candidate genes in migraine with aura.

Objective This study was designed to determine the association between the MTHFR polymorphism and plasma homocysteine levels in Japanese patients with migraine.

Methods This study consisted of 35 patients suffering from migraine with aura (MA), 56 from migraine without aura (MoA) and 71 normal controls. Genotyping for MTHFR C677T polymorphism was performed on leucocyte genomic DNA samples by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. Plasma homocysteine levels were determined by high-performance liquid chromatography (HPLC) using fasting plasma samples.

Results Plasma homocysteine concentration in MA was significantly higher than in MoA and controls (P < 0.01). Plasma homocysteine levels in the TT genotype of MA were significantly higher with respect to each genotype in both MoA and the control group (P < 0.02).

Conclusion Our results support the conclusion that the MTHFR C677T mutation was related to hyperhomocysteinemia and a genetic risk factor for MA.

Keywords: genotyping, MTHFR, homocysteine, plasma, risk factor

A015

Catechol-O-methyltransferase gene polymorphism of migraine without aura

Jeong Wook Park, Yong Jae Kim & Kwang Soo Lee

Background Recent genetic association studies have addressed the possible genetic role of the dopaminergic system in migraine. COMT (catechol-O-methyltransferase) is an
envelope which plays a crucial role in the metabolism of dopamine and this genetic polymorphism is associated with 3-4-fold variation of enzymatic activity.

**Objectives** We assessed the role of the COMT enzyme polymorphism in the genetic susceptibility to migraine and phenotypical expression in patients with migraine without aura (MoA).

**Methods** The 97 MoA and 94 healthy volunteers were included in the study. After amplifying COMT genes by PCR, we assessed genotype and allele by restriction fragment length polymorphism (RFLP). We classified all MoA patients into two groups according to their COMT genotype; individuals who have L allele (L type, N = 43) or individuals who did not (non-L type, N = 54).

**Results** The genotype frequency and allele distribution of COMT polymorphism was not different between the MoA and control groups. MoA with L type showed more severe pain intensity (P = 0.001) and over-represented associated nausea/vomiting (94% vs. 75%; P = 0.03) compared with MoA without L type during migraine attack.

**Conclusion** The genetic factor of dopaminergic system could be involved in the clinical phenotype expression of migraine without aura, although this polymorphism does not appear to be involved in a genetic predisposition to development of migraine without aura.

**Keywords:** COMT, migraine without aura, polymorphism, dopamine

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**A016**

Serotonin transporter polymorphism and harm avoidance personality in migraine without aura

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**Objective** To investigate the 5-HTTLPR and VNTR polymorphism and HA dimension in migraine without aura.

**Background** Serotonin transporter protein (5-HTT) is a key modulating protein in synaptic serotonergic neurotransmission. Two polymorphic regions of the 5-HTT gene-linked polymorphic region has been detected: promoter polymorphism located in the proximal 5-regulatory region of 5-HTT coding sequence (5-HTTLPR) and the intron 2 variable number tandem repeat (VNTR) polymorphism. 5-HTTLPR and VNTR are often associated with a number of neurological conditions, including mood disorders and difference of responsiveness to SSRI. The harm avoidance (HA) personality trait may be heritable and associated with serotonergic neurotransmitter activity.

**Methods** We amplified the 5-HTTLPR and VNTR by means of polymerase chain reaction and performed genotype polymorphism analyses and we investigated the serotonin-related personality trait by evaluating the HA dimension in a tridimensional personality questionnaire (TPQ) in 77 patients with migraine without aura (MoA) and in 100 healthy controls.

**Results** The genotype frequency and allele distribution of 5-HTTLPR was not different between the MoA and control groups. We found that 12/12 genotype of VNTR frequency was significantly higher in patients with MoA (89.6%) than in controls (77%; P = 0.03). Patients with MoA had significantly higher HA scores (21.9 ± 6.4) than controls (16.3 ± 6.1) (P < 0.001).

**Conclusions** This suggests serotonergic activity might be involved in development of migraine without aura and VNTR might be one of the genetically contributing factors.

**Keywords:** 5-HTTLPR, VNTR, polymorphism, migraine without aura, harm avoidance

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**A017**

Association studies on the GABA-receptor, endothelin system, ESR1 and MTHFR genes in a large sample of Finnish migraine with aura patients

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**Background** Polymorphisms in methylenetetrahydrofolate reductase (MTHFR) and oestrogen receptor ESR1 genes are among the few replicated genetic associations in migraine. Additional interesting functional candidates include the GABA-cluster in chromosome 15 and endothelin system genes.

**Objective** We aimed at evaluating the contribution of these genes in migraine susceptibility in a large Finnish case–control sample.

**Methods** We studied 898 unrelated migraine with aura (MA) patients with a family history of migraine and 900 migraine-free controls, originating from a population-based twin cohort and without a family history of migraine. Instead of studying only the previously migraine-associated polymorphisms, we wanted to cover the entire genes including 5′- and 3′-flanking areas and thus genotyped altogether six MTHFR, 26 ESR1, 35 GABA-receptor and 36 endothelin system polymorphisms.

**Results** GABA and endothelin genotyping is ongoing. P-values for the C677T MTHFR and the G2014A ESR1 variants were 0.827 and 0.548. ESR1 SNP rs655710 gave a P-value of 0.007, but this was not significant after correcting for multiple testing.

**Conclusion** We did not detect association to MTHFR or ESR1 in Finnish MA patients, although our study had 80–90% power. This suggests that these genes do not have a major contribution to MA at least in the Finnish population.

**Keywords:** migraine with aura, MTHFR, ESR1, GABA, endothelin

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A018

Association of migraine with genetic variants of the NOTCH3 gene
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Objective Migraine has a genetic background. CADASIL, a genetic vascular disorder caused by mutations in the NOTCH3 gene, often occurs with migraine attacks. We analysed parts of the NOTCH3 gene in migraine patients.

Methods 97 migraine patients (27 with aura; mean age 39 years, 82 female) and 97 healthy controls were enrolled. The exons 3 and 4 of the NOTCH3 gene were amplified. After sequence electrophoresis, the alleles of the two SNPs rs3815188 and rs1043994 were determined. Allele and genotype frequencies were compared.

Results We did not observe any new mutations in exons 3 and 4. Hardy–Weinberg equilibrium was shown in patients and in controls. For the SNP rs1043994, we observed a significant association in the migraine sample for genotypes (P = 0.008) and for alleles (P = 0.005). This significant association was caused by the migraine patients without but not with aura (P = 0.006; OR = 4.5, CI 1.6, 12.9).

Conclusion New mutations in exons 3 and 4 do not play a major role in migraine pathophysiology. However, there was a significant association of migraine without aura with a SNP that does not lead to an amino acid exchange. This SNP might be in linkage disequilibrium with another functional variant in the NOTCH3 gene.

Keywords: migraine, polymorphism, genetics

Neurobiology of headache

B001

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

Methods 30 healthy controls and 30 age-matched migraineurs during a 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 migraineur 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).

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

B002

Nitroglycerin enhances superoxide dismutase (SOD) activity in spinal trigeminal nucleus
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Background Nitroglycerin (NTG), an exogenous NO donor, triggers delayed migraine attacks in migraineurs. SOD (EC1.15.1.1), an antioxidative defence system but also a mediator of persistent pain (Chung, 2004), was found decreased in migraineurs’ erythrocytes and platelets. In animal studies, enhanced superoxide concentrations in lissencephalic and gyrencephalic cortices was observed after sumatriptan administration.

Objective To study the effect of NTG on SOD activity in blood and spinal trigeminal nucleus (STN), 4 h after its administration.

Methods 14 adults Wistar rats were established in two groups: group NTG (n = 7), animals receiving nitroglycerin (10 ml/kg b.w., s.c.); and group C (n = 7), rats serving as control. Animals were sacrificed 4 h after NTG injection; blood and C1-C2 spinal cord (STN) were taken for biochemical investigation.

Results Four hours after NTG administration, SOD activity in blood (units/Hb) presented no significant differences compared with control group (22.9 ± 10 vs. 28.1 ± 5.7), while in STN (units/mg protein) it was significantly (P < 0.05) increased (2.7 ± 1.01 vs. 4.48 ± 1.68).

Conclusion Our results demonstrate that NTG modifies not only the NO level in STN but also SOD activity. A disturbance in SOD activity could thus be implied in delayed migraine attacks in migraineurs after NTG administration.

Keywords: superoxide dismutase, spinal trigeminal nucleus, nitroglycerin, headache

B003

Effects of acute and chronic restraint stress on nitroglycerin-induced hyperalgesia in rats
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Background Nitric oxide (NO) plays an important role in initiation and maintenance of pain, and nitroglycerin activates spinal and brain nociceptive structures. Acute and chronic stress induce biochemical changes affecting both pain
threshold and behaviour, and the biological pattern of depression can be mimicked in the laboratory using chronic unavoidable stress paradigms (learned helplessness).

Objective To evaluate the effects of acute and chronic immobilization on pain response to nitroglycerin in the rat.

Methods Pain perception was expressed as the latency of response to a tail flick test (hot stimulus). Measures were made 1, 2 and 4 h following nitroglycerin (10 mg/kg i.p.) or vehicle.

Results Nitroglycerin caused hyperalgesia after 2 and 4 h ($P < 0.05$). Acute stress (90 min) induced a clear analgesic state ($P < 0.01$ vs. non-stressed animals), and nitroglycerin injection could not reverse stress-induced analgesia. By contrast, chronic immobilization (7 days) significantly increased pain response ($P < 0.05$); this effect was further enhanced by nitroglycerin ($P < 0.05$ vs. vehicle).

Conclusion Chronic stress conditions mimicking biological depression enhance hyperalgesia induced by nitroglycerin. This may be particularly relevant to migraine, since nitroglycerin induces spontaneous-like attacks in humans, and an unfavourable migraine outcome (transformation into a chronic daily headache) is associated with chronic stress and comorbid depression.

Keywords: hyperalgesia, immobilization, migraine, nitric oxide, nitroglycerin

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Topiramate is able to inhibit dural blood vessel dilation in a model of trigeminovascular nociception

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Objective To examine the role of topiramate, a migraine preventive and antiepileptic, in the dural trigeminovascular system using intravitral microscopy.

Methods Rats were anaesthetized with pentobarbitone (60 mg/kg) and cannulated for measurement of blood pressure and intravenous administration of experimental drugs, and supplementary anesthesia. The parietal bone was thinned to form a cranial window through which the diameter of a branch of the middle meningeal artery was measured on-line with a video dimension analyser.

Results Topiramate (30 mg/kg) was able to inhibit neurogenic dural vasodilation generated by electrical stimulation (50–300 μA) maximally after 15 min by 52% ($t_5 = 6.78, n = 6$). NO-induced dilation (4–8 μg/kg per min) was also inhibited by topiramate maximally after 15 min at both 10 and 30 mg/kg by 21% ($t_6 = 6.09, n = 7$) and 41% ($t_6 = 5.3, n = 7$) respectively. CGRP-induced dilation (1 μg/kg) was not inhibited at either dose.

Conclusion Topiramate is likely to inhibit neurogenic dural vasodilation by inhibiting the release of CGRP from presynaptic trigeminal neurons, and thus attenuating the dural vasodilation. CGRP-induced dilation was not inhibited and therefore topiramate is unlikely to be acting postsynthetically at the blood vessels. The data are consistent with a robust effect of topiramate on trigeminovascular activation which may contribute to its antimigraine mechanisms of action.

Keywords: topiramate, trigeminovascular, dura, intravitral microscopy

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Cannabinoids modulate nociceptive dural inputs in neurons of the trigeminal nucleus caudalis

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Objective To study the effects of cannabinoids on dural nociceptive inputs to the trigeminal nucleus caudalis (TNC).

Methods Rats were anaesthetized with pentobarbitone (60 mg/kg) cannulated for measurement of blood pressure and intravenous administration of drugs and supplementary anaesthesia. Anandamide and a CB₁ receptor agonist were given and antagonized with TRPV1 and specific CB₁ receptor antagonists, respectively. The effects on neurons in the TNC in response to dural stimulation were examined using electrophysiological techniques.

Results Anandamide was able to inhibit both Aδ-fibre ($F_{2,15} = 3.79, P < 0.05$) and c-fibre ($F_{2,12.4} = 3.28, P = 0.063$) TNC firing, both maximally after 5 min ($t_5 = 3.16, P < 0.05$, and $t_5 = 3.18, P < 0.05$), but only after TRPV1 receptor inhibition. CB₁ receptor activation with WIN55,212 decreased Aδ-fibre ($F_{2.9,17.3} = 12.45, P < 0.001$, maximally by 63%), c-fibre responses ($F_{3,21.9} = 3.35, P < 0.05$, maximally by 58%) and spontaneous activity ($F_{2,4,14} = 4.0, P < 0.05$, maximally by 75%) and this was reversed by a specific CB₁ receptor antagonist.

Conclusion The results demonstrate that manipulation of CB₁ receptors can affect the response of trigeminal neurons that are specific to the ophthalmic division of the trigeminal nerve, but anandamide’s effects are restricted by its agonist activity at TRPV1 receptors.

Keywords: cannabinoids, trigeminal nucleus caudalis, ophthalmic, electrophysiology

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The role of dopamine in trigeminovascular nociception

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Objective To examine the role of dopamine in the dural trigeminovascular system using intravitral microscopy.

Methods Rats were anaesthetized with pentobarbitone (60 mg/kg) and cannulated for measurement of blood pressure and intravenous administration of experimental drugs, and supplementary anesthesia. The parietal bone was thinned to form a cranial window through which the diameter of a branch of the middle meningeal artery was measured on-line with a video dimension analyser.

Results Dopamine hydrochloride (40 μg/kg) caused a significant vasoconstriction ($n = 40$, $t_9 = 7.9, P < 0.05$) and increase in arterial blood pressure ($n = 40$, $t_9 = -11.6, P < 0.05$), that was only reversed by a $\alpha_2$-adrenoceptor antagonist. Specific dopamine receptor antagonists were unable to attenuate neurogenic dural vasodilation, while dopamine hydrochloride infusion (40 μg/kg) ($n = 7$, $t_6 = 3.92, P < 0.05$) and a specific $D_1$ receptor agonist were able to attenuate the vasodilation ($n = 6$,
**B007**

**Needle-stick induced rCBF change is affected by Na\(^+\) channel blockade, AMPA/kainate antagonism and GABA agonists, but not by voltage-dependent Ca\(^{2+}\) channel or ATP-dependent K\(^+\) channel blockade**

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**Background** It is thought that regional cerebral blood flow (rCBF) changes during cortical spreading depression (CSD) represent the experimental correlate of the aura phase of migraine. Ion homeostasis and excitatory amino acid efflux are major components of CSD. We used a needle-stick model of CSD induction to study rCBF pharmacology, *in vivo*, in order to screen for promising drug targets.

**Objective** To determine the effects of Na\(^+\) channel, voltage-gated Ca\(^{2+}\) channels, AMPA/kainate receptor, GABA receptor and ATP-dependent K\(^+\) channels on rCBF.

**Methods** Cats were anaesthetised with \(\alpha\)-chloralose (60 mg/kg) and surgically prepared for physiological monitoring and drug administration. An area of parietal bone was removed and two laser Doppler probes placed 5–10 mm apart for blood flow monitoring. An area of dura mater was removed to allow passage of a 26-G needle into the cortex for CSD induction.

**Results** A Na\(^+\) channel blocker was able to inhibit rCBF changes and decreased the speed of propagation. The ATP-activated K\(^+\) channel blocker had no effect on the rCBF changes. The AMPA/kainate antagonist and the GABA agonists were able to decrease the rate of propagation, and partially inhibit the rCBF changes.

**Conclusion** In the needle prick method of rCBF changes sodium and NMDA receptors are predominantly involved, but AMPA/kainate and GABA receptors may play some role in the mechanism.

**Keywords:** regional cerebral blood flow, cortical spreading depression

**B008**

**Anatomical and functional peculiarities of cerebral haemodynamics of migraine patients**

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**Objective** We have researched anatomical and functional peculiarities of cerebral haemodynamics of migraine patients with and without aura.

**Methods** 55 migraine patients were examined by transcranial colour Doppler and duplex sonography. The control group included 25 patients with other types of headache (primary and secondary).

**Results** The anterior communicant artery did not function in 11 (29%) migraine patients without aura and eight (47%) migraine patients with aura. There was an anomaly of the incoming vertebral artery into vertebral canal among six (35.5%) migraine patients with aura. We discovered an S-twist of interior carotic artery in four (10.5%) migraine patients without aura and one (5.9%) with aura. The analysis of intracranial blood flow has shown asymmetry of blood flow in the middle cerebral artery in seven (17%) migraine patients without aura and three (20%) migraine patients with aura. 14 (36.8%) migraine patients without aura and five (29.4%) with aura have shown asymmetry vessel reaction during functional load test.

**Conclusion** The most frequent anomalies of the extracranial artery part are anomalies of the vertebral artery entrance. In migraine patients the anterior communicant artery does not function. We have not discovered any difference of anatomical structure in the group of migraine patients without aura and migraine patients with aura.

**Keywords:** migraine, aura, cerebral haemodynamics, transcranial colour Doppler, duplex sonography

**B009**

**The effect of antagonists on adrenomedullin-induced vasodilation of dural and pial arteries studied in the genuine closed cranial window model**

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**Background and objective** Large cerebral and meningeal arteries are the only cerebral structures that mediate pain and are believed to be involved in migraine pathophysiology. Adrenomedullin (ADM) belongs to the ‘calcitonin gene-related peptide’ (CGRP) family. Since CGRP is clinically involved in migraine mechanisms, it seemed worthwhile to examine ADM.

**Methods** The studies are performed in the genuine closed cranial window model. The diameter of the middle meningeal artery and the pial artery and local cerebral blood flow (LCBF) are registered together with mean arterial blood pressure (MABP) and arterial pCO\(_2\).

**Results** 15 \(\mu\)g/kg ADM induced a strong vasodilation of dural and pial arteries and an increased LCBF. MABP decreased. In both arteries the CGRP\(_{1}\)-receptor antagonist BIBN4096BS almost completely abolished the effect of ADM, but neither ADM\(_{22-52}\) nor CGRP\(_{8-37}\) was effective in antagonizing ADM.

**Conclusion** ADM exerts effects suggesting a possible involvement in migraine mechanisms. These effects are antagonized by the effective antimigraine agent BIBN4096BS but not by other CGRP antagonists.
Keywords: migraine, adrenomedullin, antagonists, MCA, MMA

B010
Distribution of the dopamine d1 and d2 receptors in the rat trigemino-cervical complex
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Background Clinical observations, particularly of the premonitory phase of migraine, suggest an involvement of dopamine in the pathophysiology of the disorder. Symptoms such as food cravings, depression, lethargy, yawning, mood changes, happen before, during and after the attack.

Objectives Investigate the role of dopamine on trigemino-cervical neurotransmission.

Methods Rats (n = 13) were anaesthetised (pentobarbitone 60 mg/kg then propofol 20–30 mg/kg/h). Extracellular electrophysiological recording was performed on neurons in the trigeminal nucleus caudalis (Vc) activated by electrical stimulation of the middle meningeal artery and on spontaneously firing units. Dopamine was administered either intravenously or via microiontophoresis directly in the Vc.

Results (i) Dopamine given intravenously did not modify Vc cell firing (P = 0.71). (ii) Cell firing was strongly and reversibly inhibited by microiontophoretic application of dopamine in a dose (current)-dependent manner: P < 0.0001 at 20–40 nA with a maximum effect 5 min after the ejection (P = 0.005).

Conclusion Dopamine strongly inhibits activation of trigemino-cervical neurons in response to MMA stimulation in vivo. This effect is only seen with microiontophoretic application and not after intravenous administration, consistent with the known poor penetration of dopamine across the blood–brain barrier. Central dopamine-containing neurons may play a role in migraine.

Keywords: migraine, dopamine, trigeminal nucleus caudalis, intravenous, microiontophoresis

B011
Kininases and NO changes: relationship with the regulation both of circulation and analgesia in migraine
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Background Kallikrein–kinin system controls vascular tone. Kininase I is a pleiotropic regulator in inflammation.

Objective To shed some light on the role of bradykinin and histamine action on the kallikrein system in migraine we measured the activity of kininase I, the enzyme responsible for bradykinin degradation, in the venous blood of 16 migraine sufferers.

Methods Levels of prekallikrein, kallikrein, nitric oxide (NO) and kininase II [otherwise named angiotensin converting enzyme (ACE)] were measured before and after the intravenous injection of histamine hydrochloride 65 μg/kg during 12 h. Histamine was chosen since it is capable of activating the effect of bradykinin that turns in a kallikrein–kinin–kinase cascade and increases bioavailability of L-arginine for NO synthesis.

Results and conclusion Histamine administration increases NO, decreases activities of prekallikrein, kallikrein, kininase II, augments kininase I (pm/l ml 12.3 ± 3.7 SD vs. pm/ml 15.6 ± 3.4 SD, P < 0.02). Nevertheless, no local or cephalic pain relates to histamine, previously reported to cure migraine when given in the mentioned dose. Inverse histamine-induced movements of both ACE (pm/ml 5.3 ± 1.9 SD vs. pm/ml 4.0 ± 1.5 SD, P > 0.04) and NO (pm/ml 26.48 ± 7.35 SD vs. pm/ml 36.8 ± 11.58 SD, P > 0.007) seemingly exclude relevant vasomotor effects. Increase of ACE suggests a balance between histamine-bradykinin and metalloendopeptidases, including kininase II: a pain/analgesia system which might correctly act in migraine.

Keywords: migraine, kallikrein, kininase I, kininase II, nitric oxide

B012
Modulation of nociceptive dural input to orexin A and B receptor activation in the rat
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Objectives To study the effects of orexin A and B on dural nociceptive input to the trigeminal nucleus caudalis (TNC).

Methods Rats were anaesthetized with pentobarbitone (60 mg/kg) and cannulated for measurement of blood pressure, administration of experimental drugs and supplementary anaesthesia. Orexin A and B were given intravenously at 30 μg/kg and the effects on neurons in the trigeminal nucleus caudalis in response to dural stimulation were examined using electrophysiological techniques.

Results Orexin A decreased the A-fibre (F1,9,9,8 = 21.93, P < 0.001) maximally after 25 min by 30% (t5 = 19.83, n = 6, P < 0.001) but not C-fibre responses to dural electrical stimulation. This effect was reversed by the orexin 1 receptor antagonist SB-334867 (F3,5,7,5 = 0.49, P > 0.7). Spontaneous activity and responses to noxious thermal stimulation of the facial skin were unaltered. Orexin B had no effect on the response to dural stimulation or noxious and non-noxious stimulation of the facial skin. Control vehicle injection had no effect.

Conclusions The results demonstrate a differential response to orexin 1 and 2 receptor activation in the rat and support the evidence for its role in nociceptive processing.

Keywords: orexin, electrophysiology, trigeminal nucleus caudalis

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Tinnitus in migraine: an allodynic symptom secondary to abnormal cortical functioning?

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Objective To describe three patients with migraine and tinnitus as their chief complaints, in whom the tinnitus intensity consistently and exclusively increased during migraine episodes.

Methods Case report of three patients.

Results We found three female patients between the ages of 45 and 59 years with a history of migraine without aura in two, migraine with and without aura in one, hemicrania continua in one and chronic Ménière’s disease in one, in whom the neurological exams were unremarkable and secondary disorders were excluded by appropriate testing. All the patients described presence of low-intensity constant ear ringing ipsilateral to the headache, the intensity of which increased to a severe level exclusively within 1 h of the headache attack. The three patients, moreover, referred skull cutaneous hypersensitivity and two patients reported bilateral decreased hearing. In one patient the tinnitus returned to previous lower intensity level 2 h after the headache, while in two patients the symptoms lasted up to 24 h.

Conclusions In headache patients, tinnitus may be related to spontaneous and aberrant neural activity at any level along the auditory axis. We hypothesize that the tinnitus intensity increase could be an allodynic symptom related to central sensitization, or could be associated with cortical hyperexcitability.

Migraine and homocysteine

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There is recent evidence that homocysteine may be involved as a risk factor for cerebral infarction. Also, the association between migraine and hypercoagulopathic states has been observed. The aim of our work was to evaluate, in a sample of subjects with migraine, the plasmatic levels of copper, iron, folate, B12 vitamin and homocysteine. Besides, in hyperhomocysteinaemic patients we gave an additional therapy evaluating its efficacy. 150 consecutive patients (112 women), mean age 37.4 (SD 16.8), suffering from migraine with aura (26) and without aura (124) were studied and 50 patients with basal hyperhomocysteinaemia were treated with B12 vitamin and folate for 60 days. We found basal blood hyperhomocysteine in 24% of patients (55% with migraine with aura and 45% with migraine without aura), having blood values of folates and B12 vitamin lower than normal and levels of copper and iron in the limits. ANOVA test made during the follow-up, in order to compare migraine indexes of treated subjects with those of controls and both with respective basal values, showed every time significant (P < 0.05) differences in treated patients, in which basal blood homocysteine levels were reduced by 40%. Our data indicate that the administration of folates and B12 vitamin is able to produce a reduction of the migraine index and homocysteine plasmatic levels.

Psychological symptom patterns and alexithymia in migraine without aura patients

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Background Negative psychological emotions seem to be closely connected with migraine disease. Accumulating evidence indicated that alexithymic feature (i.e. difficulty to identify feelings) is a predictive factor of a broad range of psychopathology.

Objective To measure alexithymic level, and to identify possible correlation with psychological symptoms, in migraine without aura patients (MoA) compared with healthy volunteers (HV).

Results Sixty-six MoA patients and 30 HV, matched for age and sex, completed these psychometric tests: Symptom Check List (SCL-90r), evaluating tendency to somatize and to identify and report the emotions, and Toronto Alexithymia Scale (TAS-20), evaluating the level of alexithymia. The MoA patients were significantly more prone to somatize, more obsessive, depressed, anxious, hostile, phobic, paranoid and showed more psychoticism then HV. Migraineurs, moreover, scored higher then HV on full TAS-20 and Factors 1 and 2, which, respectively, means more somatic sensations accompanying emotional arousal and difficulty communicating feelings to others. SCL items positively correlated with full TAS-20 and some factors. There correlations were clearer in MoA then in HV.

Conclusion Our results showed that migraine patients are psychologically distressed and possess alexithymic features. Supplementary studies are needed to establish if such emotional regulation deficits are related to depression or vice versa.

Keywords: alexithymia, TAS-20, SCL-90r
**B016**

**Distribution and origin of TRPV1 receptors and GABA containing nerve fibres innervating the dura mater**

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**Background** Origin of characteristic throbbing pain in migraine has not been fully elucidated. Recently, nociceptive stimuli such as application of capsaicin have been demonstrated to activate TRPV1 receptors mainly distributed in sensory neurons, while GABA has been supposed to be one of the putative targets in migraine treatment.

**Objective** To examine the involvement of TRPV1 receptors and GABA in migraine, we investigated distribution and origin of TRPV1 receptors and GABA containing nerve fibres innervating the dura mater.

**Methods** Five male Sprague-Dawley rats were used for immunohistochemistry. In another five animals, retrograde axonal tracer was applied on the dura mater. Two weeks later, cranial ganglia were dissected for immunohistochemistry.

**Results** Nerve fibres with TRPV1 receptor-IR were observed in the dura mater. Some of these fibres showed CGRP-IR. GABA-positive nerve fibres were also detected in the dura mater, especially along the middle meningeal artery. The accumulation of tracer was observed in the trigeminal ganglion and the dorsal root ganglion. Some tracer accumulated neurons were also shown TRPV1 receptor-IR or GABA-IR.

**Conclusion** TRPV1 receptor and GABA may be involved in the pain control system in the dura mater, the most susceptible organ to intractable pain in migraine attacks.

**Keywords:** TRPV1 receptor, GABA, dura mater, trigeminal ganglion, nociception

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**B017**

**Neuronal excitability in migraineurs measured by transcranial magnetic stimulation. Is it modified by botulinum toxin type A?**

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**Background** Botulinum toxin type A (BTX-A) has been used as migraine prophylaxis, but its central mechanism remains unknown.

**Objective** To assess the central effect of BTX-A injection on neuronal excitability in migraineurs.

**Methods** Eleven adult patients, who met the ICHDII criteria for migraine and had at least 5 migraines a month, were enrolled in this substudy of an open-label prospective trial. Medications 1 month before transcranial magnetic stimulation (TMS) study were performed before and 1 month after BTX-A (50 units) injection in migraineurs, and also in 17 healthy volunteers.

**Results** Migraine group showed higher rMT, lower relative MEP%, and shorter CSP than the control group (P < 0.01). ICI was seen in both groups but ICF was not significant in the migraine group. These parameters did not change over a month following injection despite substantial improvements in headache.

**Conclusion** Migraineurs may have altered neuronal excitability, but it remains to be elucidated whether the clinical efficacy of BTX-A was due to its central effect on altered neuronal excitability.

**Keywords:** neuronal hyperexcitability, botulinum toxin type A, transcranial magnetic stimulation

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B019

Trigeminal nociceptive evoked potentials (TNEP) in migraine

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Background A deficit of habituation characterizes cortical evoked potentials (1) and nociceptive blink reflex in migraine between attacks (2).

Objective To study habituation of the trigeminal evoked cortical potential obtained by supraorbital A-delta fibre stimulation (TNEP) with a concentric surface electrode in healthy subjects and migraineurs (3, 4).

Methods We studied 15 healthy subjects (HS) and 20 migraineurs (15 without (MoA), 5 with aura (MA)) interictally. We averaged four blocks of 25 responses during uninterrupted stimulation (1.5 × pain threshold, 300 μs, 0.2 Hz). Habituation was defined as the percentage change of the N2-P2 amplitude between 1st and 4th block.

Results TNEP habituation did not differ significantly between HS (−33.54% ± 16.89) and migraineurs (−29.22% ± 18.22%, P = 0.47). However, perception threshold and TNEP amplitude were lower in migraineurs (P = 0.02/P = 0.03), pain threshold tended to be lower (P = 0.07) and P2 latency was longer (P = 0.008). Pain threshold was correlated positively with amplitude and negatively with attack frequency in migraineurs (P = 0.04/P = 0.03). No difference was found between MoA and MA.

Conclusion This first study of TNEP after electrical stimulation does not confirm the habituation deficit found in migraineurs after CO2 laser stimulation (5). However, decreased sensory thresholds and TNEP amplitudes may reflect persisting changes in the trigeminal system interictally.

Keywords: trigeminal nociception, pain threshold, habituation, evoked potentials, migraine

References

B020

Motion sickness and headache

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Background Migraineurs are considered to be particularly susceptible to motion sickness (MS).

Objectives To evaluate the correlation between MS, migraine and other headache disorders.

Methods We interviewed hospital employees on the occurrence of childhood (before 18 years of age) and adult life MS (continued or adult onset) and headache (IHS criteria). MS severity was calculated based on the exposure to various vehicles and the frequency of symptoms.

Results We interviewed 394 subjects (37.7 ± 9 years, range 19–80 years; 63% women). Fifty-three (13%) had migraine and 66 (17%) had a non-migrainous headache. MS during childhood (childMS) was prevalent, described by 67% of the subjects, while 10% had adult MS (adMS) only. Headaches were more prevalent among subjects with adMS who had childMS (61%) compared with those with childMS only (12%), adMS only (8%) or those who never had MS (19%, P = 0.001). The headache type was not correlated to the occurrence of childMS, adMS or the MS severity or symptoms.

Conclusions Only childhood MS which continues to adulthood is related to headache but not particularly to migraine. Brainstem involvement in the pathology of both disorders could explain our findings.

Keywords: motion sickness, headache, migraine

B021

The influence of meal composition on plasma serotonin concentration in adult migraineurs compared with controls

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Background Low brain serotoninergic activity may result in sensitization of serotonin receptors, thus increasing susceptibility to migraine attack.

Objective To evaluate the influence of meal compositions on plasma serotonin concentration in migraineurs compared with normal controls.

Methods Female migraineurs without aura and controls had after a night-fast a protein meal (ProtMeal) and 1 month later a carbohydrate meal (CarbMeal). Blood samples were collected at baseline and 1, 2, 3 and 4 h after the meal. Following platelet separation, serotonin level was measured by HPLC-electrochemical detection.

Results We studied nine migraineurs (average age 29 ± 5 years; BMI 22 ± 3) and 10 controls (average age 24 ± 4 years; BMI 21 ± 2). The CarbMeal and ProtMeal increased the serotonin levels in both groups. Decreased
levels were noted only after the ProtMeal in three migraineurs and one control. Peak changes occurred at various times. The differences between the maximum serotonin levels from baseline after the ProtMeal were 36.7 ± 48 ng/ml in the migraineurs compared with 14 ± 15 ng/ml in the controls (P = NS) and 32.0 ± 24 ng/ml and 8.7 ± 8 ng/ml, respectively, after the CarbMeal (P = 0.001).

Conclusions The effect of food on plasma serotonin levels in migraineurs is significantly different from that in subjects without headaches, implying a possible relation between food and migraine attacks.

Keywords: migraine, serotonin, food

B022
Effects of flunarizine on migraine: a transcranial magnetic stimulation study
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Objective To evaluate the influence of flunarizine on the motor evoked potentials and magnetophosphene thresholds in both migraine with aura and without aura, using transcranial magnetic stimulation (TMS).

Methods In patients with newly diagnosed migraine with aura and without aura, TMS of the motor and occipital cortex interictally were given and motor evoked potentials and magnetophosphene thresholds were recorded. After the baseline TMS studies the patients were given flunarizine 5 mg/day and were asked to report every 4 weeks. Post-therapy TMS was planned after at least 4 weeks of flunarizine therapy.

Results 59 patients completed 8 weeks of treatment, and the second TMS examination was performed in 13 patients after treatment with flunarizine. A comparison between baseline values of total pain index (TPI) and the monthly follow-up values showed a significant reduction in TPI to standard values (45.70) beginning from the first month (27.4) and after the second month (10.3). The latency of the motor evoked potential after therapy was significantly shortened compared with the values before treatment. The thresholds for phosphenes between pre- and post-therapy were not significantly different.

Conclusion Flunarizine therapy resulted in marked clinical improvement in migraine and it also appeared to influence beneficially the cerebral cortex in patients.

Keywords: migraine, transcranial magnetic stimulation, visual cortex excitability, motor evoked potentials, flunarizine

B023
Study of current perception threshold in patients with headache
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Objective To demonstrate the CPT (current perception threshold) values of cranial sites and to study the diagnostic utility of CPT testing in patients with symptoms of headache.

Methods Fifteen patients with headache and 15 normal volunteers were given auto mode CPT test at trigeminal and C2 site. Three different frequencies of stimulation were used: 2000 Hz, 250 Hz and 5 Hz. Automated double-blind mode was selected. Frequencies of abnormal CPT in two groups were compared.

Results Frequency of abnormality was 87% (13/15) and 26% (4/15) in headache group and normal control, respectively. Six of seven patients who had organic disease showed abnormal CPT and there was strong correlation between the sites of abnormal CPT and the brain structures that were involved. All four patients who showed higher CPT were proved to have organic disease.

Conclusion CPT allows for non-invasive quantitative and selective measurement of sensory nerve. CPT of trigeminal and C2 site is of great help in diagnosis of patients with headache.

Keywords: current perception threshold, headache, diagnostic, noninvasive quantitative, stimulation

B024
A revised version of the rat dural plasma protein extravasation model is predictive of clinical dose and efficacy
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Background In previous versions of the dural plasma protein extravasation (PPE) model, existing and novel therapies would inhibit PPE at very low doses and predict false-positive therapies (ex. NK-1 antagonists, CP-122,288). This work was designed to revise the PPE model protocol to predict more accurately clinical doses and efficacy. The potency of sumatriptan and rizatriptan was determined while utilizing different combinations of experimental variables in the PPE model. The optimized protocol was then used to characterize additional clinically efficacious and non-efficacious compounds (selective 5-HT1F agonist LY334370, iGlu5 antagonist LY466195, 5-HT1 agonist CP-122,288 and NK-1 antagonist LY303870). Compound levels in rat plasma were determined or extrapolated at efficacious doses from the new PPE model and compared with efficacious plasma levels from the clinic.

Results Efficacious doses determined using the revised PPE model protocol correlated with efficacious clinical doses for sumatriptan (p.o. and s.c.), rizatriptan (p.o.), LY334370 (i.v. and p.o.) and LY466195 (i.v.). Plasma exposure data from rats were also in agreement with clinical exposure levels. Efficacious doses for both CP-122,288 and LY303870 were greater than the highest dose evaluated in clinical trials.

Conclusion The revised PPE model predicts clinical dose and efficacy for the set of compounds evaluated and may explain previous false-positives.

Keywords: extravasation, dura, rat, preclinical, dose
Comparison of soluble ICAM-1, VCAM-1 and E-selectin levels in patients with episodic cluster headache, superficial temporal arteritis and healthy control subjects

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Background Adrenomedullin (ADM) is closely related to calcitonin gene-related peptide, which has a known causative role in migraine. In animals ADM has a vasodilatory effect within the cerebral circulation. For these reasons, ADM is likely to be involved in migraine.

Objective To investigate the role of ADM in migraine and the cerebral circulation.

Methods 12 migraine patients without aura were included in this double-blind placebo-controlled crossover study. Human ADM (0.08 μg/kg/min) or placebo was administered as a 20-min intravenous infusion on two separate trial days. Headache and associated symptoms were registered regularly. Cerebral blood flow was measured by 133Xenon SPECT, mean blood flow velocity in the middle cerebral artery (Vmca) by transcranial Doppler and the diameter of peripheral arterices by transdermal ultrasound.

Results ADM did not induce significantly more headache or migraine headache than placebo (P = 0.58). Cerebral blood flow and Vmca was unaffected by ADM infusion (global CBF P = 0.32, rCBFmca P = 0.38 and Vmca P = 0.18). The superficial temporal artery dilated compared with placebo (P = 0.01) and facial flushing was seen after ADM administration (P = 0.001).

Conclusion ADM is not a mediator of migraine headache and does not dilate intracranial arteries. The peptide dilated extracranial arteries without causing headache, indicating that migraine mechanisms may not be of extracranial origin.

Keywords: adrenomedullin, migraine, cerebral circulation
**B028**

**No effect of BIBN4096BS on glyceryl trinitrate (GTN)-induced migraine**

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**Background** Experimental infusion of GTN induces migraine headache in migraine patients. Calcitonin gene-related peptide (CGRP) is involved in spontaneous migraine attacks and may be involved in the development of GTN-induced headache.

**Objective and hypothesis** We tested the hypothesis that GTN causes migraine via CGRP release and hence that the CGRP-receptor antagonist BIBN4096BS can prevent delayed migraine after GTN.

**Methods** 13 patients with migraine without aura (MoA) completed this double-blinded, placebo-controlled crossover study. The patients received on both trial days an initial 20-min infusion of GTN (0.5 μg kg⁻¹ min⁻¹) followed by BIBN4096BS (10 mg) or placebo 40 min later. Headache and associated symptoms were registered regularly.

**Results** 12 patients developed immediate headache after the GTN infusion (23 episodes) and 12 patients delayed headache (22 episodes). Median peak delayed headache score on placebo days was 5 (0–10) and on active days 4 (0–9). No significant difference was recorded (P = 0.69). During the delayed headache phase seven patients fulfilled MoA criteria after placebo, five after BIBN4096BS (P = 0.75).

**Conclusion** BIBN4096BS did not prevent GTN-induced migraine, indicating that GTN does not induce migraine via release of CGRP. This suggests, if both NO and CGRP are involved in spontaneous migraine, that CGRP may work higher in the migraine cascade than NO.

**Keywords:** migraine, GTN-induced headache, BIBN4096BS

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**B029**

**Cytokine expression in different phases of cluster headache**

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**Background** Cluster headache (CH) aetiology remains obscure, but activation of hypothalamus and trigeminovascular system is involved. Alterations in numbers of immunocompetent cells are described in CH compared with healthy controls. Elevated levels of interleukin-2 (IL-2) are reported during active CH periods indicating involvement of the immunological system.

**Objectives** The study includes patients with episodic CH (IHS criteria) and matched healthy volunteers. Venous blood samples were withdrawn during CH attacks, between attacks during active CH period, and in remission and once from controls. Our aim was to investigate various cytokines during phases of episodic CH.

Methods IL-2 expression was measured using real-time reverse transcription polymerase chain reaction (RT-PCR) equipment (TaqMan®, Applied Biosystems).

**Results** So far, eight patients and six controls have been analysed. IL-2 expression levels were elevated in active CH periods, between attacks (median 9.25, range 1.2–28.0, IL-2 cDNA/GAPDH cDNA) compared with controls (median 0.98, range 0.22–1.87, P < 0.01). IL-2 expression was not significantly increased during a CH attack (median 2.79, range 0.25–6.7) or in remission (median 1.63, range 0.62–2.30).

**Conclusions** This indicates that IL-2 expression is up-regulated between CH attacks during active periods, but not during attacks and remission. The interpretation of these results will be discussed.

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**B030**

**Change of brainstem and visual processing excitability in migraine exhibiting allodynia**

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**Objective** To evaluate the changes in the brainstem trigeminal pathways and the visual processing in patients with migraine exhibiting allodynia using electrophysiological testing.

Methods Blink reflexes (BRs) and pattern-reversal visual evoked potentials (PVEPs) were obtained from 13 patients with allodynic migraine (AM), 15 patients with non-allodynic migraine (NM) and 30 healthy subjects (HS). BRs were elicited by electrical paired pulses at the interstimulus intervals (ISI) of 150, 300 and 500 ms. The ratios of the area from the second R2 (R2b) to the first R2 (R2a) were calculated for each ISI. PVEPs were recorded at 0.5 and 4.0 cpd in high (98%) and low (29%) contrasts. The ratio change of the P100 amplitudes from the low to the high contrast was calculated at each spatial frequency.

**Results** AM patients had less suppression of the R2b at the ISI of 150 and 300 ms when compared with the NM and HS. The ratio change of the PVEP amplitude at 4.0 cpd in patients with AM was less when compared with the NM and HS.

**Conclusion** Our data suggest that central sensitizations in migraine, appearing clinically as allodynia, are revealed to be due to abnormal excitability in brainstem interneurons and visual processing.

**Keywords:** migraine, allodynia, blink reflex, visual evoked potential

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**B031**

**Serum cytokine/chemokine levels in patient with migraine without aura during headache-free period**

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**Objective** We simultaneously measured 16 cytokines/chemokines in serum from patients with migraine without
aura (MoA) during headache-free period, in order to address the role of inflammation in migraine.

**Methods** In this study, 13 female patients with MoA (33.0 ± 8.8 years) were enrolled. Sera were obtained during headache-free periods. 30 female healthy, headache-free patients (29.7 ± 7.8 years) were used as controls (HC). All MoA patients and HC were on no drug treatment and negative for any allergic disorders or pathologies which could interfere with the study. Serum were collected and analysed simultaneously for 16 different cytokines and chemokines, namely IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12 (p70), IL-13, IL-17, IFN-γ, TNF-α, G-CSF, MCP-1 and MIP-1β using the Bio-Plex Cytokine Assay System.

**Results** Serum MCP-1 and IL-13 in MoA patients are significantly lower than in HC (MCP-1: 40.0 ± 20.0 pg/ml vs. 55.1 ± 19.7 pg/ml, P = 0.0186; IL-13: 1.5 ± 2.3 pg/ml vs. 3.0 ± 3.8 pg/ml, P = 0.0389). Other cytokines/chemokines do not differ significantly between MoA and HC.

**Conclusion** Serum IL-13 and MCP-1 in patients with MoA during headache-free period are significantly lower than in HC.

**Keywords:** migraine without aura, cytokine, chemokine, MCP-1, IL-13

**B032**

**Effects of sildenafil on cerebral arteries in vitro**

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**Background** Sildenafil (Viagra®), a selective inhibitor of cGMP-hydrolysing phosphodiesterase5 (PDE5), induces migraine without cerebral artery dilation in vivo.

**Objective** To evaluate the activity of PDE5 in human cerebral arteries, and to investigate if sildenafil and the PDE5 inhibitor UK-114,542 (not available for human use) dilate cerebral arteries in vitro.

**Methods** RT-PCR and Western blot established the presence in human middle cerebral artery of PDE5 mRNA and protein. The effects of sildenafil and UK-114,542 on PDE activity were investigated in enzyme-assays using homogenates of human and guinea pig cerebral arteries. The vasodilator effects were studied in isolated guinea pig basilar arteries.

**Results** Sildenafil dose-dependently decreased PDE5 activity with ~ 25% at 10 nM, whereas UK-114,542 caused ~ 50% decrease at 10 nM. Sildenafil induced an endothelium-dependent vasodilation (pEC50 6.0 ± 0.3), but primarily in concentrations above the clinically effective plasma concentrations after sildenafil 100 mg (40 nM). The dilation was augmented by the nitric oxide donor, sodium nitroprusside (SNP). UK-114,542 (pEC50 8.6 ± 0.1) was a more potent vasodilator than sildenafil.

**Conclusion** Clinically relevant concentrations of sildenafil seem to dilate isolated cerebral arteries only when coadministered with SNP. These findings seem consistent with the lack of cerebral vascular effects found in humans after sildenafil administration.

**Keywords:** sildenafil, cerebral arteries, phosphodiesterase 5, human, migraine

**B034**

**Dipyridamole induces headache and migraine**

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**Objective** Our main objective was to study the migraine generating effects of dipyridamole comparing migraine patients with healthy subjects. Dipyridamole, an unspecific inhibitor

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Conclusion

period without attack (serotonin is in the normal range but significantly lower in the ric detection, radioimmunology

Keywords: melatonin levels in the genesis of cluster headache.

Methods

Dipyriramole, 0.142 mg/kg/min, was administered intravenously, in a single-blind study, including 10 patients with migraine without aura and 10 healthy subjects. Headache intensity was scored on an 11-point numerical verbal rating scale. Pain characteristics and accompanying symptoms were recorded. Blood velocity in the middle cerebral artery (V_mca), blood pressure and heart rate were measured repeatedly.

Results

Headache was induced in all migraine patients and in eight of 10 healthy subjects. The headache in five patients but only in one healthy subject fulfilled the IHS criteria for migraine without aura within 12 h (P = 0.14). There was no significant difference in headache intensity between groups. Blood velocity decreased during and after dipyriramole infusion with no difference between groups.

Conclusion

Intravenous dipyriramole may induce symptoms of migraine in migraine patients. Stroke patients with a history of migraine may need slower dose escalation than other stroke patients.

B035

Serotonin (blood, plasma and platelet) and plasma melatonin levels in cluster headache (CH)

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Objective

To determine the implication of serotonin and melatonin levels in the genesis of cluster headache.

Methods

89 patients of the Headache Emergency Centre: 64 men (71.9%) and 25 women (28.1%), mean age 38.5 years (15–62), including 77 episodic forms (86.5%) and 12 chronic (13.5%). 72 patients (79.1%) were recorded in the period without attack and 19 (20.9%) during an attack (two patients were recorded both without and during attack). We measured out dose blood, plasma and platelet serotonin levels by high-performance liquid chromatography with fluorimetric detection and plasma melatonin level by radioimmunology.

Results

Only plasma serotonin levels are significantly higher in CH than controls. Plasma, blood and platelet serotonin are significantly higher in episodic than chronic (P < 0.01). Melatonin is in the normal range but significantly lower in the period without attack (P < 0.01).

Conclusion

CH attacks could be linked to the slight increase in melatonin level. The genetic polymorphism of melatonin receptors could explain either the negative or protective effect of melatonin on CH attacks.

Keywords: serotonin, melatonin, cluster headache, fluorimetric detection, radioimmunology

B036

The relation of pain in migraine patients and serum atrial natriuretic peptide level

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Background

Although the clinical spectrum of migraine headache, known as a trigeminovascular system disease, is well established, the physiopathology of this type of headache is less clear and we need more studies to understand it. Recently, more attention has been paid to vasoactive peptides released from vascular endothelium. Studies showing the relation of increased prevalence of migraine and atrial septal defect have led to an increased attention of atrial natriuretic factor on migraine physiopathology.

Methods

The aim of this study was to evaluate the relation of pain attacks and characteristics in migraineurs with atrial natriuretic peptide serum levels by comparing 15 migraineurs with an age- and gender-matched control group. Patients with previous prophylactic migraine therapy, cardiac medication, antihypertensive treatment, or known cardiac disease history were excluded. T-test and Spearman correlation were used for statistical analyses.

Results

Migraineurs showed significantly higher serum ANP concentrations compared with the control group (12.39 ± 4.57 pg/dl, and 6.58 ± 2.54, respectively). However, there was no correlation of pain characteristics and ANP concentrations.

Conclusion

Thus, it is concluded that ANP can be effective in migraine physiopathology and further comparative studies are needed to assess ANP to understand its role in migraine physiopathology.

Keywords: atrial natriuretic peptide, migraine

B037

Increased cerebrovascular reactivity in patients with chronic migraine: a transcranial Doppler study

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Background

A dysbalance of cerebrovascular reactivity (CR) has been implicated in the pathophysiology of migraine. Yet little is known about CR in chronic migraine.

Objective

To study CR in patients with chronic migraine compared with episodic migraine and controls.

Methods

Middle cerebral artery (MCA) flow velocities on both sides were recorded before and after hyperventilation-induced hypocapnia by transcranial Doppler. Reactivity index was calculated as the percentage of change of MCA mean velocity after hypocapnia.

Results

The study included 20 patients with chronic migraine, 20 with episodic migraine and 20 controls; the three groups were matched for age and sex. There was no significant difference between the three groups as regards MCA...
mean velocities on both sides at base line, nor were they outside the reference range, while reactivity index was higher in patients with chronic migraine (44.2 ± 7.5) than episodic migraine (43.1 ± 8.9) and controls (35.1 ± 11.3) on the right side (P < 0.01). Likewise the left side: 46.1 ± 8.7 in chronic migraine, 43.9 ± 8.1 in episodic migraine, 38.4 ± 11.7 in controls (P < 0.05). Pairwise comparison of groups showed that patients with chronic migraine had higher CR compared with episodic migraine and compared with controls.

**Conclusion** Cerebrovascular reactivity is increased in patients with chronic migraine compared with episodic migraine and controls.

**Keywords:** chronic migraine, cerebrovascular reactivity, transcranial Doppler, hypocapnia

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**B038**

**Headache and serotonergic metabolism in chronic fatigue syndrome**

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**Introduction** Headache is one of main symptoms in patients with chronic fatigue syndrome (CFS). We evaluated headache and metabolism of serotonin (5-HT) in patients with CFS, comparing with patients with migraine.

**Subjects and methods** We selected 23 patients with CFS (16 men and seven women, age 37.5 ± 11.7 years, mean ± SD), 163 migrainous patients (43 men and 120 women, age 37.5 ± 11.7 years), and 224 healthy volunteers (93 men and 131 women, age 51.0 ± 7.8 years). We determined levels of 5-HT and 5-HIAA (5-hydroxyindole acetic acid) in plasma, using high-performance liquid chromatography with electrochemical detection (HPLC-ECD). We evaluated anxiety and depression in all subjects using a self-rating questionnaire for depression and anxiety for the Japanese (SRQ-ADJ).

**Result** Ninety percent of the patients with CFS were suffering from migraine-like headache, pulsating pain and episodic hemicrania often expanding to whole headache exacerbated by motion. The levels of plasma 5-HT in the CFS patients and the migrainous patients were significantly lower than in the healthy volunteers. The levels of plasma 5-HT in the CFS patients were significantly higher than in patients with migraine. The patients with CFS and migraine were more anxious and depressive than healthy volunteers.

**Conclusion** It was suggested that headache in CFS may be often migraine-like and might have a close relationship with central levels and metabolism of 5-HT like migraine.
B041

Quantitative electroencephalography (QEEG) in migraine

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Introduction Several authors have studied background EEG activity with various quantitative methods. A majority of these studies have not been blinded, and it is possible that the process of choosing the segments for analysis can affect the results (1).

Objective To examine EEG frequencies and asymmetry in migraine using a blinded design.

Patients and methods Forty patients with 2–6 migraine attacks per month and 33 age- and sex-matched controls were included. EEG was recorded on three different days. The background activity from frontocentral, temporal and occipital regions was quantified as delta, theta, alpha and beta power (and relative power) using fast Fourier transformation (FFT). Hemispheric asymmetry (absolute value of left side–right side) was also computed.

Results Significant group differences were not found in any of the power variables. Hemispheric asymmetry was not observed.

Conclusion Migraine patients do not seem to have abnormal QEEG background activity (or asymmetry), at least when the frequencies are expressed as conventional regional bandpowers. If the relationship to the previous and/or the next headache attack does influence EEG, it may explain both our present negative results and the variable results reported in the QEEG literature on migraine.

Keywords: migraine, EEG, QEEG, power

B042

Role of nNOS in cerebral blood flow increase upon trigeminovascular activation in rats

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Objective To explore the role of rNOS and 5-HT in acute migraine attacks, changes in cerebral blood flow were measured after the injection of selective nNOS inhibitor or 5-HT1B/1D receptor agonist in a rat trigeminovascular activation model.

Methods In 20 male Sprague-Dawley rats, cortical blood flow (CoBF) on the right side was continuously monitored with the Laser-Doppler flow meter system. The ipsilateral nascorial nerve (NCN) was electrically stimulated. CoBF was measured during and after electrical stimulation of NCN under intravenous infusion of 1.0 ml saline followed by nNOS inhibitor, NOS-547 (100 μg/kg in 1.0 ml saline), or 5-HT1B/1D receptor agonist, sumatriptan (25 μg/kg in 1.0 ml saline), respectively (n = 9 and n = 11).

Result CoBF was maximally increased upon electrical NCN stimulation at 20 s from the initiation of stimulation (9.0 ± 0.7%) in the control state. This increase was significantly suppressed after the administration of NOS-547 (4.3 ± 1.4%) or sumatriptan (1.3 ± 1.5%). The blood flow increase upon electrical NCN stimulation was significantly less with NOS-547 (P < 0.005) or sumatriptan (P < 0.0001) than the control.

Conclusion This result demonstrated that nNOS plays one of the most important key roles in acute migraine attacks as well as 5-HT.

B043

Habituation of the visual evoked responses is modulated by diffuse noxious inhibitory controls (DNIC)

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Background The antinociceptive subcortical nuclei, raphe nucleus in particular, was hypothesized to modulate the habituation phenomena of visual evoked potentials (VEPs) described in healthy volunteers (HV), and its deficit observed in migraineurs between attacks (Schoenen, 1995). These subcortical formations, such as the above-mentioned raphe nucleus, the locus coeruleus, the diffuse noxious inhibitory control (DNIC) and the periaqueductal grey region (PAG), are implicated in the beginning of migraine attack.

Objective To investigate the effects of DNIC, using cold pressor test (CPT), on VEP habituation in a group of HV.

Results We recorded VEP habituation (N1-P1 percentage change between the 1st and 6th block of 100 sweeps) in eight HV and in four experimental conditions: baseline; not painful (25°C); pain (by means of the CPT to active the DNIC, 2–4°C); after-effects. We found a normal habituation at baseline and no-pain session (−10.5 and −6.9%) in all the HV. Instead, the recordings during the CPT showed a lack of habituation in seven subjects (±10%, χ² P < 0.05), persisting in the last session in six subjects (±3.4%, P < 0.05).

Conclusions It could be hypothesized that DNIC exerts its role via subcortical nociceptive nuclei and therefore its activation could modulate the visual information processing, by changing the VEPs’ habituation curve.

Keywords: habituation, VEPs, DNIC, antinociception
Involvement of 5-HT_{2A} receptor in central sensitization secondary to tissue inflammation

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Background The process of central sensitization is complex and involves several neurotransmitters. The role of 5-HT_{2A} receptor in this process is not known.

Objectives To investigate the effect of 5-HT_{2A} receptors in central sensitization induced by peripheral tissue inflammation.

Methods Male Wistar rats were divided into inflammation and control groups (10 rats each). In the inflammation group, tissue inflammation was induced by subcutaneous injection with complete Freund’s adjuvant (CFA, 0.05 ml) into forepaw. Three days after injection, a 5-HT_{2A} agonist, ketanserin (0.3 mg/kg BW) was given. Nociceptive behaviours (licking, lifting and favouring) were recorded. The paw withdrawal latency in response to noxious heat was recorded.

Result Rats receiving CFA injection exhibited nociceptive behaviour. The response to the noxious heat was enhanced in this group as indicated by shortening of the paw withdrawal latency. Pretreatment with ketanserin did not prolong the paw withdrawal latency in non-inflamed limb, indicating the lack of intrinsic analgesic effect. However, this drug significantly reduced the nociceptive behaviour and prolonged the paw withdrawal latency on the inflamed side.

Conclusion Our findings indicate that although 5-HT_{2A} receptor does not play a primary role in nociception, it may be considerably involved in the process of central sensitization, hence inducing nociceptive facilitation.

Keywords: pain, sensitization, 5-HT_{2A} receptor

Effect of sensitization of trigeminal nociceptive system on development of cortical spreading depression and trigeminal vanilloid receptor expression

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Background Sensitization of trigeminal nociceptive system is important in the pathogenesis of headache. Its effect on the cortical excitability and vanilloid receptor (VR1) expression is unknown.

Objectives To study the effects of inflammation-induced sensitization on the generation of cortical spreading depression (CSD), trigeminal nociception and VR1 expression in trigeminal ganglia (TG).

Methods Wistar rats were separated into sensitization and control groups (eight rats each). Trigeminal nociceptive system was sensitized by subcutaneous injection of complete Freund’s adjuvant (CFA, 0.1 ml) into the forehead area. CSD was induced by cortical application of KCl (3 mg). Expression of Fos in trigeminal nucleus caudalis (TNC) and VR1 in TG was determined using immunochemistry.

Results The development of KCl-induced CSD was enhanced in the CFA-treated group. The area under the curve of each CSD wave and the number of CSD waves developed within 1 h were significantly greater in the sensitized group compared with the control. Sensitization also led to the facilitation of trigeminal nociception as shown by increased Fos-immunoreactive cells in TNC. The VR1-immunoreactive cells in TG were also increased in the sensitized groups.

Conclusion The central sensitization can facilitate the development of CSD, potentiates the trigeminal nociceptive system and up-regulates VR1 expression.

Keywords: inflammation, sensitization, cortical spreading depression, Fos, VR1

Secretoneurin levels in the internal jugular blood of migraine patients assessed ictally are related to nitrates but not endothelin-1 levels

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Background Experimental evidence supports the involvement of the 33 amino acid neuropeptide secretoneurin in neurogenic inflammation.

Objective This study was aimed at determining secretoneurin levels in the internal jugular blood (IJB) samples taken serially during attacks from 10 migraine without aura (MoA) patients and to verify the relation between these levels and those of endothelin-1 (ET-1) and nitrates.

Methods Secretoneurin and ET-1 levels were measured by radioimmunoassays, nitrite levels by high-performance liquid chromatography.

Results A significant increase in secretoneurin levels was found during attacks compared with headache free-period with a peak at the first (P < 0.02) and second hours (P < 0.01). A parallel increase in nitrite levels was observed at the same time points, which were correlated with secretoneurin (R = 0.51, P < 0.01) and ET-1 (R = 0.62, P < 0.03). Higher ET-1 levels were found at each time of attack but no correlation was evident between these values and those of nitrates and secretoneurin.

Conclusion Secretoneurin seems to play a role in stimulating endothelial cells during migraine attacks as suggested by the parallel increase in nitrite levels. The rise in ET-1 levels seems to be a response to shear stress, instead of being a specific compensatory response to the effect of secretoneurin on cerebral endothelium.

Keywords: secretoneurin, migraine attacks, jugular blood, endothelin-1, nitrates
B047

Nociceptin and PGE2 levels in cerebrospinal fluid of chronic migraine and fibromyalgic patients
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Background Experimental findings have supported the involvement of the nociceptin/ORL-1 system in the mechanisms of pathological pain.

Objective The present study was aimed to investigate the cerebrospinal fluid (CSF) levels of nociceptin and PGE2 in 20 chronic migraine (CM) patients, 20 patients with probable chronic migraine (PCM) and probable analgesic-overuse headache (PAOH) and 20 patients affected by primary fibromyalgia syndrome (PFMS). Control values for nociceptin and prostaglandin E2 (PGE2) were obtained from the CSF of 20 subjects, for whom laboratory and instrumental investigations excluded diseases of the central and peripheral nervous system.

Methods CSF nociceptin and PGE2 levels were determined by sensitive immunoassays.

Results Nociceptin and PGE2 levels were significantly higher in the CSF of patients with CM, PCM + PAOH, and PFMS compared with controls (nociceptin = P < 0.01, P < 0.02, P < 0.01 and PGE2 = P < 0.03, P < 0.02, P < 0.01, respectively), without significant differences among patient groups. A significant correlation emerged between CSF nociceptin and PGE2 levels in CM (R = 0.62, P < 0.01), PCM + PAOH (R = 0.60, P < 0.02) patients and also PFMS patients (R = 0.48, P < 0.01).

Discussion A pro-nociceptive action of nociceptin related to PGE2 secretion can be hypothesized in both chronic migraine and fibromyalgia, where it seems to be related to PGE2 secretion and does not appear to be influenced by analgesic abuse.

Keywords: nociceptin, chronic migraine, cerebrospinal fluid, fibromyalgic, prostaglandin E2

B048

Endocannabinoid levels in chronic migraine: cerebrospinal fluid findings suggest a failure of this system
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Background Based on experimental evidence of antinociceptive action of endocannabinoids and their role in modulating trigeminovascular system activation, we hypothesized a dysfunction in chronic migraine (CM).

Objective To test this hypothesis, we determined the levels of anandamide (AEA), palmitoylethanolamide (PEA) and 2-arachidonoylglycerol (2-AG) in the cerebrospinal fluid (CSF) of 15 patients with CM, 15 patients with probable chronic migraine (PCM) and probable analgesic-overuse headache (PCM + PAOH) and 15 controls.

Methods Endocannabinoids purified from CSF by high-performance liquid chromatography (HPLC), and quantified by isotope dilution gas-chromatography/mass-spectrometry. Calcitonin gene-related peptide (CGRP) levels were determined by RIA method and nitrates by HPLC.

Results CSF, AEA and PEA were significantly lower in CM and PCM + PAOH patients than in controls (P < 0.01 and P < 0.02, respectively). In contrast, levels of 2-AG were below detection in both patient and control groups. A negative correlation emerged between AEA, PEA, CGRP and nitrite levels in both patient groups.

Conclusions The finding of reduced AEA and PEA levels in CSF related to the increased CGRP and nitrite production may reflect an imbalance in the endocannabinoid system in CM and PCM + PAOH patients and support the potential role of the cannabinoid CB(1) receptor as a possible therapeutic target in these patients.

Keywords: endocannabinoids, analgesic overuse, cerebrospinal fluid, chronic migraine

B049

Effects of dihydroergotamine on capsaicin- and CGRP-induced canine external carotid vasodilatation
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Background Migraine is associated with increased plasma concentrations of calcitonin gene-related peptide (CGRP), a neuropeptide released from trigeminal nerves.

Objective To investigate pharmacologically the effects of dihydroergotamine on canine external carotid vasodilator responses induced by capsaicin and exogenous CGRP.

Methods Twenty-four anaesthetized mongrel dogs prepared for measurements of external carotid blood flow (ECBF) were divided into three groups (n = 8 each). The first two groups received intracarotid (i.c.) infusions of, respectively, capsaicin (10–100 μg/min) and human α-CGRP (0.1–10 μg/min) and were subdivided into two subgroups (n = 4 each) that received i.c. infusions of, respectively, saline (1 ml/min) and dihydroergotamine (180 μg/min). The third group, subdivided into two subgroups, received i.c. capsaicin followed by the antagonists SB224289 (300 μg/kg; 5-HT1D) and BRL15572 (300 μg/kg; 5-HT1D), respectively, given i.v.; then, each subgroup received i.c. dihydroergotamine. Subsequently, the responses to capsaicin and CGRP were reanalysed.

Results Capsaicin and CGRP induced dose-dependent increases in ECBF, which remained unaffected after saline. Interestingly, the vasodilator responses to capsaicin, but not those to CGRP, were significantly inhibited after dihydroergotamine, a response reverted by BRL15572, but not by SB224289.

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**Conclusion** Dihydroergotamine seems to activate presynaptic 5-HT1β receptors that inhibit the trigeminal release of CGRP induced by capsaicin.

**Keywords:** CGRP, capsaicin, external carotid blood flow, dihydroergotamine

**B050**

**Occurrence and distribution of vanilloid, purinergic and serotonergic receptors in the trigeminovascular system of the rat—possible pain control system in migraine**

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**Objective** To clarify the role of receptors in the pain control system in the rat, distribution of vanilloid receptor (TRPV1), the ion-channel type ATP (P2X3) receptor and 5-hydroxytryptamine 1B (5-HT1β) receptor were explored in the rat trigeminovascular system.

**Methods** A total of 15 Sprague Dawley rats were perfused with fixative. The trigeminal (TG), dorsal root (DRG) ganglia, lower brain stem and spinal cord as well as the circle of Willis with its major branches, which consist of the trigeminovascular system, were dissected. TRPV1, P2X3 receptors, and CGRP were detected immunohistochemically.

**Results** TRPV1 receptors were distributed in the neurons of TG, DRG and those of dorsal column. Most of those TRPV1-positive neurons also revealed 5-HT1β receptors. The P2X3 receptors were observed in the neurons of TG, DRG and the nerve fibres in the trigeminal nucleus caudalis and the dorsal column. These P2X3-positive neurons and fibres also contained CGRP.

**Conclusion** TRPV1 and P2X3 receptors appeared in the sites where primary sensory fibres form synapses in the trigeminovascular system. Since those receptors were known to act as nociceptive receptors in pain transmission, TRPV1 and P2X3 receptors are possibly involved in the pain control system involved in migraine headache.

**Keywords:** TRPV1, P2X3 receptor, 5-HT1β receptor, trigeminovascular system

**B051**

**Lack of habituation of visual evoked gamma band oscillations in migraine patients between attacks**

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**Background** Between attacks, migraineurs lack habituation on evoked potentials and experience more visual discomfort. Visual stimuli evoke high-frequency oscillations in the gamma range (GFOs, 20–60 Hz) generated both by pre- and postsynaptic mechanisms.

**Objective** To search in migraine for abnormalities of the GFOs embedded in the classical pattern-reversal evoked potential (PR-VEP).

**Methods** The six peaks of GFOs were analysed regarding amplitude and habituation in six successive blocks of 100 averaged PR-VEPs in healthy volunteers (HV, n = 15) and interictally in patients suffering from migraine with (MA, n = 15) or without aura (MoA, n = 15).

**Results** The amplitude of the three early GFO components in the first PR-VEP block were significantly increased in MA patients (P = 0.03). There was a significant habituation deficit of the late, but not of the early, GFO peaks in migraineurs (MA and MoA) compared with HV (P < 0.05).

**Conclusions** The habituation deficit of late GFOs mimics that of the broad band PR-VEP and may suggest that postsynaptic mechanisms are responsible for this interictal abnormality of sensory processing in migraine. On the other hand, the increased amplitude of early GFOs might be related to the visual discomfort more frequently reported in MA, a hypothesis that merits to be tested.

**Keywords:** gamma band, habituation, VEPs, visual discomfort

**B052**

**COX-2 expression in primary trigeminal ganglion neurons—implications for the pathophysiology of migraine**

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NSAIDs are powerful inhibitors of cyclooxygenases (COX-1 + -2) and widely used for the treatment of migraine attacks. However, the precise role of COX in the pathophysiology of migraine is unknown. Prostaglandins are reaction products of COX. In experimental pain models prostaglandins (PG) contribute to sensitization which appears to be an important feature in migraine.

We examined the expression and function of COX-2 in rat primary trigeminal ganglion neurons. IL-1β caused a time + dose-dependent expression of COX-2 mRNA as demonstrated by real-time PCR. We identified neurons as the primary source of COX-2 using immunohistochemistry methods. COX-2 expression is mediated by IL-1 receptors and independent of nitric oxide. IL-1β stimulation of trigeminal neurons led to prostaglandin E2 release after 4 h but not after 1 h. PGE2 release could be blocked by selective and non-selective COX-2 antagonists while sumatriptan was without effect. These findings indicate that COX-2 is the major source of PGE2 release.

In summary, we could detect that primary trigeminal neurons are capable of producing COX-2 which leads to a significant release of PGE2. A similar mechanism could contribute to the generation of migraine or the sensitization of neurons during migraine attacks.

**Keywords:** migraine, COX-2, trigeminal, prostaglandin
**B053**

Cerebrospinal fluid glutamate levels are decreased in chronic migraine patients using triptans


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**Introduction** There is a putative role of glutamate in migraine pathophysiology. Little is known about the role of glutamate neurotransmission in acute medication overuse and chronic migraine.

**Objective** To analyse cerebrospinal fluid glutamate levels in chronic migraine patients using analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), ergotamines, and triptans with or without overuse.

**Methods** We studied 20 patients (eight using analgesics, NSAIDs and ergotamines, with overuse, five without overuse and seven using triptans). The patients were diagnosed with chronic migraine (CM) or probable CM according to the International Headache Society diagnostic criteria (2003). They underwent a lumbar puncture in order to rule out idiopathic intracranial hypertension. Cerebrospinal fluid (CSF) glutamate levels were measured by high-performance liquid chromatography.

**Results** CSF glutamate levels were lower in chronic migraine patients using triptans compared with patients using other medications with or no overuse (0.19 ± 0.06 vs. 0.34 ± 0.23 μmol/l) (P < 0.02).

**Discussion** Our study shows decreased glutamate levels in the CSF of CM patients using triptans compared with patients using analgesics, NSAIDs and ergotamine. The hypothesis of increase in the glutamatergic system activity in CM patients is supported by this study. Triptans may be involved in the modulation of glutamate, decreasing their levels in migraine.

**B054**

A61603-induced vasoconstriction in the porcine isolated meningeal artery: possible involvement of a novel receptor

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**Background** α1-adrenoceptors mediate vasoconstriction in the porcine carotid vasculature (1), but the underlying mechanisms are yet to be investigated.

**Objective** To characterize pharmacologically the contraction to the putative α1<sub>1A</sub>-adrenoceptor agonist A61603 (2) (N-[5-(4,5-dihydro-1H-imidazol-2-yl)-2-hydroxy-5, 6, 7,8-tetrahydrophenalen-1-yl] methane sulphonamide) in the porcine isolated meningeal artery.

**Methods** Segments of PMA were placed in Mulvany myographs and concentration response curves were constructed.

**Results** Ergotamine, dihydroergotamine, isomethyptene and sumatriptan all failed to contract the PMA (E<sub>max</sub> < 2% of contraction to 100 mM K<sup>+</sup>). In contrast, 5-HT (E<sub>max</sub> 64 ± 17%; pEC<sub>50</sub> 6.65 ± 0.25) and noradrenaline (E<sub>max</sub> 205 ± 29%; pEC<sub>50</sub> 5.72 ± 0.24) induced contractions that were antagonized by, respectively, ketanserin (10 nM) or prazosin and rauwolscine (100 nM each). Moreover, the CGRP antagonist BBN4096BS antagonized the relaxation to CGRP (E<sub>max</sub> 57 ± 4%; pEC<sub>50</sub> 8.20 ± 0.23; pK<sub>B</sub> 7.70 ± 0.15), whilst the α<sub>2A/2C</sub>-adrenoceptor antagonist OPC28326 antagonized the contraction to noradrenaline (pK<sub>B</sub> 7.46 ± 0.31).

**Conclusion** Our data demonstrate that the carotid vasooconstriction by current antimigraine drugs in anaesthetized pigs (1, 2) does not involve the PMA. Thus, other vasculature, such as arteriovenous anastomoses, may have a prominent role in migraine pathophysiology. The actions of OPC28326 and BBN4096BS suggest that α<sub>1</sub> agonists and CGRP antagonists may be future antimigraine drugs.

**Keywords:** α-adrenoceptors, BBN4096BS, CGRP, 5-HT, OPC28326

References


**B055**

Effects of current and prospective antimigraine drugs in the porcine isolated meningeal artery

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**Background** Vasoconstriction to agonists at 5-HT<sub>1</sub> receptors (1) and α-adrenoceptors (2), as well as vasodilation to CGRP (3), is well characterized in the carotid vasculature of anaesthetized pigs, but the exact location of the vasomotion remains to be investigated.

**Objective** To analyse the responses to current and prospective antimigraine drugs in the porcine isolated meningeal artery (PMA).

**Methods** Segments of PMA were placed in Mulvany myographs and concentration response curves were constructed.

**Results** The contraction to A61603 (E<sub>max</sub> 253 ± 49%; pEC<sub>50</sub> 7.17 ± 0.19) was more efficacious and more potent than that to noradrenaline (E<sub>max</sub> 204 ± 29%; pEC<sub>50</sub> 5.73 ± 0.24). Antagonists such as prazosin (α<sub>1</sub>; 1–100 nM) or rauwolscine (α<sub>1</sub>; 1–1000 nM) concentration-dependently antagonized the contractions to A61603. Interestingly, the mixed 5-HT<sub>1</sub>/<sub>2</sub> and α<sub>1</sub>/<sub>2</sub>-adrenoceptor antagonist methiothepin induced an even more pronounced antagonism.

**Conclusion** Considering its low affinity for 5-HT<sub>1</sub>/<sub>2</sub> receptors (3), our results suggest that A61603 contracts the porcine meningeal artery via α<sub>1</sub>-adrenoceptors and a novel (methiothepin-sensitive) receptor unrelated to the 5-HT<sub>1</sub>/<sub>2</sub> types. This novel receptor may be a target for future antimigraine drugs.

**Keywords:** α-adrenoceptors, A61603, 5-HT, methiothepin

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References

B056
Evidence for generalized hyperalgesia in patients with chronic tension-type headache
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Background Sensitization of the CNS may play an important role in the pathophysiology of chronic tension-type headache. Previous studies using pain thresholds as a measure of central pain sensitivity have given conflicting results, and only few studies have examined perception of pure muscle pain without involvement of adjacent tissues. Suprathreshold testing might be more sensitive than threshold measurements in evaluation of central hyperexcitability in CTTH.

Aims The aim of the study was to compare pain ratings to suprathreshold single and repetitive (2 Hz) electrical stimulation of muscle and skin in cephalic and extracephalic regions between patients with CTTH and healthy subjects.

Methods Twenty-one patients with CTTH and 21 healthy controls were included. Pain sensitivity was assessed by intramuscular needle and cutaneous electrodes in temporal, trapezius and anterior tibial regions. Two types of electrical stimulation were used: single pulse and 2 Hz. Subjective pain ratings (0–100 mm VAS) to single and repetitive electrical stimulation with intensity of 1.5 times the individual pain threshold were assessed.

Results Pain ratings to both single and repetitive suprathreshold stimulation (VAS) were higher in patients than in controls both in skin and muscle in both cephalic and extracephalic regions (P < 0.04).

Conclusions Patients with CTTH exhibit generalized cutaneous and muscular hyperalgesia when stimulated by suprathreshold electrical stimulation. This strongly supports that pain sensitivity is increased in the CNS in patients with chronic tension-type headache.

B057
Migraine, transient ischaemic attacks; methylenetetrahydrofolate-reductase gene polymorphism (C677T-MTHFR) associations and questions.
A retrospection in bibliography
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Background Since 1969, when McCully made the clinical observation linking homocysteinaemia with vascular disease, much epidemiologic evidence and many clinical studies have supported him.

Objective Since the C677T-MTHFR gene variant is diversely responsible for vascular disease, and in connection with a patient homozygous for C677T-MTHFR suffering from migraine and transient ischaemic attacks, it is discussed whether homocysteinaemia is related to this pathological condition.

Methods A 43-year-old woman with positive family history came to us because of recurrent intense episodes of migraine and transient ischaemic attacks. The pathological findings included homocysteinaemia, increased levels of protein C, low levels of vitamin B12 and homoyzygotic for the C677T polymorphism. MRI revealed leukoaraisis.

Results There are conflicting studies regarding the association of homocysteinaemia with cerebral atherosclerosis and with migraine. Although it is generally accepted that homocysteinaemia is directly related to cerebral vascular disease, it is yet to be determined whether or not it induces ischaemic strokes or is the result of the tissue dysfunction after the ischaemic stroke. The relationship of homocysteinaemia with migraine was adequately supported only in case of migraine with aura.

Conclusion While homocysteinaemia is an independent risk factor for transient ischaemic attacks, it is a point of further study whether or not it induces migraine.

Keywords: migraine, stroke, homocysteinaemia, C677T-MTHFR

B058
What kinds of aminergic tones correlate with migraine or medication overuse headache?
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Background Many biochemical studies of migraine have noted serotoninergic abnormalities.

Objective To investigate the personality dimensions related to aminergic activity in patients with migraine or medication overuse headache.

Methods From a consecutive series of 210 patients with primary headaches, we selected patients with migraine or medication overuse headache. All patients were assessed by means of the TPQ and Zung’s self-rating depression scale.

Results Fifty-four patients with migraine headaches and 10 patients with medication overuse headache were recruited. The results show that both groups of patients had significantly higher harm avoidance scores (P < 0.01) than control group (n = 20). Furthermore, patients with migraine headaches had a significantly lower score in the novelty seeking dimension (P < 0.01). Comparing only the two headache groups, we found that only the reward dependence dimension was significantly lower in patients with medication overuse headache (P < 0.05).

Conclusion The TPQ results support the use of the serotoninergic system in migraine pathophysiology. Dysfunction of the dopaminergic tone also seems to be a specific feature of migraine headaches. Moreover, dysfunction of the noradrenergic tone may have an effect on medication overuse headaches that have migraineous backgrounds.
Keywords: personality, Cloninger’s tridimensional personality questionnaire, migraine, medication-overuse headache

**B059**

**Increased plasma substance P and CGRP levels, and high ACE activity in migraineurs during headache-free periods**

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**Background** Substance P (SP), calcitonin gene-related peptide (CGRP), and angiotensin converting enzyme (ACE) may have roles in trigeminovascular nociceptive mechanisms.

**Objective** To investigate possible alteration of SP, CGRP and ACE activity in migraineurs between attacks.

**Methods** Forty-one patients suffering from migraine with aura (MA), 54 without aura (MoA), and 52 non-headache subjects (controls) participated in this study. Blood samples were collected from cubital veins during interictal periods. Samples were prepared by extraction on C18 reverse-phase columns. Plasma levels of SP and CGRP were measured by enzyme immunoassay. ACE activity was measured spectrophotometrically.

**Results** The mean interictal plasma levels of SP in MA (6.6 *±* 3.7 pg/ml; mean *±* SD) and in MoA (6.6 *±* 3.2) were significantly higher than in controls (4.8 *±* 2.4). CGRP levels in each group were 18.8 *±* 8.8, 19.1 *±* 9.4 and 13.4 *±* 4.4 pg/ml, respectively (*P* < 0.01 vs. controls). Mean ACE activity in MA was significantly higher than that in MoA and controls. There was a weak but significant positive correlation between SP and CGRP levels, and between SP and ACE activity. However, the relation between ACE activity and CGRP was not observed.

**Conclusion** Plasma SP and CGRP were increased in patients with MA and MoA during headache-free periods and ACE activity was increased in MA.

**Keywords:** substance P, calcitonin gene-related peptide, angiotensin converting enzyme, migraine

**B060**

**Effects of nitroglycerin on the nociception specific blink reflex**

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**Background** Nitroglycerin (NTG), a NO donor, induces an attack in migraine patients 4–6 h after administration. The causative mechanisms are not known. The long delay leaves room for a central effect, e.g. sensitization in the trigeminal nociceptive pathway. The nociception-specific blink reflex (nBR) is mediated in the brain stem and abnormal in migraine.

**Objective** To explore the central effects of NTG by studying its effects on the nBR in healthy volunteers.

**Results** The nBR was recorded in 10 healthy volunteers before, 1 h and 4 h after NTG administration (1.2 mg sublingual). We calculated the R2 area under the curve (AUC) by averaging five rectified sweeps, obtained by stimulating the supraorbital nerve at 1.5 times the pain threshold. We used the AUC/i2 ratio to compare AUC obtained with different stimulation intensity (i). After NTG administration, we found a significant decrease of pain (1 h: *P* = 0.004; 4 h: *P* = 0.003) and reflex thresholds (1 h: *P* = 0.009; 4 h: *P* = 0.011); while AUC/i2 was increased at both delays (1 h: *P* = 0.006; 4 h: *P* = 0.005).

**Conclusion** In healthy volunteers NTG increases trigeminal pain sensitivity and amplitude of the nBR. These findings suggest that sensitization in the trigeminal system at the level of the brainstem may play a role in the attack-triggering properties of NTG in migraine. Studies of the effect of NTG on the nBR in migraineurs are underway.

**B061**

**Distribution of TRPV1 receptors and P2X3 receptors in the trigeminovascular system of the rat. Possible involvement in migraine pathogenesis**

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**Objective** In order to elucidate involvement of TRPV1 receptors and P2X3 receptors in the pathophysiology of migraine, we investigated the distribution of these receptors in the trigeminovascular system of the rat.

**Methods** A total of 12 Sprague-Dawley rats, weighing 350–450 g, were perfused with Zamboni’s fixative. The trigeminal (TG), dorsal root ganglia (DRG), medulla and cervical segments of spinal cord, the circle of Willis with its major vascular branches were dissected. The specimens were sectioned at 4 μm thick and the pial arteries were processed as the whole mount preparation. TRPV1 receptors were detected by goat anti-rat VR1 receptor antibody (Santa Cruz Biotech. Inc.) as 1 : 1000, and P2X3 receptors were detected by guinea-pig anti-P2X3 receptor polyclonal antibody (Chemicon International Inc.) as 1 : 1000.

**Results** TRPV1 receptors were observed in the neurons of TG, DRG, spinal trigeminal nucleus and the nerve fibres around the pial arteries and P2X3 receptors were observed in the neurons of TG, DRG and the nerve fibres around the pial arteries and in the spinal trigeminal nucleus.

**Conclusion** TRPV1 receptors and P2X3 receptors are known as a nociceptor and observed in the trigeminovascular system, so that these receptors are likely to be involved in migraine pathogenesis.

**Keywords:** TRPV1 receptor, P2X3 receptor, trigeminovascular system, migraine
B062
Changes in temporal summation threshold of the nociceptive flexion reflex in medication overuse headache after withdrawal treatment
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Background It has been postulated that chronic exposure to antimigraine and/or analgesic treatment may interfere with the pain control system, leading to a central sensitization phenomenon responsible for chronic headache.

Objective The present study investigates the temporal summation threshold (TST) of the RIII reflex in medication overuse headache (MOH) patients before and after withdrawal therapy.

Methods Twenty-three MOH patients before and after withdrawal treatment and 21 age- and sex-matched controls were evaluated. TST of the RIII reflex and the subjective painful withdrawal treatment and 21 age- and sex-matched controls were enrolled. Serum Mg2+ levels were measured (mEq/l) with atomic absorption. Mean values were compared, using t-test.

Results Forty migraineurs and 40 healthy subjects enrolled. Respectively, their mean Mg2+ levels were 1.56 ± 0.27 vs. 1.55 ± 0.29 (P > 0.05), and mean Ca2+ levels were 8.04 ± 1.18 vs. 7.56 ± 0.82 (P < 0.05). Without vs. with aura subjects had lower serum Mg2+ (1.56 ± 0.26 vs. 1.76 ± 0.24 mEq/l), and higher serum Ca2+ (8.10 ± 1.23 vs. 7.64 ± 0.65) (P > 0.05). Migraineurs, with more than 3 monthly attack rate vs. lesser attack rates, had lower Mg2+ and Ca2+ (1.48 ± 0.23 vs. 1.58 ± 0.29) and (7.95 ± 0.42 vs. 8.09 ± 1.85) (P > 0.05). Menstrual migraineurs vs. non-menstrual migraineurs had lower serum Mg2+ and Ca2+ (1.47 ± 0.24 vs. 1.76 ± 0.25 and 7.77 ± 0.59 vs. 8.80 ± 2.77) (P < 0.05).

Conclusion These results confirm the role of reduced magnesium level in lowering the attacks’ threshold. Also, low Mg2+ and high Ca2+ levels in migraine without aura could exhibit a demonstrable calcium channelopathy, and also raise questions about the possibility of different mechanisms for ‘with and without aura’ migraine.

Keywords: headache, migraine, magnesium, calcium

B063
Serum ionized magnesium and calcium level in adult migraineurs during interictal period in comparison with control group
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Background Magnesium and calcium are supposed to be involved in the pathophysiology and treatment of migraine.

Objective To compare serum ionized magnesium and calcium levels in migraineurs during interictal period and control group.

Methods Migraineurs who met IHS criteria and healthy controls enrolled. Serum Mg2+ and Ca2+ levels were measured...
No increase of calcitonin gene-related peptide (CGRP) in external jugular or peripheral venous blood during migraine attack

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Background Increased calcitonin gene-related peptide (CGRP) in external jugular venous blood during migraine attack is one of the most cited findings in the headache literature. The finding, based on comparison with historic controls, has not been convincingly reproduced. We therefore investigated the issue using an intrapatient comparison design and two different assays.

Methods CGRP level was measured in the external jugular (17 patients) and cubital vein (17 + 4 patients) during and outside migraine attack without aura, with assay (I) used in most previous studies and a newer validated assay (II).

Results Assay I. Mean CGRP concentration in external jugular venous blood during attack 17.18 pmol/l compared with 15.88 pmol/l outside of attack. Mean difference 1.29 pmol/l (95% CI 2.88, 6.41, P = 0.44). In peripheral blood 16.86 pmol/l compared with 17.57 pmol/l. Mean difference – 0.71 pmol/l (95% CI 4.64, 3.06, P = 0.69). Assay II. External jugular CGRP concentration during attack 32.59 pmol/l/1 compared with 30.59 pmol/l outside of attack, mean difference 2.00 pmol/l (SE 2.39, 95% CI 3.07, 7.07, P = 0.416). In peripheral blood 33.37 pmol/l compared with 31.84 pmol/l, mean difference 1.53 pmol/l (SE 1.90, 95% CI 2.46, 5.51, P = 0.431).

Conclusion CGRP is not increased in external jugular venous blood during migraine without aura. Previous findings of elevated CGRP could not be confirmed.

Absence of direct anatomical connections between circadian and trigeminovascular systems in a higher primate

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Background Periodicity in migraine and cluster headache depends on complex relationships either involving areas that integrates multiple inputs, like posterior hypothalamus, or hormonal systems.

Objective We investigated anatomical connections between these systems in a higher primate.

Methods In four macaque monkeys, injection or apposition of anatomical tracers in the pineal gland (PG), unilaterally in suprachiasmatic nucleus (SCN) and middle meningeal artery (MMA), were followed by histological examination of brain structures. MMA was also electrically stimulated during 15 min and c-fos expression examined in the trigeminal caudal nucleus (NTC).

Results Tracer injected in the PG was present in sphenopalatine ganglia (SPG) on both sides. Tracer injected in the SCN was absent from trigeminovascular structures. Tracer apposed around the MMA was absent from circadian structures and present in ipsilateral TG and SPG. Tracers from the PG and MMA were not colocalized in SPG. C-fos was expressed in ipsilateral NTC after 15 min stimulation, showing that anatomically studied MMA was innervated by functional trigeminal sensory fibres.

Conclusion Circadian and trigeminovascular systems do not exhibit direct anatomical connections in higher primate, suggesting that biological rhythmicity in migraine and cluster headache depends on complex relationships either involving areas that integrates multiple inputs, like posterior hypothalamus, or hormonal systems.

Keywords: periodicity, migraine, cluster headache, anatomy

Re-evaluation of SSRI as prophylactics for tension, migraine and cluster headache

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Objective Re-evaluating selective serotonin reuptake inhibitor (SSRI) as prophylactics for tension, migraine and cluster headache.

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Methods Paroxetine 20 mg had been prescribed to outpatients with tension, migraine and cluster headache for 8 weeks. Severity, duration and associated symptoms of headache, effectiveness and adverse events of paroxetine were recorded and categorized in our ‘Headache Diary’.

Results The 35 patients (tension 23, migraine seven and cluster five), based on ICHD-II over a year went through this prospective analysis. Paroxetine were effective in 94% of patients. All types of headache, frequency and severity, were relieved along with reductions in attack duration. In particular, paroxetine had a dramatic effect in relieving patients with cluster headache within 3 days following prescription.

Conclusion Paroxetine is effective as prophylactics for cluster headache, particularly. At an early stage, patients complained of only minor adverse events, such as lack of appetite or sleep disorder, etc.

Keywords: SSRI, prophylactics, paroxetine, migraine and cluster headache

B069
Indomethacin increases tumour necrosis factor-alpha (TNF-α) in paroxysmal hemicrania (PH) and hemicrania continua (HC) patients

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Background PH and HC are headaches that respond absolutely and exclusively to indomethacin, as equipotent doses of other NSAIDs are not equally effective. TNF-α is a cytokine involved with a series of inflammation processes.

Objective To address the influence of indomethacin on the serum TNF-α levels in PH and HC patients, and the effects of indomethacin or acetyl salicylic acid (ASA) on healthy mice.

Methods TNF-α serum levels have been measured prior to and after oral indomethacin therapy in 11 2004 IHS female PH and HC patients. Fifteen healthy mice were tested for comparison. The first mice group did not receive any treatment, the second was treated with indomethacin and the third group received ASA.

Results TNF-α increased following indomethacin treatment in the majority of patients to a substantial extent. Before the drug administration, TNF-α concentration was 24.1 ± 59.8 (0–192) pg/ml. After indomethacin, levels rose to 202.9 ± 249.4 (0–642) pg/ml, P = 0.027. In all animals TNF-α did not reach the detection threshold, regardless of the use of drugs.

Conclusion Since TNF-α increases after NSAID intake in the presence of inflammation, the results suggest that inflammatory mechanisms might be involved with the pathophysiology of the indomethacin-responsive headaches.

Keywords: paroxysmal hemicrania, hemicrania continua, indomethacin, tumour necrosis factor

B070
The mechanism of chest symptoms after oral sumatriptan

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Background There are patients who complain of some chest symptoms after oral or subcutaneous injection of sumatriptan. The aetiology in most is still unknown except for a few patients who had ischaemic coronary changes. Chest symptoms are important problems because the patients who had chest symptoms after sumatriptan would drop out of triptan therapy. The aim of the study is to clarify the mechanism of chest symptoms after oral sumatriptan.

Objective A 24-year-old woman who has migraine with aura was recruited for the study with informed consent. She always had chest symptoms for 3 or 4 h after oral 50 mg sumatriptan.

Methods Surface electromyograms (EMG) of her cervical muscles were recorded before and after oral 50 mg sumatriptan. After the appearance of chest symptoms, 0.3 mg of atropine sulphate was injected via forearm vein to clarify whether the chest symptoms originated from the muscle contraction of the neck and chest or not.

Results The muscles of her neck continuously contracted on EMG after oral sumatriptan and completely relaxed after venous injection of atropine sulphate.

Conclusion Chest symptoms induced by oral sumatriptan originated from the continuous muscle contraction due to the release of acetylcholine by sumatriptan.

Keywords: sumatriptan, chest symptoms, electromyograms, atropine sulphate, acetylcholine

B071
Activation of the transcription factor NF-kappaB in the nucleus trigeminalis caudalis in an animal model of migraine

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Background Nitroglycerin (NTG) induces an inflammatory state in perivascular meningeal tissues of rat via the activation, inter alia, of nuclear factor kappa B (NF-kappaB).

Objective In the present study we sought to elucidate whether NF-kappaB activation might have a role in the determinism of migraine attacks also at the neuronal level. Therefore, we investigated the transcriptional activity of NF-kappaB in the brainstem of rats systemically injected with NTG and in control animals.

Methods Activation of NF-kappaB in brain areas was detected by means of both the immunohistochemical technique and Western blot analysis.

Results A significant increase of nuclear immunostaining of p65, an indicator of NF-kappaB activation, was detected in lamina I and II of nucleus trigeminalis caudalis in rats injected
Comparative analysis of the neuronal activation and cardiovascular effects of nitroglycerin, sodium nitroprusside and L-arginine

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Background Nitric oxide donors are often used to evaluate the biological effects of nitric oxide, and nitroglycerin has been used extensively in the case of migraine.

Objective In this study, we compare the effects of different nitric oxide modulators (nitroglycerin, sodium nitroprusside and L-arginine) in the rat.

Methods Fos expression and cardiovascular responses induced by the three nitric oxide donors where evaluated in male Sprague-Dawley rats.

Results Nitroglycerin and sodium nitroprusside induced a similar pattern of neuronal activation in several areas. However, only nitroglycerin activated the periaqueductal grey and nucleus trigeminalis caudalis. L-arginine-induced neuronal activation was restricted to the paraventricular and supraoptic nuclei of the hypothalamus. As regards cardiovascular effect, both nitroglycerin and sodium nitroprusside induced moderate hypotension (nitroglycerin ~23.3%, sodium nitroprusside ~24.3%) that lasted 40 min in the case of sodium nitroprusside and 80 min in the case of nitroglycerin. L-arginine did not significantly influence blood pressure.

Conclusion These data suggest that modulators of nitric oxide are associated with different biological effects on both the cardiovascular and central nervous systems. In the paradigm adopted in this study, nitroglycerin is the only drug with the capacity to activate the brainstem areas implicated in nociception.

Keywords: nitroglycerin, nitric oxide, migraine, Fos, nucleus trigeminalis caudalis

Paediatrics

C001

Sodium valproate in the prophylactic treatment of acute confusional migraine

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Background Acute confusional migraine (ACM) is recognized as a kind of paediatric migraine equivalent.

Case report A 10-year-old girl first visited our hospital because of severe headache with nausea and vomiting after complaining of visual aura, and she was diagnosed as having migraine with typical aura. Oral sumatriptan was tried and her headache severity was reduced. But another episode of ACM developed 3 months later. Severe right-frontal pulsating headache and vomiting after visual aura occurred and she developed somnolence and disorientation. Electroencephalography showed generalized slow waves without seizure discharges during the attack. She suffered five more attacks of ACM. Therefore, 400 mg/day of sodium valproate (VPA) was initiated to prevent these attacks. They have been controlled after increasing her dosage to 600 mg/day which resulted in a VPA blood level of 66.0 μg/ml. Intracranial magnetic resonance angiography (MRA) during the last ACM attack indicated narrowing of left middle and posterior cerebral arteries. However, MRA during the attack-free period at 41-day follow-up showed normal vessels.

Conclusion This case indicates that VPA is an effective treatment for the prophylaxis of ACM and that MRA is considered helpful for the diagnosis of this kind of migraine in children because of non-invasive neuroimaging.

C002

The prevalence and character of chronic headache in Japanese high-school students

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Background There are only a few reports about the prevalence and character of chronic headache in Japanese high-school students.

Objective To investigate prevalence and character of a chronic headache in high-school students in Japan.

Methods A questionnaire for headache diagnosis according to the international classification of headache disorders (ICHD) wasa distributed to 2462 high-school students.

Results The overall headache prevalence was 41.0% in boys, 55.3% in girls, and the headache onset was 12.7 years old in boys, 12.9 years old in girls. The prevalence of migraine without aura was 5.5% in boys, 6.1% in girls according to ICHD-I and 13.7% in boys, 17.5% in girls according to modified ICHD-II diagnosis criteria. For tension-type headache, it was 23.0% in boys, 30.6% in girls according to modified ICHD-I...
diagnosis criteria. High-school students with chronic headache tend to take painkillers easily, but are much less likely to visit physicians.

**Conclusion** Our data showed that the prevalence of headache, especially migraine, in Japanese high-school students was almost similar to past world-wide findings, and suggest that its impact on the quality of life can not be ignored. Therefore, headache education must be important and a necessity in a high school.

**Keywords:** headache prevalence, high school student, ICHD-II, Japanese, headache education

**C003**

**Headache prevalence in adolescents aged 12–17: a student-based epidemiological study in Bursa**

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**Objectives** To investigate the prevalence and sociodemographic characteristics of headaches among Turkish adolescents aged 12–17 years in the Bursa province of Turkey.

**Methods** A multistep, stratified, cluster sampling method was used for subject selection. The estimated sample size for 12–14-year-old students was 1270 and for 15–17-year-old students 1117. Our study sample included 6.5% of the secondary students aged 12–17 years in the Bursa province of Turkey. The study was conducted in two phases: the questionnaire phase and the face-to-face interview phase.

**Results** The prevalence of recurrent headache in the study population was 52.2%. Girls (59.8%) had significantly more recurrent headache than boys (45.1%). The prevalence of recurrent headache increased from 42.2% up to 60.7% by age. In multivariate logistic regression analysis age and gender differed significantly between adolescents with and without recurrent headache groups. Frequent episodic tension-type headache was the most common (25.9%) headache among Turkish adolescents, followed by migraine (14.5%).

**Conclusion** Age and gender appeared to be demographic factors increasing adolescent headache prevalence. Frequent episodic tension-type headache was the most common headache, followed by migraine.

**Keywords:** adolescent, migraine, tension-type headache, prevalence, epidemiology

**C004**


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**Method and results** One case of sudden onset chronic migraine was observed in a population of 379 adolescents subsequently suffering from headache (mean age 12.8 ± 3.5 SD) in the period 1994–1997. Conversely, in 457 subsequent young patients (13.02 ± 3.9 SD) observed in the period 2001–2004, 34 were affected by sudden onset chronic migraine. Age of onset was 15.10 ± 2.2 SD. Severity of pain was 92.05 ± 7.8 SD on a 0–100 VAS, superimposed attacks were A3 in 67% of cases. Vegetative phenomena were non-relevant. Compared with matched controls, parental bonding instrument (PBI) indicates an abnormal overprotection of one of the parents. (PBI-MPI 18.2 ± 4.9 SD vs. 14.0 ± 6.0 SD, P < 0.005; PBI-PP 17.5 ± 5.5 SD vs. 14.1 ± 4.5 SD, P > 0.013). The other parent was ‘non-interested’. Where both parents were overprotective (n = 10), they conflicted about adolescent behaviour. In half of cases parents were divorced. In all cases patients were highly rewarded by school life and economic life before the beginning of chronic migraine. In spite of the declaration of patients’ normal mood given by parents, Wang (25 ± 7.5 SD) and Zung test (49.7 ± 6.4 SD) always exceeded cut-off values (18 and 40, respectively).

**Conclusion** Results suggest both an abnormal parenting and a family conflict which might induce adverse stress evoking a breakdown of analgesia.

**Keywords:** chronic migraine, adolescents, parental bonding instrument, Wang test, Zung test

**C005**

**Semantic memory and metamemory in adolescents suffering from migraine**

Maria Nicolodi

**Background** Randt Memory Test seems a test suitable to evaluate semantic, visual memory, short-term and long-term memory.

**Methods** The test was administered following the exclusion of adolescents scoring higher than 18 and 40 in Wang and Zung tests, respectively. Randt Memory Test was administered to 70 adolescents suffering from migraine, i.e. to 36 chronic migraine sufferers (mean age 16.7 ± 4.1 SD) (Group 1) and to a matched group of 34 episodic migraine sufferers (mean age 17.1 ± 2.3 SD) (Group 2).

**Results and conclusion** Group 1 showed a global deficit in mnesic performance that overlapped that of 70-year-old control subjects. Following the test administration, subjects included in Group 1 suffered a migraine attack. That affected long-term memory. In fact, the latter parameter was 15.11 ± 3.40 SD. The result was partly determined by a peculiar metamemory determining intrusion of word pairs into short history. Conversely, patients in Group 2, who did not suffer a migraine attack following the test, showed: (a) lower global deficit in mnesic performances (99.5 ± 21.33 SD vs. 65.1 ± 3.4 SD, P > 0.0001), (b) long-term semantic memory scoring higher (23.5 ± 7.5 SD, P > 0.0001) without metamemory in recall. Since, during the attack, electroencephalogram of Group 1 showed abnormalities, their relationship with altered memory processes is proposed.

**Keywords:** migraine, adolescents, semantic memory, metamemory, electroencephalogram
C006

Prevalences of primary or recurrent headaches and abdominal pain at school entry. A population-based epidemiological survey of preschool children and their parents

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Objectives The self-designed questionnaire FSEKB (Fragenbogen zur simultanen Erfassung von Kopf- und Bauchschmerzsymptomen) simultaneously collects the defined symptoms of primary headache and abdominal pain (IHS, 2004; ROME-II, 1999) in context with health-related life quality. Prevalences of pain experiences in preschool children are reported.

Methods An unselected sample of preschool children and their parents answered separately FSEKB during the official healthcare examination at school entry in 2004.

Results 885 school beginners (55.1%/44.9%) are reported officially. 23.3% of the parents refused participation; 14.1% declined in spite of at least three official invitations. 555 children/parents (62.6%/54.6%; 45.2%) cooperated. Prevalence of children vs. parents: isolated headaches 3.6% vs. 4.7%; isolated abdominal pain 31.9% vs. 23.4%; headache + abdominal pain from children 29.8%/44.7%; from parents 27.2%/21.40% vs. 24.3%/21.9%; no pain: 8.6%/5.8% vs. 10.3%/8.5%. There are no gender differences, either in children's judgments (mean ranks 279.73/268.12, $P = 0.352$) or in parents' judgments (mean ranks 253.42/265.70, $P = 0.314$).

Conclusions These findings are in concordance with earlier international studies and suggest no further increase in prevalences. High prevalences in combined headache and abdominal pain support the suggestion to assess both symptom complexes simultaneously.

Keywords: gender-specific prevalences, primary headache, abdominal pain, preschool children

C007

Gender differences in the prevalences of primary and recurrent headaches and abdominal pain at school entry. An analysis on judgements of preschool children and their parents

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Objectives Primary and recurrent headache and abdominal pain are relevant and underestimated problems for children.

Methods In this cross-sectional study, data were collected from January 2004 to September 2004. The headache-specific module of the questionnaire (based on HIS Criteria-II, 2004) was answered by children and their parents separately during the official healthcare examination at school entry.

Results Participation rate: 62.6% ($N = 555$; 54.7%/45.3%; mean ± SD: 6.0 years ± 0.25). 291 children (52.4% [55.7%/44.3%] and 282 parents (50.8%; 53.2%/46.8%) reported headache events.

Conclusions These findings are in concordance with earlier international studies and suggest no further increase in prevalences. High prevalences in combined headache and abdominal pain support the suggestion to assess both symptom complexes simultaneously.

Keywords: gender differences, primary headache, abdominal pain, preschool children

C008

Headache symptoms in preschool children. A population-based study on the epidemiology of headache reported by preschool children and their parents

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Objectives Only few international epidemiological studies on headache in preschool age have been conducted. German investigations have not considered this age group yet. This study aims to determine the prevalence of headache symptoms in preschool children and analyse their characteristics (location, intensity, frequency).

Methods In this cross-sectional study, data were collected from January 2004 to September 2004. The headache-specific module of the questionnaire (based on HIS Criteria-II, 2004) was answered by children and their parents separately during the official healthcare examination at school entry.

Results Participation rate: 62.6% ($N = 555$; 54.7%/45.3%; mean ± SD: 6.0 years ± 0.25). 291 children (52.4% [55.7%/44.3%] and 282 parents (50.8%; 53.2%/46.8%) reported headache events.

Conclusions These findings are in concordance with earlier international studies and suggest no further increase in prevalences. High prevalences in combined headache and abdominal pain support the suggestion to assess both symptom complexes simultaneously.

Keywords: gender differences, primary headache, abdominal pain, preschool children
**Conclusions** Headache frequently influences the everyday life coping of German preschool children. In addition to the parents’ information, the children’s own description of pain perception should be taken into account. The data collected call for further investigation on potential triggers and (gender-specific) risk factors.

**Keywords:** primary headache, preschool children, location, intensity, frequency

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**C009**

The character of recurrent abdominal pain (RAP): an epidemiological study based on the judgements of preschool children and their parents

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**Introduction** As there are no reliable particulars about RAP in preschool age, the intention of our study is to gain insights into the present situation. We analyse how RAP is characterized according to symptoms (frequency, duration, intensity) and gender relation.

**Methods** This cross-sectional study relies on an unselected sample of preschool children and their parents. 555 school beginners and their parents participated (62.6% of the sample; mean age 6.0 years ± 0.25).

**Results** RAP is defined as three or more compromising pain episodes within a period of three sequent months. 44.7% of children with recurrent headaches (mean = 8.00) have a value >3.15, F = 0.527. RAP is characterized in the following areas: abdominal pain, frequency, duration, intensity.

**Conclusion** RAP may have a negative impact on children’s everyday life. With these data as a basis it will be possible to follow up the developing course of pain experience. Due to better knowledge of the pain’s character it may serve for prevention measures.

**Keywords:** abdominal pain, frequency, duration, intensity, preschool children

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**C0010**

The impact of headache and abdominal pain on health-related life quality in preschool children

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**Objectives** Subjective and psychological health dimensions should be integrated into the diagnostic process of pain. Studies including life-quality measures are rare for preschool children. The impact of medically defined headache and abdominal pain symptoms on life quality is analysed.

**Methods** During the official healthcare examination an unselected population-based sample of preschool children (N = 555, 54.6% / 45.2%; mean age 6.0 ± 0.25) reported about life quality (LQ, Kiddy-Kindl), headache (HE) and abdominal pain (AP). The LQ scores are compared for six life areas and between the pain groups (HE, AP, HE + AP, NP no pain) by an analysis of variance (SPSS). Gender specific differences are computed for the total quality of life index.

**Results** Preschool children report a good life quality over all six areas (values ranging from 4.5 to 5.6 (from ± 0.82 to ± 1.2). Gender differences in the total life quality index: HE 30.5 ± 3.15 vs. 30.6 ± 2.91, F = 0.401, d.f. = 1; P = 0.527. The LQ areas differ significantly for all pain groups (psychological area: HE HE LQ 29.6 ± 2.8; AP: HE LQ 30.7 ± 2.7; HE + AP HE LQ 30.0 ± 3.1, NP HE LQ 32.1 ± 3.20; analysis of variance F = 3.525; d.f. = 3; P = 0.015).

**Conclusions** Already preschool children present a loss in life quality because of pain experiences, especially through headaches. These results underline that subjective health-related variables should be integrated into the diagnostic process of pain.

**Keywords:** life quality, Kiddy-Kindl, preschool children, headache, abdominal pain

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**C011**

Headache experiences and the influence on perception organization. A comparison of healthy children and children with recurrent headaches

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**Objectives** The perception organization of healthy children (HE) and children with recurrent headache (RH) were examined in the first year of primary school. The children (N = 22), identified by their parents as ‘recurrent pain expected’, were recruited in 2004 from an unselected population-based sample of preschool children (N = 555) shortly before school entry. It is hypothesized that children with recurrent headaches show a worse perception organization than healthy children. The data acquisition will be completed in summer 2005.

**Methods** N = 24 healthy and N = 7 children with recurrent headaches were examined here. The level of development and the achievement of the perception organization are determined by the mosaic test (mosaic test, HAWIK III). The group comparisons are computed with t-tests (SPSS).

**Results** The age-adjusted standard range for perception organization lies between 7 and 13 (min = 1, max = 19). Healthy children (mean = 11.96) are within the normal range. Children with recurrent headaches (mean = 8.00) have a value in the low norm area (HE > RH; t-value = 2.585; P = 0.03; confidence interval = 95%, d.f. = 8.98).

**Conclusions** Explicitly significant influence can be found for children experiencing recurrent headaches. It is assumed that the analysis of the whole sample as well as an increasing
duration of the headache experiences in the developmental course strengthens the formulated hypothesis.

Keywords: perception organization, pain experiences, recurrent headache

C012

About the impact of recurrent headache and abdominal pain on the information processing speed of children in the first year of primary school

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Introduction This experimental study analyses the impact of recurrent headache and abdominal pain experiences on the information processing speed. The healthy and pain experienced children were traced by their parents’ judgements and recruited from an unselected population-based sample of preschool children (N = 885). It is suggested that first-graders without recurrent pain experiences show a faster information processing speed than children with pain experiences.

Methods The sample consists of N = 41 children (N = 24 healthy and N = 17 pain experienced children). The performance of 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 (scaling from 1 to 19). Healthy children (mean 12.66) as well as children with recurrent pain experiences (mean 9.00) are within the normal range. The children without recurrent pain experiences show a significantly higher information processing speed than those with recurrent pain experiences (t = -3.156, P = 0.004, confidence interval = 99%, d.f. = 29.08)

Conclusion There is a significant impact of pain experiences on the quality of information processing speed. Although the results of both groups are within the normal range, healthy children perform better.

Keywords: information processing speed, recurrent headache, abdominal pain, preschool children

C013

Development of information processing speed in healthy children. Are there influences of experienced headache intensities?

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Introduction The influences of gender, developmental stage and experienced headache intensity on the speed performance in healthy children are analysed and reported here.

Methods This cross-sectional experimental study included N = 139 healthy children (71 boys, 68 girls). The developmental aspect was defined by school age (N = 22 preschoolers, N = 24 first-graders, N = 20 second-graders, N = 24 third-graders, N = 19 fourth-graders, N = 30 youngsters in class 8, age 13–15). The information processing speed has been detected by means of number symbol test (subtest ZS of HAWIK III). The children were divided into groups with higher and lower intensity of experienced headaches (VAS) by median test. The influence of the independant factors have been determined by analysis of variance (SPSS).

Results School age has no influence on the adjusted standard range of information processing speed (F = 1.524, d.f. = 5, P = 0.187, m 10 636–12 667) measured by number symbol test. There is a tendency of gender influence on the examined factor (F = 3.367, d.f. = 1, P = 0.069, m boys = 11 099; girls = 11 985).

In this sample of healthy children experienced headache intensities have no impact on information processing speed (F = 0.048, d.f. = 1; P = 0.826).

Conclusions In healthy children the information processing speed is a stable developmental factor. Isolated headache experiences have no influence on this cognitive function. More insights are expected from future comparisons of healthy children with children suffering from recurrent headaches.

Keywords: development, gender, information processing speed, headache intensity, healthy children

C014

Personality traits and central information processing in migraine children

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Objective Migraine children are characterized by increased amplitude and reduced habituation of the early component of the contingent negative variation (CNV). In this study, we investigated the relation between well-replicated migraine-specific personality characteristics and the early CNV.

Methods 58 children with migraine without aura and 48 healthy children were studied using State-Trait-Anxiety Inventory and Hamburg Neuroticism/Extraversion Scale. CNV recordings were performed in all participants.

Results Migraine children differed significantly from controls according to neuroticism (P = 0.0092) and trait anxiety (P = 0.05), demonstrating higher scores for these traits. We found significant correlations between amplitude of the early CNV and neuroticism (r = 0.62, P < 0.01) as well as trait anxiety (r = 0.51, P < 0.05). The perfomed cutoff of the groups into persons with high and low neuroticism/anxiety scores revealed significant differences between them: individuals with high neuroticism/anxiety were characterized by higher CNV amplitude (P = 0.021) and more pronounced loss of the early CNV habituation (P = 0.038).

Conclusion The healthy CNV may be discussed being a neurophysiological correlate of high neuroticism/trait anxiety in migraine patients. A shared disposition for CNV and the described personality traits may be hypothesized.

Keywords: contingent negative variation, neuroticism, anxiety, migraine

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C015

Meningismus: a major clinical syndrome of tension-type headache in children and adolescents

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Background Neurological status in children with tension headaches is usually believed to be normal. This is the first study of meningeal signs in such patients.

Objective Examination of detailed neurological status in children with chronic tension headaches.

Method 837 patients with complaints and anamnesis that could be diagnosed as tension-type headache (aged 5–17 years) were examined by a paediatric neurologist in a routine out-patient practice over a 7-year period. Particular attention was paid to meningeal signs.

Results The meningismus syndrome (positive Kernig’s sign, Brudzinski’s lower sign, the ‘tripod’ sign, nuchal rigidity and/or pain in head, neck and epigastrium when bending the head forward) was present in 97% of the patients. For treatment we used a method that is usually applied in ‘post lumbar puncture headaches’: bed rest during 7–10 days in a recumbent position. This brought relief from the headache in most cases. In addition, the meningeal signs had disappeared.

Conclusion The major clinical syndrome of chronic tension headaches in children is meningismus, possibly caused by chronic, sterile, perhaps autoimmune origin, mild pachymeningitis, which most likely originates from a minor trauma of the head and/or back, or of infectious agents.

Keywords: headache, meningismus, tension-type headache, pachymeningitis

C016

Clinical characteristics, sensitivity and specificity of adolescent headaches according to age and gender: a student-based study

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Background and objectives To investigate the characteristics of tension-type headache and migraine, to find the sensitivity and specificity of the diagnostic criteria of the IHS classification according to age and gender.

Methods A multistep, stratified, cluster sampling method was used. The estimated sample size was 2387. The study was conducted in two phases: the questionnaire phase and the face-to-face interview phase. During the semistructured interview a clinical diagnosis has been made and clinical characteristics have been recorded.

Results All headaches fulfilled the criteria of duration. The most common feature of migraine was moderate to severe pain (92.4%) followed by pulsating quality of pain (79.2%). For ETTH bilateral localization (91.3%) and mild to moderate pain intensity (90.6%) were the most common features. Younger adolescents had mixed headache characteristics.

Highest sensitivities for migraine were duration (100%), moderate to severe pain (92.4%) and pulsating quality of pain (79.2%). Vomiting, trigger factors foods and alcohol had a high specificity for migraine.

Conclusion Age and gender have some influence on headache, particularly migraine. In early adolescence headaches might present with mixed headache characteristics. Therefore, careful evaluation is needed in this age group and proper diagnosis may be difficult.

Keywords: adolescent, migraine, tension-type headache, age, gender

C017

Prevalence of migraine in Thai students

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Background Migraine in children is common but the prevalence in Thai children is not well established.

Objective To determine the prevalence of migraine in Thai 7th grade students.

Methods A cross-section study in the 7th grade students aged 12–14 in four junior high schools in Bangkok, Thailand was conducted by a 13-item questionnaire screening survey followed by interview and physical examination. Students who reported two out of six items, included in the 2nd ICDH for diagnosis of migraine, received individual interview and physical examination by paediatric neurologists to verify the diagnosis. Characteristics, severity and precipitators of migraine were collected.

Results Among 1789 students, migraine was diagnosed in 248 (13.5%) consisting of 111 boys (44.7%) and 137 girls (55.3%). 119, 128 and one students had common migraine, classic migraine and complicated migraines, respectively. Six children had chronic daily headache in addition to migraine. Migraine in relatives was found in 27%. Migraine precipitators were reported in 33.8%, including stress from daily school activities (52.3%). Two students had a history of taking prophylactic medication.

Conclusion The prevalence of migraine in Thai 7th grade students is as high as that in Western countries. Precipitators were reported in one-third of the children.

Keywords: migraine, children, prevalence, precipitators, Thailand

C018

Familial occurrence of migraine in a Japanese paediatric clinic

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Objective We investigated familial occurrence of migraine with and without aura to analyse clinical characteristics of migraine in children.
Methods Our study involved 160 children who visited our clinic complaining of headaches. They were diagnosed according to ICHD-II. 125 children diagnosed with migraine and their families were studied.

Results Of 125 children with migraine, 75 were girls aged 11.2 ± 2.5 years (mean ± SD) and 50 were boys aged 10.9 ± 1.0 years. Eighty-eight children (70%) had a family history of headache. They had 112 first-degree relatives; 73 (65%) mothers, 27 (24%) fathers and 12 (11%) siblings. In this study, 73 mothers of 43 girls and 30 boys were interviewed. Thirty-seven of 43 girls (86%) and 27 of 30 boys (90%) had mothers with migraine. The rate of co-occurrence of migraine type in mothers and children was 16% in girls and 4% in boys for migraine with aura. However, the rate for migraine without aura was 49% in girls and 74% in boys.

Conclusion Our study indicated that the maternal occurrence rate of migraine was significantly high in children; however, there was no difference in this rate between girls and boys.

C019
The pet therapy and childhood headache: a new therapeutic course
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Pet therapy (PT) is a behavioural therapy, which has been used for some time for the treatment of psychomotor retards and psychic disturbances in childhood. The purpose of the study is to evaluate PT as a therapy for headache linked to psychosocial disturbances. After preliminary work on 25 young patients (YP) (1), a study was conducted on 48 YP (25 F, 23 M, 41 MoA, 7 MA, range 6–15 years). The therapeutic scheme has been of 15 weekly sessions lasting 1 h each. The PT takes place in a 1000-m² garden with trees, animals (dogs, cats, rabbits, birds, sheep), psychotherapists and three groups of YP aged 6–8, 9–11 and 12–15 years. The data controlled at T0 and T30 weeks for headache: duration and frequency; psychological tests CDI, FAB-C; parents’ indication in the new way of handling the psychosocial disturbances. Headache has shown a reduction of >40% (M.I. 13.3 ± 8, 6.8 ± 3.3, P < 0.005); the psychological characteristics have given better results: CDI (13.3 ± 3.6, 9.6 ± 3.1, P < 0003); Culture-Free Self-Esteem Inventory (24.5 ± 6.2, 28.7 ± 5.9, P < 0.05); FAB-C (12.4 ± 2.9, 10.5 ± 2.9, P < 0.05); but above all, the ability of the children has changed in dealing with the triggering events. We think that the PT may have acted to improve security, ability to socialize, to deal with a precise task. We therefore believe that this intervention may be very useful for childhood headache.

Reference

C020
Headache and cerebral neoplasia in children—a case report
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We present the case of a 5-year-old child suffering for a few months from widespread intense headache. He presented 4 days after head trauma, which had accentuated headache with one morning vomiting. Upon admittance the neurological examination (NE) was negative. A first CAT was made, which showed new formation in the back cranial fossa. Ten days later there was worsening of headache, uncontrolled vomiting, drowsiness, irritability, NE pluridirectional lateropulsion to Rosemberg, bilateral dysmetria, dysarthria; anti-oedemigenous therapy was applied. A NMR showed voluminous expansive process on the upper portion of the cerebral hemisphere. Operated: anaplastic medulloblastoma AN (IV WHO). One month later good general conditions, negative neurological NO. Two months later first chemotherapy cycle, radiotherapy, corticosteroids. Eight months later the child is well, shows only ETT the day before chemotherapy. AN is a very soft child’s tumour, which adjusts to spaces causing nervous compressions and diagnostic delay. The common symptoms are endocranial hypertension from obstructive hydrocephalus, widespread headache, vomiting, walking disturbances, often late and indistinct. Post-traumatic symptoms, notwithstanding the negative NE, have led to make an early neuroimage, thus enabling a still useful intervention. It was the cranial trauma to accentuate the headache or the expansive process to cause the first compressive phenomena.

C021
The dependence of headache character on iron deficiency anaemia (IDA) in adolescent
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Aim To study the interconnection between headache and IDA in adolescent girls. We examined 80 adolescents from 11 to 18 years of age. Among them 75 were girls. By questionnaires we determined headache duration, locality, time and speed of appearance, as well as the levels of haemoglobin, serum iron and ferritin.

Results We marked headaches in 71.2% (57 subjects, all adolescent girls). At the same time, in 31.5% of them we found anaemia in haemoglobin level not less than 120 g/l. The duration of headache (over 24 h) in the group with IDA was met evidently more often (P = 0.05) than in the group with normal haemoglobin (16% vs. 2%, respectively). Intensive headache (an obstacle to performing usual activities) in the group with IDA was met evidently (P = 0.01) more often than in the normal haemoglobin group (27% vs. 5%, respectively). In the group with normal haemoglobin in combination with lowered iron and ferritin the intensive headache was met evidently (P = 0.05) more often than in the group with normal
biochemical indices of iron complex (12% vs. 0%, respectively).

Conclusion Probably, there is a link between iron deficit and the appearance of headaches in adolescent girls.

Keywords: headache, adolescent, iron deficiency, anaemia

C022
Prevalence of headache and migraine in urban Siberian school children
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The prevalence of headache in children varies greatly depending from the region and the criteria for diagnosis.

Aim To determine the prevalence of migraine headache in urban school children of Siberia.

Study design We carried out a cross-sectional study of 353 children aged from 7 to 16 years (44.9% boys and 55.1% girls) using parent-structured questionnaires, which includes migraine diagnosis criteria for children, adopted by the International Headache Society (IHS, 1988) and revised IHS criteria (D. Winner et al. 1997).

Results Among the children 82.7% suffered from recurrent headaches. 2.1% of school children were relevant to IHS criteria. Migraine without aura was diagnosed in 1.1% of school children. 1.8% of school children were relevant to diagnosis criteria of migraine without aura when the criterion of minimal headache duration changes to 1 h, with hemiconal addition, with inclusion of two-sided location of headache and elimination of the presence of both photophobia and phonophobia.

Conclusion The prevalence of migraine in urban school children of Siberia, revealed by parent interview, is considerably lower than in the data, distributed before, regarding school children of Europe and North America. Probably, correct results could be obtained from children questionnaires and ‘headache diary’.

Keywords: headache, prevalence, children

C023
Paintings and poetry are good supplements to questionnaires for evaluation of the burden of headache as well as headache diagnosis in children and adolescents
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Objective Our aim was to register the presence and impact of headache in school children.

Methods We distributed a small questionnaire to 15 randomly chosen primary schools in Norway. It contained questions about headache days and characteristics, duration, and absence from school because of headache. 708 questionnaires were returned. The participants were children between 10 and 16 years. There were 358 boys, 316 girls, the rest with no reported sex. They also submitted paintings and poems of their headaches and there were prizes for the best contributions.

Results 76% of the children reported headache more than once a month. 61% had headache attacks lasting less than 2 h and 30% of them less than 30 min. More than two-thirds reported bilateral headaches and one-third had pain located in their forehead. One in four children had been absent from school during the last 2 months because of headache.

Conclusion Headache is a common disorder in school children, and a common reason for absence from school. The headache lasts shorter than 2 h in the majority of the children. The paintings give additional insight into the burden of headache.

Keywords: headache, children, art, paintings

C024
Zolmitriptan 5 mg nasal spray is effective and well tolerated in the acute treatment of adolescent migraine
Andrew D. Hershey1, Paul Winner2, Donald Lewis3 & Warren Wasiewski4, on behalf of the adolescent migraine steering committee: ‘Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, USA, 2Palm Beach Headache Center, West Palm Beach, FL, USA, 3Division of Pediatric Neurology, Children’s Hospital of the King’s Daughters, Norfolk, VA, USA, and 4AstraZeneca, Wilmington, DE, USA

Objective To evaluate zolmitriptan nasal spray (NS) vs. placebo for the acute treatment of adolescent migraine.

Background Migraine in adolescents differs from that in adults, with shorter attack duration and high placebo headache responses in clinical trials.

Methods 248 adolescents entered this multicentre, randomized, double-blind, placebo-controlled, two-attack crossover trial with a single-blind placebo challenge. Each attack was initially treated with placebo NS; if a headache response was obtained at 15 min, no further medication was taken. If headache pain remained moderate or severe, patients were treated with randomized zolmitriptan NS or placebo NS. The presentation will discuss all endpoints and the implications of this unique approach compared with a traditional evaluation.

Results The ITT population comprised 171 patients. Zolmitriptan NS produced significantly higher headache response rates than placebo at 1 h postdose (58.1% vs. 43.3%; P < 0.02), with an onset of action as early as 15 min. Importantly, zolmitriptan NS produced a significant pain-free response at 1 h (27.7% vs. placebo 10.2%; P < 0.001). Adolescents experienced a lower incidence of adverse events than usually seen in adults, with no serious adverse events or withdrawals.

Conclusions Zolmitriptan NS is effective and well tolerated in adolescent patients with migraine, with a fast onset of action.

C025
Migraine and puberty: a casual or a causal relationship
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The aim of the study is to understand if migraine arises together with puberty or afterwards. Twenty-four girls were included (21 MoA, three MA, age range 10–14 years) followed
for about a year before puberty and 1 year after without therapy prophylaxis. Follow-up was at three time points: 6 months before (3–11), 6 and 12 months after.

At the three follow-ups: hormones: LH, FSH, PRL, 17β-estradiol; psychological test: anxiety test, CDI, FAB2; headache: TPI (DxFxI), associated symptoms. To avoid the results being linked to puberty variations, psychological tests were compared with those of a control group of 20 girls.

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35% medium hormonal increase, 25% increase of headaches (TPI 93.6 ± 6.8, 107.5 ± 8.3, 118.49 ± 7.5; P < 0.05), more nausea, vomiting, photo/phonophobia. Anxiety and insecurity are increased due to the social role, but these situations seem to be mainly due to a real instability rather than to a true change.

Conclusions Even if these data are scant, we reckon that the migraine variations, at least in the first puberty period, are linked to psychophysical changes that generate insecurity, rather that a true hormonal reaction. We think that following the same patients, it will be possible to define when and how much the neuro-hormonal impacts on the individual, rather than the specific behavioural changes.

C026

How the loss of either parent affects a child’s headache

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An event having strong affective valence, such as the loss of a family member, has often been indicated as a causative factor of headache. Purpose of this work was to compare headache characteristics of a group of patients without either parent. In 6 months 320 patients were checked, 51 (15.8%) without either parent (separation 68.7%; divorce 23.5%; death 7.8%). These were compared with young headache sufferers (HS) having both parents. The characteristics of headache and psychiatrie comorbidity were evaluated.

First group: 51 (25 M; 26 F), age range 3–18, mean 11.4 ± 2.9 years; second group: 51 (24 M; 27 F) age range 3–18, mean 9.9 ± 2.7 years.

ETTH and MoA were reviewed. MoA [first group 29; 17 F, 12 M, M.I. (DxF) 8 ± 2.4; second group 23: 14 F, 11 M, M.I. 3.7 ± 3.4, P < 0.0001]; ETTH (first group 12: 7 F, 5 M, M.I. 6 ± 2.6; second group 21: 9 M, 13 F, M.I. 3.5 ± 3.8, P < 0.0001).

Only in 10% for the first group did the onset of headache coincide with the loss either parent (three MoA, one ETTH). Anxiety was higher in the ETTH first group, depression in the MoA first group.

The loss of a family figure is suffered by HS with more evident headache, but often is not a causative factor. The high level of anxiety and depression show the great involvement of HS. Greater attention to the child’s environment is per se a therapeutic intervention.

C027

Transient focal neurological symptoms in migraine of childhood

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Background Migraine of childhood can be diagnosed according to the diagnostic items (such as visual, sensory, speech disturbances or duration of aura, etc.) of the International Classification of Headache Disorders, 2nd Edition (ICHD-II), the same as in adults.

Objective To investigate the prevalence and clinical features of transient focal neurological symptoms (TNS) in migraine without aura (MoA) and migraine with aura (MA) of childhood, whose diagnoses were based on ICHD-II.

Methods I studied a sample of 83 children (58 girls, 25 boys) with MA and MoA and checked their headache diaries and pictures (1 January 2004 to 31 January 2005).

Results In MoA (girls 35, boys 16, mean age 10 years and 2 months) transient visual disturbances (TVD, 19.3%) and transient sensory disturbances (TSD, 13.3%) were observed. In MA (girls 23, boys 9, mean age 10 years and 8 months) there were TVD (9.6%), TSD (3.6%), perceptual disturbances (8.4%; such as micropsia or distortions of body images, etc.) and other symptoms (4.8%; such as auditory hallucination, etc.).

Conclusion In migraine of childhood, there are many other symptoms than the diagnostic items of ICHD-II, which are TVD, TSD in MoA and perceptual disturbances in MA.

Keywords: migraine of childhood, transient focal neurological symptoms

C028

Lamotrigine and flunarizine prophylaxis in childhood migraine

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Background Migraine is an important cause of recurrent headache in childhood. Calcium channel blockers, anti-convulsants, beta-adrenergic blockers are the prophylactic drugs used most commonly for preventive treatment in childhood migraine.

Objective The aim of the study is to determine the efficacy and security of lamotrigine and flunarizine in prophylaxis in children and teenagers.

Methods 40 children with migraine according to International Headache Society criteria were included in the study. Their ages ranged from 6 to 17. Therapy continued for at least 3 months; the lamotrigine dose was 25–50 mg/day, flunarizine 5 mg/day. We compared total number of headache attacks, its frequency and duration before and after 3 months’ drug
therapy. All subjects were asked to keep a headache diary for 12 weeks. In all patients EEG records were performed.

**Results** We have found beneficial effects of lamotrigine and flunarizine in the treatment of headache attacks and its severity in all children. Lamotrigine is more effective for the therapy of migraine with aura. The good clinical response correlated with the reduction of paroxysmal activity in EEG. Flunarizine is effective also in transformed migraine, which was observed in five children. Adverse effects associated with flunarizine in three teenagers included sedation and weight gain. Side-effects have not been reported by younger children. None required drug withdrawal.

**Conclusion** Lamotrigine and flunarizine appear to be effective and safe in selected patients with childhood migraine.

**C029**

Transcranial Doppler examination in migraine and tension-type headache in children

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**Background** Migraine has a complex pathomechanism which is partly explained by the vasomotor theory of Wolff, whereas the pathomechanism of tension-type headache is still not clarified. Among many factors, the structural changes in blood vessels should be considered.

**Aim** To compare haemodynamic changes assessed by TCD in children with migraine, with tension-type headache and in control group.

**Materials and methods** 20 children with migraine (nine with aura, 11 without aura) and 20 patients with tension-type headache aged 8–15 years hospitalized in Department of Developmental Neurology, Medical University of Gdansk were analysed. Control group consisted of 20 healthy children without headache of similar age. Doppler examination with an instrument DWL Multi Dop T1 (2001), including evaluation of blood flow velocity (BFV) of ACAs and MCAs was performed. The statistical analysis was provided.

**Results and conclusion** There were differences in cerebral blood flow parameters among children suffering from migraine, tension-type headache and control group. The obtained results can be helpful in the diagnosis of the type of headache and its pathomechanism.

**C030**

Change of clinical picture of migraine from childhood to adolescence

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**Objective** The clinical picture of child migraine is different from that of an adult. We examined this changing process from childhood to adolescence.

**Patients and methods** Three hundred and fifty-nine migraine cases ranging in age from 7 to 18 years and diagnosed according to Maytal’s criteria, were analysed clinically. The cases were divided into four groups: 7–9, 10–12, 13–15 and 16–18 years old at the first consultation. Clinical findings of each group were compared.

**Results** Boys were more than girls below 12 years old, and the peak was 54.4% in the 10–12-year-old group. Ipsilateral headache accounted for 50.0%, 63.2%, 76.6% and 75.6%, respectively, in the four groups. Pulsative pain was 63.2%, 34.0%, 41.9% and 51.5% in that order. Duration of headache within 4 h was 43.3%, 51.6%, 36.9% and 26.8%, respectively. Scintillation scotoma was 2.1%, 7.8%, 9.5% and 27.2% and vomiting was 37.5%, 33.0%, 23.8% and 25.2%, respectively.

**Conclusion** The present study revealed the changing process from child to adult clinical figure in migraine. The results of this study will be especially useful in understanding child migraine.

**Keywords:** migraine, childhood, adolescence, clinical picture

**C031**

A retrospective review of the efficacy and tolerability of zonisamide in prophylaxis of refractory paediatric headaches

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**Objective** Zonisamide is an anti-epileptic drug which has recently been reported to have potential utility in headache prophylaxis. Our goal was to (1) evaluate the relative efficacy and tolerability of zonisamide used for headache prophylaxis in children with refractory headaches and (2) make preliminary observations regarding comorbid conditions potentially influencing patient response to zonisamide for headache prophylaxis.

**Methods** Retrospective chart review was completed on patients followed in our paediatric headache clinic who were treated with zonisamide for headache prophylaxis. Records were reviewed for data on patient history, headache type, treatment and response. Pre- and post-treatment headache frequency was analysed using analysis of variance. Descriptive analysis was used for remaining data.

**Results** Eleven patients were identified (seven girls). Age range 9–17 years; mean = 14.6 years. Four had episodic migraine, seven had chronic daily headaches. This patient cohort had previously failed other medication trials (x = 2.4). 6/11 had = 50% reduction in headache frequency with zonisamide. Average dose was 5 mg/kg/day. Two patients had adverse events: anorexia (1), behavioural changes (1). 6/11 had comorbid psychiatric diagnosis; 50% were positive responders.

**Conclusion** Zonisamide had efficacy in decreasing headaches in a small retrospective study of refractory patients and was well tolerated. Further prospective studies are warranted.

**Keywords:** zonisamide, headache, children, migraine

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C032
Cannabis use masquerading as cyclical vomiting related to migraine
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Background IHCD-II describes cyclical vomiting (CV) as a self-limited episodic condition of childhood which has been suggested to be related to migraine. In adults, a similar disorder has been described and speculated to represent a migraine variant. Chronic cannabis use has been linked to CV in adults in the gastrointestinal literature.

Objective Description of two cases of CV in adults linked to chronic cannabis use.

Methods Case reports.

Results Two men, aged 25 and 50 years, each presented with histories of 2–3 years of episodic severe nausea and vomiting of 6–48 h duration. Average frequency was one attack every several weeks. Neither patients’ attacks were accompanied by headache, nor was there a history of migraine. Extensive gastrointestinal investigations failed to elicit the cause of attacks. Both had normal neurological examinations. Each patient had a history of chronic cannabis use preceding the onset of CV; one had urine that contained cannabinoids. Discontinuation of cannabis was advised and in one patient with 3 months of follow-up, the episodes ceased.

Conclusion Chronic use of cannabis can cause CV. A history of cannabis use should be sought, and drug screening should be considered. The disorder remits with cessation of cannabis use.

Keywords: cannabis, cyclical vomiting, migraine, adults

C033
Quality of life in children and adolescents with migraine: a controlled study
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Background Quality of life (QoL) is a major aspect of migraine management.

Objectives To evaluate QoL in children and adolescents with migraine without aura (MoA) and to compare MoA patients from a tertiary care centre and from public schools with headache-free subjects.

Methods We used the ‘Inventory of Quality of Life in Children’ developed by Mattejat to assess QoL by self and parents’ report in 60 clinic patients (mean age 11.5 years) with MoA and in 154 age-matched controls approached in schools. Seventy-three controls had MoA and 81 had no lifetime history of headache.

Results QoL was significantly reduced in clinic-based and school-based migraineurs and the two groups did not differ from each other. Patients and parents reported a reduced total QoL and an increased prevalence of physical, psychological and school problems. Migraine attacks were more severe in clinic patients, but frequency and duration were similar in clinic-based and school-based migraineurs. Among the latter, more than 75% had never been seen by a physician.

Conclusion In children and adolescents with MoA, QoL is similarly reduced in patients from a tertiary care centre and in subjects from public schools. Consultation rates are low and must be increased by adequate education.

Keywords: quality of life, migraine, children and adolescents, headache centre, school

C034
Pattern of regional brain dysfunction in paediatric migraine. A SPECT and VEP study
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Objective The aim was to research the topography of metabolic and electrophysiological dysfunctions in paediatric migraine.

Methods We have investigated interictally 66 children and adolescents aged 8–18 years, suffering from migraine with aura (MA) and without aura (MoA). Regional cerebral blood flow (rCBF) was evaluated by SPECT with 99mTc HMPAO. Standard visual evoked potentials (VEP) were recorded with monocular and binocular system.

Results Substantial prolongation of P100 and N145 latencies and reduction of N75/P100, P100/N145 amplitudes in comparison with healthy subjects were found in both MA and MoA. Brain SPECT showed that rCBF was both reduced and asymmetric in 73% of the patients. A correlation between localized hypoperfusion mainly involving the posterior regions of the brain, the pattern of VEP and symptoms of migraine were estimated.

Conclusion The presence of neuronal dysfunction in migraine at visual pathway even in headache-free period was shown. Indication of interhemispheric differences without interocular changes of VEP points to their unilateral localization confirmed by asymmetric rCBF. These results support the hypothesis that the aetiology of both subtypes of migraineous headaches is the same and differences are related only to the intensity of clinical symptoms appearing in patients.

Keywords: VEP, SPECT, paediatric migraine

C035
A case of infant with intractable cyclic vomiting syndrome treated with sumatriptan
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Introduction Cyclic vomiting syndrome (CVS) has recently been re-classified in the 2nd edition of the International Classification of Headache Disorders as childhood periodic syndromes that are common precursors of migraine.

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Case report An 18-month-old Japanese boy was diagnosed as CVS at 3 months of age. He started having frequent vomiting, face exanthema and drowsiness at 2 months old. His vomiting episode lasted for 3–5 days and the frequency was two to three per month. Because he vomited every 5–30 min in the first to second days of episode, he was given intravenous drip infusion every time. Extensive examination demonstrated no aetiology for his symptoms. Amitriptyline, cyproheptadine, valproic acid and propranolol had no prophylactic effect on his vomiting episode. We tried to treat him with sumatriptan. Sumatriptan 2 mg/m² was administered approximately 12 h after vomiting episode had begun and after a second dose 6–8 h later. This treatment protocol was approved by the institutional ethics committee. Frequent vomiting decreased to one-tenth or less after sumatriptan injection and his activity during the episode improved. Any adverse effect was not detected. His motor and mental development is within normal range.

C036
Primary headache in children and adolescents: psychiatric comorbidity and the relationship between headache characteristics
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Background There is conflicting evidence about the relationship of primary headache disorders and psychiatric comorbidity. There are also few data about the effect of headache characteristics on having associated psychiatric disorders.

Objective In order to determine comorbid psychiatric disorders and relationship between headache characteristics and this comorbidity we performed a clinical based prospective study.

Methods Children were evaluated by the same neurologist for the IHS-II-based headache diagnosis and by the same Child and Adolescent Psychiatry specialist using the Child Beck Depression Inventory (CBDI), Trait-State Anxiety Score (STAI-C) and Piers-Harris Children’s Self-Concept Scale (PHCSCS) in addition to clinical evaluation. Using appropriate statistics, results were evaluated.

Results In total, 112 patients were evaluated and 58.9% of them were girls. Headache diagnoses were migraine (14.3%), tension-type headache (57.1%) and others (28.6%). Eighteen percent of patients had comorbid psychiatric diagnoses, predominantly depression and anxiety disorders. The most important determinators of psychiatric disorders in patients with headache were sociodemographic characteristics of family, headache history of family and headache subtypes.

Conclusion It was concluded that headache-associated comorbid psychiatric disorders are important in these age group and should be included in the headache coping strategies.

C037
Secondary migraine-like headache as a symptom of cerebral AVM in a 10-year-old girl—a case report
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We report a 10-year-old girl, admitted to hospital because of the first attack of migraine-like headache. She had no neurological disabilities. Her EEG showed slow waves, fundoscopic examination and laboratory tests were normal. Transcranial colour duplex Doppler ultrasonography (TCCD) showed a complex of cerebral vessels at the region of the left anterior cerebral artery with high velocities and with abnormal spectral velocity waveform in both anterior cerebral arteries, suspected on arteriovenous malformation (AVM).

Magnetic resonance imaging showed an area of serpiginous multiple loss of signal at the left frontal region, which corresponded to vascular structures. Magnetic resonance angiography showed arteriovenous malformation located in the area of mediocortical part of the left side upper frontal gyrus, affecting the anterior edge of nucleus caudatus. The diagnosis was confirmed by the digital subtraction cerebral angiography (DSA) which showed an AVM at the frontal region.

The treatment of AVM was embolization. After that treatment, the girl is in optimal condition, she has no headaches, paraesthesias or motor disturbances and she is on anticonvulsant therapy. Control TCCD shows normal morphological findings of great cerebral arteries, but with high velocities in arteries of left hemisphere. Control DSA and embolization are planned for next year.

C038
Psychiatric comorbidity and primary headache: investigation on 200 parents and their children
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Background The psychiatric comorbidity (Psi-co) in headache raises questions on the likely common aetiological mechanism and direction of influence.

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

Methods Headache history and symptomatology have been collected in a clinical sample of 200 patients and their families, using a semistructured interview which covered all items required for diagnosing headaches according to IHS criteria (2004). The questionnaire was composed of different sections in which we assessed the Psi-co in parents, according to DSM-IV criteria. \( \chi^2 \) was computed in order to analyse contingency tables.
Results Ninty-four mothers (47%) and 51 fathers (25.5%) had at least one psychiatric disorder, mainly mood and anxiety disorders. It is noteworthy that patients of mothers with Pisco showed a higher recurrence of psychiatric disorders than children whose mothers had no history of psychiatric disorders ($P < 0.05$), without differences across headache subtypes.

Conclusion The occurrence of psychiatric disorders is high in children with headache, but also in their parents and common to all headache subtypes. It may be due to a genetic mechanism, but also to the shared familial environment.

Keywords: psychiatric comorbidity, family, child, migraine

C039

The so-called ‘migraine personality’: a comparative study on headache and recurrent abdominal pain

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Background Personality characteristics (e.g. rigidity, perfectionism and aggressiveness) have been linked to the onset and clinical course of headache and recurrent abdominal pain (RAP) in childhood.

Objective Studying characteristics of personality in children (8 and 13 years old) with headache and RAP compared with a control group.

Methods We examined a clinical sample of subjects grouped into 63 migraineurs, 40 suffering from tension-type headache, 40 with RAP and 123 control subjects. We administered to all the Big Five Questionnaire for Children to test personality characteristics (Barbaranelli et al. 1998).

Results Results of ANOVA did not show significant differences between the headache, RAP and control subjects in any of the scales of the Big Five Questionnaire for Children.

Conclusion The study did not show the existence of a bidirectional relation between personality profiles and migraine. The definition of ‘migraine personality’ seems to be useless, even if the relevance of psychiatric comorbidity is well-known in migraine and tension-type headache in children (Guidetti et al. 1998).

Keywords: psychological factors, personality, child, migraine

C041

Attack anticipation and susceptibility to stress in migraine children

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Objective As demonstrated previously, migraine attacks are anticipated by different neurophysiological changes. The mechanisms of the attack anticipation, however, remain unknown. In this study, we investigated variations of daily hassles and mood as well as changes of stress hormones in relation to a migraine attack.

Methods 15 children with migraine (12.6 ± 3.2 years) kept a headache diary and a diary for evaluation of daily hassles for 1 month. The school, family and time pressure stress as well as positive and negative mood experience were estimated using visual analogue scales. During the whole time of observation, samples of night urine were obtained and the concentrations of cortisol, adrenaline and noradrenaline in relation to creatinine were analysed.

Results Migraine children demonstrated a significant increase in stress experience and negative mood changes before a migraine attack (day before an attack compared with a day during the interval for summated stress: $P = 0.02$; for school stress: $P = 0.04$; for negative mood: $P = 0.05$). Changes in subjective stress experience were related to variations in catecholamines. On the day of migraine attack, a significant increase in cortisol level was observed.

Conclusion This study emphasizes the important role of psychosocial stress in precipitation of migraine attacks in children.

Keywords: daily hassles, cortisol, catecholamines, migraine, children
**C042**

**Headache disorders as risk factor for sleep disturbances in school-aged children**

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**Background** Several studies have shown the presence of comorbidity between various types of sleep disorders (SD) and headache subtypes.

**Objective** To assess the risk for SD in a prepubertal headache population.

**Methods** 170 children aged 5–10 years (mean age 8.12±0.44) referred to university third-level headache centre of Naples and Rome were studied with Sleep Disturbance Scale for Children questionnaire to assess SD, and compared with 170 matched children. They were selected according to IHS criteria (2004), and absence of other disorders (e.g. epilepsy, behavioural problems) evaluated by clinical interviews as well as by neurophysiological recordings (wake and sleep EEG).

**Results** Headache subgroups were: MA 20%, MoA 38.24%, ETTH 19.41%, CTTH 22.35%. MoA is a sensible risk factor for initiating and maintaining sleep disorder (OR 8.2500), and CTTH for sleep breathing disorders (OR 15.231). Headache disorder is a cumulative risk factor for excessive daily somnolence (OR 15.061).

**Conclusion** Excessive daily somnolence is strongly related to all types of headache, even in the absence of sleep breathing-related disorder, in prepubertal population, even if few studies have focused on the whole sleep/wake cycle and disorders on the circadian aspects of headache.

**Keywords:** sleep, excessive diurnal sleepiness, child, primary headache

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**C043**

**Neonatal hyperreactivity and migraine risk: a 15-year follow-up study**

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**Background** Reactivity is an early temperamental trait. Some infants show low threshold of sensory stimulation and a lack of habituation to stimuli: hyperreactive (IPR) neonates. Recent studies suggested that migraineurs have a lower threshold of neurophysiological reactions and a lack of habituation, as the principal interictal abnormality of sensory processing.

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

**Methods** In 2003, we contacted 100 children (M = 60, F = 40; m.a. = 17.5), 50 with at least two symptoms of IPR, 50 without; the groups were similar for age and gender. All infants were visited between 1 and 18 months of life, at the Puericulture Institute of ‘La Sapienza’. We administered a revised headache questionnaire (IHS, 2004). \( \chi^2 \) test had been used.

**Results** Twenty-one (43.2%) IPR infants suffered from migraine (69% are 1.6.1), vs. five (10.3%) of the control group (25% are 1.6.1) \( (P < 0.05) \); 19 (37.8%) suffered from TTH (57% are 2.4.1), vs. 15 (30.7%) of the control group (83% are 2.4.1).

**Conclusion** IPR, part of negative emotionality (already proved to be related to psychosomatic disorders) (Hagekull & Bohlin, 2004) of temperament, is an important risk factor for developing migraine, but not other primary headaches.

**Keywords:** migraine, newborn, reactivity, temperament

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**C044**

**Pre- and perinatal complications in headache children and adolescents: a study on 200 patients and their mothers**

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**Background** Genetic and environmental factors are hypothesized to be involved in the pathogenesis of migraine with a similar ratio. The study of environmental factors is compelling, as well the genetic studies.

**Objective** Analysing if/what factors from the history of headache patients differentiate migraineurs vs. other primary headache.

**Methods** In a sample of 200 patients diagnosed with headache and their mothers (IHS criteria, 2004), we analyse the presence of factors from the patients’ history, by means of a semistructured interview administered to the mothers. \( \chi^2 \) was computed in order to analyse contingency tables.

**Results** Sixty-four percent of patients showed at least one pre/perinatal problem: 35.5% (71/200) reported prenatal problems and 28.5% (57/200) perinatal problems. There was no difference according to the occurrence of migraine or tension-type headache in patients. Analysing the headache subtypes of mothers, migraineurs had had children with more pre/perinatal problems (40.6%, 28/61) than mothers that did not suffer from headache (24.6%, 17/73) \( (P < 0.05) \).

**Conclusion** Headache patients show a very high prevalence of pre/perinatal problems compared with data from general population (10–15%) (Waldie, Poulton 2002). Moreover, migraine in mothers is a risk factor both for developing migraine in children and for the occurrence of pre/perinatal complication. The data have important aetiological and pathophysiological implications.

**Keywords:** migraine, risk, neonatal problems, mother, child

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**C045**

**Familial recurrence of headache: a study on headache clinical characteristics in 200 children and adolescents**

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**Background** Migraine is a complex disease, where genetic and biology interact with environmental factors, determining a polygenic multifactorial aetiology.
Objective Analysing if migraine clinical characteristics change according to familial recurrence of headache compared with other headache subtypes (oHs).

Methods Two hundred children (92 M; 108 F; range 4.6–17.9 years) and their parents were enrolled. To record headache history and symptomatology: a semistructured interview, according to IHS criteria (2004). Data were collected on the occurrence of headache in first- and second-degree relatives. \( \chi^2 \) was computed in order to analyse contingency tables.

Results Prevalence of headache of any kind in parents is 81%, with a predominance in family of migraine patients compared with oHs: 22 patients do not have any parents with headache (12% vs. 8.5% Hs); 42 have only mother (22.4% vs. 8.5% Hs); 25 only father (13.3% vs. 5.3% Hs) and 49 have both parents (26% vs. 10.6% Hs). The clinical characteristics of migraine were not influenced by the presence of headache in parents, but considering second-degree relative (double familial loading), differences in headache characteristics were found: aura and photophobia (\( P < 0.05 \)).

Conclusion Children with migraine more often have first- and second-degree relatives with migraine (mainly maternal line). No difference in clinical phenotype exists in migraine and second-degree relatives with migraine (mainly maternal line). No difference in clinical phenotype exists in migraine and second-degree relatives with migraine (mainly maternal line). No difference in clinical phenotype exists in migraine and second-degree relatives with migraine (mainly maternal line).

Keywords: familial recurrence, genetic, migraine, child, symptoms

C046

Headache in schoolchildren: pain comorbidity and family history of pain

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Background Limited information exists about associations between different headache types, other pain and a family history of pain among children from the general population. Objective To find out whether reports of pain and physical symptoms differ between children with migraine, tension-type headache and without primary headache as well as between their first-degree relatives.

Methods Semi-structured interviews with a stratified, randomized sample of 130 children, 70 girls and 60 boys, aged 7–17 years together with a parent.

Results Children with headache, especially those with migraine, reported other pains and physical symptoms more frequently than children without primary headache. In addition, first-degree relatives of children with headache suffered from more migraine, other pains, and physical symptoms compared with first-degree relatives of children without primary headache.

Conclusion In schoolchildren, pain and physical symptoms cluster within individuals as well as their families. Therefore, when treating a child with headache, other pains should be asked for and treated as well.

Keywords: children, migraine, tension-type headache, pain, family history

C047

Alexithymic traits in mothers of children and adolescents suffering from primary headache

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Background Alexithymia is a specific disturbance in emotional processing indicating a diminished ability to identify and/or communicate feelings to other people. The role of negative emotionality since the early child–mother relationship in influencing headache has been evidenced (Hagekull & Bohlin 2004) and needs further studies.

Objective Investigating alexithymia in mothers of children and adolescents suffering from migraine and tension-type headache vs. a control (non-headache) group.

Methods Headache diagnoses in mothers and children by IHS criteria (2004). Toronto Alexithymic Scale (TAS-20) has been administrated to 100 subjects: 50 mothers (17 headache-free; 22 MoA; six MA; five frequent ETTH) of patients (32 MoA; four MA; 11 frequent ETTH; three chronic TTH) attending the Headache Centre and 50 from the general population (26–54 years old). \( \chi^2 \) has been used.

Results Findings indicate that the mothers of headache patients showed more clinical scores (9/50) than mothers of the control group (0/50) (\( P < 0.01 \)). Furthermore, mothers of migraineurs are more prone to show alexithimic traits than mothers of tension-type headache patients (\( P < 0.006 \)).

Conclusion The association between headache and alexithymia should be further explored in prospective studies to understand the presence in parents of a deficit in emotion regulation, particularly in migraine.

Keywords: headache, alexithymia, mother, child, adolescent

C048

Recurrent abdominal pain and headache: a controlled study by CBCL

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Background Recurrent abdominal pain (RAP) and headache are among the most common reasons for paediatric consultation: recurrent, paroxysmal, painful symptoms since the youngest age characterize the two disorders. Similar psychological characteristics have been also evidenced for both disorders.

Objective Comparing the occurrence of internalizing and externalizing disorders in headache, RAP and control groups.

Methods Child-Behaviour-Check-List (CBCL 4–18, Achenbach 1991), a semistuctured interview, had been administered to the accompanying parent of 25 headache patients (range 4–17; 9: 12 MoA, five MA, five episodic TTH, three chronic TTH) recruited at the Child and Adolescent Headache Centre of the University of Rome ‘La Sapienza’. Headache diagnosis according to IHS criteria (2004). Children with RAP (\( N = 25 \)) have been recruited from Department of Paediatric

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Gastroenterology of the University ‘La Sapienza’ and control matched sample (N = 25) in different schools. Mann–Whitney test had been used.

**Results** Forty-eight percent of headache children and 64% of children with RAP showed statistically significant scores for Internalizing Scale compared with the control group (only 4%) (P < 0.0001). No one score of Externalizing Scale is shown to be significant.

**Conclusion** Headache and RAP patients show a similar psychopathological liability (anxiety/mood disorders), related to somatization disorders.

**Keywords:** recurrent abdominal pain, migraine, internalizing disorders, child

C049

Efficacy of nimesil use in vasomotor headaches in children

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**Introduction** The large arsenal of medicinal agents is used for treatment of various types of headache at present, among which the non-steroidal anti-inflammatory agents have a large place, because the process of neurogenic oedema and inflammatory factor have a significant role in the genesis of the primary headache. Among NSAIDs Nimesil of Berlin-Chemie firm is a preparation with minimal side-effects.

**Materials and methods** We have investigated 30 children (girls 21, boys 9) from 11 to 14 years with vasomotor cephalalgia. The studied patients underwent accurate investigation of vegetative status, vegetative reactivity, vegetative activity maintenance. The patients received electropuncture diagnosis by Nakatani technique.

**Results and discussion** The variants of the data obtained from electropuncture diagnosis by Nakatani technique revealed that in the majority of patients (95%) an increase in bioenergetic indicators from 77.9 ± 3.4 to 97.8 ± 5.9 Com was noted. There was noted sharp reduction of intensity of headaches in the study group and improvement of vegetative status and bioenergy of organism after therapy with Nimesil. The intensity of vegetative indicators reduced from 98 balls to 79 balls. The patients noted a positive effect of Nimesil in decreasing intensity of headache attacks.

**Conclusion** Nimesil is a highly effective preparation for treatment of vasomotor cephalalgia, stabilizing not only vegetative but also bioenergetic body parameters.

C050

Examination to the effect of 5HT1B/1D receptor operation medicine on cyclic vomiting syndrome in Japan

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Conception of cyclic vomiting (abbreviated with CVS) was proposed in 1882 by Gee. The clinical feature is automatic neuropathy-shaped sudden intense vomiting, headache and endocrinological aberration to repeat itself. We often see patients presenting such a symptom in medical paediatric care.

In recent years automatic neuropathy has received increasing attention in Europe and America and it is positioned as a disease of non-epileptic paroxysmal disorders and one of the migraine variants because of the efficacy of tranquilizing agent. However, ‘autointoxication’, ‘acetonic vomiting’ and ‘periodicity ACTH-ADH ejection symptom-complex’ are some of the various names it is given in our country, and there are various hypotheses, such as autonomic nerve aberration, aberration of endocrinology, digestive system aberration, metabolic disorder, and it is controversial.

We had reported before that we treated CVS with 5HT1B/1D receptor agonist and achieved a good effect. We report on our comparison of the relationship between CVS and migraine.

**Keywords:** CVS, 5HT1B/1D receptor agonist, migraine, paediatrics

C051

Headache prevalence among adolescents in Germany: a large population-based study of recurrent headache

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**Objective** This population-based study examined the prevalence of headache, recurrent headache, migraine, and tension-type headache (TTH) among adolescents aged 12–15 years in Germany.

**Methods** 3234 students from 20 randomly selected schools (50% of all schools) in the region of Pomerania (Germany) completed a standardized headache questionnaire during one regular school lesson. The questionnaire complied with the respective criteria of the International Headache Society (IHS). ‘Modified criteria’ changed the items ‘duration’ in migraine (>30 min instead of >4 h) and ‘frequency’ in TTH (relaxation of minimum number of lifetime episodes).

**Results** The overall 3-month prevalence of headache was 69.4%, with 6.2% of adolescents suffering from frequent and severe headache. The 3-month prevalence of migraine was 2.6% applying the strict IHS criteria for adults and 6.9% with the modified criteria and 4.5% and 13.3%, respectively, for TTH. Recurrent headache and migraine were more common in girls than in boys and in teenagers aiming at higher education levels. The frequency of headache did not change significantly with increasing age.

**Conclusion** Recurrent headaches and primary headache disorders are common complaints among German adolescents, especially among girls.

**Acknowledgements**

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from Astra Zeneca, Berlin Chemie, Boots Healthcare, Glaxo-Smith-Kline, MSD Sharp & Dohme, Pfizer, and Woelm Pharma.

**Keywords:** headache, migraine, tension-type headache, prevalence, adolescents

### Hormones and headache

**D001**

**The effect of combination oral contraceptives on headache**

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**Background** Headache is commonly considered to be a side effect of combination oral contraceptive (COC) use, and is a frequently cited reason for discontinuation.

**Objective** This review sought to examine the risk of new onset or worsening of pre-existing headache as a potential or actual consequence of COC use.

**Methods** We conducted a systematic review of COC clinical trials published between 1966 and June 2004. We included only trials with a control group, in order to assess headache risk attributable to OC use, and separate it from the high background rate of headache in this population.

**Results** The literature review identified 121 studies. Only seven met all criteria for inclusion in this review. Because of differences in study populations, oral contraceptive formulations, trial endpoints and trial duration, it was not possible to pool data. Results are presented in tabular form.

**Conclusion** Available evidence does not suggest that COCs have a clinically important effect on headache activity in most women. Headache that occurs during early cycles of COC use tends to improve or disappear with continued use. Some subgroups of women may be at higher risk of developing new or worsening headache or headache-associated symptoms on COCs.

**Keywords:** combination oral contraceptives, headache, systematic review

**D002**

**A case of benign bath-related headache (BBRH) appearing after leuprorelin acetate therapy**

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**Background** Since BBRH was first described by Negoro et al., 13 patients have been reported without any hints on its pathophysiology.

**Objective** This report indicates an aetiological importance of fluctuations of oestrogen and related hormones.

**Methods and Results** (case report) A 37-year-old Japanese woman with no past history of migraine started to have a monthly injection of leuprorelin acetate, a gonadotropin-releasing hormone (Gn-RH) analogue, for 6 months to treat endometriosis. The treatment was successfully finished.

About 1 month after the final injection, she experienced unexpected severe pulsatile headache with nausea and vomiting soon after pouring hot water over the neck to wash her hair. The duration was about 4 h and the attack repeated three times on washing her hair in 2 weeks thereafter without recurrence. Neurological and laboratory examinations revealed normal findings including brain MRI and cerebrospinal fluid.

**Conclusion** Gn-RH analogue strongly reduces oestrogen, FSH and LH levels for about 1 month after its injection. Our patient experienced BBRH during that period when the Gn-RH effect might disappear. BBRH in this patient may have a close relationship to fluctuations of hormonal levels induced by the Gn-RH analogue in addition to a headache-prone hereditary and ethnic background.

**Keywords:** benign bath-related headache, Gn-RH analogue, oriental female

**D003**

**The possible role of pituitary pace-maker in menstrual migraine**

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**First trial—method** 359 females were monitored over 20 years since the age of 33.

**Results and conclusion** Main outcomes were: during the first quarter of pregnancy (n = 115) 98 reported moderate 4–12-h migraine having the same monthly pattern of menstrual migraine. Pregnancy is characterized by oscillation in oestrogens without any relationship with migraine attacks. That suggests the role of the pituitary–hypothalamic system intended as a pace-maker of biological rhythms.

**Second trial—method** To act on pituitary gland we used melatonin (9 mg/g orally once a day) in 170 menstruants. A matched group of 156 women receiving only analgesics represented the control group.

**Results** Melatonin reduced pain following a 3-month therapy (VAS 0–100, 74.3 ± 11.9 SD vs. 34.7 ± 12.9 SD, P > 0.0001) and during 10 months of the 1-year follow-up period (54.2 ± 13.1 SD, P > 0.0001). In 157 cases, 10.2 months ± 5.8 SD after therapy there was a switch: i.e. pre-menstrual migraine became post-menstrual and vice versa. In both groups the pre-menopausal phase, characterized by low gonadotropin pulse and hypo-oestrinaemia, overlapped a worsening of migraine. In menopausal and post-menopausal phase a menstrual-like pattern of migraine remained in 80 of 134 sufferers in the first period: 20.6 months ± 7.3 SD.

**Conclusion** Results suggest a role of pituitary gland intended as pace-maker also relating to internal/external inputs.

**Keywords:** migraine, menses, oestrogens, melatonin, pituitary gland

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EMICA. Evaluation of menstrual migraine: a French survey performed by general practitioners
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Background The frequency of menstrual migraine (MM) is based mostly on clinical experience and is not well documented.

Objective An epidemiological survey was undertaken to evaluate the frequency, severity, the factors associated with MM and the type of treatment dispensed.

Methods The survey was conducted among 769 GPs and involved 14,331 menstruating females. Among them, 6,201 (43%) were identified as migraineurs according to IHS criteria. MM was defined as attacks that occurred 2 days before through the last day of the menstrual period. Associated factors with MM were evaluated using multiple logistic regression.

Results Among the 6,201 migraineurs 70% had MM. 25% of MM patients were misdiagnosed by the GP. Associated factors with MM were oral contraceptives use, a history of migraine beginning before the age of 20 and age under 47 years. Thirty-six percent of patients reported that the intensity of their MM was more severe than their non-menstrual migraine attacks. Migraine-specific medications (triptans or ergot derivatives) were prescribed 45% of the time.

Conclusion MM has a high prevalence among menstruating women and is often misdiagnosed. Factors associated with MM are age, the age of migraine onset and use of oral contraceptives. Migraine-specific medications (triptans and ergots) are prescribed in 45% of women.

Keywords: menstrual migraine, survey, frequency, associated factors, severity, treatment

A possible predictive factor of migraine outcome after menopause
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Background It is well known that perimenopause marks a time of exacerbation or regression of migraine, for many women. Up to now, no data have existed predicting the outcome of the illness after the onset of menopause.

Objective In order to discover some predictive factors in the development of the illness, we studied the course of post-menopausal migraine in a number of mothers and daughters.

Methods 99 women (age 42–75 years) suffering from migraine according to ICHD-II criteria, referring for the first time to the Turin University Headache Centre in the years 2000–2004, whose mothers suffered from the same illness, were studied. We asked these women if and how the characteristics of their migraine changed during menopause, then compared these data with their mothers’.

Results 26 (54.2%) daughters improved out of 48 (48.5%) mothers with the same tendency and seven (77.8%) daughters worsened out of nine (9.1%) mothers (P = NS, 2 test).

Since the power of the test was below the desired level, these data should be interpreted cautiously.

Conclusions On the basis of these data, in the majority of cases daughters’ migraine seems to follow the mothers’ pattern. More interviews are needed to assess this tendency.

Keywords: migraine, menopause, outcome, predictive factors

Menstruation-related migraine in Korean nurses—Hallym University Migraine in Nurses Study
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Background and objectives It is known that migraines in women are associated with menstruation. We analysed the data of the Hallym Medical Centre nurse study to identify the prevalence and clinical features of menstruation-related migraine in Korean nurses.

Method All 1501 nurses working at Hallym Medical Centre were given a 72-item questionnaire on migraine including general information, occupational environments and characteristics, characteristics of headache, triggering factors, management of headache, migraine-related disabilities and characteristics of sleep. We categorized participants as having menstruation-related migraine (MRM) who answered that migraine attacks were related to menstruation.

Results 89.2% of participants completed the questionnaire. All were female with mean age of 27.5 ± 5.7 years. According to IHS criteria, 17.5% were classified as having migraine. 25.1% of migraineurs had MRM. Among MRM, 61.0% had migraine attacks in premenstrual period, 22.0% in menstruation period, 1.7% in postmenstrual period. 15.3% of migraineurs reported a varying relationship between migraine attacks and menstruation. There were no significant differences in attack frequency, headache severity or MIDAS scores between MRM and non-MRM.

Conclusion 25.1% of nurses with migraine had MRM. Migraine attacks occurring in the premenstrual period were the most common form of MRM. MRM showed some different clinical features from those of non-MRM.

Migraine prevalence in Iranian postmenopausal women
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Background Although previous studies have disclosed that the vast majority of migraine sufferers tend to improve after physiological menopause, it can become worse or even occur for the first time in women vulnerable to hormonal changes. According to these studies we try to elucidate the prevalence of menopausal migraine in our society based on our outpatient neurological department.

Methods and materials A cross-sectional hospital-based survey was undertaken among Iranian women aged between 50 and 75 years in Isfahan province (located at the centre of our country), Iran. We recruited 125 women suffering from...
headache in the age range 50–75 years. All subjects were evaluated for migraine headache by a practising neurologist according to International Headache Society classification criteria. Menstrual history, including a past or current history of premenstrual syndrome, was obtained. In addition, all our cases were evaluated for hypertension and familial history of migraine.

**Results** Our data indicate that 41.6% of patients had had menopausal migraine. Among them, 84.61% had a positive history of migraine before menopause and in the remainder no previous history of migraine was detected. Meanwhile, 57.69% demonstrated a positive history of familial migraine in their close relatives.

**Conclusion** To our knowledge, there is no documented report present in our community indicating the prevalence of menopausal migraine based on a population survey, but this study supported the impression that migraine prevalence declines after spontaneous menopause. In the other words, our women suffer more from menopausal migraine compared with other nations.

**D008**

**Effects of oral contraceptives (OCP) in Iranian women with migraine headache**

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**Background** Migraine is most common in women of childbearing age, the same population that also uses oral contraceptives. Because the most common method for contraception in Iranian women is the oral contraceptive pill, we decided to investigate the effects of OCP on intensity of migraine headache.

**Methods** In this study we selected 44 women less than 40 years old who had migraine, attending the Neurologic Clinic of Noor in Isfahan University. This study was a clinical trial. We compared severity, duration of attacks and frequency of migraine in this group, before and after two cycles of oral contraceptive pill (type LD) use.

**Results** Severity in 52.3% was unchanged, in 36.6% was worsening and in 11.4% headache was improved (P < 0.05). Duration remained unchanged in 45.5%, worsened in 38.6% and improved in 15.9% (P < 0.05). Frequency in 50% was unchanged, in 34.1% was increased and in 15.9% was decreased (P > 0.05).

**Conclusion** In our population we have differences between before and after oral contraceptive use in severity and duration of headache attacks but no significant difference in frequency; this means that oral contraceptive use changes the severity and duration of headache attacks but does not change the frequency significantly.

**D009**

**Long-term analgesic effect of octreotide on headache in patients with acromegaly**

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**Background** Octreotide has been used for the treatment of acromegaly and the strong analgesic effect is well known. However, the long-term analgesic effect has not been well documented.

**Objective** We report three acromegaly patients treated with octreotide to elucidate the long-term effects.

**Methods** They underwent octreotide treatment for 70, 149, and 150 months respectively. All patients complained of headache. The pain intensity was assessed using a visual analogue scale.

**Results** Self-injection of octreotide exhibited strong analgesic effect on severe headache in all three patients. Headache resolved in a patient after surgery, medical treatment including octreotide and radiotherapy. His serum GH and IGF-I levels normalized and no medication was required. Two other patients also underwent surgery, medical treatment and radiotherapy. However, endocrinological remission has not been achieved and they still have headache. The two patients have been treated with octreotide. Octreotide showed strong analgesic effect even after long-term administration in all patients. A patient developed a dependency on octreotide soon after the initiation.

**Conclusion** The present study showed the long-term effectiveness of octreotide on acromegaly including analgesic effect as well as GH reduction.

**Keywords**: octreotide, headache, acromegaly, long-term

**D010**

**Headache before and during menstruation: a diary study in 327 migraineurs**

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**Background** Menstrually-related migraine has been defined as occurring on days –2 to +3 of menstruation.

**Objectives** To calculate the risk of onset and persistence of headache in migraineurs before and during menstruation.

**Methods** A total of 327 migraineurs (86.5% females) filled in a comprehensive diary for 3 months. Differentiating (1) the 2 days before menstruation, (2) the first three and (3) the remaining days of menstruation we calculated univariate and stepwise multivariate Cox regression analyses in all patients (n = 327), in menstruating women (n = 196), and in menstruating women without hormonal contraception (n = 102).

**Results** The risk of headache onset was increased premenstrually in the entire group (hazard ratio 1.26, P = 0.005) and in menstruating women (hazard ratio 1.34, P = 0.002), but not in women without hormonal contraception and it was
similarly increased in all groups on all days of menstruation (hazard ratios 1.47–1.98). The risk of headache persistence was increased in all groups during all days of menstruation, but not premenstrually.

**Conclusion** In migraineurs, the risk of headache onset and persistence is increased not only in the first 3 days of menstruation, but also on days 4+. The risk of headache onset is increased premenstrually. Hormonal contraception has no negative effect.

**Keywords:** menstruation, migraine, headache onset, headache persistence, hormonal contraception

**D011**

**Association between headache and menstruation in Japanese women**

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**Background and objective** Approximately 60% of women with migraine are reported to be associated with menstrual cycles. We investigated the association between headache and menstruation in Japanese women.

**Methods** Patients kept their headache diary to record the days of headache occurrence, severity, disability, use of triptans or NSAIDs. The menstrual period was marked.

**Results** Forty-six women 37 ± 8.2 years old were studied. Twenty-nine women had migraine without aura (63%), 17 had both migraine without aura and tension-type headache (37%). The menstrual cycle was 31 ± 7.7 days among 138 cycles analyzed. Two had pure menstrual migraine without aura (4.4%), 25 had menstrually-related migraine without aura (55.5%). Headache occurred most frequently on the first 2 days of the period, and the drug was most frequently consumed on these days. Out of 21 attacks treated by NSAIDs and triptan, NSAIDs were taken prior to triptan.

**Conclusion** As many as 59.9% of migraine attacks were associated with their menstrual cycles in Japanese women. Headache occurred most frequently on the first 2 days, and NSAIDs was usually taken as the first choice and often followed by triptan.

**Keywords:** multiple sclerosis, migraine, brainstem lesions, MRI

**E002**

**Transcranial Doppler findings in patients with medication-overuse headache**

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**Objective** To investigate intracranial blood flow velocities (BFV) in patients suffering from medication overuse headache (MOH).

**Methods** Twenty-three females with ergotamine overuse headache (EOH), 23 females with analgesic overuse headache (AOH) and 15 female healthy controls participated. All patients suffered migraine without aura. Mean BFV of bilateral middle and anterior cerebral (MCA and ACA) and basilar arteries (BA) were measured by transcranial Doppler TCD.

**Results** There was no significant difference between the mean ages of the patient and the control groups (EOH: 42.5 ± 4.81, AOH: 41.31 ± 6.59 and control group: 41.14 ± 4.16 years) or between the patient groups in mean primary headache and mean MOH duration. Mean BFV of BA was significantly increased in EOH group compared with that of AOH and control groups (EOH: 46.81 ± 9.79, AOH: 40.63 ± 6.07 and control group: 40.92 ± 2.09 cm/s) (P < 0.05). Mean BFV of MCA was significantly increased in EOH group in comparison with AOH (EOH: 65.14 ± 13.38, AOH: 53.8 ± 12.14 and control group: 56.25 ± 3.77 cm/s) (P < 0.05). No significant difference in BFV of ACA was observed between any of the groups (EOH: 57.2 ± 12.51, AOH: 51.29 ± 10.14 and control group: 53.5 ± 6.04 cm/s) (P > 0.05). Mean BFV of all vessels in AOH group was lower than control and EOH groups but failed significance.

**Conclusion** Our results support 5HT1B/D receptors being located on MCA and BA.

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E003
A fetal circle of Willis and white matter abnormalities in migraine
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Objective The purpose of this study is to evaluate whether a fetal circle of Willis contributes to white matter abnormalities (WMAs) in migraineurs.

Methods Brain MRI, MRA using 3D time-of-flight sequence, and cardiovascular risk factors were analysed among 415 migraineurs (233 women), 54 migraineurs with aura (MA), 361 migraineurs without aura (MoA), and 356 age- and sex-matched controls.

Results The cardiovascular risk profile did not differ among the four groups. Clinical hallmark of migraineurs revealed frequency of 1 attack per month and mild degree of headache severity. Appearance of cerebral WMAs (%) did not significantly differ among the migraine (6.3), MA (13.0), MoA (5.3) and control groups (5.1). Percentage of fetal patterns did not significantly differ among 17.6 in migraineurs (17.0 in men and 18.0 in women), 22.2 in MA sufferers and 16.9 in MoA sufferers and 16.0 in controls (14.7 in men and 17.6 in women). The presence of cerebral WMAs (%) decreased in migraineurs with fetal patterns (2.7) compared with migraineurs without fetal patterns (7.0), controls with fetal patterns (5.3) and controls without fetal patterns (5.0).

Conclusion The data indicate the possibility that a fetal circle of Willis protects against appearance of cerebral WMAs in migraineurs.

Keywords: migraine, a fetal circle of Willis, white matter abnormalities, cardiovascular risk factors

E004
Cerebral haemodynamic assessment in primary headache patients
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Purpose Assessment of the main cerebral blood haemodynamic parameters in primary headache patients.

Materials and methods Migraine with aura patients, over 18 years old and chronic tension-type patients of the same age group. (1) Prospective neurological intraindividual comparison in headache patients. (2) Routine neuroimaging of all patients to exclude secondary headaches. (3) Retrospective evaluation of headache patients in order to assess the CBF, CBV and MTT using perfusion analysis before and in attack period using by MedX program 3.4.1. (4) Post-processing perfusion analysis for assessing perfusion parameters.

Results Perfusion changes occur only in migraine with aura subjects during the attack (decreasing of CBF on 16–53%, CBV on 6–33%, and increasing MTT). Cerebral oligaemia in migraine with aura patients correlates with reduction of r-CBF of this stage. Patients with chronic TTH tried to have higher CSF pressure because they possibly have an increased CBV.

Conclusions Chronic tension-type headache patients have increased intra CBV, which causes a slight elevation of the CSF pressure. In contrast to this, in migraine patients there may be changes in the intracranial blood volume depending on stage of progression of migraine attack, with a lower blood volume at the beginning and an increased volume at the later stages.

E005
A case of radionuclide cisternography in spontaneous intracranial hypotension with multiple leaks
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Background Spontaneous intracranial hypotension is characterized by postural headache, low CSF pressure and specific MRI findings. The pathogenic mechanism of spontaneous intracranial hypotension has suggested spontaneous cerebrospinal fluid leakage from a spinal dural tear without previous history of head trauma or lumbar puncture. Most common site of CSF leakage was C-T spine junction, almost all cases were single or double lesion and multiple leaks were very rare.

Case A 35-year-old man complained of headache. The character of headache was orthostatic and associated with severe nausea and vomiting. The headache was not relieved by analgesics. He had no history of trauma or lumbar puncture. Neurological examination showed no lateralizing and localizing sign. Brain MRI demonstrated diffuse thickening and enhancement of the meninges. No signs of venous sinus thrombosis were identified. There was no downward displacement of the cerebellar tonsils. The radionuclide cisternography showed cerebrospinal fluid leakage at both C-T junction level and multiple thoracic spine levels. After epidural blood patch was performed twice, his symptom was improved.

Conclusions We presented the very rare case report of a patient of spontaneous intracranial hypotension, in which radionuclide cisternography demonstrated multiple CSF leaks. To localize multiple leaks, radionuclide cisternography should be performed with a patient in various positions just before images are obtained.

E006
MR angiography during the aura in the patient with migraine. A case report
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Background Some authors report vasospasm during and/or after the headache in patients with migraine by MR angiography (MRA). This paper is the first report of abnormal MR vascular imaging during the aura in a patient with migraine.

Case presentation A 61-year-old woman with a 7-year history of migraine with aura (scintillating scotoma) was admitted to our hospital due to the right hemiplegia and aphasia. MR imaging was immediately performed, and MRA showed diffuse narrowing of the intracranial arteries and severe stenosis of the inferior branch of the left middle cerebral artery. The right hemiplegia and aphasia disappeared 1 h after symptom onset, but she did not suffer from migraine.
headaches. Follow-up MRA 2 days after admission showed resolution of the vasospasm. Two months later, she suffered from attacks of scintillating scotoma without headache. MRA revealed severe stenosis of the right posterior cerebral artery. At the same time, she suffered from left central retinal vein occlusion due to the venous thrombosis. Increased tendency of platelet aggregation was revealed. After the administration of antiplatelet drugs, migraine attacks were decreased.

**Conclusion** To the best of our knowledge, this paper is the first report of the vasospasm during the aura in a patient with migraine by MRA.

**Keywords**: aura, migraine, MRA, platelets

**E007**

**Headaches associated with Rathke’s cleft cyst**

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**Objective** Headaches are a common presentation in patients with Rathke’s cleft cyst (RCC). This study was conducted to elucidate the underlying mechanisms.

**Methods** 33 patients were retrospectively studied. 23 patients underwent surgical intervention, 22 patients with trans-sphenoidal surgery (TSS).

**Results** Headaches were the most common symptoms occurring in 16 patients (48.5%) and were the only presentation in seven patients. Five patients suffered sudden severe headache mimicking that of pituitary apoplexy. Three patients had repeated the episodic headaches. Presence of headaches did not correlate with cyst size but was more frequent in RCCs of T1 high- and iso-intensity than those of T1 low intensity on MRI ($P = 0.0309$). Among six patients with intense chronic inflammation at the cyst wall, five patients had a T1 high intensity RCC ($P = 0.0220$), and four patients associated hypopituitarism ($P = 0.0249$), none of which improved after surgery. Headaches improved after TSS in 11 patients (84.6%). Episodic headaches disappeared in every patient.

**Conclusion** Headaches, particularly episodic headaches, are common manifestation in patients with RCCs and may indicate intermittent inflammatory reactions. Patients who repeat episodic headaches should undergo TSS to prevent extension of the inflammation that can potentially cause irreversible endocrine dysfunction.

**Keywords**: headache, pituitary tumour, Rathke’s cleft cyst, MRI, trans-sphenoidal surgery

**E008**

**MRI prevalence of subclinical cerebellar stroke in a highly selected migraine population**

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**Purpose** To determine the prevalence of subclinical cerebellar infarction in a highly selected population of migraine patients.

**Background** Investigators have reported that in a sample of individuals with migraine drawn from the general population, brain MRI may demonstrate a prevalence of subclinical cerebellar infarction which significantly exceeds that observed in migraine-free controls matched for age, gender and place of residence.

**Methods** The brain MRI scans of 100 consecutive patients with migraine and no clinical history of stroke who presented to a headache clinic and selectively had undergone brain MRI and the MRIs of 50 patients with a history of stroke were reviewed by a board-certified neuroradiologist blinded as to patient diagnosis. The neuroradiologist was asked to assess each scan according to the presence vs. absence of infarction and the location(s) of any infarction noted.

**Results** None of the MRI scans performed on the 100 patients with migraine and no clinical history of stroke was felt to demonstrate evidence of cerebellar infarction.

**Conclusion** Our results conflict with those reported previously by others and suggest that MRI evidence of subclinical cerebellar infarction may not occur at a greater frequency in migraineurs than in non-migraineurs.

**Keywords**: cerebellar infarction, MRI, migraine

**E009**

**MR myelography findings in patients with spontaneous intracranial hypotension**

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**Background** There are limited published reports of non-invasive MR myelography in patients with spontaneous intracranial hypotension (SIH).

**Objectives** To report findings for CSF leakage of MR myelography in patients with SIH.

**Methods** We recruited consecutive SIH patients between April 2003 and January 2005. The diagnosis of SIH was based on the criteria of headache attributed to spontaneous low CSF pressure proposed by the ICHD-2, 2004, code 7.2.3. Every patient received brain MRI plus MR myelography using Single-Shot Fast Spine-Echo method during an acute stage and at follow-up when headaches resolved.

**Results** Seven patients (3 males/4 females) were enrolled. MR myelography demonstrated CSF leakage in five patients (71%): three cervical and two thoracic spine. Compared with follow-up MR myelographies, positive findings for CSF leakage were evidenced as either an oblique stripe originating from the dural sac ($n = 3$) or irregular root sleeves ($n = 2$). Further, an accumulation of pleural effusion at the thoracic paraspinal region ($n = 1$) might be an indirect sign of CSF leakage. Perineural cysts should not be taken as a positive sign.

**Conclusions** Since symptoms might worsen after diagnostic dural punctures, the alternative of non-invasive MR myelography might be used to screen for CSF leakage in patients suspected SIH.
**E010**

**Observation of cerebral cisterns and ventricles with fine, flexible fibrescopes by percutaneous lumbosacral route**

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**Objective** To establish the minimally invasive method for a diagnostic as well as manipulative tool of CNS diseases, we visualized the cerebral cisterns and ventricles by percutaneous lumbosacral route by using the newly developed fine flexible fibroscope.

**Methods** Flexible fibrescopes, 0.5, 0.9, and 1.4 mm in diameter, were introduced up to the cerebral cisterns and ventricles through percutaneous lumbosacral puncture in 31 wakeful patients with chronic headache and/or neck pain or undergoing spinal surgery, in whom MRI did not disclose any particular abnormalities in the brain.

**Results** In 25 of 31 patients, the cerebellomedullary and/or pontine/interpeduncular cisterns were easily and safely reached and the brainstem structures were visualized. Further advancement of the fibrescopes to the 4th and 3rd ventricles was successfully made in two patients tested. Numbers of arachnoidal filaments were found in the cerebellomedullary cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern in four patients (two with chronic spinal arachnoiditis, one with spinal arachnoid cyst, one with post-traumatic pain cistern

**Conclusions** This method may provide a minimally invasive and safe way to observe the cerebral cisternal and brainstem regions, and can be applied at the bedside for the diagnosis of cerebral ventricular system diseases.

**Keywords:** cerebral cisterns, fibrescopes, lumbosacral puncture

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**E011**

**Grey matter decrease in patients with chronic tension-type headache**

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For cluster headache, but not for migraine, local morphological alterations have recently been detected. To answer the question, whether the brain of patients suffering from chronic headache shows morphological alterations, we investigated 40 patients suffering from CDH, consisting of 20 patients suffering from chronic tension-type headache (CTTH) and 20 patients with a medication overuse headache (MOH) before and after medication withdrawal, and compared them with 40 healthy controls with no headache history. Using MRI and voxel based morphometry (VBM) we found that the brain of patients suffering from MOH or episodic migraine, developed a significant decrease in grey matter in the midbrain, the insula, anterior and posterior cingulum, parahippocampus and fronto-orbital cortex. Our data suggest that the brain grey matter may be altered in regions known to play a substantial role in pain transmission and antinociception. In contrast to CTTH, patients suffering from migraine or medication overuse headache failed to show any global or regional structural changes. Our finding challenges the notion that the brain of idiopathic headache sufferers is normal and implies that the alterations are specific to CTTH rather than simply representing a response to chronic head pain or chronicity per se.

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**E012**

**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. We utilized gastric scintigraphy studies to compare gastric motility in migraineurs in the ictal and interictal periods compared with normal controls.

**Methods** Ten migraine (M) subjects were compared with equal numbers of age- and sex-matched normal controls (NC). Gastric scintigraphy using a standard meal was performed in NC (n = 10), in M subjects in the interictal period (n = 10) and in the ictal period migraine (n = 9).

**Results** Time to half emptying was delayed in migraineurs ictally (78%) and interictally (80%) using institution normative data. Gastric stasis was less pronounced ictally (149.9 min) compared with interictal period (188.8 min). There was a significant delay in M interictally compared with NC (M 188.8 vs. NC 111.8 min; P < 0.05). These findings were replicated using a second endpoint, percentage of radioactive material remaining in the stomach at 2 h.

**Conclusions** Contrary to previous belief this study has demonstrated that migraineurs suffer from gastric stasis both during and outside an acute migraine attack. This suggests that migraineurs may have an abnormal autonomic function compared with non-migrainous controls.

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**E013**

**MRI for patients with headache: is it necessary for a diagnosis?**

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**Background** Taking a history about headache is most important for a diagnosis of headache. It is also important to exclude headache caused by organic lesions.

**Objective** To assess the importance of MRI for a diagnosis of headache.
Methods In serial 160 patients (69 men, 91 women, 60.1 ± 18.7 years) who underwent brain MRI study were evaluated.

Results Fifty-three of 160 patients (33.1%) suffered from headache. The patients with headache (14 men, 39 women, 49.5 ± 19.0 years) were significantly younger than the patients without headache (55 men, 52 women, 65.3 ± 16.3 years). Patients with headache were more women than the patients without headache. On brain MRI, abnormal findings were detected in 90 of 160 patients (56.3%). The difference in the ratio of abnormal findings on MRI was not significant between patients with headache (24/53, 45.3%) and patients without headache (66/107, 61.7%). Among 30 patients with primary headache, four (13.3%) had sinusitis which worsens their primary headache and it could be found with MRI. Seventy-seven of 160 patients had ischaemic cerebral lesions on MRI.

Conclusion Even if patients fulfil diagnostic criteria for primary headache, MRI is useful for a diagnosis of coexisting headache and also useful for the prevention of cerebrovascular disease.

Keywords: headache, diagnosis, MRI

E014 Vertebrobasilar artery dissection as a cause of occipital headache
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Objectives To evaluate the frequency of headache and neck pain in patients with brainstem and cerebellar infarction due to vertebrobasilar artery dissection (VBAD) at onset.

Subjects and methods We enrolled consecutively 51 patients with acute brainstem or cerebellar infarction within a month of onset due to VBAD during a 4.5-year observation period. The diagnosis of VBAD was done by gadolinium-enhanced T1 weighted thin slice image from 1.5-T MRI. We surveyed retrospectively the occurrence of headache and neck pain from medical records on admission.

Results VBAD was found in about 20% of the patients with all brainstem and cerebellar infarctions. One half of the patients with medullary infarction had VBAD. Ten of 51 patients (19%) with VBAD complained of either occipital headache or neck pain on admission.

Conclusion VBAD is one of the main causes of brainstem and cerebellar infarction, especially in patients with medullary infarction. Occipitalgia and neck pain is highly specific in VBAD but not chronically symptomatic. Because of low occurrence of headache and neck pain, we should make a diagnosis of VBAD not only with clinical symptoms but in first MR findings among patients with suspicious brainstem infarction.

Keywords: brainstem infarction, vertebrobasilar artery, dissection, neck pain

E015 Near infrared radiation spectroscopy (NIRS) evaluates triptan effect
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Objective NIRS is a non-invasive method to determine oxygen saturation of circulation blood on the surface of the brain. We used this method to evaluate the time course of the effect of triptan (rizatriptan) which constricts blood vessels.

Methods NIRS determination of oxygen saturation was accomplished in out-patients complaining of attacks of migraine or cluster headache. After a control period of 5 min, triptan (rizatriptan 10 mg) was given p.o. Evaluation continued for 90 min.

Results Five patients (two men with cluster, three women with migraine, mean age 33 years) took triptan. Oxygen saturation of brain surface diminished progressively during 30-min period following triptan. Cluster headache was often relieved prior to significant decrease in oxygen saturation determined by NIRS.

Conclusion NIRS proved to be useful for objective diagnosis of migraine and cluster headache and drug treatment of migraine and cluster headache.

Keywords: NIRS, migraine, cluster headache, triptan and rizatriptan

E016 Transcranial Doppler sonography (TCD) in the evaluation of headache sufferers at different moments during attack
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Objective To compare TCD values in headache sufferers during various phases of attack and interictal period.

Methods TCD examinations were performed in: 43 migraineurs, 12 tension-type sufferers (TTH), 10 chronic daily headache sufferers (CDH) and 45 age- and sex-matched controls at different moments during attack, as well as during headache-free period. Blood flow velocities, resistivity index and breath holding index were measured. Headache intensity was rated on a 10-point scale. When appropriate, a Wilcoxon rank sum, a signed rank test and Pearson’s correlation coefficient were used.

Results Our results show a trend towards (a) higher values of mean blood flow velocities (MFV) in interictal migraineurs than in controls (P<0.05), (b) lower velocities in migraine periods with relatively high intensity of pain when compared with interictal phase. Correlation analysis revealed a linear relationship between changes in MFV at different moments during attacks and correspondent changes in pain intensity scale (r = 0.59, P<0.05). The TTH and CDH sufferers had no significant increase in interictal MFV values (P>0.05). Variability of repeated TCD measurements, assessed by intraclass correlation coefficient, was low.
Conclusion The differences in TCD parameters between migraineurs and controls suggest some degree of altered vascular reactivity in basal and ictal conditions.

Keywords: transcranial, Doppler, sonography, headache

E017
Focal cerebral blood flow changes in two cases of migraine
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Objective We examined focal cerebral blood flow (CBF) during the attacks of two migraine patients using 99mTc-ECD-SPECT. CBFs in the interictal period of each patient were measured as the baseline.

Methods SPECT was performed in two cases. Case 1: A 10-year-old girl, first attack of migraine with aura. On first SPECT, she had headache but her visual symptom was resolved. Second SPECT was performed on the day after the attack. Case 2: A 14-year-old boy, diagnosed as sporadic hemiplegic migraine. His first SPECT was performed during the asymptomatic period. He had headache, nausea, left hemiparesis and confusion on second SPECT. We calculated subtracted SPECT images. CBFs on the attacks subtracted from the asymptomatic periods. Focal CBF changes during the attacks were evaluated using the subtracted SPECT/MRI fusion images.

Results Right temporo-occipito-parietal region, cingulate gyrus and mesial temporal showed hyperperfusion, bilateral thalamus and subthalamic region showed hyperperfusion in case 1. Right hemisphere and bilateral cingulate gyrus showed hypoperfusion and dorsal brainstem showed hyperperfusion in case 2.

Conclusion Hypoperfusion areas during the attacks almost support preceding studies. Perfusions of the limbic system, brainstem and subthalamic regions were also changing and thought to be related on migraine attack.

Keywords: migraine, 99mTc-ECD-SPECT, limbic, brainstem, subthalamic lesion, migraine

E018
The role of brain MRI in patients with chronic headache who have normal neurological examinations
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Background and objectives There is a low likelihood of discovering significant disease in evaluating chronic headache patients with normal neurological examinations by magnetic resonance imaging (MRI) because previous studies considered silent brain infarct (SBI) as not significant lesion. We investigated the incidence of abnormal findings including SBI in MRI of the brain for the patients who have normal neurological examinations.

Methods We retrospectively reviewed the medical records and MR images of 425 patients with chronic headache between January 2001 and December 2002. Only 212 patients with normal neurological examinations were included in this study.

Results The patients were diagnosed as having tension-type headache (67.8%), migraine (26.7%), and atypical type headache (5.4%). Clinical significant abnormalities on MRI were found in 29 patients (13.7%) which were silent infarct, tumour, AVM and aneurysm. The most common abnormality on MRI was SBI (65.5%). We found that SBI in chronic headache with normal neurological examinations were related not only to hypertension and heart disease, but also to types of headache.

Conclusion These results indicate that brain MRI in chronic headache is a useful tool for detecting SBI, which may be an independent risk factor for symptomatic brain infarcts.

Keywords: chronic headache, MRI, silent brain infarct

Therapeutic advances in acute headache

F001
Is cold therapy effective in migraine attacks?
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Background Some patients with headache report that they have frequently used physical therapies such as application of cold. There are a few studies related to cold therapies.

Objective In this study, we investigated the effect of cold application in migraine patients.

Methods Twenty-eight migraine patients were included. Cold therapy was applied to the patients by gel cap. Patients used this cap during their two migraine attacks. Before the cold therapy, headache severity was recorded by using visual analogue scale (VAS). Patients used this cap for 25 min. Just after the therapy, 25 min, 1 h, 2 h and 3 h later, they recorded their VAS score.

Results Twenty-six patients had migraine without aura and two patients had migraine with aura. Twenty-five minutes after the treatment of first attack, VAS score was decreased from 7.89 ± 1.93 to 5.54 ± 2.96. Twenty-five minutes after the treatment of the second attack, VAS score was decreased from 7.7 ± 1.8 to 5.4 ± 3.55. Two courses of cap therapy were found to be effective in migraine attacks (P < 0.05).

Conclusion In this study we found that cold therapy was effective in the migraine attacks. Cold treatment may be a useful treatment choice for migraine patients.

Keywords: migraine, headache, cold, therapy

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F002

Efficacy of switching to eletriptan in migraine patients unsuccessfully treated with NSAIDs

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The current study evaluated the efficacy and tolerability of switching to the 40-mg dose of eletriptan in triptan-naive patients who reported a poor response to non-steroidal anti-inflammatory drug (NSAID) therapy. Patients (N = 106) meeting International Headache Society criteria for migraine, and who reported dissatisfaction with their current NSAID, received open-label treatment with a 40-mg dose of eletriptan for one migraine attack. Headache and pain-free response rates at 2 h and 4 h postdose, respectively, were 60%/32% and 83%/54%. At 2 h, relief of baseline associated symptoms was achieved by 67% of patients with nausea, 62% of patients with phonophobia, and 61% of patients with photophobia. Functional response was achieved by 61% of patients by 2 h post-dose. Initial response was maintained over 24 h, with only 22% of patients experiencing a headache recurrence, and only 14% using a second dose of eletriptan. At 24 h, 81% of patients rated eletriptan as being preferable to any previous treatment they had taken for migraine. Overall, eletriptan was well tolerated with the majority of the adverse events being transient, and mild-to-moderate in severity. No serious adverse events were reported. The results of this open-label study suggest that eletriptan is well-tolerated and highly efficacious treatment option in triptan-naive patients who were poor responders to NSAIDs.

F003

Efficacy of Diclofenac-Potassium Sachets in migraine: a randomized, double blind, cross-over study with Diclofenac-Potassium Tablets and placebo

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Background Rapid onset and effective pain reduction are important in migraine treatment. A new drinkable Diclofenac-Potassium Sachet (Volfast®, Catafast®) formulation enables fast intestinal absorption.

Objective This multicentre, controlled, cross-over study evaluated the clinical efficacy of single-dose (50 mg) Diclofenac-Potassium-Sachets (DPS) on pain intensity and analgetic onset time, compared with Diclofenac-Potassium-Tablets (DPT) and placebo (PLA).

Methods 328 out-patients with established diagnosis of migraine were randomized to double-blind treatment for three separate migraine attacks. Patients recorded headache diary over 8 h using verbal 4-point score and visual analogue scale (VAS). Percentage of patients pain free at 2 h and headache response were compared by logistic regression analysis, VAS ratings were compared by ANCOVA.

Results 317 patients received treatment. At 2 h, 24.7% were pain-free with DPS compared with 18.5% and 11.7% with DPT and PLA (P < 0.01). For DPS, DPT and PLA, headache response was achieved in 46%, 42% and 24% (P < 0.01). VAS headache reductions were significantly greater for DPS and DPT than PLA at all time points. Onset to analgetic effect was 15 min for DPS and 60 min for DPT.

Conclusion Diclofenac-Potassium-Sachets provide rapid onset, effective treatment for migraine pain.

F004

Photoplethysmography may predict oral sumatriptan responsiveness in migraineur

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Background Although triptan’s efficacy has been demonstrated all over the world, no predictive factor for responsiveness has been identified. In the previous study, we disclosed that the ageing index in the second derivative of the waveform of photoplethysmography (SDPTGAI) is significantly higher in migraine patients between attacks than in normal control.

Methods SDPTGAI was obtained from 52 migraine patients before attacks or 50 mg oral sumatriptan. After converting the SDPTGAI into the ‘vascular age’ in each patient, the differences between ‘vascular age’ and real age and the ratios of ‘vascular age’ to real age were compared between the responders and non-responders.

Results Forty-six of 52 patients were involved in the final assessment (male : female = 10 : 36); 32 were responders (M : F = 3 : 29) and 14 non-responders (M : F = 7 : 7). Both the differences and the ratios are significantly higher in the responders than in the non-responders (P = 0.010 and 0.017, respectively). With the cut-off, 10 years in the differences or 1.2 in the ratios, the positive predictive values were 0.89 or 0.91, respectively.

Conclusion An SDPTGAI obtained beforehand may be a predictive marker in oral sumatriptan treatment for acute migraine attacks.

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F005

Modulation of nociceptive pathway activity in the trigeminocervical complex by BK<sub>Ca</sub> channel blockers and NS1619

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**Background** Large conductance, voltage- and calcium-activated potassium channels (BK<sub>Ca</sub>) are regulators of neuronal excitability and synaptic transmission. Iberiotoxin (IbTx) and slotoxin (SloTx), peptide blockers of BK<sub>Ca</sub> channels, promote hyper-excitability in some neurons.

**Objective** To examine using microiontophoresis the effects of IbTx and SloTx, and the benzimidazolone potassium channel opener NS1619, on activity evoked in nociceptive pathways in the trigeminocervical complex.

**Methods** Cats (<i>n</i> = 15) were anaesthetized and physiologically monitored. Their superior sagittal sinus was stimulated to activate trigeminovascular nociceptive neurons. Extracellular recordings were made from neurons in the trigeminal nucleus caudalis that received mechanoreceptor input from ipsilateral cutaneous <i>V</i><sub>i</sub> or <i>V</i><sub>ii</sub> receptive fields.

**Results** Sixty-five cells were reversibly excited by microiontophoresis of L-glutamate. IbTx and SloTx facilitated L-glutamate evoked firing in 70% and 71% of these cells, respectively, suggesting a subpopulation of neurons in the trigeminocervical complex express toxin-sensitive BK<sub>Ca</sub> channels. NS1619 reduced the firing rate in 74% of cells tested. In 10 out of 10 cells examined, this inhibition was reversed by slotoxin, suggesting that the action of NS1619 was mediated through BK<sub>Ca</sub> channels.

**Conclusion** These data suggest the presence of BK<sub>Ca</sub> channels in the trigeminocervical complex that could be a novel migraine therapeutic target.

**Keywords:** MaxiK, NS1619, potassium channel, trigeminal, headpain

F006

The effect of antimigraine herbal extracts on nitric oxide level in cultured vascular endothelial cells

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**Objective** The present work was designed to study the effect of a number of herbal extracts, which have been prescribed in migraineous subjects, on the level of nitric oxide (NO) in cultured endothelial cells.

**Methods** We applied aqueous extracts of the herbs on cultured mouse endothelial cell F-2 and determined the NO levels by Griess method. Lavandula stoechas, Origanum vulgare, Foeniculum vulgare, Coriandrum sativum and Viola odorata were the herbs that have been chosen for this study. Different concentrations of each herb were applied.

**Results** Concentrations of 200 and 400 μg/ml of Lavandula stoechas reduced the level of NO, 35.6% and 41%, respectively. Concentrations of both 200 and 400 μg/ml of Origanum vul-
Satisfaction with current migraine therapy: experience from three centres in USA and Sweden

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Objective To assess the level of satisfaction with migraine usual care (UC).

Design/methods Patients seen in three headache centres completed standardized questionnaires assessing levels of satisfaction with UC using a five-point scale (where 1 was strongly agree, 3 was neutral and 5 was strongly disagree).

Results We assessed 175 subjects (74.8% women, mean age 39.3 years). UC consisted of a single drug or combination of: conventional triptan tablets, 62%; disintegrating triptan tablets, 8%; sumatriptan nasal spray, 9%; sumatriptan injection, 9%; non-triptans, 19.6%. Most (54%) had no benefit within the first hour of treatment. The maximum benefit took more than 1 h to be reached in 69%, and more than 2 h in 36%. After the maximum benefit, pain worsened in 61%. Although 58% were satisfied with the degree of relief, 37% were dissatisfied with the speed of effect, 50% with the recurrence of pain and 42% with the need for a second dose. Most were satisfied with the tolerability (56%). Interestingly, most (79.7%) said they were willing to try another acute medication.

Conclusions An important subset of patients is dissatisfied with the speed of returning to normal functioning, including a large subgroup of patients using conventional triptan tablets. This study was supported by an unrestricted grant from AstraZeneca.

Zolmitriptan nasal spray vs. usual care in the acute treatment of migraine: a preference study

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Objective To compare zolmitriptan nasal spray 5 mg (ZNS) vs. usual care (UC) in a randomized prospective study.

Design/methods Migraineurs were randomized to treat three consecutive attacks with UC and three with ZNS 5 mg, in counterbalanced order. Efficacy and tolerability were assessed using headache forms and diaries. Participants also expressed their satisfaction and preference in regard to several parameters.

Results Our sample consisted of 175 subjects; in most UC consisted of triptans other than ZNS (80.4%). More patients started to notice benefit within 1 h in the ZNS group (74% vs. 60%, P < 0.01), as well as reaching maximum benefit within 90 min (54% vs. 43%, P < 0.01). No significant difference was found in the maximum relief of pain. Moderate or severe disability continued after treatment in 24% of those using UC vs. 13% of the ZNS group (P < 0.01). Consistency was higher in the ZNS group (three out of three, 61% vs. 47%, P < 0.01). Tolerability and recurrence were not different. A total of 61% preferred ZNS vs. UC.

Conclusions Most patients preferred ZNS to UC (mostly other triptans) for the acute treatment of migraine, with speed of onset and consistency being the most important determinants of preference.

This study was supported by AstraZeneca.

Abolition of migraine attacks by normalization of cardiac dysfunction with digitalis

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Background It is known that during migraine attacks there is cerebral ischaemia. However, the relationship between this finding and transient cardiac dysfunction is still unknown.

Objective The aim of the present study was to evaluate the cardiac function and benefit of digitalis in migraine attacks during overload produced by phenylephrine test (PT).

Methods By two-dimensional direct M-mode echocardiography was measured: percentage of systolic shortening (ΔD), ejection fraction (EF) and mean velocity of circumferential fibre shortening (Vcf) in 18 patients and 10 normal subjects. These measures were performed in three different periods: during attack-free intervals, attacks and after 1 mg digoxin/24 h oral.

Results Cardiac size and function were normal at rest in both groups. However, during migraine attacks PT provoked a significant decrease in ΔD, EF and Vcf, followed by a concomitant increase of headache severity. After digitalis the PT did not cause changes in cardiac function with regression of migraine attacks, but during the attack-free period and in the control group PT did not show changes in cardiac function.

Conclusion The normalization of cardiac dysfunction by digitalis during the PT leads to abolition of migraine attacks, suggesting that this transient and reversible dysfunction is the pathophysiological mechanism that causes headache.
Clinical efficacy of eletriptan in the acute treatment of migraine

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Objectives To evaluate the clinical efficacy of eletriptan 20 mg in Japanese patients with migraine.

Methods We provided a headache diary to out-patients with migraine, and evaluated the efficacy and safety of eletriptan based on the records.

Results We investigated a total of 82 attacks in 31 patients (three males, 28 females; mean age 42.8 years, mean duration of disease 19.4 years, mean frequency of attacks 3.5 times/month). In 81.7% of the patients, improvement of headache was achieved 2 h after oral administration. Eletriptan significantly improved pain, duration for which the effects appeared, functional disability, and migraine-associated symptoms (nausea/vomiting, photophobia, phonophobia) compared with previous therapy (sumatriptan, zolmitriptan, prescribed analgesics, OTC analgesics). The presence of tension-type headache did not influence the improvement rating. Mild adverse events, such as nausea, dizziness and chest pain, were observed in five patients.

Conclusion Eletriptan is useful for patients suffering migraine attacks.

Keywords: eletriptan, migraine, clinical efficacy

Efficacy of triptan on alcohol-induced headache

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Background Despite the ease of inducing alcohol-induced headache (AIH), only a few trials have studied treatment of AIH.

Objective Since pulsating headache due to AIH resembles migraine, we investigated the effects of triptan on immediate and delayed AIH in a non-blinded study.

Methods Fifteen healthy young Japanese volunteers (11 men, four women) were asked to drink the alcoholic beverage of their choice. After the appearance of immediate or delayed type of disease, 19.4 years, mean frequency of attacks 3.5 times/month. In 81.7% of the patients, improvement of headache was achieved 2 h after oral administration. Eletriptan significantly improved pain, duration for which the effects appeared, functional disability, and migraine-associated symptoms (nausea/vomiting, photophobia, phonophobia) compared with previous therapy (sumatriptan, zolmitriptan, prescribed analgesics, OTC analgesics). The presence of tension-type headache did not influence the improvement rating. Mild adverse events, such as nausea, dizziness and chest pain, were observed in five patients.

Conclusion Eletriptan is useful for patients suffering migraine attacks.

Keywords: eletriptan, migraine, clinical efficacy

Almotriptan in Japanese subjects, a phase I study

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Objective To explore safety, tolerability and pharmacokinetics of almotriptan after single oral doses of 6.25, 12.5 (usual dose), 25 and 50 mg in Japanese healthy male volunteers.

Methods Single-centre, randomized, double-blind, single ascending dose, alternating placebo-controlled trial.
subjects were allocated 50% to two groups. Group A received almotriptan 6.25 mg or placebo and, after 15 days, almotriptan 25 mg or placebo. Group B started 7 days after group A, receiving almotriptan 12.5 mg or placebo and, after 15 days, almotriptan 50 mg or placebo. The placebo/active ratio was 1:3. A cross-validation of almotriptan plasma levels obtained by LC/MS/MS and HPLC techniques was performed in four subjects, one from each dose level.

Results There were neither adverse events of clinical concern nor a dose-dependent increase in their incidence. The drug absorption was rapid, and t½ was approximately 3–4 h. Dose-dependent increases were observed in Cmax, AUC and Aν, while λz, t½, CL/f, Vz/f, and CLr were not dosage-affected. AUC and Cmax showed a linear pharmacokinetic profile for almotriptan. Almotriptan plasma levels were equivalent using LC/MS/MS or HPLC techniques.

Conclusion Almotriptan was well tolerated by Japanese subjects, and pharmacokinetic data found are in line with those observed in previous almotriptan studies in caucasians.

Keywords: almotriptan, Japanese, pharmacokinetics, safety, tolerability

F016
Cross-over, double-blind, clinical trial comparing almotriptan vs. ergotamine + caffeine in migraine treatment
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Objective Efficacy and tolerability of almotriptan 12.5 mg tablets vs. ergotamine 2 mg + caffeine 200 mg tablets in migraine.

Methods 24 Spanish centres, double-blind, randomized and cross-over study. Patients diagnosed following IHS criteria for at least 1 year, with 1–6 attacks/month and aged between 18 and 65 years were included to treat two attacks, one with each study medication.

Results 229 patients (86.9% female) took at least one tablet. Average age was 33.5 years (SD 9.4 years). Main efficacy results for the 182 patients that fulfilled protocol requirements and had at least one pain measurement data after treatment intake for both attacks were: 2 h pain free: 20.88% with almotriptan vs. 13.74% with ergotamine + caffeine (P < 0.05); 2 h pain relief: 57.69% with almotriptan vs. 44.51% with ergotamine + caffeine (P < 0.01); 24 h sustained pain free: 20.33% with almotriptan vs. 11.54% with ergotamine + caffeine (P < 0.05); rescue medication use: 38.46% with almotriptan vs. 48.35% with ergotamine + caffeine (P < 0.05). No difference was found in recurrence at 24 h (P = 0.42). Adverse events in safety population (n = 229) were present in 7.42% of almotriptan attacks, vs. 12.23% of ergotamine + caffeine attacks (P = 0.06).

Conclusion Treating migraine attacks, almotriptan provides better efficacy than ergotamine + caffeine. A clear trend towards better tolerability of almotriptan was also found.

Keywords: almotriptan, ergotamine + caffeine, migraine, cross-over

F017
Zolmitriptan nasal spray is effective in the acute treatment of cluster headache: a double-blind, placebo-controlled, crossover study
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Background Cluster headache is a form of primary headache whose attacks are rapid in onset with very severe pain. The mainstays of acute therapy are inhaled oxygen and sumatriptan by injection and nasal spray.

Objective To determine if zolmitriptan nasal spray is effective in the acute treatment of cluster headache.

Methods Ninety-two patients, aged 42 ± 10 years, 80 males and 12 females, with either episodic or chronic cluster headache by IHS criteria, were randomized into a placebo-controlled, double-blind, crossover study treating three attacks with either of placebo, or zolmitriptan nasal spray 5 or 10 mg (ZNS5, ZNS10). The primary endpoint was headache relief, reduction from moderate, severe or very severe to nil or mild pain, at 30 min. The study was approved by appropriate Ethics Committees. Multilevel multivariate analysis with MLwinN (http://www.ioe.ac.uk) tested the primary endpoint.

Results Sixty-eight patients were available for an intention-to-treat analysis. Response rates for the primary endpoint were 21% (placebo), 38% (ZNS5) and 60% (ZNS10), which represented a significant difference for ZNS5 or ZNS10 against placebo (Wald test, χ² = 29.4, P < 0.001).

Conclusions Zolmitriptan 5 and 10 mg intranasal is effective in the treatment of acute cluster headache.

F018
Randomized controlled trial of relaxation therapy on recalled headache intensity in tension-type headache patients
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Objective The aim of this study was to investigate the effect of relaxation therapy (RT) on recalled headache intensity in tension-type headache (TTH) patients.

Methods Fifteen men (40.3 ± 9.9 years) and 39 women (36.6 ± 10.4 years) with TTHI were randomly assigned to 8-week sessions of a RT group or to a waiting list control (WLC) group. The patients rated their headache intensity during the last week using a 100-mm visual analogue scale before and after the treatment and the waiting period. We compared headache intensity within the groups and between the groups using repeated measures ANOVA in the whole patients and separately in chronic and episodic TTH patients.
Results In within-group comparisons, recalled headache intensity was significantly reduced after RT in the whole patients ($P = 0.002$). In between-group comparisons, recalled headache intensity was significantly reduced after RT in the RT group compared with the WLC group in chronic TTH patients ($P = 0.04$), although there was no significant difference in the whole patients or in the episodic TTH patients ($P = 0.18$ and 0.51, respectively).

Conclusion RT might be effective in improving recalled headache intensity in chronic TTH patients.

Keywords: tension-type headache, relaxation therapy, randomized controlled trial.

F019

Headache treatment and discharge instructions in the Emergency Department

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Objective To evaluate headache care that patients at an urban emergency department receive.

Background We analysed patterns of care that can be used to design interventions to improve headache care within and beyond the ED.

Methods Patients who presented to the ED with a complaint of headache were interviewed and an ED chart review was done. Inclusion criteria: patients 18 years or older with a non-traumatic headache of less than 1 month in duration. Exclusion criteria: patients with a history of a lumbar puncture or epidural procedure in the previous 7 days.

Results 219 of 364 patients were eligible and consented. 19 (21.8%) had no pain upon leaving the ED, 37 (42.5%) mild pain, 20 (23%) moderate pain and 11 (12%) severe pain. 89 (40.6%) were asked to follow up with a physician and, of these, 22 (10%) were asked to follow up with a specialist. 27 (12.3%) left AMA, four (1.8%) were imaged, 16 (7%) were admitted. Triptans were prescribed for five (2.2%), non-opioids for 30 (13.6%) and opioids for 22 (10%). 137 (62.6%) received no discharge medications. 36 (64%) of 56 people who responded said the headache returned within 24 h of leaving the ED.

Conclusion ED headache discharge instructions were often vague and did not include headache-specific treatment.

Keywords: emergency department, headache, discharge, treatment, disposition.

F020

Transcranial magnetic stimulation (TMS) for migraine headache

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Objective This randomized control study examined the effects of transcranial magnetic stimulation (TMS) to control migraine headache pain.

Methods Forty-two (42) subjects, mean age 41 years, 35 females and seven males, received two impulses of TMS over the area of reported pain (intensity ranged from 30% to 50% of the maximum output). Pain intensity was measured on a 1–5 Likert scale (5 worst score) pre- and poststimulation. Patients kept diaries pre- and poststimulation.

Results Twenty-nine 29/42 (69%) received immediate relief on first stimulation (T1). Repeated trials indicated that 20/23 (87%) and 9/11 (82%) got immediate relief after a second and third stimulation set. No adverse effects were recorded after any trial.

Conclusion Efficacy results are 69%, 87% and 82% without any adverse effects and are comparable with current treatment interventions.

Keywords: migraine, TMS.
F022

Inhibition of neurogenic blood flow increases in the rat cranial dura mater by a CGRP-binding Spiegelmer
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Background Calcitonin gene-related peptide (CGRP) has a key function in the pathogenesis of primary headaches. Elevated concentrations of CGRP are found in jugular vein blood samples during migraine attacks. CGRP released from trigeminal afferents is the main vasodilator in the meninges that mediates neurogenic blood flow changes.

Objective In an animal model of trigeminovascular activation and meningeal blood flow the inhibitory effect of a new high-affinity CGRP-binding RNA-Spiegelmer, which is a bio-stable aptamer composed of mirror-image nucleotides, was examined.

Methods Increases in meningeal blood flow caused by periodic local electrical stimulation of the exposed rat cranial dura mater were analysed using laser Doppler flowmetry. The CGRP-binding Spiegelmer was applied topically (10^{-7}–10^{-5} M) or i.v. (5 mg/kg).

Results The Spiegelmer caused dose-dependent, significant inhibition of the evoked blood flow responses to about 50% of the control. Topical application was most effective. Basal blood flow and systemic arterial pressure were unchanged.

Conclusion Neurogenic blood flow increases in the meninges are reduced by binding of the released CGRP to the Spiegelmer, thereby preventing it from activating vascular CGRP receptors. The Spiegelmer may open a new therapeutic strategy in diseases that are linked to excessive CGRP receptors.

Keywords: headache, migraine, CGRP, Spiegelmer, meningeal blood flow

F023

Successful treatment for allodynia accompanied with migraine attack using intravenous injection of Mecobalamin
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Objective Migraine attack with allodynia is reported to be not effective for triptans. But we succeeded in providing rapid relief for such patients.

Patients and methods Nine migraine patients without aura, who ordinarily showed efficacy for triptans, consulted our clinic with severe headache in spite of the use of triptans and with numbness of the face or temporal. The duration between triptan intake and consultation was within 4 h. 500 μg of Mecobalamin was given intravenously with 20% glucose of 20 ml. The change in the symptoms was investigated 10–15 min after.

Results Skin allodynia completely recovered in seven cases (77.8%), remarkably in one (11.1%) and moderately in one (11.1%). Severe headache almost completely recovered in three (33.3%), and moderately in six (66.6%). These effects continued until the expected time when the attack would end.

Conclusion It is unknown whether these results were due to the efficacy of Mecobalamin alone or to the additional come-back effect of triptans. This is the first report of rapid rescue by allodynia with migraine. We recommend this therapy not only for its speed but also for its being easy to perform for any doctor with no side-effects.

Keywords: migraine, alldynia, Mecobalamin

F024

Rapid relief for cranial neuralgias using intravenous injection of Mecobalamin

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Objective Although Vitamin B12 is known to be effective for neuralgias, not so general clinically. In the present study, we examined the quickness of the efficacy of Mecobalamin for cranial neuralgias.

Patients and methods Cranial neuralgias of 721 cases (trigeminal 138, occipital 566, greater occipital and trigeminal neuralgia syndrome (GOTS) 17) were examined. There were 264 male cases and 457 female. The ages ranged from 11 to 85 with the mean of 50.6 ± 16.9. For the patients only recognized by Valleix’s point of tenderness, 500 μg of mecobalamin + 20% glucose 20 ml (for diabetic patients, 0.9% of saline) was given intravenously. After 10 min, the change in tenderness was observed.

Results Mecobalamin was remarkably effective in 39 cases (5.4%), moderately in 610 (84.6%), and not effective in 72 (10.0%). The ratio of effective cases in each neuralgia was 72.2% in trigeminal neuralgia, 72.7% in greater occipital, 72.5% in minor occipital, 63.0% in greater auricular and 60.0% in combinations of each occipital neuralgia. GOTS was 100.0% among 17 cases.

Conclusion When neuralgia is decreased, for some time the patient is maintained in a good state and will remain in a generally good condition, so Mecobalamin, which is an active type of Vitamin B12, is very useful. Benefical points are that it is not only rapidly efficacious, but also easy to use by the medical staff. No side-effects were seen, and the drug is reasonably priced for patients.

Keywords: trigeminal neuralgia, occipital neuralgia, Mecobalamin, greater occipital and trigeminal neuralgia syndrome (GOTS)

F025

Preference for rizatriptan 10-mg wafer versus eletriptan 40-mg tablet for acute treatment of migraine

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Objective To compare patient preference for rizatriptan 10-mg wafer vs. eletriptan 40-mg tablet for acute treatment of migraine.
Methods Multicentre, open-label, two-period, crossover study. Out-patients were randomly assigned to treat the first of two moderate to severe migraines with rizatriptan or eletriptan and the second with the alternate therapy. Patients completed diary assessments at baseline and 24 h after taking study medication. At the last visit, patients completed a psychometrically validated preference questionnaire.

Results A total of 372 patients treated two migraine attacks, and 342 patients (92%) expressed a preference for treatment. Significantly more (P ≤ 0.001) patients preferred rizatriptan 10-mg wafer [61.1%; 95% confidence interval (CI) 55.7, 66.3] to eletriptan 40-mg tablet (38.9%; 95% CI 33.7, 44.3). The most common reason given for treatment preference was speed of headache relief. At 2 h, 80% and 69% of patients reported that rizatranip and eletriptan, respectively, was convenient or very convenient to take.

Conclusions In this head-to-head study designed to evaluate global patient preference, significantly more patients preferred the rizatriptan 10-mg wafer to the eletriptan 40-mg tablet for acute treatment of migraine. The single most important reason for preference was speed of relief.

Keywords: rizatriptan wafer, eletriptan, patient preference

F026

Triptans are not always the patient’s choice

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Background The triptans, selective serotonin (5-hydroxytryptamine, 5-HT) 5-HT1B/1D receptor agonists, are currently the drugs of choice for the acute treatment of moderate-to-severe attacks of migraine. Several decision-making models addressed the difference between the triptans and tried to assess which triptan should be prescribed. Only few studies tried to assess patients’ preferences in using triptans and other analgesics in acute attacks.

Methods Prescription filling information of 2003, in the southern district of a large HMO, were reviewed. All the patients prescribed any triptan during this year were evaluated using the HMO computerized database.

Results In 2003, 1450 patients were prescribed triptans. Fifty-eight percent (n = 939) of the patients never filled a second prescription. Only 28% of the patients filled a third prescription. There was no difference between the users of different triptans.

Conclusion Our data suggest that after using triptans for the first time, many patients choose not to use it again. This observation can be explained by low effectiveness (absolute or compared with previously used medications), side-effects and cost of the drug. It seems that triptans are appropriate for only some migraine patients.

Keywords: triptan, migraine, HMO, primary care

F027

Pharmacokinetic profile of rizatriptan 10-mg tablet and rizatriptan 10-mg orally disintegrating tablet administered with or without water in healthy subjects: an open-label, randomized study

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Objectives To compare the pharmacokinetic profiles of rizatriptan conventional tablet, rizatriptan orally disintegrating tablet with water (ODTc), and rizatriptan ODT without water (ODTs).

Methods This was an open-label, single-dose, three-period crossover study of rizatriptan plasma concentration profiles in 24 adults. At each of the three periods, subjects received a single dose of either 10-mg rizatriptan tablet, 10-mg rizatriptan ODTs, or 10-mg rizatriptan ODTc. The primary hypotheses were that rizatriptan ODTc had a greater geometric mean AUC0–2h, than rizatriptan ODTs and that rizatriptan ODTc had a greater geometric mean AUC0–1h, than rizatriptan tablet. Time to maximum plasma concentration (Tmax) was also compared.

Results Rizatriptan ODTc had a significantly greater geometric mean AUC0–2h compared with rizatriptan ODTs (33.84 h/ng/ml vs. 18.83 h/ng/ml; P < 0.001). Rizatriptan ODTc had a slightly, but not statistically, greater geometric mean AUC0–1h compared with rizatriptan tablet (17.07 h/ng/ml vs. 13.32 h/ng/ml). The median Tmax was 0.67 h for ODTc, 1.33 h for ODTs, and 0.67 h for tablet.

Conclusions Rizatriptan ODT has a faster absorption rate with water. Rizatriptan ODT with water showed a slightly, but not significantly, faster rate of absorption compared with rizatriptan tablet. Further studies are warranted to determine if this acceleration of pharmacokinetic profile translates into an improvement in efficacy.

F028

Atrial fibrillation induced by sumatriptan—a case report and review

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Background Triptans are 5-hydroxytryptamine 1B and 1D receptor antagonists used commonly as an effective acute treatment for migraine. Safety concerns include their potential to induce ischaemic cardiac or cerebrovascular vascular events if used inappropriately.

Case report We describe a 54-year-old male with migraine without aura without contraindications to triptan usage who developed acute atrial fibrillation (AF) immediately after first use of oral sumatriptan. The atrial fibrillation was persistent and required intervention. Subsequent cardiological investigation did not identify an alternative cause of AF. Rechallenge was not performed.

Conclusion Non-cardiac chest pain is described in 3–15% of patients using triptans and not always associated with
ischaemic ECG changes. Sumatriptan is the drug most frequently reported as causing chest pain. Triptan use is contraindicated in patients with established ischaemic cardiac disease and also in those at risk as myocardial infarction has very rarely been reported as a consequence of triptan use. Cardiac arrhythmias including atrial fibrillation are rarely described as side-effects following sumatriptan use. We describe a rare side-effect of sumatriptan in the absence of obvious cardiac disease.

**Keywords:** sumatriptan, atrial fibrillation

**F029**

Etizolam on NSAID in tension-type headache

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**Objective** To study the effect of etizolam on NSAID in tension-type headache (TTH) by a randomized controlled study.

**Methods** The study design was a RCT of 100 patients. The diagnosis of TTH was based on ICHD-I. The changes in degree of headache and shoulder pain were graded in terms of visual analogue scale (VAS) before and after administration of drugs. NSAID alone (N) and etizolam plus NSAID (EN) group were randomized and given to the patients.

**Results** VAS for headache was decreased significantly from 5.55 ± 1.79 to 2.46 ± 2.17 for shoulder pain from 5.91 ± 2.24 to 3.65 ± 2.36 totally [both N and EN groups (P < 0.01)]. However, there was no significant difference between N and EN group for headache. VAS for shoulder pain was decreased from 5.91 ± 2.24 to 3.65 ± 2.36 in the total group (P < 0.01). In addition, EN group showed stronger efficacy than N group for shoulder pain. Side-effects were seen in 24.4% of patients, sleepiness, fatigue and stomach ache being the commonest.

**Conclusion** Although both N and EN groups showed a significant decline of VAS for headache and shoulder pain, efficacy of etizolam on NSAID may have an advantage for shoulder pain treatment in TTH.

**Keywords:** etizolam, NSAID, tension-type headache, TTH, VAS

**F030**

Satisfaction of Spanish patients and neurologists with acute migraine treatment

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**Objective** To evaluate satisfaction of Spanish patients and neurologists with acute migraine treatments used under actual clinical practice conditions.

**Methods** A cross-sectional, retrospective, multicentre study involving 1313 patients and 230 neurologists, funded by Pfizer Spain (the ‘Rescate’ Study). Satisfaction of patients and neurologists with treatments used over the past 3 months was evaluated. Subjects were considered ‘satisfied or highly satisfied’ when the score in a 0–10 scale was ≥6.

**Results** The proportion of patients receiving each treatment was: triptans 61.3%, NSAIDs 53.8%, analgesics 29.0% and ergot derivatives 7.8%. The proportions of patients and neurologists satisfied or highly satisfied with the most commonly used treatments were: eletriptan (n = 93, 87.7% and 87.6%), almotriptan (n = 206, 81.7% and 78.7%), rizatriptan (n = 242, 79.9% and 74.8%), zolmitriptan (n = 265, 79.3% and 74.4%), sumatriptan (n = 70, 72.4% and 64.3%), naproxen sodium (n = 181, 62.3% and 52.5%), naproxen (n = 94, 57.4% and 46.8%), ibuprofen (n = 399, 57.1% and 47.5%), ergotamine (n = 63, 50.8% and 31.1%), metamizol (n = 125, 46.7% and 33.3%), and acetaminophen (n = 187, 34.5% and 26.1%). The comparison of ‘triptans’ vs. ‘non-triptans’ significantly favoured the former (P < 0.001).

**Conclusion** Use of triptans by Spanish neurologists is high. Satisfaction of patients and neurologists with triptans is markedly higher compared with other treatments.

**Keywords:** triptans, migraine, satisfaction, patients, neurologists

**F031**

Are there differences between neurologists with and without migraine as regards management of their migraine patients?

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**Objective** To establish whether the existence of migraine in neurologists may affect their therapeutic management of migraine patients.

**Methods** A subanalysis of a cross-sectional, retrospective, multicentre study involving 1313 patients and 230 neurologists, funded by Pfizer Spain (the ‘Rescate’ Study). Main variables compared between neurologists with migraine vs. neurologists without migraine: mean MIDAS score, mean number of attacks, and proportion of patients with preventive treatment in the past 3 months; for the last attack, proportion of patients using triptans and satisfaction of patients and neurologists (0–10 scale) with acute treatment.

**Results** 28.5% of neurologists stated that they had migraine. Statistically significant differences were found between neurologists with and without migraine in the following patients variables: mean number of attacks in the past 3 months (11.4 ± 10.8 vs. 9.2 ± 8.6; P = 0.0006), proportion of patients using triptans for the last attack (45.8% vs. 52.4%; P = 0.0425), and satisfaction of neurologists with acute treatment used in the last attack of patients (5.9 ± 3.3 vs. 6.3 ± 2.9; P = 0.0429).

**Conclusion** These data suggest that when the neurologist has the same disease as the patient, interpretation of pain of others may be distorted, and diagnosis and treatment may be affected.

**Keywords:** triptans, migraine, satisfaction, patients, neurologists
F032

Efficacy of rizatriptan administered in an early intervention model: the rizatriptan TAME (Treat A Migraine Early) Study

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Background The current study examined the efficacy of rizatriptan for the early treatment of acute migraine, while pain is mild.

Methods This was a randomized, double-blind study. Migraineurs treated with rizatriptan 10 mg or placebo within 1 h of headache onset. During the next 24 h, patients assessed pain severity, presence of associated symptoms, use of rescue medication, degree of functional disability, and reported any adverse experiences. The primary endpoint was pain freedom at 2 h; the secondary endpoint was 24-h sustained pain freedom (no headache recurrence, no rescue medication use).

Results Of 583 patients randomized to treatment, 530 (91%) treated a study migraine. The percentage of patients reporting pain freedom at 2 h postdose was significantly greater for rizatriptan than for placebo (57.3% vs. 31.1%, P < 0.001), as was the percentage of patients reporting 24-h sustained pain freedom (42.6% vs. 23.2%, P < 0.001). All other efficacy endpoints favoured rizatriptan.

Conclusion Rizatriptan 10 mg was superior to placebo for treating mild migraine, as measured by pain freedom at 2 h and 24-h sustained pain freedom. When previously reported data for moderate/severe migraine are considered, these results support the efficacy of rizatriptan regardless of timing of migraine treatment and baseline pain severity.

F033

The fixed combination of acetylsalicylic acid, paracetamol and caffeine is superior to the single substances and dual combinations in the treatment of headache

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Objective We investigated efficacy, safety and tolerability of the fixed combination of acetylsalicylic acid, paracetamol and caffeine in comparison with the combination without caffeine, the monotherapies, and placebo in a randomized, placebo-controlled, double-blind study in patients treating their tension-type headache or migraine attacks with non-prescription (OTC) analgesics.

Methods 133 centres included a total of 2336 out-patients. After the prephase evaluation 353 patients were withdrawn due to inability to comply with the study procedures. 1983 patients were randomized, but 94 thereof did not take study medication, 146 patients did not return their diaries with VAS data, or returned diaries with obviously unreliable entries, which left a total of 1743 patients in the ITT dataset. The primary efficacy endpoint was the calculated time to 50% pain relief based on the pain intensity recorded on a 100-mm visual analogue scale. Secondary endpoints comprised time until reduction of pain intensity to 10 mm, weighted sum of pain intensity difference, extent of impairment of daily activities, global assessment of efficacy and tolerability as well as incidence of adverse events. Results of secondary endpoints will be presented.

Results For the primary endpoint with the ITT dataset, the fixed combination of acetylsalicylic acid, paracetamol and caffeine was statistically significantly superior to the combination without caffeine, the mono-substances ASA, paracetamol, caffeine. Treatment contrasts with the secondary endpoints consistently confirmed the evaluation with the primary endpoint. All treatments were safe and well tolerated.

Keywords: Migraine, tension-type headache, fixed analgesic combinations, ASA, paracetamol, caffeine

F034

A retrospective study to assess the safety and efficacy of intravenous lignocaine for the acute treatment of headaches

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Background Approximately 5% of headache patients have chronic daily headaches. Some of these are hospitalized for more intensive treatment. There is a lack of data on in-patient intravenous (i.v.) medications and this study will provide information on the efficacy of intravenous lignocaine in treating these patients.

Objective To determine safety and efficacy of lignocaine for treatment of patients.

Methods The medical records of 12 patients admitted and treated with i.v. lignocaine were reviewed upon discharge.

Results There were three male and nine female patients. Five patients had chronic migraine with analgesic rebound, four had chronic migraine without rebound, one had NDPH and two had status migrainous. Their pretreatment pain scores ranged form 2 to 8 and post-treatment scores decreased to 0–4. They were treated with 75–175 mg of intravenous lignocaine as a continuous infusion for 72 h. Out of these 12 patients, 10 patients responded to treatment. Two patients did not respond to therapy. Nine patients did not experience adverse events from therapy.

Conclusion Patients treated with intravenous lignocaine showed significant improvement in their headaches. They tolerated treatment well with few adverse events. I.v. lignocaine is a viable addition to the armamentarium for in-patient headache therapy.

Keywords: lignocaine, in-patient, infusion, chronic migraine, NDPH
F035
Migraine-free data with sumatriptan fast disintegrating tablets: results from two double-blind, placebo-controlled trials
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Background Two clinical trials were conducted to determine the onset of headache relief with the fast disintegrating formulation of sumatriptan tablets. Pooled data results reported onset of relief in 20 min for 100 mg, and 30 min for 50 mg followed by 2 h relief in up to 72% of patients using 100 mg and 67% using 50 mg (1). Migraine-free results (no pain and no migraine-associated symptoms) were a secondary endpoint.

Methods Two double-blind, single-attack, out-patient studies were conducted at 272 centres in the US/Canada and Europe. 2696 patients were randomized to placebo, 50 mg, or 100 mg. Patients treated one moderate/severe attack and reported pain severity and associated symptoms using a hand-held electronic diary.

Results Pooled data results showed migraine-free response for placebo, 50 mg and 100 mg at 2 h: 12%, 31% and 37%; and at 4 h: 21%, 47% and 53%, respectively; all statistically significant vs. placebo (P < 0.001). The individual studies showed similar results.

Conclusions Sumatriptan in the fast disintegrating formulation delivers migraine-free response in up to 37% of subjects at 2 h and 53% of subjects at 4 h after treating a moderate to severe attack.

Keywords: migraine, sumatriptan, fast disintegrating, onset

Reference

F036
Headache recurrence with sumatriptan fast disintegrating tablets: results from two double-blind, placebo-controlled trials
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Background Two clinical trials were conducted to determine the onset of headache recurrence using the fast disintegrating sumatriptan tablet formulation. Pooled data results reported onset of relief in 20 min for 100 mg and 30 min for 50 mg, followed by 2 h relief in up to 72% of patients using 100 mg and 67% of patients using 50 mg (1). Headache recurrence/ time to recurrence were secondary endpoints.

Methods Two double-blind, single-attack, out-patient studies were conducted at 272 centres in the US/Canada and Europe. 2696 patients were randomized to placebo, 50 mg or 100 mg. Patients treated one moderate/severe attack and reported pain severity and associated symptoms at 2 and 4 h using a hand-held electronic diary.

Results Pooled data results showed headache recurrence rates over 2–24 h after treatment with placebo, sumatriptan 50 mg and 100 mg, of 46%, 27% and 29%, respectively. The median time to recurrence was 4.3, 11.2 and 12.5 h, respectively. The individual studies showed similar results for placebo, 50 mg and 100 mg as in the pooled data analysis.

Conclusion Sumatriptan 50 mg and 100 mg in the fast disintegrating tablet formulation is associated with headache recurrence rates of less than 30%.

Keywords: sumatriptan, fast disintegrating, migraine, recurrence

Reference

F037
Sustained pain relief and sustained pain-free rates with sumatriptan fast disintegrating tablets: results from two double-blind, placebo-controlled trials
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Background Two clinical trials were conducted to determine the onset of headache recurrence using the fast disintegrating formulation sumatriptan tablets. Pooled data results reported onset of relief in 20 min for 100 mg and 30 min for 50 mg followed by 2 h relief in up to 72% of patients using 100 mg and 67% of patients using 50 mg (1). Sustained pain relief (SPR) and sustained pain-free measures (SPF) (pain relief or pain-free at 2 h after treatment, without headache recurrence or use of further acute medications up to 24 h after treatment) were secondary endpoints.

Methods Two double-blind, single-attack, out-patient studies were conducted at 272 centres in the US/Canada and Europe. 2696 patients were randomized to placebo, 50 mg or 100 mg. Patients treated one moderate/severe attack and reported pain severity and associated symptoms using a hand-held electronic diary.

Results Pooled data results showed SPR rates for placebo, 50 mg and 100 mg of 18%, 39% and 41%, respectively, and SPF rates of 8%, 21% and 25%, respectively; all statistically significant vs. placebo (P < 0.001). The individual studies showed similar results.

Conclusion Sumatriptan fast disintegrating tablets deliver SPR in around 40% and SPF in 20–25% of patients.

Keywords: pain relief, sumatriptan, fast disintegrating, migraine
**Preliminary evidence for improved efficacy when patients treat with sumatriptan 100 mg formulated with RT technology during visual aura in migraine**

Sheena K. Aurora, Patricia M. Barrodale, Susan M. McDonald & Rami Burstein

**Background** Several studies have indicated early treatment, i.e., during mild phase of migraine, results in better treatment outcomes. Previous studies done to treat migraine during aura have shown no benefit. These studies, however, lacked intrapatient consistency.

**Introduction** This study was designed to be a 4-way cross-over study of migraine patients to establish earliest points of treatment.

**Methods** 32 migraine with visual aura patients were recruited, mean age 39.8, mean duration of illness 21.3 years. Patients used sumatriptan 100 mg for three baseline (B) headaches to establish eligibility. Nineteen patients were eligible.

**Results** Nineteen patients treated eight attacks each (three B, one headache 5 h after onset of aura (L) and two each within 1 h of onset of pain (E) and during aura (A)). Mean time to treatment for B 113 min after aura vs. E 85.2 min after aura vs. A 2.3 min after aura. Late, early and aura attacks were treated with 100 mg of sumatriptan RT. Pain freedom at 2 h was greater if patients treated during A 89 vs. E 82 vs. B 60. Sustained pain freedom was also greater if patients treated during A 84 vs. E 68 vs. B 51. Results of associated symptom control were similar. At B 35% had alldynia vs. E 25% vs. A 5%.

**Conclusion** Correlations between answers to key questions and scores of HIT-6, MigSev and QVM questionnaires are in favour of the construction validity of ANAES questions developed empirically. These results suggest the clinical pertinence in daily practice of the four key questions from French guidelines for the assessment of acute migraine treatment.

**Keywords:** migraine, French guidelines, HIT-6, MigSev, QVM

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**ARAIMG: study of the management of migraine in general practice in France**

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**Background** Despite improvements in the management of migraine in France, recent studies suggest the persistence of certain shortages in primary care.

**Objective** To analyse the medical management of migraine attacks in French daily practice.

**Methods** Negative answers to at least one of the four key questions from guidelines regarding failure of usual acute treatment, issued by the French National Agency Accreditation and Evaluation (ANAES), were compared with data collected in daily practice from questionnaire MigSev (severity of migraine attack), HIT-6 (migraine impact), QVM (quality of life), and drugs for acute treatment prescribed by practitioners.

**Results** 1228 patients mean age 39.9 years and sex ratio 5.46 F/M were recruited. Medications were aspirin (30%), NSAIDs (48%), ergots (15%) and triptans (35%) and choice of NSAIDs or triptans was correlated to scores of the HIT-6, MigSev, and QVM.

**Conclusion** These results suggest a positive evolution in the prescription of acute treatment in daily practice according to severity of migraine attacks.

**Keywords:** migraine attack, acute treatment, HIT-6, MigSev, QVM

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**Reference**

F041

Comparative efficacy of eletriptan and sumatriptan in reducing headache recurrence in high-risk migraine patients

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Background Eletriptan has been shown to significantly reduce recurrence rates among patients achieving a headache response within 2 h.

Objective The goal of the current study was to compare the efficacy of eletriptan and sumatriptan in reducing recurrence in patients at high risk for recurrence.

Methods Data were pooled from 10 double-blind, placebo-controlled trials in migraine. Multivariate regression analyses identified significant predictors of recurrence within 24 h of initial treatment response. Patients qualified for inclusion in the high-risk subgroup if they had at least three of the most significant predictors of recurrence (high baseline pain severity, female, age ≥ 35 years).

Results Among patients qualifying for the high-risk subgroup, recurrence rates at 24 h were lower on eletriptan 40 mg (E40; 35%) compared with both sumatriptan 100 mg (S100; 51%; P < 0.005) and placebo (48%; P = 0.058) when the analysis was limited to patients with severe headache pain at baseline (N = 511). Recurrence rates at 24 h were also lower on E40 (29%) compared with both S100 (40%; P < 0.005) and placebo (43%; P < 0.001) when the analysis was limited to patients with moderate headache pain at baseline (N = 1314).

Conclusion Eletriptan was more effective than sumatriptan in reducing the risk of headache recurrence among high-risk patients.

Keywords: migraine, headache, eletriptan, sumatriptan, recurrence

F042

Efficacy and tolerability of eletriptan in triptan-naive vs. triptan-experienced patients: results of a combined analysis

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Background Triptan-naive (TN) patients (starting a triptan for the first time) represent a clinical subgroup with different treatment needs than triptan-experienced (TE) patients.

Objective To evaluate the efficacy and tolerability of eletriptan in TN vs. TE patients.

Methods Efficacy and tolerability data were analysed from 10 double-blind trials in patients treated with eletriptan 20 mg (E20; TN vs. TE, N = 179 vs. 255), eletriptan 40 mg (E40; TN vs. TE, N = 1381 vs. 1971), and placebo (PBO: TN vs. TE, N = 735 vs. 988).

Results 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). Sustained response at 24 h was also significantly higher in TN and TE patients on E20 (34% and 29%) and E40 (45% and 41%) vs. PBO (20% and 9%; P < 0.0001 for all comparisons with PBO). 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%).

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

Keywords: migraine, headache, triptan, eletriptan, meta-analysis

F043

Functional impairment in migraine: validation of a work productivity questionnaire

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Background Functional impairment is a core criterion for diagnosing migraine.

Objective To validate a 7-item Work Productivity Questionnaire (PQ-7) designed to measure attack-related impairment in ability to perform work-related activities.

Methods Eletriptan 40 mg treatment data were analysed from an acute, double-blind migraine study (N = 207). Impairment on the PQ-7 was compared with the traditional 4-point global functional impairment scale (FIS), and with the recently validated Activity and Participation subscale of the Functional Assessment in Migraine scale (FAIM-A&P). Convergent and discriminant validity were evaluated by calculating Spearman coefficients.

Results The Spearman correlations between the FIS and PQ-7 standard scores were −0.57 at baseline and −0.69 at 2 h, while the Pearson correlations between the PQ-7 and the FAIM-A&P standard scores were 0.57 at baseline and 0.77 at 2 h. The PQ-7 had good discriminant validity: at baseline, the mean (± SD) PQ-7 standard score in patients with mod/severe headache pain was 43.1 ± 27.1, while patients who were pain free at 2 h had a mean PQ-7 standard score of 89.7 ± 19.3.

Conclusions These results confirm the validity of the PQ-7, with the level of correlation suggesting that the PQ-7 is measuring a dimension that is semi-independent from existing functional measures.

Keywords: eletriptan, migraine, headache, work productivity, validation study

F044

Is it wise to use topimimate for migraine prophylaxis in poor countries

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Objectives Migraine is a common disorder with a relatively high cost of treatment from both society’s and the patient’s
standpoint. To reduce the cost of migraine treatment preventive medication is an option. There are several agents (propranolol, amitriptyline, verapamil, valproic acid and flunarizine) for this purpose. Recently, topiramate, an antiepileptic agent, was studied and found more effective than placebo in prevention of migraine attacks.

**Methods** In this study we aimed to evaluate the cost-effectiveness of topiramate and compare it with standard preventive treatment options, using the drug and patient care costs available in Turkey. The main parameters were price per migraine attack reduced, monthly preventive medication cost.

**Results** The effectiveness data for all corresponding agents were obtained from different well-designed placebo or active-controlled, double-blind, randomized clinical trials. For some points calculation was performed with an assumption of equal effectiveness for all agents with the lowest doses reported as effective in placebo-controlled trials. Both of the parameters used show clearly that topiramate has the highest monthly drug cost for prevention of migraine attack and price per migraine attack reduced.

**Conclusion** The results indicate that even though the idea of preventing is more cost-effective than to treat the migraine attacks, our and previously reported studies show that this hypothesis may not be valid for certain agents, which is the case for topiramate in migraine prophylaxis in Turkey.

**Keywords:** topiramate, cost-effectiveness, migraine

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**F045**

Functional response in migraine: efficacy of eletriptan using four concurrently administered functional assessment measures

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**Background** Functional response is an important assessment measure for diagnosing migraine.

**Objective** To evaluate the efficacy of eletriptan in normalizing functional impairment using four concurrently administered scales: the 7-item Work Productivity Questionnaire (PQ-7), the FAIM Activities and Participation subscale (FAIM-A&P) and Mental Functioning subscale (FAIM-IMMF), and the traditional 4-point global functional impairment scale (FIS).

**Methods** Out-patients with an IHS diagnosis of migraine were randomized to double-blind treatment with either eletriptan 40 mg (E40; N = 196) or placebo (N = 194). Patients with moderate-to-severe impairment were identified on each of the four disability scales, and 2-h functional response was compared for E40 vs. PBO.

**Results** Functional response at 2 h was significantly higher on E40 vs. PBO on the measure of work productivity (PQ-7: 56% vs. 34%; P < 0.011), on mental functioning (FAIM-IMMF: 50% vs. 34%; P ≤ 0.015), and on the ability to participate in a range of activities (FAIM-A&P: 63% vs. 36%; P ≤ 0.0001). These rates were similar to functional response rates on the traditional 4-point FIS: 75% vs. 45%, P < 0.0001. Impairment in mental functioning showed a somewhat more delayed time-to-remission on eletriptan compared with work productivity and other non-mental functional activities.

**Conclusion** Eletriptan is effective in normalizing functioning across multidimensional domains in individuals experiencing attack-related disability.

**Keywords:** eletriptan, triptan, migraine, headache, disability

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**F046**

Eletriptan and headache recurrence

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**Background** The recommended dose of eletriptan is 20 mg (E20) in Japan and 40 mg (E40) in the USA and Europe.

**Objective** The current analysis evaluates the effect of dose on headache recurrence in patients with mild and moderate-to-severe headache in both settings.

**Methods** Data were pooled from three placebo-controlled trials in migraine conducted in Western countries comparing E20 (N = 322) and placebo (PBO; N = 183); and one study of E20 (N = 51) and placebo (N = 46) in Japan.

**Results** In the pooled Western studies, recurrence rates were not different on E20 (31%) compared with PBO (31%) in patients with moderate-to-severe headache. However, in patients with mild headache, recurrence rates were reduced on E20 compared with PBO (14% vs. 41%). In contrast, in Japan, reduction in recurrence was achieved on E20 (10%) compared with placebo (24%; P = 0.06) regardless of headache severity.

**Conclusion** The 20-mg dose of eletriptan provides reduction of recurrence in Japan regardless of headache severity, and the 20-mg dose appears effective in Western settings when headache pain is mild.

**Keywords:** migraine, headache, triptan, eletriptan, recurrence

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**F047**

Efficacy of eletriptan in migraine patients at high risk for non-response

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**Background** Eletriptan is a safe and efficacious treatment in patients initiating triptan therapy for the first time. The other end of the clinical spectrum consists of patients who are at high risk for non-response.

**Objective** The goal of the current study was to evaluate the efficacy of eletriptan 40 mg (E40) in this high-risk patient group.

**Methods** Data were pooled from 10 double-blind, placebo-controlled trials in migraine. Multivariate regression analyses identified significant predictors of non-response to treatment. Patients qualified for inclusion in the high-risk subgroup if they had at least three of the most significant negative
predictor variables (high baseline pain severity, female, age ≥ 35 years; N = 1052).

**Results** Among the high-risk subgroup of patients, headache response at 2 h was significantly higher on E40 (49%) vs. placebo (17%; P < 0.0001); pain-free response at 2 h was also significantly higher on E40 (27%) vs. placebo (4%; P < 0.0001). Improvement in headache pain was associated with significantly higher functional response at 2 h on E40 (50%) vs. placebo (21%; P < 0.0001). At 24 h, sustained response was higher on E40 (30%) vs. placebo (8%; P < 0.0001).

**Conclusion** Eletriptan is efficacious in the difficult-to-treat subgroup of patients at high risk for non-response.

**Keywords:** migraine, headache, triptan, eletriptan, treatment resistant

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**F048**

**Impact of rizatriptan on functional disability in an early intervention model: results from the TAME Study**

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**Background** Early treatment of migraine has been demonstrated to improve efficacy measures, but its effect on functional disability has not been extensively studied.

**Methods** This was a randomized, double-blind study. Migraineurs treated their headache with rizatriptan or placebo within 1 h of onset. During the next 24 h, patients assessed pain severity, degree of functional disability, and reported adverse experiences. The primary endpoint was pain freedom at 2 h. This tertiary analysis examined functional improvement (mild or severe disability at baseline improving to no disability at 1 and 2 h).

**Results** Of 583 patients randomized to treatment, 530 (91%) treated a study migraine. Before treatment, 68% of patients reported mild impairment of ability to perform daily activities, and 41% reported severe impairment. The percentage of patients that experienced functional improvement with rizatriptan treatment was significantly greater than with placebo by 1 h postdose (40.5% vs. 29.9%, P = 0.015) and was further increased by 2 h (69.5% vs. 46.3%, P < 0.001).

**Conclusion** Functional disability exists in a significant proportion of patients early in the course of migraine, when the pain is mild. Early treatment with rizatriptan relieved migraine-related functional impairment significantly by 1 h and in the majority of patients by 2 h.

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**F049**

**A case of headache attributed to otitis media chronica cholesteatomatica with cerebral sigmoid sinus thrombosis**

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**Objective** This case of a 31-year-old man showed the importance of ear disease as a cause of headache in terms of differential diagnosis.

**Chief complaint** Headache, earache, vomiting, and vertigo.

**Present illness** Two years ago he had stuffed up his right ear with tissue paper because of a noise and sometimes had right ear discharge. One month before admission he had right occipital headache with right earache and fever. One day before admission he had vomiting. Vertigo developed on the day of admission.

**Physical examination** The level of consciousness was somnolence. The temperature was 36.9 °C. The blood pressure was 112/68 mmHg. Meningeal sign was obvious. Cerebrospinal fluid examination showed a cell count of 32/3 mm³. Brain magnetic resonance imaging (MRI) revealed right otitis media chronica cholesteatomatica and right cerebral sigmoid sinus thrombosis.

**Course** He became conscious and his symptoms improved after administration of ampicillin and ceftriaxone sodium. A diagnosis of headache attributed to disorder of ears was made on the basis of symptoms and MRI findings. Otitis media chronica cholesteatomatica was thought to be the cause of cerebral sigmoid sinus thrombosis and meningitis.

**Conclusion** In case of headache with earache, headache attributed to disorder of ears should be considered.

**Keywords:** otitis media chronica cholesteatomatica, cerebral sigmoid sinus thrombosis, meningitis, headache with earache, MRI

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**F050**

**Triptan-induced allodynia: central response to triptan?**

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**Background** Allodynia can be induced by systemic sumatriptan administration.

**Objective** We investigated the clinical expression of allodynia induced by oral triptans.

**Methods** 200 migraineurs were requested to complete a questionnaire looking for allodynia during untreated migraine and to treat attacks with a triptan and complete the questionnaire. Patients treated three consecutive attacks with a triptan and tested several triptans. Quantitative sensory testing (QST) was performed in patients experiencing both migraineous and triptan-induced allodyneas, outside attack, during migraineous allodynia, and triptan use.
Results 41 patients reported migrainous allodynia, 21 patients reported triptan-induced allodynia, one patient reported both. Migrainous allodynia concerned the face in 28 patients and was tactile in 38 patients. Allodynia was induced by a triptan in 18 patients, with several triptans in seven patients. Triptan-induced allodynia developed when relief was complete, lasted 1–24 h, was thermal allodynia in the face and four limbs. QST confirmed static and dynamic facial tactile allodynia during migrainous allodynia and diffuse thermal allodynia after triptan use.

Conclusion Thermal allodynia may be a central phenomenon different from migrainous allodynia occurring with all triptans after relief.

Keywords: allodynia, triptan, side-effect

Reference


F051

Treatment with sumatriptan 50 mg in the mild phase of migraine attacks in patients with infrequent attacks. A randomized, double-blind, placebo-controlled study

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Background Many migraine patients with infrequent attacks are currently not treated with specific medicine such as triptans. It is unknown how these patients respond to specific treatment.

Objective To investigate the efficacy and tolerability of sumatriptan 50 mg vs. placebo in migraine patients with infrequent migraine attacks taken during the mild phase of an attack.

Methods This study was a double-blind, placebo-controlled, randomized, parallel-group clinical trial. Migraine patients were recruited by general practitioners and referred to one of four study centres. Additional patients were recruited by announcement. Patients were eligible for the study if they had 6-12 migraine attacks per year. Patients were instructed to take the medication during the mild phase of a single attack. The primary efficacy measure was the proportion of patients pain free after 2 h.

Results One hundred and one patients treated an attack. Forty-seven percent of treated attacks were moderate or severe. In the intention-to-treat analysis sumatriptan (20/51) was superior to placebo (8/47) (P < 0.05). Adverse events occurred more frequently after sumatriptan (40%) than after placebo (13%) (P < 0.05).

Conclusion In this migraine population with infrequent attacks sumatriptan was superior to placebo. Sumatriptan was generally well tolerated.

Keywords: migraine, sumatriptan, infrequent attacks

F052

Effect of zolmitriptan in migraine occurring at work

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Background Migraine’s impact on society is not negligible. Indirect costs are related, among other aspects, to attacks occurring during work.

Objective To address zolmitriptan efficacy in reducing pain and promoting full work capacity in migraine occurring in the workplace.

Methods Volunteers suffering from 1988 IHS migraine from six different work environments enrolled and received four 2.5-mg zolmitriptan tablets each. A diary for efficacy measurement was completed. Work capacity was approached using a visual work capacity scale.

Results A total of 44 patients recorded 64 treated attacks; two were mild, 24 moderate, 26 intense and 21 excruciating. In 37 attacks, zolmitriptan was used before 1 h. Fifty-eight attacks responded to zolmitriptan and six attacks did not respond. The time required for improvement was 2.16 ± 1.86 h. Total pain reduction was observed in 72.4% before 2 h. Three patterns of productivity recovery following zolmitriptan were noticed: fast recovery to full work capacity; slow recovery; and no recovery. These curves were influenced by the pain intensity, the response to zolmitriptan and the side-effects. Following zolmitriptan, full work conditions were achieved in 3.5 ± 4.3 h.

Conclusion Zolmitriptan is efficient for migraine during work, reducing not only the pain but also restoring full work capacity.

Keywords: migraine, zolmitriptan, treatment, impact

F053

The effect of food, migraine and a second tablet on the pharmacokinetic profile of a single tablet combining sumatriptan RT Technology™ and naproxen sodium for the acute treatment of migraine

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Background Migraine involves activation of nociceptive and inflammatory responses. Acute therapy that targets both may confer additional therapeutic benefit.

Objective To assess the pharmacokinetic (PK) profile of a single tablet combining sumatriptan 85 mg RT Technology™ and naproxen sodium 500 mg (SumaRT/Nap)® in the fasted/fed states, (2) during and in the absence of migraine, and (3) following a second tablet.

Methods Three phase-I, crossover, open-label, single-centre studies (n = 18–24/group).

Results Food: Administration of food did not affect the bioavailability of naproxen or sumatriptan with respect to either AUC0–inf or Cmax. Food had no affect on naproxen Tmax but delayed sumatriptan Tmax by 40 min (95% CI 15, 65). During absence of migraine: There were no differences in PK parameters for either sumatriptan or naproxen. Two-tablet study: For
naproxen, the mean $C_{\text{max}}$ and AUC increased by a factor of 1.5 and 1.6, respectively, when a second dose of SumaRT/Nap was given after 2 h. For sumatriptan, there was a dose-proportional increase in AUC and $C_{\text{max}}$ by a factor of 1.6 following a second dose of SumaRT/Nap.

**Conclusion** SumaRT/Nap was well tolerated with minor PK changes noted when given with food or followed by a second dose after 2 h.

**Keywords:** sumatriptan, naproxen sodium, pharmacokinetic, migraine, inflammation

**F054**

**Improved absorption of sumatriptan tablets formulated with RT Technology™ (SumaRT)**

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**Background** SumaRT tablets are bioequivalent ($C_{\text{max}}$, AUC$_{0-\infty}$) to conventional sumatriptan tablets (conv tab). Evidence suggests benefits from reformulation of sumatriptan, e.g. 5x faster in vitro dissolution; $T_{\text{max}}$ 15 min earlier and 8% increase in AUC$_{0-2\text{h}}$ (Walls 2004); clinical onset of efficacy by 20 min (Sheftell 2004); 75% patients pain free at 2 h (Carpay 2004).

**Objective** To evaluate differences in time to disintegration, emptying, and absorption between conv tab and SumaRT.

**Methods** Four-way cross-over study of five migraineurs (ICHDI-II 1.21 or 1.1) interictally of conv tab and sumaRT using gamma scintigraphy (time to disintegration, emptying, absorption). Patients swallowed a 100-mg sumatriptan radio-labelled tablet (Indium-111) with water ($^{99m}$TC DPTA) at each session; images taken every minute for 30 min and 10–15 min for 4 h. Time to 50% gastric emptying and plasma samples were analysed.

**Results** Five migraineurs (mean age 30.8 years; migraine history of 17.2 years) completed the sessions. SumaRT disintegrated 6x faster (6.2 vs. 38.8 min, respectively), emptied 30 min faster (57.9 vs. 94.2 min, respectively), and plasma levels were higher at earlier time points compared with conv tab.

**Conclusion** Intercital administration of sumatriptan tablets formulated with RT Technology result in faster disintegration, emptying, and absorption than the conventional tablet.

**Keywords:** sumatriptan, gastric emptying, absorption

**F055**

**Pharmacokinetics of a single-tablet formulation of sumatriptan RT Technology™ and naproxen sodium**

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**Background** Pain and inflammatory mechanisms are activated during migraine, suggesting that multiple mechanisms may be targets for treatment. Combining these therapies along with RT formulation may improve the PK profile for acute migraine treatment.

**Objective** To evaluate the PK profile of sumatriptan RT Technology™ (SumaRT) 85 mg and naproxen sodium 500 mg given as a fixed-dose single-tablet formulation (SumaRT/Nap).

**Methods** The results of two single-centre, open-label, incomplete 3-way crossover, healthy volunteer, phase-I studies are summarized ($n = 24–29$/group).

**Results** AUC$_{0-1.5}$ for sumatriptan following SumaRT/Nap was 40.2 h/μg/ml, which was 51% greater vs. sumatriptan conventional formulation (CF) 100 mg (26.7 h/μg/ml). The $C_{\text{max}}$ for naproxen from SumaRT/Nap was 68.0 μg/ml: a decrease of 31% and 26%, respectively, vs. Anaprox® 550 mg (98.0 μg/ml) and naproxen sodium 500 mg (91.0 μg/ml). The $T_{\text{max}}$ for naproxen given as SumaRT/Nap was delayed (median 7.0 h; range 0.5–8.0 h) vs. Anaprox (median 1.0 h, range 0.5–3.0 h) or naproxen sodium given alone (median 1.0 h, range 0.5–4.0 h). In a second study, similar results were observed. Overall exposure, AUC$_{0-\infty}$, was similar for sumatriptan and naproxen when given as sumaRT/Nap and individual components.

**Conclusion** The single-tablet SumaRT/Nap exhibits consistent and reproducible enhanced early absorption of sumatriptan and an extended availability profile for naproxen.

**Keywords:** sumatriptan, naproxen sodium, pharmacokinetics

**F056**

**Population-based assessment of oral sumatriptan efficacy and safety in migraine patients**

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**Background** Sumatriptan introduction has become a breakthrough in controlling migraine attacks.

**Objective** The common usage of this agent in such patients provides an opportunity for population studies on its efficacy and safety.

**Methods** The analysis included 17 199 oral administrations of sumatriptan in 798 migraine patients aged 17–87 years. Non-responders were excluded from the study after treating the second migraine attack. The assessment also included the number and intensity of adverse effects.

**Results** Of 798 patients, in 412 (51.6%), sumatriptan evoked a good clinical effect without any significant adverse effects. A further 44 patients (5.5%) achieved a good clinical effect, but failed to take the second sumatriptan dose due to its adverse effects. In 102 individuals, the effective dose was 50 mg, in 28–25 mg. A total of 242 patients took sumatriptan more than 50 times; 187 showed no decline in its efficacy. Any adverse effects were noted in 195 patients (24%).

**Conclusions** The results confirm the clinical efficacy of sumatriptan in more than 55% of migraine sufferers. In more than 77% of individuals on chronic therapy, sumatriptan shows long-term efficacy. Approximately one-quarter of patients experience adverse effects, but no serious effects have been observed.

**Keywords:** sumatriptan, migraine, acute treatment, efficacy, safety

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Prevention and progression

G001

To study the efficacy and safety of levetiracetam in refractory migraine.
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Background Antiepileptic drugs are being employed in migraine prevention. Levetiracetam has patient-friendly pharmacokinetics that might facilitate management of migraine.

Methods Patients with refractory migraine (failed two migraine prevention drugs from different class), satisfied IHS criteria for migraine, were aged 18–45, and had at least four headaches/month were included. Women on oral contraceptives, lactating or pregnant, patients with comorbid neurological or psychiatric illness and mixed headache types were excluded. Dose escalation was weekly until 1500 mg/day was reached within 1 month. Rescue medications for acute attacks were allowed. Follow-up was done at months 1 and 3 after withdrawal therapy. Tapering analgesics gradually in conjunction with inpatient withdrawal treatment in difficult cases suffering from analgesics abuse headache.

Results Twenty-two patients average age of 32 years (range 18–45), women n = 19, men n = 6 were included. There was a 67% reduction in headache number (P < 0.001), 78.3% reduction in headache days (P < 0.001). Emergency visits were reduced by 74% (P < 0.001), rescue medication reduced by 84.3% (P < 0.0001) and headache severity cut down by 47% (P < 0.05). Three patients discontinued medication due to sleepiness, nausea, light-headedness and agitation, n = 1.

Conclusion Levetiracetam was effective in reducing headache number, days, severity, emergency visits, rescue medication and was well tolerated in patients with refractory migraine. A double-blinded comparison trial of levetiracetam is underway.

G002

Long-term prognosis of analgesics abuse headache
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Objective To evaluate the long-term prognosis of analgesics abuse headache.

Methods Ninety-five consecutive patients with analgesics abuse headache were treated for 6 years from November 1997 to October 2003. Seventy-three patients (76.8%) had migraine, 18 (19.0%) had tension-type headache and four (4.2%) new daily persistent headache. Seventy-seven (81.1%) were females and 18 (18.9%) males. A total of 69 patients were available for interview as of October 2004 at a mean time interval of 41.5 months after drug withdrawal therapy. Twenty-two patients were admitted to our in-patient withdrawal unit and 25 patients were treated by out-patient withdrawal therapy. Tapering analgesics gradually in conjunction with instituting preventive therapy treated 22 patients.

Results Intake of analgesics; days/month: in-patient, nine cases (41%) on ≤8, five cases (23%) on 9–15 and eight cases (36%) on >15. Three cases (14%) developed recurrent analgesic abuse. Out-patient (abrupt discontinuation), 12 cases (48%) on ≤8, five cases (20%) on 9–15 and eight cases (32%) on >15. One case (4%) reported on recurrent analgesic abuse. Out-patient (tapering analgesics gradually), one case (5%) on ≤8 and 21 cases (95%) daily intake. Fifteen cases (68%) reported continuous analgesic abuse.

Conclusions These results demonstrate the efficacy of inpatient withdrawal treatment in difficult cases suffering from analgesics abuse headache.

G003

Topiramate has a locus of action outside of the trigeminocervical complex
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Background Inhibition of the trigeminocervical complex, or neurons that modulate sensory input, are plausible mechanisms for the action of migraine preventives.

Objective To facilitate understanding its preventative action we examined the effect of topiramate (TPM) on trigeminocervical activation.

Methods Cats (n = 14) were anaesthetized and physiologically monitored. Their superior sagittal sinus (SSS) was stimulated to activate trigeminovascular nociceptive neurons. Extracellular recordings were made from these neurons in the trigeminal nucleus caudalis.

Results Microiontophoretically delivered TPM (–80; −160 nA) produced no significant inhibition of SSS linked trigeminocervical cells activated by microiontophoresis of L-glutamate (n = 15 cells). Cell firing linked to electrical stimulation of the SSS was partly inhibited (30.0 ± 9.8% at 15–30 min) by 30 mg/kg i.v. TPM (n = 9 cells). Overall there was no inhibition of SSS-evoked activity by microiontophoretically applied TPM (−160 nA; n = 13 cells). However, after i.v. TPM (30 mg/kg) profound inhibition (70.7 ± 9.5%) of L-glutamate-evoked firing of SSS linked cells was observed (n = 7).

Conclusion These data suggest that TPM acts outside the trigeminocervical complex. This distinction from triptans may be crucial in understanding the mechanisms by which TPM agent acts as a preventive.

Keywords: topiramate, preventive, microiontophoresis, trigeminal, headpain

G004

Acetazolamide inhibits trigeminovascular nociceptive transmission in the cat
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Background Inhibition of the trigeminocervical complex, or neurons that modulate sensory input, are plausible mechanisms for the action of migraine preventives.
Objective To facilitate understanding their action we examined the effect of acetazolamide on trigeminocervical activation.

Methods Cats \((n = 5)\) were anaesthetized (\(\alpha\)-chloralose 60 mg/kg) and physiologically monitored. The superior sagittal sinus (SSS) was stimulated to produce a model of trigeminovascular nociceptive activation. Cumulative dose–response curves were constructed for the effect of acetazolamide at doses of 3, 5, 10, 30 and 50 mg/kg on SSS-evoked firing of trigeminocervical neurons.

Results Acetazolamide reduced SSS-evoked firing in a dose-dependent fashion. The maximum effect was seen over 30 min for the cohort taken together. At 3 mg/kg firing was reduced by 21 ± 10% (mean ± SEM) after 15 min. At 5 and 50 mg/kg firing was reduced by 62 ± 17% and 77 ± 6%, respectively, after 30 min.

Conclusion Inhibition of the trigeminocervical complex directly, or neurons that modulate sensory input, possibly involving altered properties of voltage-gated ion channels, may play a role in migraine.

Keywords: acetazolamide, preventive, nociception, trigeminal, migraine

**G005**

Topimarate and sodium valproate prevent migraine

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Background Both topimarate (TPM) and sodium valproate (SV) have been proved to be effective for migraine prevention in USA.

Objective To test TPM efficacy in Chinese and compare its efficacy with SV.

Methods Total of 102 patients with episodic migraine were randomized into two groups: TPM (53) and SV (49). TPM was titrated by 25 mg/week for 2–4 weeks. SV was given at 200 mg twice daily during initial titration of therapy. The patients’ headache diaries were recorded and the severity of headaches was rated on a 0–10 rating scale.

Results Mean frequency of headache occurrence decreased from 7.2 to 2.0 \((P < 0.05)\) and 7.0 to 2.5 \((P < 0.05)\) per month in the TPM and SV group, respectively. No significant difference existed in mean frequency of headache between the two groups. Mean severity decreased from 8.0 to 2.0 \((P < 0.05)\) in the TPM group and from 7.6 to 3.6 \((P < 0.05)\) in the SV group, showing a significant difference between the two groups \((P < 0.05)\).

Conclusion Both TPM and SV prophylaxis therapy for episodic migraine yielded a significant reduction in migraine frequency and severity in Chinese. TPM is better in reduction of migraine severity than SV.

Keywords: topiramate, sodium valproate, episodic migraine

**G006**

Efficacy of topiramate in migraine patients. Randomized, double-blind, placebo-controlled group

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Background Some evidence suggests topiramate, a broad-spectrum anticonvulsant, can prevent migraine.

Objective The efficacy of topiramate in migraine prophylaxis was examined.

Methods 56 patients were analysed. The diagnosis of migraine was made according to the IHS criteria. The migraineurs were randomly assigned to treatment with either topiramate 100 mg/day or placebo for 8 weeks.

Results Headache frequency showed 75.3% reduction in the topiramate-treated group, whereas there was a 18.8% reduction in the placebo group. Headache intensity showed a 40.0% reduction in the topiramate-treated group, and a 9.7% reduction in the placebo group.

Conclusion Topiramate is an effective prophylactic agent in migraine patients.

Keywords: topiramate, migraine, placebo

**G007**

Paraesthesia in Korean migraineurs with topiramate shows better clinical outcome

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Objective Purpose of study is to determine the clinical outcome of migraineurs with topiramate, with or without adverse events, such as paraesthesia, fatigue, memory difficulty, loss of appetite and weight loss.

Methods 260 migraineurs (mean age 48.2 ± 12.0; 39 male, 221 female) were included. Medication was given from 25 mg/day and gradually increased up to 100 mg/day weekly. Headache frequency and adverse events were recorded and evaluated up to 10 months.

Results 66 patients were unable to make follow-up, due to adverse events, mostly paraesthesia, fatigue and memory complaint. 155 patients who took medication for more than 1 month also reported paraesthesia (52.9%), fatigue (27.0%), memory difficulties (29.0%), and loss of appetite (12.3%). At 3 months, those with paraesthesia showed 60% level of headache frequency compared with baseline, and it decreased to 40% at 6 months. However, patients without paraesthesia showed a 70% level at 3 months and 60% at 6 months. Effect of weight loss, memory or other adverse effects does not seem to be related to headache frequency. Paraesthesia commonly subsided spontaneously, usually in 2–3 months.

Conclusion Even though paraesthesia is the most common troublesome adverse effect, migraineurs with paraesthesia showed a better clinical outcome.

Keywords: topiramate, migraine, paraesthesia, headache frequency
G008

Prevalence of headache in students of Kanazawa University
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Objective To study the prevalence and characteristics of headache in university students.

Methods We performed a questionnaire study based on the diagnostic criteria of the International Headache Society (IHS) for students in Kanazawa University on the occasion of the annual health examination in 2001.

Results Of 5320 students, 92% (4917) had at least one experience of headache and 23.5% (1251) had repeated headache episodes. Two hundred and two students had migraine with aura, 164 had migraine without aura, 192 had episodic tension-type headache, and 41 had chronic tension-type headache. Most students with migraine had their first attack during elementary school, and those with tension-type headache had the first episode during junior high school. Prevalence of migraine and tension-type headache was significantly higher in females than males. The score of self-assessment of pain strength was higher in students with migraine than in those with tension-type headache. The most common trigger of headache attack was stress in both migraine and tension-type headache. When headache occurred, students tended to take rest and few students consulted physicians. Only 10% of students recognized the category of their headache.

Conclusion Promotion of health education and support for individuals who have severe headache are important issues in university healthcare.

Keywords: migraine, tension-type headache, questionnaire, epidemiology, risk factor

G009

Chronic migraine is the earlier stage of migraine chronification
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Objectives To test the hypothesis that early in the course of migraine chronification, the frequency of migraine attacks is high and that as illness progresses the frequency of non-migraine headaches increases.

Methods We collected information on 402 adults with more than 15 days of headache per month, and history of episodic migraine. Group 1 also had more than 15 days of migraine per month, while Group 2 had less than 15 days of migraine per month. We modelled risk factors for number of migraine days per month using logistic regression.

Results Of 402 subjects, 121 (30.1%) were in Group 1. The proportion of Group 1 subjects decreased with age, from 71% below the age of 30 years to 22% aged 60 or above. The corresponding proportion of Group 2 sufferers increased from 29% to 78%. More than 15 days of migraine per month were independently predicted by younger ages (<40 years, \( P = 0.003 \)), and shorter interval from episodic to daily headaches (<5 years, \( P = 0.003 \)), and shorter time since the development of daily headaches (<6 years, \( P < 0.0001 \)).

Conclusions Chronic migraine appears to represent an earlier stage of migraine transformation. As disease evolves, fewer attacks fulfil criteria for migraine.

G010

The influence of the body mass index on headache frequency and severity
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Objective To assess the influence of the body mass index (BMI) on the frequency, severity and clinical features of primary headaches in the population.

Design/methods We interviewed 143 433 individuals and identified 30 850 subjects with at least one headache attack in the prior year and BMI information. We defined five categories based on BMI: 1, underweight (<18.5), normal weight (18.5–24.9), overweight (25–29.9) and obese (30–40.0), and morbid obesity (>35). We modelled headache frequency as a function of BMI, adjusted by covariates.

Results More than 15 days of headache was more common in obese (5.2%) than in the normal weighted group (4.1%, \( P < 0.001 \)). Prevalence was highest in the morbidly obese group (7.1%, \( P < 0.001 \)). Having missed work activities for more than 4 days due to headache was more common in obese (33%) compared with overweight (27.2%), normal (27.2%) and underweight (26.1%). Obese subjects also reported severe pain more often than the other groups (35.7% vs. 31.7%, 29.5%, 30.3%, \( P < 0.001 \) OR = 1.223 vs. normal). Severity of pain and disability significantly correlated with obesity.

Conclusions Obesity is associated with headache frequency, headache severity, and headache-associated disability in the population.

Study supported by: The MHS was collected by IMR, Inc., a division of Caremark. Analysis of these data was supported by OrthoMcNeil, Inc., a division of Johnson and Johnson.

G011

Comorbidity of chronic frequent headache in the general population
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Objective To study the nature and extent of comorbidity of chronic frequent headache (CFH) in the general population.

Methods Subjects with CFH (headache on > 14 days/month) were identified in a general health survey. We sent a second questionnaire including open questions on comorbidity with CFH and subjects with infrequent headache (IH) (1–4 days/
Objective
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 analysing method with nine stage displays is used. Subjects were consecutive 13 patients for (1) and nine patients for (2), who showed platelet hyper-aggregability.

Results
Excellent preventive effects on migraines were obtained in all cases. (1) Days of missed 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. (2) Migraine attacks did not appear completely in all nine cases for many years. In addition, the scintillating scotoma itself disappeared completely in seven cases. In one of two cases that were using triptans, it became not necessary.

Conclusion
Based on these results, the author proposes that the fundamental cause of migraine is the long-standing platelet hyper-aggregability. The effect must be elicited by stabilizing the serotonin metabolism by correcting the platelet hyper-aggregability. If the platelet hyper-aggregability is not corrected, white matter lesion will develop and progress rapidly, and finally it becomesBinswanger’s dementia. Thus, this is the best preventive treatment for migraine and dementia. The author strongly recommends applying this method.

Keywords: platelet hyper-aggregability, prevention of migraine, MIDAS scale, migraine accompanying scintillating scotoma

G014
Curative preventive effect of the platelet hyper-aggregability correction (1) on migraine evaluated by MIDAS scale and (2) on migraine accompanying scintillating scotoma

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Objective
To investigate the preventive effect of correction treatment of the platelet hyper-aggregability on severe migraine.

Results
CFH subjects (n = 176) had higher comorbidity scores than the IH subjects (n = 141). Mean CIRS score: CFH, 2.85, IH, 1.53, mean difference 1.32 (95% CI 0.85, 1.80). Median number of categories selected was two in the CFH group vs. one in the IH group. Fifty percent of CFH subjects had a comorbidity severity level of at least two, indicating disorders requiring daily medication compared with 28% of IH subjects, mean difference 22% (95% CI 12, 33). In both groups the most prevalent comorbid disorders were in the gastrointestinal and musculoskeletal categories. CFH subjects reported more heartburn, bowel problems, musculoskeletal problems (joint operations and arthritis), endocrine/breast and psychiatric pathology than the IH subjects.

Conclusions
Patients with chronic frequent headache have more comorbid disorders than patients with infrequent headaches. Many CFH patients have a comorbid chronic condition requiring daily medication.

Keywords: chronic frequent headache, comorbidity, CIRS

G015
Psychological risk factors for the transformation of migraine to chronic migraine and medication overuse headache: a possible role for dysfunctional coping strategies

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Objective
About 5% of the population suffer from daily or near daily headache, mostly evolved from an episodic type of headache. Somatic factors as well as psychological factors play an important role in this transformation. Dysfunctional coping strategies, especially endurance behaviour, have high predictive value for chronification of low back pain. Similar mechanisms might be important for headache.

Methods
We investigated 211 patients with different kinds of headaches regarding pain coping behaviour, depression and somatic factors. Diagnosis was based on IHS criteria. Depression was evaluated using the ‘Allgemeine Depressions Skala’ and coping behaviour assessed using the ‘Kiel Pain Inventory’.

Results
Depression was high in the overall sample, with significant differences between patients with episodic and chronic migraine. Two-thirds of all patients used dysfunctional coping strategies with high prevalence of ‘endurance’ behaviour with marked differences between chronic and episodic headache types.

Conclusion
Headache patients employ many dysfunctional coping strategies. It is likely that they have the same impact on chronification as in low back pain patients. The results of this study suggest that headache patients at risk need
behavioural and psychological guidance in addition to adequate medication to prevent chronication.

**Keywords:** chronic migraine, psychological risk factors, pain chronication, medication overuse headache

**G016**

The prevalence of headaches and associated factors in an urban multiracial sample of older adults

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**Background** Epidemiological data about headaches in urban elderly are lacking.

**Objective** We examine the prevalence of headache and associated factors among older adults in New York City.

**Methods** 225 Caucasians and 848 Blacks aged 55+ (mean 68 years) were interviewed using scales that assessed physical and mental health, social supports, coping and psychosocial stressors. Data were analysed using a model with 13 independent variables, and a dependent variable dichotomized into headaches that bothered respondents ‘none or little of the time’ vs. ‘some, good part, or most of the time’ in the past few weeks.

**Results** 18% met headache criteria. For the entire sample, headaches were significantly associated ($P < 0.05$) with anxiety symptoms, religiosity, and a smaller proportion of confidantes. There were no demographic differences. When examined separately, we found that among Blacks, headaches were significantly associated with anxiety symptoms, larger social networks and greater financial strain. Among Caucasians, headaches were associated with anxiety symptoms, smaller social networks, religiosity, physical illness, and higher daily functioning.

**Conclusion** Psychiatric factors are known to be comorbid with headache. These results implicate other psychosocial factors and they may differ by race. These findings are important with respect to the aetiology and management of headache in older adults.

**Keywords:** headache, epidemiology, race, age, psychiatric disorders

**G017**

Combined therapy of coenzyme Q10 and magnesium as a migraine preventive

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**Background** Earlier studies in the field of preventive migraine treatment have shown effective benefits both from CoQ10 and magnesium independently given, in order to reduce the frequency and duration of migraine attacks.

**Objective** The objective of this study was to evaluate the potential benefit of combined therapy of coenzyme Q10 and magnesium as a preventative for migraine.

**Methods** Combined daily therapy with CQ10 2 × 100 mg and magnesium 2 × 300 mg was given to the first group of patients ($N = 78$; $F: M = 54 : 24$) suffering from migraine with or without aura (IHS criteria), with frequency ≥ 3 and ≤ 8 (average 4.72) of migraine attacks per month. The second group of patients ($N = 68$; $F: M = 49 : 19$), formed according to the same criteria, was given placebo therapy, had had 4.52 attacks per month. After the 1 month baseline period, the treatment period was performed during 3 months. During both periods, the number and duration of migraine attacks was evaluated.

**Results** At the and of the study, the first group of patients has shown significant reduction of the migraine attack frequency from 4.72 to 2.23 per month, with significant statistical response ($P < 0.0001$), in comparison with the placebo group, where the frequency reduced from 4.52 to 4.34. Also, the average days of migraine attacks from the baseline period were reduced from 8.92 to 2.56 ($P < 0.0001$).

**Conclusion:** Combined CoQ10 and magnesium therapy in migraine prevention has shown a significant effect on reducing migraine.

**Keywords:** migraine, coenzyme Q10, magnesium, prophylaxis, treatment

**G018**

The efficacy of lomerizine in the long-term prophylactic treatment of migraine

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**Objective** Lomerizine, a calcium antagonist, is used clinically as an oral migraine prophylaxis in Japan. Previous studies have demonstrated a decrease in frequency of migraine attacks with administration of lomerizine in 12 weeks or less. We investigated the efficacy of lomerizine in the long-term prophylactic treatment of migraine.

**Methods** Forty-one patients (men six, women 35, mean age 34.9 years) suffering from migraine with and without aura according to ICHD-II criteria received treatment with lomerizine 10 or 20 mg per day. Follow-up ranged from 6 to 42 months (mean 17.7 months). Patients suffering from chronic tension-type headache and medication-overuse headache were excluded. Efficacy parameters were frequency of headache attacks.

**Results** Five patients (12%) were almost free from headache attacks and 30 patients (73%) had more than 50% reduction of headache frequency. These improvements continued for follow-up period (maximum 42 months). Three patients had insufficient reduction of headache frequency and three patients were non-responders to lomerizine. No major adverse effects were noted in any patients.

**Conclusion** These data suggest that lomerizine may be useful in the long-term prophylactic treatment of migraine.

**Keywords:** migraine, lomerizine, prophylactic treatment
The epidemiological and clinical characteristics of sports-related headache

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Background Previous studies have suggested sports as a potent trigger of headaches. Compared with other headache syndromes, sports-related headaches (SRH) have attracted little academic interest. Therefore, the precise epidemiology and clinical characteristics of SRH remain uncertain.

Objective To investigate the epidemiological and clinical characteristics of SRH.

Methods We used a self-designed questionnaire, which was completed by 500 Korean university students. The subdivision of SRH was based on the clinical patterns.

Results The prevalence of SRH among the university students was 29.6% (148 of 500). The prevalence of SRH in male students was slightly higher than that in female students (30.3 and 29.2%, respectively). The most common subtype of SRH was an effort/exertion headache. This type of headache was slightly more prevalent in female students than in the male counterparts (94.4 and 92.2%, respectively). Where basketball and football predominately initiated headache in male students, sprinting and long distance running was the most frequent cause in female students. Precipitating factors were varied, the most common being cardiopulmonary overloading.

Conclusions This study demonstrated that sports- and exercise-related headaches are a common problem among university students. Our results might be helpful in understanding the characteristics of SRH and provide some basic information for further studies.

Keywords: sports, headache

Tobacco and alcohol use in relation to headache. The Head-HUNT Study

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Background Conflicting evidence exists whether tobacco is a risk factor of headache. Compared with other headache syndromes, sports-related headaches (SRH) have attracted little academic interest. Therefore, the precise epidemiology and clinical characteristics of SRH remain uncertain.

Objective To examine a possible association between tobacco, alcohol and headache in a large population-based cross-sectional study.

Methods 51,383 subjects completed a headache questionnaire, and of these 48,576 (94.5%) answered questionnaires on tobacco and 45,635 (88.8%) on alcohol consumption. Potential confounders such as age, sex, education level, anxiety and depression, coffee consumption, hypertension and use of anti-hypertensives were adjusted for.

Results Smokers had higher prevalence rates of headache compared with never smokers, most evidently for those under 40 years smoking ≥ 10 cigarettes/day (OR 1.5, 95% CI 1.3, 1.6). For those above 40 years, the association was less clear. Also, previous and passive smokers had higher headache prevalences. For alcohol use, there was a tendency of decreasing prevalence ORs of headache, particularly migraine, with increasing alcohol consumption compared with alcohol abstinence.

Conclusion The association between headache and smoking found in the present study raises questions about a causal relationship. The relations between alcohol use and headache are probably explained by the headache-precipitating properties of alcohol.

Keywords: alcohol, tobacco, headache, migraine, epidemiology

Quality of life in migraine measured by two different tools

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Background Migraine worsens patients’ quality of life (QoL) significantly, limiting their working and social possibilities.

Objective To investigate the QoL in migraine patients according to clinical features, anxiety and depression levels.

Methods Migraine QoL questionnaire QVM, modified Goetheborg QoL Inventory (GQI), Spielberger’s Questionnaire, Beck’s Inventory, MIDAS and 10-point VAS scale were used in an open-label study of 40 migraine patients aged 16–57 (average 38.45 years).

Results The group showed poor QoL (GQI score 34.16; QVM Global Index 52.43). Correlation was found between GQI score and levels of anxiety and depression. GQI score did not depend on length, frequency of migraine attacks and VAS score. The QVM score correlated with the length of attacks, VAS score, anxiety and depression levels and with the results of MIDAS inventory. Frequency of attacks, length of the disease and the amount of acute medications per attack did not influence QVM results.

Conclusions In this survey QoL in migraine depended mostly on the length of attacks and the severity of pain and correlated with anxiety and depression levels. Migraine-specific questionnaire (QVM) is preferable in QoL measurements.

Keywords: migraine, headache, quality of life, anxiety, depression
in episodic migraine as well as the medications effective in CDH in placebo-controlled studies. The aim of this open clinical study was to determine the efficacy of different preventive medications in CDH. The comparison between amitriptyline, propranolol, verapamil, magnesium, divalproex and fluoxetine was done in 332 CDH patients, diagnosed as chronic migraine, chronic tension-type headache and medication overuse headache. The number of responders, patients with at least 50% reduction in number of headache days, adverse events as well as the number of patients with CDH relapses in a 48-month follow-up period was determined for every treatment. Amitriptyline had the best efficacy of examined medications with 45.9% responders. Propranolol, divalproex, fluoxetine, verapamil and magnesium had lower efficacy than amitriptyline in this order. Divalproex had the highest number of patients with adverse events, 30.9% and fluoxetine had the lowest number of adverse events, 5.0%. The highest number of patients with relapses, 28.6%, was in the divalproex group and there were no relapses in the verapamil and magnesium groups.

**Keywords:** chronic daily headache, preventive therapy, effectiveness

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**G023**

**Importance of the first medical consultation on migraine management—FRAMIG 3 results**

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**Background** Only 20% of all migraine subjects are medically followed up in France.

**Objective** To investigate the impact of the first medical consultation on migraine management.

**Methods** 1652 subjects, who were identified by a postal screening questionnaire, had participated in the second phase of the mailed survey of Framig 3 survey.

**Results** The mean time lag between onset of migraine symptoms and first consultation was 3.7 ± 5.8 years. 983 migraine subjects who had consulted expressed their expectations of the first consultation. After the first migraine consultation, 28% of patients had stopped to consult. The five expectations which had been significantly less satisfied for migraine subjects who had lapsed consulting compared with those who had continued to consult were how to organize daily living with migraine, disease consequences and seriousness, underlying causes of attack, to obtain an efficacious treatment and to know migraine trigger factors. Physician listening, duration of the consultation, information regarding the causes of the attacks were scored significantly less satisfactory for subjects who had lapsed consulting. 38% of subjects with a prescription after the first consultation continued to consult vs. 20% without.

**Conclusion** Quality of the first migraine medical consultation appears a determinant of subsequent consultation behaviour.

**Keywords:** first migraine consultation, migraine management

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**G024**

**Development of a four-item Migraine Specific Quality of life questionnaire (MSQ4) to evaluate the need for a migraine preventive treatment in general practice (GP)**


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**Background** Many guidelines recommend evaluating migraine-related disability before initiating a prophylactic treatment. This evaluation is difficult in GP because no easy and pragmatic questionnaire is available.

**Objective** To develop a 4-item MSQ questionnaire that can be used easily in GP to decide the initiation of a preventive migraine treatment.

**Methods** 338 patients of the PROMISE trial (Pradalier et al. CNS Drugs 2004) followed up in GP completed the whole 14-item MSQ Questionnaire (Martin et al. Headache 2000) before randomization. Best subset regression model with four variables was used to identify the four items. Spearman correlation coefficient was calculated between the global score and the best subset of questions.

**Results** The identified questions were items 5, 6, 10 and 13 of the MSQ questionnaire. Thus, the three dimensions, restrictive, preventive and functional, are still represented. The information lost by this reduced version of MSQ is small because the Spearman coefficient between the global score and the MSQ4 score is 0.947 (P < 0.001).

**Conclusion** Waiting for the final validation, the MSQ4 seems to be an easy and comprehensible questionnaire to be used in GP to evaluate the need for migraine preventive treatment.

**Keywords:** migraine, preventive treatment initiation, quality of life

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**G025**

**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.

**Objective** 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 to the headache diagnosis.
Results 523 (253 men, 270 women) participated. In women tenderness was increased in chronic and frequent episodic tension-type headache compared with women without headache ($P < 0.001$). There was no significant difference 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: $P = 0.73$).

Conclusion 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.

Keywords: general population, tension-type headache, migraine, tenderness, pressure pain threshold

G026

A prospective, controlled, open-label, long-term study of the efficacy and tolerability of topiramate in the prophylaxis of chronic tension-type headache

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Objective To assess the effectiveness and safety of topiramate for the prophylaxis of chronic tension-type headache (CTTH).

Background Topiramate has been shown to be a highly effective monotherapy in patients with new-onset partial epilepsy or generalized tonic clonic seizures, as well as in migraineurs.

Design 50 patients with CTTH completed a 12-week baseline, and 47 of them a planned 24 weeks of treatment with topiramate. Dosing was titrated from 25 mg to 100 mg daily dose by treatment week 4. Primary endpoint was determined as a 50% reduction in headache days per month.

Results Overall headache frequency declined from 23.50 (baseline, mean, SD ± 5.32) to 20.83 days through week 12 ($P > 0.005$) and to 12.58 (mean, SD ± 6.28) from week 12 to week 24 ($P < 0.0001$), with frequency of severe headaches dropping from 8.18 at baseline to 3.14 days through week 24 ($P < 0.0001$). Average headache intensity dropped from 2.13 to 1.07 (1-to-4 scale); peak intensity declined from 2.85 to 1.25 ($P < 0.00001$). Also improved were mood, sleep, quality of life ($P < 0.00001$) as well as the Beck Depression Inventory-II ($P < 0.0001$). Six patients reported mild-to-moderate adverse events, four patients discontinued treatment. Additional highly significant weight loss was observed between baseline (71.64, SD ± 10.65) and week 24 (69.50, SD ± 10.04) ($P < 0.0001$).

Conclusions The results provide preliminary support for the efficacy, safety and tolerability of topiramate in the prophylaxis of chronic tension-type headache.

Keywords: chronic tension-type headache, prophylactic treatment, topiramate, anticonvulsant
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.

Conclusion 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.

Keywords: migraine, prognosis, follow-up studies, epidemiology

G029

Prevalence of migraine and non-migraine headaches in female medical workers

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Object This study was carried out to assess the prevalence of chronic headaches in female medical workers.

Subject and methods Data on headaches were obtained through a self-administered questionnaire distributed among 1584 female employees working in four hospitals and three pharmacies, during January and May of 2003. Of the 1584 subjects, 1410 responded (89.0%). Subjects included 106 doctors, 1080 nurses, 105 pharmacists and 119 others. Subjects ranged in age from 19 to 65 with a mean age of 29.5 years.

Results Experience of chronic headache was noted in 64.5% of the subjects without significant differences between occupations. According to the International Headache Society criteria, 6.2% of the samples were classified as having migraine and 37.3% as tension headache. The age distribution of migraine was 4.9% under 30, 10.3% in their 30s, 10.6% in their 40s, and 21.1% over 50. Daily life activities or work productivity were affected in 61.4% of migraineurs. Only 14% of subjects with headaches consult a doctor or go to hospital regularly, and 60% are using OTC. Recognition of triptans was as low as 9.2% of nurses compared with 62.5% of doctors and 69.7% of pharmacists.

Conclusion Headache sufferers, even amongst medical workers, are underdiagnosed and should be encouraged to receive the proper diagnosis and better management.

G030

Efficacy of acupuncture in migraine attack prophylaxis: a randomized sham-controlled trial

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Objective To evaluate acupuncture efficacy in preventing migraine attacks.

Methods Sixty-two migraine patients were randomized to the real or sham acupuncture groups. Both groups were treated with 16 acupuncture sessions in 12 weeks. Treatment was individualized in the real acupuncture group following the Traditional Chinese Medicine (TCM) principles and minimal acupuncture was used in the sham acupuncture group not respecting the TCM rules.

Results The first primary endpoints adopted, the percentage of patients with reduction ≥ 50% in their migraine attack frequency, showed no difference between groups. The second, the total of migraine days, showed that real acupuncture group improved with a statistically significant difference in all treatment periods (P = 0.013). Serious secondary parameters evaluated showed the improvement of the real acupuncture group with statistically significant difference, such as: the total duration of migraine pain in hours per 4-week headache diary (0.009); average duration of a migraine attack (P = 0.017); number of attacks (P = 0.014). There were no statistically significant differences between groups when the average headache severity, rate of rescue medication used as well as nausea and vomiting frequency were evaluated. Nevertheless, both groups improved in almost all parameters. No serious adverse events were reported.

Conclusion Individualized acupuncture should be an interesting option to reduce migraine attacks.

Keywords: acupuncture, migraine, prophylaxis, randomized controlled trial, efficacy

G031

The long-lasting effects of acupuncture treatment for migraine prophylaxis: 44 weeks’ post-treatment follow-up

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Objective The objective of this present trial was to evaluate the long-lasting effects of acupuncture treatment for migraine prophylaxis.

Methods Sixty-two migraine patients were randomized to the real or sham acupuncture groups and treated with 16 acupuncture sessions for 12 weeks. Treatment was individualized in the real acupuncture group and minimal standard acupuncture was used in the sham acupuncture group. The post-treatment follow-up was done for 44 weeks with headache diaries.

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Results Fifty-three patients concluded follow-up for 20 weeks and only 41 completed 44 weeks. However, no additional change was observed between groups from the end of the treatment to the end of the follow-up period. The improvement observed in almost all parameters evaluated during the treatment period in both groups was preserved for all follow-up periods with little and expected variations. There were no statistically significant differences between groups in primary and secondary parameters evaluated (P > 0.05).

Conclusion The real and sham acupuncture groups maintained the effects reached in the treatment period. Therefore, acupuncture has long-lasting effects; nevertheless, there were no differences between groups.

Keywords: acupuncture, migraine, prophylaxis, randomized controlled trial, efficacy

G032
The prevalence of Helicobacter pylori and CagA-positive strains in patients with chronic headache
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Objective To explore the correlation of Helicobacter pylori (Hp) infection with the pathophysiology of chronic headache, we evaluated the presence of Hp infection in patients with migraine (MIG) in patients with tension-type headache (TH) and in headache-free control subjects (CTL). We also evaluated CagA-positive strains in Hp-positive patients and CTL subjects.

Methods ELISA was used to determine the presence of Hp infection in 168 patients with MIG, 77 patients with TH, and in 163 CTL. Specific serological IgG against CagA in infected subjects were detected using ELISA.

Results The prevalence of Hp infection was 40% in patients with MIG, 43% in patients with TH and 28% in CTL subjects. The prevalence of Hp infection was significantly higher in the patients with MIG than in CTL subjects (P < 0.05). Classifying the prevalence of Hp infection into groups according to age in MIG patients and CTL subjects who were under 40 years of age, the prevalence of Hp infection was significantly higher in patients with MIG than in CTL subjects (P < 0.05). We evaluated CagA-positive strains in Hp-positive patients. No significant differences in CagA-positive strains were found between samples.

Conclusion Our results show a direct correlation between Hp infection and migraine, especially in younger patients.

Keywords: migraine, tension-type headache, Helicobacter pylori, CagA

G033
The effect of preventive treatment with topiramate in chronic migraine psychiatric comorbidity
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Introduction Psychiatric comorbidity in chronic migraine (CM) is one of the most important management issues. Anxiety and depression can be found in up to 75% of cases. Little is known about the effect of migraine preventive treatment in comorbid disorders.

Objectives To analyse the effect of chronic migraine prevention with topiramate in psychiatric comorbidity.

Methods Sixty-four patients were enrolled in the study. Fifty patients completed criteria for analysis. An intention-to-treat method was used for the analysis. All patients met diagnostic criteria for chronic migraine according to the IHS-2004. Eighty-four percent of patients had at least one DSM-IV diagnosis, 76% anxiety, 50% mood disorders. Trait-state anxiety, HAM-anxiety, HAM-depression and Beck scores were used at baseline, titration and follow-up visits.

Results Frequency, intensity and duration of migraine attacks were significantly reduced. Mood and anxiety scales significantly reduced (P < 0.001) with topiramate treatment (median dose 100 mg), when comparing the initial visit with month 1, 2 and 3 data. The effect was already significant (P < 0.001) at the first month of treatment.

Discussion/conclusion Patients with chronic migraine and psychiatric comorbidity treated with topiramate reduced significantly their anxiety and depression levels in addition to their migraine attacks.

G034
Epidemiology of chronic daily headache in Koreans—the Korean Migraine Study
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Background Chronic daily headache (CDH) refers to a frequent headache syndrome (≥15 days/month). Although CDH has a great impact on the quality of life, little has been reported on Korean people.

Objective To investigate the prevalence of CDH and its causative factors in the general population in Korea.

Methods The Korean Migraine Study is the first government-supported epidemiological survey of headache disorders in the Korean population. A door-to-door survey was conducted by direct interviews among people aged between 15 and 65 years. Stratified systematic household sampling was performed and 2038 subjects (1032 men, 1006 women) were recruited. We used a standardized questionnaire using the algorithm based on the ICHD-II. Demographic, clinical and risk factors were surveyed.

Results The prevalence of CDH was 1.47% (M 0.97%, F 1.99%) and increased with age in both genders with the peak rate (7.7%) in women aged in the 60s. Most CDH subjects...
were in the medication overuse state or abused caffeine-containing beverages like coffee or green tea.

**Conclusion** The prevalence rate of CDH in Korea is lower than in previous reports from other countries (around 5%). Medication overuse and caffeine abuse were prevalent in afflicted subjects.

**Keywords:** Korean Migraine Study, chronic daily headache, epidemiological study

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**G035**

**Efficacy of topiramate for the prevention of migraine in patients with or without symptoms of aura**

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**Background** Topiramate 100 mg/day is approved for the prophylaxis (prevention) of migraine headache in adults. The most common pivotal-trial adverse events were paraesthesia, fatigue, anorexia, nausea, cognitive impairment.

**Objective** To characterize the efficacy of topiramate 100 mg/day for migraine prevention in subjects experiencing aura symptoms or migraine without aura in three 26-week, randomized, double-blind, placebo-controlled trials.

**Methods** Change in mean monthly migraine frequency (MMMF) and mean monthly aura episodes were compared. Between-group differences were analysed from baseline to endpoint for pooled intent-to-treat subjects who reported aura [topiramate 100 mg/day (n = 135), placebo (n = 125)], or migraine without aura [topiramate 100 mg/day (n = 249), placebo (n = 247)] during the 28-day, baseline phase (ANCOVA).

**Results** Topiramate 100 mg/day significantly reduced MMMF by 2.0 ± 3.6 (mean ± SD) from baseline (MMMF = 5.4) to endpoint for subjects experiencing aura symptoms (placebo reduction: 1.3 ± 2.6; placebo baseline MMMF = 5.6) (P = 0.034). In subjects experiencing migraine without aura, topiramate 100 mg/day significantly reduced MMMF by 2.0 ± 2.8 from baseline (MMMF = 5.3) to endpoint (placebo reduction: 0.8 ± 2.6; placebo baseline MMMF = 5.3) (P < 0.001). In addition, topiramate 100 mg/day significantly reduced the mean number of aura episodes by 0.42 ± 1.41 from baseline (mean = 0.90 auras/month) to endpoint compared with placebo (mean reduction: 0.19 ± 1.00; placebo baseline = 0.76 auras/month) (P = 0.020).

**Conclusions** Topiramate was equally effective at significantly reducing MMMF in subjects with and without migraine aura, and effectively reduced monthly aura episodes.

**Keywords:** topiramate, migraine, prophylaxis, prevention, aura

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**G036**

**Adverse event incidence rates during titration and maintenance periods of placebo-controlled, topiramate migraine prevention trials**

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**Background** Topiramate 100 mg/day is approved for migraine prophylaxis (prevention) in adults. Common topiramate-associated adverse events (AEs) in the pivotal trials included paraesthesia, fatigue, anorexia, cognitive impairment, nausea and somnolence. Most AEs were mild to moderate in severity.

**Objective** Compare AE incidence during titration and maintenance periods of four randomized, double-blind, placebo-controlled, topiramate migraine-prevention trials.

**Methods** The pooled safety population (mean age = 40 years, female = 85%) took ≥1 study medication dose during the double-blind phase. Topiramate was titrated in 25-mg weekly increments to assigned/maximum-tolerated dose (50 mg/day, 100 mg/day, or 200 mg/day). Double-blind maintenance period was up to 18 weeks. Onset of specific AEs, during titration/maintenance, was assessed.

**Results** For all topiramate doses, AE incidence rates were consistently higher during titration vs. maintenance. For example, for patients on topiramate 100 mg/day (n = 386, titration; n = 294, maintenance) or placebo (n = 445, titration; n = 392, maintenance), paraesthesia incidence rates were 49% (topiramate 100 mg/day) and 4% (placebo) during titration, vs. 12% (topiramate 100 mg/day) and 2% (placebo) during maintenance. Incidence rates for difficulty with memory were 6% (topiramate 100 mg/day), 2% (placebo) during titration; vs. 2% (topiramate 100 mg/day), 1% (placebo) during maintenance. Somnolence incidence for topiramate 100 mg/day was 6% during titration (5%, placebo) and 1% during maintenance (both groups).

**Conclusions** TPM-associated AE incidence rates were consistently higher during the titration period than during maintenance at assigned/maximum-tolerated doses.

**Keywords:** topiramate, migraine, prevention, prophylaxis, safety

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**G037**

**Assessing the effect of topiramate on the quality of life of patients with migraine in three placebo-controlled, migraine prevention trials**

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**Objective** Evaluate health-related quality-of-life (HRQoL) changes in subjects receiving topiramate 100 mg/day during three randomized, double-blind, placebo-controlled trials;
assess interactions between reduced monthly migraine frequency and improved HRQoL.

**Background** Topiramate is approved for the prophylaxis (prevention) of migraine headaches in adults. A favourable response to migraine preventives is defined as showing ≥50% reductions in monthly migraine frequency. The most common AEs in the pivotal trials included: paraesthesia, fatigue, anorexia, nausea, cognitive impairment.

**Methods** Migraine-Specific Questionnaire (MSQ) scores were compared across trials for pooled ITT subjects (mean age 39.8 years; female = 84%) receiving topiramate 100 mg/day (n = 384), vs. placebo (n = 372). For additional analysis, patients receiving topiramate 100 mg/day or placebo were combined and classified by response < 50% (n = 492), ≥50% (n = 262). All between-group differences were analysed using ANCOVA.

**Results** Significantly more patients on topiramate 100 mg/day were ≥50% responders vs. placebo (46% vs. 23%; P < 0.001). Favourable responders had a 2- to 3-fold greater improvement on MSQ scores vs. less favourable responders (P < 0.001). Topiramate 100 mg/day-treated subjects experienced significant improvements on all three MSQ domains throughout the double-blind phase, vs. placebo (P = 0.024 at week 8; P < 0.001 at weeks 16 and 26 for Role Prevention; P < 0.001 for Role Restriction and Emotional Function, all time points).

**Conclusions** Greater reduction in migraine frequency was associated with significantly higher improvement in HRQoL. Topiramate 100 mg/day significantly improved HRQoL throughout the 6-month study.

**Keywords:** topiramate, migraine, prevention, prophylaxis, quality of life

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**G038**

**Patients’ preference for migraine preventive therapy**

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**Background** Understanding the factors influencing patients’ preference increases the ability to make rational choices in selecting appropriate acute migraine therapy. However, unlike acute migraine treatment, patients’ preferences for migraine preventive treatment have never been studied.

**Objective** To evaluate patients’ preference for migraine prevention.

**Methods** We enrolled 250 patients with a primary headache diagnosis at the Jefferson Headache Center and IIEP-Albert Einstein. Patients were asked to rate seven aspects of headache prevention (efficacy, speed of onset, out-of-pocket expenses, side-effects, formulation of therapy, type of treatment, and frequency of dosing) in order of importance (1–7). Each patient also evaluated 12 different clinical scenarios, each one containing a simulation of two hypothetical headache preventive treatments, where patients could choose product A, B or neither. Each product had efficacy data, side-effect profile, and dosing frequency.

**Results** Most patients rated effectiveness the most important aspect, and were more likely to choose treatments with higher efficacy rates, less side-effects and less frequent dosing schedule. Patients preferred treatment options with higher efficacy rates even in the presence of side-effects and more frequent dosing schedule.

**Conclusions** Patients rated efficacy the most important aspect in preventive and preferred treatment options with higher efficacy rates.

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**G039**

**Prophylactic treatment of migraine with a novel herbal remedy**

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**Background** Migraine is under-treated worldwide and needs new drugs for limiting pain and modulating the course of disease.

**Objective** To determine the efficacy of herbal remedy (Origanum vulgare, Lavandula stoechas, Coriandrum sativum, Foeniculum vulgare and Viola odorata) in the prophylaxis of migraine.

**Methods** Volunteer migraineurs according to IHS criteria entered the study. After 1st month basement follow-up (m₀), intervention was made for 2 months using inhalation of herbal remedy 20 nights monthly (m₁ and m₂). Patients followed for 2 months after the end of treatment. Headache characteristic recorded using a self-reporting diary from m₀ to m₄. Monthly attack-rate (MAR), days with migraine (DWM) and weighted migraine severity (WMS) calculated from diary and compared using repeated measure ANOVA.

**Results** Thirty migraineurs entered with mean age of 30.07 ± 10.41 years, 25 female (83.3%) and five male (16.7%). Mean MAR, DWM and WMS of m₁ vs. m₀ decreased (5.20 ± 1.47 to 3.27 ± 2.72, 10.00 ± 5.25 to 5.44 ± 5.13 days and 10.62 ± 3.26 to 7.32 ± 6.14, respectively) (P < 0.01). All indexes showed a short, but not significant (P > 0.05), increase in m₃ vs. m₀.

**Conclusion** Study revealed good preventive effect of this herbal remedy. Although there was a short increase in indexes after the end of therapy, the effect of treatment 2 months after the end of therapy was acceptable.

**Keywords:** headache, migraine, preventive treatment

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**G040**

**The efficacy and tolerability of anticonvulsants in the prophylaxis of migraine: an updated systematic review**

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**Background** In July 2004, in a Cochrane systematic review, we demonstrated that anticonvulsants, considered as a class,
were effective in reducing migraine frequency compared with placebo, and were reasonably well tolerated.

**Objective** To present an updated review including recently published trials.

**Methods** Medline (1966–2005) and the Cochrane Controlled Trials Register were systematically searched for prospective, randomized controlled trials of anticonvulsants taken regularly to prevent the occurrence of migraine attacks and/or to reduce the intensity of those attacks.

**Results** Seventeen papers met the criteria for inclusion in the review. Sixteen trials compared anticonvulsants with placebo, and one compared an anticonvulsant with an active control. Preliminary analyses indicate that two recently published trials do not substantially affect our previous conclusions. In addition, the increasing number of trials of topiramate demonstrates good overall efficacy. For example, in four trials of topiramate 100 mg daily, the number of patients in whom the frequency of attacks was reduced by 50% or more is significantly greater for topiramate vs. placebo (OR = 3.27, 95% Cl 2.21, 4.85).

**Conclusion** Anticonvulsants appear to be effective and moderately well tolerated as migraine prophylactics, although there is noticeable variation amongst individual agents. Reasonably substantial evidence bases are available for valproate/divalproex and topiramate.

**Keywords:** migraine, prophylaxis, anticonvulsants, systematic review, Cochrane Collaboration

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**G042**

**Primary headaches population studied in a computer company in Japan**

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**Objective** This study presents the prevalence of primary headaches, influence of headache on work and consultation rate to medical staff at one of the computer companies in Japan.

**Methods** After informed consent to this survey, 1706 employees (men 1479, women 227) were given a questionnaire. Diagnosis of headache was based on 1988 IHS criteria.

**Results** The response rate was 74.3%. The lifetime prevalence of headache was 55.7% (men 54.8%, women 69.5%). The prevalence of migraine was 10.3% (men 9.9%, women 15.3%), tension-type headache was 27.4% (men 27.4%, women 31.1%). Among migraine sufferers, 42.7% had one to three migraine attacks per month and 39.7% reported severe pain. Among migraine sufferers, 38.2% lost working days or left work early due to headache, and 20.5% of tension-type headache sufferers lost working days. Among migraine sufferers, 78.4% reported reduced quality of work. Among tension-type headache, 62.2% reported reduced quality of work during headache. The consultation rate to the company medical staff was 30.5% for migraine sufferers and 13.0% for tension-type headache sufferers.

**Conclusion** Although migraine attacks influenced work, 70% had never consulted company doctors or nurses. It is necessary to educate workers and prepare a system for migraine sufferers to consult physicians.

**Keywords:** primary headache, prevalence, company workers

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**G043**

**Efficacy of progressive muscle relaxation training in migraine prophylaxis—a single-centre, randomized, controlled trial**

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Departments of Neurology and Surgery, Medical University of Vienna, Vienna, Austria

**Background** Progressive muscle relaxation training (PMR) is frequently recommended for migraine prophylaxis.

**Objectives** To evaluate the efficacy of three different therapeutic settings of PMR in migraine patients.

**Methods** We randomly assigned 124 migraineurs with or without coexisting tension-type headache to home-based PMR (PMR-H, n = 61), clinic-based group therapy (PMR-G, n = 33) or clinic-based single therapy (PMR-S, n = 30). The study comprised 4 weeks of baseline, 6 weeks of treatment and 8 weeks of follow-up. All patients were advised to train regularly at home. For PMR-H the patients used an audio CD. The sessions of PMR-G and PMR-S were held weekly by an experienced psychologist. Each PMR-G group comprised 5–7 patients. PMR-S was complemented by respiratory biofeedback. Primary outcome measure was the number of headache days during the last 4 weeks of follow-up.

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Global campaign against headache. A Spanish population in education success was 100%.

Results The number of headache days decreased significantly in all three groups (P < 0.001). The median reduction of headache days was 33% in PMR-H, 40% in PMR-G and 64% in PMR-S. PMR-S was more effective than PMR-H (P = 0.012) and PMR-G (P = 0.019). The number of completers was 97% in PMR-S, 79% in PMR-G and 69% in PMR-H.

Conclusion In migraine prophylaxis, biofeedback-assisted PMR-S is more effective than PMR-H and PMR-G.

Keywords: migraine, prophylaxis, progressive muscle relaxation training, respiratory biofeedback

G044

Migraine in the Institute of Cukurova University Medical Sciences students: the first study with ID Migraine™

Sebnem Bicakci, Nafiz Bozdemir, Esra Saatci, Yakup Sarica & Fahri Over

The purpose of this study was to investigate migraine in the Institute of Medical Sciences Students (Medical and Dentistry Faculties) of Cukurova University, using The ID Migraine™. A questionnaire, consisting of 43 items, was administered and the students were interviewed. Students were informed about the study by the investigators. The aim of the first 34 items was to analyse social and demographic data (age, gender, living conditions, etc.). Only the cases were involved in the study regarding the presence of headache for lifetime in the 35th question and in the last year in the 36th question. Headache was evaluated in the 37–43rd questions. Migraine diagnosis was established according to the presence of functional loss, nausea and sensitivity to light (ID Migraine). Hindering effect of migraine in education success, referral to physician and use of medication for migraine were evaluated. 542 of 636 cases in the study have described headache in the recent year. Migraine was diagnosed in 3.7%, 5% female and 45% male. The mean age in the migraine group was 22.2 (17–31). Educational success ratio was 60% in this group. Use of medication ratio was 70% for headache. The preventive effect of headache in education success was 100%.

G045

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 the 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 in 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 twice a week. 84% thought that the health system should increase the awareness about headache. Only 35% had a medical diagnosis (65% in the severe cases), only 42% used prescribed medication and 7% received preventive treatment. 25% reduced activity during migraine.

Conclusion Even severe headaches still remain undiagnosed and undertreated in Spain and most people think that the health system should change its attitude in relation to this problem. We hope to improve the situation with the campaign in the next 2 years with interventions at all levels.

G046

Comparison of amitriptyline and venlafaxine in the prophylaxis of migraine without aura

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Background Tricyclic antidepressants are of the most commonly used medications in the prophylaxis of migraine. It has been shown that serotonin specific reuptake inhibitors can also be helpful in this regard.

Objective To compare amitriptyline and venlafaxine (SSRI) in the prophylaxis of migraine without aura regarding their efficacy and side-effects.

Methods 88 subjects with migraine without aura (the International Headache Society criteria) who needed medical prophylaxis were enrolled in a double-blind clinical trial. They were randomly assigned to receive amitriptyline 25 mg/day or venlafaxine 75 mg/day. After 5 weeks, the subjects were visited every 2 weeks for 6 months. The frequency and intensity of migraine attacks as well as the side-effects of the medications were reported in each visit.

Results 80 subjects completed the study. The frequency and intensity of migraine attacks were reduced significantly in each group (P < 0.05); however, this reduction was much more significant in the subjects taking amitriptyline. Meanwhile, the frequency of anticholinergic side-effects was significantly higher in the amitriptyline than the venlafaxine group.

Conclusion Although the side-effects are less frequent with venlafaxine compared with amitriptyline, the latter is more efficacious in the prophylaxis of migraine with the doses mentioned.

Keywords: migraine, amitriptyline, venlafaxine
**G047**

Efficacy of angiotensin II receptor blocker for the prophylaxis of migraine in Japanese patients

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**Background**
A few reports have demonstrated beneficial effects of angiotensin II receptor blocker (ARB), Candesartan, for migraine prophylaxis. We investigated the prophylactic effect of other lipophilic ARBs on the attacks of migraine.

**Objective**
To determine whether treatment with ARB, losartan or olmesartan, could be an alternative choice of drug for migraine prophylaxis.

**Subject and methods**
A series of 12 patients with migraine according to the IHS criteria, who presented with systolic pressure over 130 mmHg, were included in the study. Two were men and 10 were women. The age range was 33–65 years with a mean of 49.6. After a month’s wash-out observation period, patients took 50 mg of losartan or 20 mg of olmesartan every day for 3 months. We assessed from headache diary changes in frequency, severity, consumption of triptans and/or analgesics. Disability with MIDAS questionnaire was also used for evaluation.

**Conclusion**
This study showed losartan and olmesartan are effective and safe for migraine prophylaxis.

**Keywords:** migraine, prophylactic treatment, angiotensin II receptor blocker

**G048**

Migraine patient therapy evaluation of Moscow migraine population in Russia

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

**Methods**
The value of migraine therapy was studied by specific original valuation inventory, which consist of four parts: social-demographical part, asking for medical aid, taking medications, migraine influence on the quality of life, 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 did not have any tax or medical insurance refunds. Most patients were out-patients; they did not have free care and paid directly to their doctor 21 USD on average. Migraine patients asking for neurologist or general practitioner six times a year on average. Doctors prescribed medications during 1–2 months a year. Patients paid transport expenses themselves; they consisted of 2 USD for one doctor’s consultation.

**Conclusion**
Migraine is an expensive and important social disease. Patients do not have medical insurance and occasionally pay directly themselves for their consultations and medications. Their direct and indirect costs constituted 30% of a full year’s patient’s income.

**Keywords:** migraine, therapy valuation, pharmacoeconomy analysis, direct, indirect costs

**Headache clinics**

**H001**

Rheumatoid pachymeningitis mimicking spontaneous intracranial hypotension

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**Background and objective**
Central nervous system involvement of rheumatoid arthritis (RA) is a very rare occurrence and most of them have been incidental postmortem cases. The patient with RA suffering from orthostatic headache and showing corresponding neuroimaging findings on brain MRI is exceptional.

**Results**
A 67-year-old woman suffering from RA for 10 years complained of an intractable headache with postural dependency. Brain MRI showed a diffuse pachymeningeal enhancement and the biopsy of meninges revealed a thickened dura with fibrosis and proliferation of arachnoid meningothelial cells.

**Conclusion**
We report a case of rheumatoid pachymeningitis which resolved excellently with high-dose steroid therapy.

**Keywords:** rheumatoid pachymeningitis, dural enhancement, postural headache

**H002**

The actual state of migraine obtained from neurosurgical examinations

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**Objective**
Since 1988, I have proposed that migraine is a disease with a close relation to epilepsy. I would like to report on the pertinent findings of migraine obtained from neuro-surgical examinations.

**Methods**
Sixty-seven patients with migraine (men 25, women 42) were studied CT, TCD and EEG in their interictal period. In the case of no advent of abnormal waves on resting EEG, megimide activation was added.

**Results**
CT showed tight brain findings including either small ventricle or shallow sylvian fissures or both in 54 of 67 patients (80.0%). TCD indicated increased blood flow velocity (65 cm/s) in the MCA trunk was found in 42.9% (33 patients). Fourteen patients had uninterpretable TCD. If they are excluded, the incidence of this finding becomes 62.3% (33 of 53 patients). EEG disclosed epileptiform discharge (ED) including theta wave, multiple sharp wave bursts and atypical spike and wave in 68.7% on resting EEG and 31.3% on megimide activation. All the patients showed ED on either EEG.

**Conclusion**
ED was the most important finding in the patient. Both high velocity (vessel constriction) and tight brain signs (chronic brain swelling) were other important findings. The latter two findings are considered to correlate with the former.

**Keywords:** CT, TCD, EEG, epileptiform discharge, megimide activation
How long do patients take to describe their headaches?

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Unidad de Neurología, Hospital de Mataró, Mataró, Spain

**Background** The time taken by a patient to describe his/her headache spontaneously without interruption is not studied.

**Objective** To examine the effects of mass media announcements (by local newspapers and television) of ‘opening of the headache clinic’ on patients with migraine.

**Methods** To demonstrate that thunderclap headache (TH) may be the initial manifestation of spontaneous intracranial hypotension (SIH) caused by a CSF leak.

**Design/methods** We evaluated 24 patients with SIH. Four of them (16%), three women and one man with mean age of 31 years (range 25–43 years), initially experienced an excruciating headache of instantaneous onset.

**Results** One patient was affected by Marfan’s syndrome. Excruciating pain duration range was 10 s to few minutes. The pain was described as head swelling or as a hard stroke on the head, followed by gravitative occipito-nucal and frontal orthostatic headache. Mild neck stiffness was present in one
patient. CT scan, cerebral angiography (1 patient), and MRI angiography (1 patient) were unremarkable. The patients also underwent lumbar puncture (3 patients), brain MRI, spinal MRI and MRI myelography (3 patients), CT myelogram (1 patient), and radioisotope cisternography (1 patient). CSF pressure was low. Brain MRI showed diffuse pachymeningeal enhancement in all patients. CSF leak was demonstrated only in one patient at cervical level. Three patients received supportive measures only (bed rest, hydration). Patient with cervical CSF leak underwent epidural blood patch.

**Conclusion** We suggest that SIH should be included in the differential diagnosis of TH.

**H007**

**Investigation of headache management of general practitioners in Yamaguchi, Japan**

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**Background** Patients with headache have been underdiagnosed and undertreated in Japan.

**Objective** The aim of this study is to investigate the present condition of headache management of general practitioners in Yamaguchi, Japan.

**Methods** We mailed the questionnaire about the present headache management to 519 members of Ube and Yamaguchi, Yamaguchi prefectural medical association.

**Results** 211 (41%) of them answered completely. 63% of 211 were interested in headache practice. 70% had experienced any troubles in treating headache patients: 49% in diagnosis, 43% in treatment and 14% in examination. 53% thought headache practice was difficult, and 32% answered that headache practice was troublesome. The reasons were that there were no objective markers for diagnosis of headache or that it took a long time to get information of patients’ headache characteristics and evaluate them. 57% had information about the International Classification of Headache Disorders. 79% were sure of triptans, and 47% had prescribed them. 47% wanted to participate in the regional network for headache management if it was constructed in their district of medical practice.

**Conclusion** Although general practitioners are interested in headache practice, they might have difficulty because of their inexperience and insufficient knowledge for headache care.

**Keywords:** general practitioners, headache practice, migraine, triptan

**H008**

**A prospective randomized comparative efficacy and safety study of zolmitriptan vs. cafergot in Japanese patients with migraine**

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**Objective** This is a prospective, randomized, cooperated study of zolmitriptan (Z) vs. cafergot® (C) patients for the acute treatment of migraine (M) in Japanese patients.

**Methods** Z (2.5 mg) and C (100 mg) were prospectively prescribed randomly to out-patients with M. Patients recorded in their headache diary, including severity, duration and associated symptoms of M, the effectiveness and side-effects of the two therapies in a comparative study.

**Results** A total of 11 225 patients (>20 years) were randomly divided into two groups for their M attacks. Effective response after 2 h was noted in 78% of 5567 Z and 40% of 5558 C. The recurrence rate was 22% to Z and 47% to C. The adverse events were 25% for Z and 47% for C. The appearance of side-effects and abnormal laboratory data during this study in C were significantly more than in Z. In Z more would want to take Z than C in repeated M attacks.

**Conclusion** Z was significantly more effective and safe than C. These results were discussed in this presentation.

**H009**

**Comparison of validity and reliability of the Iranian migraine disability assessment (MIDAS) vs. headache impact test (HIT)**

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Isfahan University of Medical Sciences, Iran

**Background** During previous years researchers designed two questionnaire tests as Headache Impact Test (HIT) and Migraine Disability Assessment (MIDAS) with the aim of improving migraine care. These two tests provide a standard measurement of migraine’s affect on people’s life style that divided patients into four groups (grades) from the view point of headache intensity, as a means of standardizing the information that doctors receive from their patients.

**Objective** During this survey, we used two new tests (HIT and MIDAS) in same patient’s migraines at the same time and our goal is to compare the validity and reliability of these two test results.

**Materials and methods** This study was designed as a multicentre, descriptive study to compare validity and reliability of Persian versions of MIDAS and HIT questionnaires in 240 males and females with a migraine diagnosis according to the criteria for headache and facial pain of the International Headache Society (IHS).

**Results** According to our study, there was a high correlation between the two tests (R = 0.94). There were differences of 15% (one-grade difference) and 8.4% (two-grade difference) that all of these patients (8.4%) were housekeepers.

**Conclusion** This finding demonstrated that the Persian version of HIT has the same validity and reliability as MIDAS.
Quality of life of headache sufferers in Turkey: a university hospital-based study, part I

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Economic impact of primary headaches in Turkey: a university hospital-based study, part II

Necdet Karlı, Asist. Prof.1, Mehmet Zariçoğlu, Prof.1, Mustafa Ertaş, Prof.1, Sabahattin Saip, Assoc. Prof.2, Vesiştir Oztürk, Assoc. Prof.2, Debnem Bıyakçıkçı, Assist. Prof.2, Cavit Boz, Assoc. Prof.2, Deniz Şelçuki, Prof.2, Atilla Oğuzhanolu, Assoc. Prof.2, Munife Neyal, Prof.2, Ceyla Yrkeč, Prof.2, Hakan Kaleaşy MD2, Tulay Kansu, Prof.2, Yakup Sarıça, Prof.2, Nebahat Tăşdemir, Prof.2, Nevzat Uzuner, Assoc. Prof.3, Fethi İdiman, Prof.4 & Aksel Siva, Prof.4
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Headache in the Greco-Roman world: from Zeus to Alexander of Tralles

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Methods Review of Greek and Roman texts on headaches.

Results Hippocrates’ interest in the prognostic value of symptoms explains his emphasis on the significance of headache in disease outcome in the Hippocratic corpus. Aretaeus of Cappadocia (2nd century AD) described his migraine and the first migrainous aura as Heterocrania. His contemporary, Galen, described variations of migraine as Cephalalgia, Cephalea and Hemicrania. Several herbs and medicines are classified in Dioscorides’ pharmacology. While physicians debated about the terminology, Plato through Socrates mocked them in Charmides and introduced the concept of a psychosomatic approach. Terms including Heterocrania, Holocrania and Hemicrania struggled until Alexander of Tralles (6th century AD) finally established the term Hemicrania, from which migraine has derived.

Conclusion Greek and Roman physicians’ approach to headache provided the terminology, symptom description and prognostication.

Keywords: migraine, history of medicine

H013

Amaterasu, the progenitrix of the Japanese imperial line, might suffer from migraine

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Background Amaterasu omikami is the principal female deity of Japanese mythology, identified with the sun and regarded as the progenitrix of the imperial line (Queen Himoko). She has been famous for the Amano-iwato legend that she hid herself in a cave. This legend has been explained as a mythology of the solar eclipse, the winter solstice, or Himiko’s death followed by her daughter’s succession.

Methods I propose a new hypothesis that she suffered from migraine.

Case report She was assigned to rule the High Celestial Plain. Deeply offended by the misdeeds of the younger brother, she hid herself in a cave, leaving the universe in complete darkness and chaos. Lured out of the cave by the merrymaking of the other divinities, she shone forth again and order was restored.

Conclusion The reasons why I consider she suffered from migraine are as follows: (1) she is female and might be younger; (2) there is a precipitating factor of migraine that she was under severe mental stress; (3) the cave was shut by the rock and seemed quiet and dark, suggesting photophobia and phonophobia; (4) although the duration of illness was not described, several days is most likely and compatible with migraine, contradicting other hypotheses.

H014

A comparative study of precipitating factors for tension-type headache between a large city and a small one in Japan

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Background Although various precipitating factors for tension-type headache are well known, there have been few systematic studies and the new criteria, ICHD-II, do not address this subject.

Methods I deduced precipitating factors from structural interviews for patients with tension-type headache only by myself at two out-patient clinics in Chiba, Japan; one was Chiba University Hospital located in a prefectural capital with a population of a million people (1993–2002; n = 134) and the other Kameda Medical Centre located in a small, local city with 36 000 people (2003–4; n = 91).

Results Male to female ratios were 48 : 86 and 41 : 51 and ages were 44 ± 16 (mean ± SD) and 57 ± 17, respectively. Top three factors were specified as lack of bodily exercise (53% and 45%, respectively), mental stress or neurotic tendency (46% and 63%) and bad posture of the neck or hard work (33% and 38%). Others included orthopaedic (31% and 36%), dental (18% and 14%), ophthalmological (15% and 19%), otorhinological (11% and 12%) and weather factors (10% and 5%).

Conclusion Although there are small differences between the two groups possibly due to regional or generation differences, the main precipitating factors for tension-type headache seem similar.

H015

Roller coaster headache

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Background Roller coasters are popular attractions at amusement parks around the world. Despite their relative safety, roller coaster riding has been documented as a cause of secondary headaches and neck pains through various mechanisms such as subdural haematoma or arterial dissection.

Objective To clarify the characteristics of secondary headaches and neck pains associated with roller coaster riding.

Methods Literature databases and the internet were searched from 1965 to February 2005.

Results Twenty-eight patients were found, including two of ours; there were seven patients with subdural haematoma, six carotid artery dissection, four vertebral artery dissection, two CSF leak, one post-traumatic headache, one glaucoma, one syringomyelia (syringebulbia), one expansion of intracranial cyst and one bleeding from arteriovenous malformation. Five of six young (<30 years old) patients showed no predisposing factors. Durations between riding and onset were variable, from immediate to 2 months. One patient died and some had mild sequelae.

Conclusion Causes and mechanisms of roller coaster headaches and neck pains were variable. Physicians should be aware of these risks.

H016

Migraine and spinal arteriovenous malformation (SAVM): an unusual association

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Objectives To demonstrate that SAVM may cause migraine-like symptoms and to discuss mechanism involved.

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**Case report** A 23-year-old man had a 9-year history of migraines without aura often triggered by physical exercise. He presented to our hospital 3 days after onset of a typical migraine attack for worsening of the pain and vomiting. The headache was not explosive and within few hours spread from cranial localization to the vertebral column. Neurological examination revealed a slight neck stiffness with no signs of medullary involvement. Cerebral CT scan was negative. Cerebrospinal fluid (CSF) was haematic with high opening pressure. MRI of the whole central nervous system showed flow voids at D12. Spinal angiography demonstrated an extramedullary SAVM. Surgery was performed without any complications. Two years later his neurological examination remained normal and he never suffered from migraine.

**Discussion** We hypothesize that patient’s migraine represented episodic bleeding from SAVM into the subarachnoid space, triggered by physical exercise. Two mechanisms of headache are possible: (1) bleeding caused obstruction of CSF outflow and increased intracranial pressure; (2) considering possible migration of subarachnoid blood from spinal to cranial level, the stimulation of the trigeminal nociceptive receptors may induce migraine-like symptoms.

**Keywords:** migraine, spinal arteriovenous malformation

**H017**

Patka headache an external compression headache—report of five cases

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**Introduction** The external compression headache is a rare kind of cranial neuralgia caused by continued external pressure over the head. Patka is a special cloth used by Sikhs to cover their head continuously throughout the day. This is a new observation noticed in a specific religious Indian population. We describe symptoms and signs of five patients with headache caused by use of tight patka.

**Patients** Five patients out of 757 patients evaluated in headache clinic of tertiary care hospital from 2001 to 2004 were diagnosed to have external compression headache. All our patients were male in the age group 14–25 years. The onset of headache was after 2–3 years of continuous use of patka. Headache used to start 60–90 min after tying the patka. Headache was a generalized, non-pulsating, dull ache with no nausea or vomiting and resolved about 10–20 min after patka was removed. One patient also gave a history of episodic headache suggestive of migraine without aura. Patients received many therapies for headache with variable responses.

**Conclusions** We conclude that headache associated with use of tight patka is caused by external compression and headache relief can be obtained simply by not wearing patka.

**Keywords:** patka, external compression, headache

**H018**

Migraine and headache treatment in general medical practice: efficacy of treatment by greater occipital nerve blockade

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**Objective** Testing the efficacy of an inexpensive treatment on acute onsets of migraine and headache in a general practice environment.

**Methods** In an open series of 73 patients spontaneously consulting once or several times for heavy complaints of acute headache, 1.5 ml lidocaine (20 mg/ml) with 1/80 000 adrenaline were injected on both epicranial emergencies of greater occipital nerve (GON). Response was considered as positive if complaints completely disappeared within 120 min, and negative if relief occurred later or was incomplete.

**Results** Fifty-two patients (71%) responded positively, and 82 onsets of headache (76%) out of 108 were completely relieved in due time. No side-effects were observed. Results were compared with virtual groups of patients or of onsets supposedly treated by placebo with positive responses in 50% of the cases. Positive differences were highly significant at Yates’ $\chi^2$.

**Conclusion** GON blockade could be considered as an inexpensive and efficacious alternative to costlier systemic treatments.

**Keywords:** greater occipital nerve blockade, general practice

**H019**

Anxiety and depression in patient with headache—comparison with non-headache subjects

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**Introduction** Migraine and tension-type headache have been the most common headache in every society. To date it has been proved that most of the chronic headaches are accompanied with psychological and moral factors.

**Material and methods** A case–control study was conducted from March to November 2003. 125 patients who were suffering from migraine and tension headache referring to Neurology Outpatient Department and 125 control group have been studied in term of depression and anxiety.

**Results** In this study of patients (29.6% male and 70.4% female), 16% had migraine with aura and 45% migraine without aura and 45% had tension headache. The prevalence of depression in case group was 65.2% vs. 52.8 in control group. The severity of depression in case group was moderate in 36% vs. 47.2% without depression. The prevalence of anxiety in case group 76.6% vs. 52% in control group. Comparison of the two groups indicates that depression and anxiety were more prevalent in case group ($P < 0.001$).

**Discussion** Our results indicate that migraine and tension headache can often be accompanied by comorbid anxiety and or depression, as well as increase severity and consistency of headache.
**Keywords:** migraine, tension-type headache, aura, depression, anxiety

**H020**

**Symptomatic hemicrania due to high cervical meningioma**

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A 56-year-old woman suffered from left hemicrania since 6 months. The headache was disabling, pressing and associated with phonophobia. In the beginning, it occurred in attacks lasting 2–3 h. After a few weeks, the headache became constant. Clinical examination was normal. Before referral to our centre, carbamazepine and a left suboccipital steroid infiltration were tried without success. To exclude atypical hemicrania continua, we prescribed indomethacin (150 mg/day) which was ineffective, and had a CT scan performed. The latter showed a contrast-enhancing tumour located in the spinal canal at C1–C2 on the left side. Cervical MRI was compatible with an intradural meningioma which compressed spinal roots and was accompanied by mild oedema of the adjacent spinal cord and lower medulla. A few days later the patient developed a mild left hemiparesis and the meningioma was completely resected. After surgery both the left hemicrania and the motor deficit rapidly disappeared. To our knowledge, this is the first case of a cervical meningioma presenting initially for several months as monosymptomatic hemicrania. Compression by the meningioma of the left spinal trigeminal nucleus and tract and/or C2 spinal nerve was probably responsible for the headache.

**Keywords:** symptomatic hemicrania, cervical meningioma

**H021**

**Migraine aura without headache, study of 77 cases**

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**Objective** To analyse the clinical pattern of patients consulting because of neurological transitory deficit diagnosed as migrainous aura without headache (MAwoH).

**Methods** 77 patients consecutively seen in our Neurology Department over the last 10 years. All patients meet the diagnostic criteria of MAwoH according to the IHS classification.

**Results** 77 patients (59 women), mean age at first MAwoH was 36 (12–72, SD 14.48). Isolated visual symptoms were the most frequent 63 (83%), 15 patients (19%) suffered a second type of aura. Mean duration of MAwoH was 27 min (5–60, SD 14.48). Mean progression 9 min (acute 30 min, SD 6.11). Migraine history was present in 56 (73%), without aura in 22 (29%) and with aura in 34 (44%). No history of headache was reported in 16 (21%). Family migrainous history was found in 34 (44%). No differences were observed between patients with acute or progressive onset. Patients with history of headache started MAwoH younger than patients without headache (P = 0.013).

**Conclusion** MAwoH occurs more frequently in middle-aged women with monthly visual episodes. Headache history is present in most of them and family history in half.

**Keywords:** migraine aura without headache, migraine aura

**H022**

**Attachment styles and headache**

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**Background** The internal working model on attachment dimensions changes with significant emotional experiences.

**Objective** Purpose of this study was to evaluate if and how the internal working models correlate with primary headaches.

**Methods** 114 subjects [68 with migraine, 23 with tension-type headache (according to ICHD-I criteria); 23 with chronic daily headache (according to Silberstein’s criteria)] were studied and compared with a control group of 57 subjects (matching in sex, age and social level) not suffering from any primary headache. Attachment dimensions were investigated using Adult Attachment Questionnaire (AAQ) and Attachment Style Questionnaire (ASQ). The data were statistically analysed using χ2 test, t-test for independent sample and ANOVA univariated.

**Results** AAQ showed that in the headache sufferers’ group there was a much higher percentage of subjects with an ‘uncertain’ attachment style when compared with the control group (P < 0.01). The ASQ mean scores, where the scale of Relationships Subordination is concerned, show meaningful differences between the sample and the control groups (P < 0.05).

**Conclusions** Our study showed that headache sufferers seem to be characterized by internal working models of the ‘uncertain’ type. In particular, they seem to feel extremely ill at ease if there is a reduction of the interpersonal distance.

**Keywords:** migraine, tension-type headache, chronic daily headache, attachment styles

**H023**

**Secondary headache due to brain tumours; comparison with meningiomas and gliomas**

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**Objective** In secondary headache due to a brain tumour, we reviewed whether the clinical features varied in glioma as a malignant tumour and meningioma as a benign tumour.

**Methods** The brain tumour case that developed headache was chosen among 148 meningioma cases and 307 glioma cases admitted at Niigata University. Imaging and pathological diagnoses were made in all cases.

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Objective

To describe the behaviour of disability and quality of life, headache, migraine (MIDAS), Headache Needs Assessment survey (HANA), sex.

Results

Among 148 patients with meningioma, in 25 cases the primary symptom was just headache (17%). There was intracranial hypertension in five cases (3%). As for the headache occurring in 47 cases (15%) among 307 patients with glioma, the increased intracranial pressure case was 10 (3%). In localization of meningioma, posterior fossa accounted for 28%. Tumour size was an average of 4.8 cm, and a massive tendency was present. Localization of tumours did not have the characteristic findings in the glioma patients. Glioblastoma was seen histopathologically and accounted for 44.7%. The period from the onset to admission was 16.4 months in patients with meningioma. On the other hand, it was 3.9 months in patients with glioma.

Conclusion

A feature of secondary headache was typical in the meningioma that was benign tumour. In the case of malignant brain tumour, history of headache and clinical findings should be diagnosed precisely.

Keywords: secondary headache, brain tumour, IICP, meningioma, glioma

H024

Factors linked to disability and quality of life in patients with migraine

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Objective

To describe the behaviour of disability and quality of life (QOL) in patients suffering from migraine and to identify the factors associated with these variables.

Methods

A non-experimental study based on observation was conducted with 116 patients diagnosed as having migraine, who were consecutively admitted to the casualty department at the Institute of Neurology and Neurosurgery. The chief variables used in the study were disability, QOL and the overall evaluation of their state of health. The remaining variables employed included demographic variables and clinical variables such as length and intensity of the bouts and the number of days with headache. The Migraine Disability Assessment questionnaire (MIDAS) was used to evaluate disability, while QOL was measured with the Headache Needs Assessment survey (HANA).

Results

The mean total score on the MIDAS was 40.8, and 58.6% of the patients were in grade IV disability. The mean number of days with headache over a 3-month period was 32.25 and the mean headache intensity was 8.50. The mean score on the HANA was 76.37.

Conclusion

The factors associated with disability were the number of days with headache and comorbidity with high blood pressure, whereas their QOL was linked to the number of days with headache, the intensity of the pain and female sex.

Keywords: Migraine Disability Assessment questionnaire (MIDAS), Headache Needs Assessment survey (HANA), quality of life, headache, migraine

H025

Narcotic analgesics for acute migraine in Emergency Room; are we meeting IHS guidelines?

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Background

Acute migraine patients are often treated with injectable analgesics in the ER. International Headache Society recommends use of narcotic analgesics as a last resort.

Objective

Our study aimed to find out whether practice in a tertiary care hospital ER in Karachi meets IHS guidelines.

Methods

All patients with acute migraine visiting ER at The Aga Khan University were reviewed during a 3-month period. Patients with headaches other than migraine and patients requiring hospitalization were excluded from the study.

Results

A total of 161 patients were included in study. 103 (64%) were female. Age range was 18–59 years (mean 34 years). Associated nausea, vomiting, photophobia were present in 94 (59%) patients. 65 (40%) patients had pain for less than 6 h. Neurological examination was normal in all patients. 126 (72%) patients were treated with injectable analgesics. 35 patients received only oral analgesics. 126 (75%) received injectable analgesics. 34 (22%) received opioid analgesics, while 92 (56%) received non-opioid analgesics. Pain was completely relieved in 100 (62%) patients, partially relieved in 50 (31%) patients and was not relieved in 11 (7%) patients.

Conclusion

Most patients received non-narcotic analgesics.

The current practice at our ER somewhat meets IHS guidelines.

H026

Coexistent pathologies in patients affected by primary headaches

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Objective

Finding the most frequently associated pathologies in patients referred to our Headache Centre.

Methods

1486 adult patients consecutively visited in our Headache Centre from 1 January 2000 to 31 December 2001: 1008 women and 478 men. Headache was classified according to IHS 1998; coexistent pathologies were drawn by clinical history: the diagnosis had to be made by a specialist.

Results

Type of headache: migraine without (MoA, n = 718) and with aura (MA, n = 124), episodic type-tension headache (ETTH, n = 105), chronic type-tension headache (CTTH, n = 94), cluster headache (CH, n = 59), overuse medication headache (OMH, n = 33). Coexistent pathologies: 28% of patients presented arterial hypertension, 11.1% depression, 11.04% gastritis, 6.39% allergic rhinitis, 5.11% allergic asthma, 4.24% insomnia, 3.77% hypothyroidism, 2.77% peptic ulcer, 2.49% anxiety, 2.42% allergic dermatitis, 1% hiatus hernia; <1% hyperthyroidism, panic disorder, epilepsy, diabetes, systemic lupus erythematosus, coronary artery disease, coeliac disease and stroke.

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H027
The influence of psychiatric comorbidity on migraine-related disability in a clinical population of patients with migraine without aura
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**Background** Previous studies have revealed that migraine-related disability, as measured by MIDAS Questionnaire, does not reflect only migraine intensity and frequency. Factors other than migraine severity may play a role in determining individual variation in disability levels.

**Objective** To define predictors of migraine-related disability in patients referred to a specialty headache clinic focusing on psychiatric comorbidity and personality characteristics.

**Results** 233 consecutive patients, suffering from migraine without aura, were evaluated using MIDAS, BDI for depressive symptoms, STAI-T and STAS-T for trait anxiety and anger, TAS-20 for alexithymia and SCID-I for the categorical diagnosis of axis I psychiatric disorders. Multiple regression analysis showed that disability was higher in those patients experiencing a higher number of headache days per month, more severe pain intensity, more severe depressive symptoms, and more prolonged migraine attacks. Other independent predictors of the total MIDAS score were female gender and having full-time employment. The model was highly significant ($F = 18.96, P < 0.00001$) and explained 35% of the observed variance (adjusted $R^2$).

**Conclusions** Our findings demonstrate that, with the exception of depressive symptoms, psychiatric comorbidity has a limited influence in modulating the impact on every-day functioning.

**Keywords:** disability, MIDAS, psychiatric comorbidity

H028
Hypnic headache presenting with typical migraine aura
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**Background** The hypnic headache syndrome of recurrent, brief, nighttime headaches occurring in elderly patients was first described by Raskin (1). It usually lacks autonomic symptoms and has few accompanying symptoms like nausea, photophobia and phonophobia. While typical migraine aura has been associated with several non-migraine conditions (cluster headache (2), hemicrania continua (3), and paroxysmal hemicrania (4)), it has not been described in hypnic headache.

**Case** A 64-year-old woman described middle-of-the-night pancephalic pain accompanied by ‘bright lights, blurred vision, dark lines and numbness’ (head, hand) nightly for 2.5 years. Episodes lasted 30–60 min. She also described a history of unilateral headaches accompanied by nausea, photophobia and phonophobia, occurring once to twice per month since age 20. Brain MRI was normal. Lithium 300 mg at bedtime led to dramatic reduction in the frequency and severity of the nighttime headaches.

**Discussion** This is the first case of hypnic headache described with typical migraine aura. While migrainous aura may result from a process independent of typical migraine physiology, the coexistence of migraine in our case suggests a possible mechanistic link with the hypnic headache syndrome. Interestingly, our patient’s migraines were unassociated with aura.

**Keywords:** hypnic headache, aura, migraine

**References**

H029
Prosopanomia as migraine aura manifestation
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**Background** Although aphasic aura occurs in 15–20% of migraineurs with aura, prosopanomia has not yet been described as migraine aura.

**Objective** Report a case of selective category aphasia. People describe anomia (prosopanomia) as migraine aura.

**Methods** A 52-year-old man presented due to acute difficulty in naming persons, which appeared during fitness activity. He was unable to name the other participants, the attending physician or the trainer. The physician considered that speech comprehension was intact and that the speech was fluent, except for the striking inability to remember names of people including his family members. Prosopanomia lasted about 40 min and was followed by throbbing headache. The patient had had classic migraine for 30 years with aphasic aura in many attacks.

**Results** The neurological examination, language assessment, brain CT and EEG were normal. This patient developed prosopanomia during migraine attack. Prosopanomia was usually associated with left tempo-parietal lesions. During aura, transient oligogaemia spread across the cortex, starting at the visual cortex. Extension of oligogaemia to the left angular gyrus and to Brodmann area 17 may produce prosopanomia.

**Conclusion** Isolated prosopanomia may be a feature of aphasia during migraine attack.

**Keywords:** prosopanomia, migraine, aura
H030
Is medication overuse a kind of behaviour of substance dependence?
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Background Medication overuse (MO) is a common disorder in the headache clinics. It is debatable if these patients experience dependence.

Objective To explore the prevalence of substance dependence by DSM-IV criteria and the predictors among chronic daily headache (CDH) patients with MO.

Methods We recruited consecutive patients with CDH at a headache clinic from November 1999 to June 2004. Each patient filled in a headache intake form, a dependence questionnaire modified from DSM-IV and the Hospital Anxiety and Depression Scale (HADS). The MO was defined based on the ICHD-2, 2004.

Results 1861 CDH patients (1369 F/492 M, mean age 49.6 ± 15.4 years) were recruited. Of them, 895 patients (48%) met the criteria of MO. According to the DSM-IV dependence criteria, 606 of the 893 MO patients (67.9%) were classified as dependence, whereas 191 of 968 patients without MO (19.7%) were classified as dependence [OR = 8.6, (7.0–15.4), χ² test, P < 0.001]. The anxiety and depression scores of HADS did not differ between patients with and without MO. The logistic regression analyses revealed that dependence was the most significant predictor for MO after controlling for other variables.

Conclusion Among CDH patients, MO was associated with a behaviour of substance dependence defined by the DSM-IV.

Keywords: medication overuse headache, chronic daily headache, dependence

H031
The natural course of migraine attacks. A prospective analysis of untreated attacks compared with treated
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Objective This study was designed to document prospectively and explore scientifically the natural course of untreated migraine attacks in detail.

Methods A new, integrated, time-intensity method for self-assessment of the intensity of symptoms was tested on 18 adult HIS migraineurs who volunteered to refrain from treatment during one attack. The area under the curve (AUC) during 72 h of untreated attacks was compared with attacks treated with a triptan.

Results Migraine attacks are heterogeneous both inter- and intra-individually. In untreated attacks, the pain can stabilize and fluctuate around a plateau with a wavelength of hours. In general, the symptoms of each separate migraine attack follow a similar temporal course, with only moderate deviations. In some cases photo- and/or phonophobia (hypersensitivity) were not experienced at all, despite severe pain and nausea. Moreover, there was sometimes no nausea despite severe pain and hypersensitivity. Vomiting does not always correlate to the intensity of nausea and is not always followed by decreased headache intensity. Treatment with a triptan usually only temporarily distorts the basic pattern of attacks. Hypersensitivity can respond before pain to treatment.

Conclusion These genuine findings of the classic symptoms of migraine attacks support the notion of a reciprocal underlying pathophysiological mechanism.

Keywords: migraine, natural course, triptans

H032
Headache in Parkinson disease
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Objective The aetiology of headache accompanied with Parkinson disease is not well known. Based on the findings of the present study, we propose a new aetiological consideration.

Methods Sixty-seven patients with Parkinson disease were investigated. Twenty-seven were male and 40 were female. The age ranged from 42 to 87 years old with the mean of 70.7 ± 9.8. Yahr stage was six cases in degree I, 47 cases in II, 11 cases in III and three cases in IV. Among these patients, the headache patients were examined.

Result Seventeen cases (25.4%) were found to suffer from headaches. The nature of the pain was non-vascular type in 15 cases (88.2%). Sixteen cases showed bilateral headache. Among them, eight cases revealed a decrease in pain when in the supine position. These eight cases showed orthostatic hypotension.

Conclusion The aetiology of the headache accompanied by Parkinson disease is heterogeneous. But in the present study, some headache patients of all headache in Parkinson disease might have developed due to low CSF pressure. Since these patients showed orthostatic hypotension, automatic dysfunction due to Parkinson disease might occur due to decreased CSF pressure.

Keywords: Parkinson disease, low pressure headache, orthostatic hypotension

H033
Headache in cerebrovascular infarction
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Objective Few reports have been made on headaches among chronic cerebrovascular infarction patients in Japan.

Method A total of 106 cerebrovascular infarction out-patients in the chronic phase were examined in the present study. Seventy-five cases were male and 31 were female. Their ages were from 42 to 94 years old with the mean of 71.1 ± 8.6.
Result Before CVD, 26 cases showed headaches, but after the disease decreased to eight cases. Among 80 patients who had no headache before CVD, 13 cases developed headache. Among them six cases (46.2%) showed hemispheric pain. The side of the headache was the same as the CVD lesion in five cases.

Conclusion There were two interesting results in the present study. First, in patients who developed headache after CVD, the headache side tended to correspond to the lesion side. Second, patients who had headache before CVD recovered after CVD in 69.2% of the cases. From these results, apparently the intracranial abnormality influences the mechanism of headache occurrence.

Keywords: cerebrovascular infarction, out-patient, chronic CVD phase, headache-side

H034

The migraine postdrome: an electronic diary study

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Background Many migraineurs have residual non-headache symptoms after resolution of their headache: the postdrome. These have not been systematically studied.

Methods A prospective electronic diary study of 120 patients with frequent migraine was carried out over 3 months. For each postdrome, data were collected on: spectrum of non-headache symptoms; duration; headache relief medication taken; overall level of functioning, on a visual analogue score, and severity of the previous headache.

Results Before the study, 67% of patients reported migraine postdromes. Four hundred and twenty-five diary entries with at least one non-headache feature in the postdrome were recorded. The most frequent symptom was ‘tired/weary’ (88% of entries), followed by ‘difficulty in concentrating’ and ‘stiff neck’. Many patients also reported a mild residual headache. There was no relationship between medication taken for the previous headache and the duration of the postdrome. Overall state of health scores remained low during the postdrome [mean 57 (81 interictally)].

Conclusion Non-headache symptoms in the postdrome account for a significant degree of the distress of a migraine. Postdrome symptoms should be taken into account in clinical trials of acute and prophylactic migraine medication.

Keywords: postdrome, migraine, headache

H035

Outline of clinical picture in Japanese migraine patients

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Objective Clinical analysis of migraines in many cases has been rare in Japan. In the present study, we gathered clinical findings from the first consultation by each patient.

Patients and methods There were 3138 adult (≥19 years old) migraine patients (male 786, female 2352) who consulted our headache clinic over 19 years and were investigated.

Results The ratio male vs. female was 1:3. On the first consultation, patients in their 40s were the most numerous (29.8%). 361 cases had migraine with aura (11.5%), against 2777 (88.5%) without aura. The affected side was the right in 19.3%, left in 21.0%, alternating in 26.2%, bilateral with a difference between the right and left in 22.0%, and completely bilateral in 11.5%. Duration of one attack was 12.4% within 6 h, 6.9% between 6 and 12 h, 42.3% between 12 and 24 h and 38.4% over more than 24 h. Frequency of attack per month was 9.0% less than 1, 53.1% from one to five, 15.3% from six to 10, and 22.6% more than 11. Nausea was 43.0% and vomiting was 32.9%. Photophobia was 69.4% and phonophobia was 69.0%.

Conclusion These results might be considered to reflect the standard clinical findings in Japanese migraine patients. Total laterality is clear, and nausea, vomiting, photophobia and phonophobia are less in Western cases reported in the literature.

Keywords: migraine, symptomatology, clinical analysis

H036

Validity of the Turkish ID-Migraine Screener in workers and the impact of migraine on productivity

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Background ID migraine Screener (IDMS) was initially developed by Lipton and colleagues to facilitate migraine diagnosis.

Objective To validate this test in Turkish population in a workplace setting and to evaluate the burden of disease using SF-36 and migraine’s impact on quality of life (QoL); and to compare the results with the original study (OIDMS) (1).

Methods Subjects who reported two or more headaches in the previous 3 months and responded positively to one of the ID-Migraine prescreening questions were included. They were given IDMS by a primary care physician and received MIDAS questionnaire for evaluation of disability, and SF-36 for QoL assessment. Migraine cases were diagnosed according to IHS criteria by headache experts blinded to IDMS results.

Results Of 227 subjects (65.6% female, mean age 31.9 ± 5.9 years), 46.7% was migraine-positive according to IDMS and 51.5% was migraine-positive according to IHS criteria. The correlation between these two tools was moderate (κ 0.50, P < 0.001) (sensitivity 70.9%, specificity 79.1%). According to MIDAS, the loss of work days of migraine-positive and -negative subjects were 8.7 ± 9.5 days and 4.9 ± 6.6 days, respectively.

Conclusion The Turkish version of IDMS was found to be a useful screening tool to identify migraine patients in the workplace.

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Keywords: migraine, screener, diagnosis, validity, disability

Reference

H037
Prevalence and clinical characteristics of headache in university students in Japan
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Background Headache is one of the most common complaints in medical practice. To our knowledge, there are almost no investigations of chronic headache in university students in Japan.

Objective The aims of this study were to determine the type, degree and frequency of headache in university students, examine associated factors and medication.

Methods This study included 1760 university students who were interviewed by a questionnaire.

Results 1759 students (99.9%) completed the questionnaire. The lifetime prevalence of headache was 33.7%. The diagnostic impressions of the different types of headache were migraine without aura (6.3%), migraine with aura (1.4%), tension-type headache (21.4%) according to modified ICHD-I diagnosis criteria. Disabilities due to headache were reported by 31% of migraine and 5% of tension-type headache sufferers for academic performance. When the students with headache were asked what they did to obtain relief, 49% of migraine and 18% of tension-type headache students took medication. Only 20% of migraine and 10% of tension-type headache students had visited a physician for treatment of headache.

Conclusion Since a university student’s recognition over a headache is low, it is important for them to perform the education to chronic headaches continuously in consideration of productivity after employment.

Keywords: headache, prevalence, university student, migraine, tension-type headache

H038
Three patients of cardiac cephalagia (ICHD-II: 10.6)
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Background In the recent International Classification of Headache Disorders (ICHD-II), the cardiac cephalagia (10.6) is a subtype of headache attributed to disorders of homeostasis and develops concomitantly with myocardial ischaemia.

Objective Owing to the very rare occurrence of headache as a symptom of myocardial ischaemia, diagnosis is difficult and requires a high degree of suspicion.

Methods Patient I: A 68-year-old women developed intermittent headache with epigastric discomfort, suddenly. Treadmill exercise-stress test demonstrated ST depression on the electrocardiogram (ECG) as the headache appeared. The exertional headaches were cured after nitrates were prescribed. Patient II: A 46-year-old man developed headache with left chest and shoulder pain, simultaneously. A coronary angiogram and holter-monitoring studies revealed variant angina with right coronary artery stenosis. The headaches disappeared after coronary stent insertion. Patient III: A 44-year-old women presented headache and substernal tightness. Coronary catheterization with acetylcholine provocation study demonstrated the right coronary artery spasm with headache, substernal tightness and ischaemic ECG changing. The headaches disappeared after nitrates and calcium channel blocker were prescribed.

Results A short duration of headache and relationship with exercise should alert physicians to the possible cardiac origin of headache.

Conclusion Paradoxical relief and prevention of the headache by nitrates is a strong clue to diagnose cardiac cephalagia (ICHD-II: 10.6).

Keywords: myocardial ischaemia, referred headache, nitrates, ICHD-II, angina

H039
Frontal lobe dysfunction in the interictal phase of migraine without aura: case–control study
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Objective To investigate frontal lobe functions in subjects with migraine without aura, and to relate cognitive performances to migraine characteristics.

Methods 45 young adults with migraine without aura and 90 migraine-free controls matched for age and education underwent a cognitive battery including tasks assessing frontal lobe functions. The following migraine features were collected: length of migraine history, frequency, duration and intensity of attacks.

Results Migraineurs showed a worse performance in tasks exploring focused and divided attention and cognitive planning and flexibility (P from 0.005 to 0.0001). Multiple linear regression models revealed that intensity of migraine attacks was significantly associated with the performance of the Trial Making Test A (β = 0.261, P < 0.05), a task exploring selective attention. Length of migraine history was associated with the scores obtained on the Trial Making Test B (β = 0.276, P < 0.05) and with the perseverative errors of the Wisconsin Card Sorting Test (β = 0.382, P = 0.01), two tasks evaluating cognitive planning and flexibility.

Conclusions Migraine without aura in the interictal phase is associated with frontal lobe dysfunction. This findings may be associated with the cumulative effects of repeated migraine attacks causing covert subcortical white matter lesions.
Keywords: migraine without aura, frontal lobe dysfunction, neuropsychology

H042

Efficacy of candesartan in treatment of migraine in hypertensive patients

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Background Triptans can not be administrated to patients who have trouble with cardiac or cerebral vascular systems, which are commonly accompanied by hypertension.

Objective This prospective study shows efficacy of angiotensin II receptor blocker, candesartan in migraine treatment in hypertensive patients.

Methods After the patients were diagnosed with migraine, candesartan was prescribed if their attacks were frequent. Because candesartan can be prescribed only in hypertensive patients in Japan, hypertensive patients were picked up.

Results A total of 28 patients (mean age 51.8 years, men 12, women 16) were administrated candesartan. Degree of severity was measured by Migraine Disability Assessment score (MIDAS). MIDAS was improved from 40.9 points to 6.7 points.

Conclusion Because many patients have vascular diseases, candesartan is thought to be one of the attractive choices in the treatment of hypertensive migraine patients.

Keywords: candesartan, migraine, preservation

H043

Pressure-pain threshold changes in scalp and forearm during different phases of a migraine cycle

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Background Scalp tenderness is a common finding in migraine, and increased forearm skin sensitivity is reported in migraine.

Objective To measure pressure-pain threshold on the headache and non-headache sides of scalp and both forearms during a migraine cycle.

Methods A Fischer pressure-algometer measured pain threshold in kg. Ten migraineurs with unilateral migraine, preceded by prodrome, and 10 non-headache controls were entered in the study. Readings, blinded to investigator and subject, were taken on scalp headache side and scalp non-headache side, and forearms, during prodrome, headache, postdrome and interictally, during a single migraine cycle. Controls were measured at similar sites at a single visit.

Results Significant changes in scalp pain threshold occurred on headache side during different phases of the migraine cycle; lowest during headache (0.27 kg), highest interictally (1.16 kg) (P < 0.0001). A similar pattern existed on non-headache side at higher threshold levels. Prodrome thresholds (0.59 kg), in absence of headache, were also below interictal.

Forearm threshold fell on headache side during headache. Scalp thresholds (1.63 kg) were higher in non-migraineurs.

Conclusion Significant changes in scalp pressure-pain threshold occur during a migraine cycle. A fall in threshold occurs during prodrome. This increased tenderness may provide an early warning signal of impending headache.

Keywords: botulinum toxin, tension-type headache

H045

Sleep deprivation headache in medical students

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Background For over a century, the relationship between sleep and headaches has been studied. However, the mechanisms of sleep-related headaches are still not clearly known. Both sleep deprivation and excessive sleep may result in headaches. However, although prolonged sleep is a recognized cause of headaches, insufficient sleep is rarely mentioned in the literature; therefore, we investigated the clinical characteristics of sleep deprivation headaches (SDH) to obtain some basic information for future studies on sleep deprivation headaches.

Methods A survey, which included 15 questions about the clinical features of SDH, was completed by 416 medical students.
Results All but two of the students responded. Of the 414 respondents, 287 (69.3%) experienced SDH. The incidence of SDH was higher than that in a previous report. The characteristics of SDH varied greatly and were fairly different from other headache types.

Conclusions The results of the present study suggested that SDH are an independent headache type, which may be related to insufficient functional restoration of the central nerve system due to lack of sleep.

Keywords: sleep, deprivation, headache

H046
Investigation on agreement between recalled headache intensity and momentary headache intensity using computerized ecological momentary assessment technique
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Objective Computerized ecological momentary assessment (EMA) has been developed to avoid problems such as recall bias and fake compliance involved by recall or paper-and-pencil diaries. The aim of this study was to investigate the agreement concerning headache intensity between recall and computerized EMA in tension-type headache (TTH) patients.

Methods Forty-four patients with TTH (40.0 ± 10.8 years) wore a watch-type computer for 1 week. With this device, scheduled recordings of headache intensity were performed approximately every 6 h. Event-contingent recordings were also performed at acute exacerbations. At the end of the week, the subjects rated their headache intensity during the week by recall. We calculated four indices from EMA recordings: the averages of all the recordings (HI1), of the scheduled recordings only (HI2), of the event-contingent recordings only (HI3) and of the recordings only when headache existed (HI4). We divided the subjects into lowSD and highSD groups at the median of standard deviation of headache intensity from EMA recordings.

Results Intra-class correlation coefficients of absolute agreement of weekly recall and HI1-4 for the lowSD/highSD groups were 0.75/0.21, 0.75/0.16, 0.81/0.21 and 0.77/0.29, respectively.

Conclusion The agreement between EMA recordings and weekly recall might be very low, especially in subjects whose headache intensity varies.

Keywords: computerized ecological momentary assessment, recall bias, fake compliance, intraclass correlation coefficient, tension-type headache

H047
Epidural blood patches for a patient with orthostatic headache after suboccipital craniectomy
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Although orthostatic headache after spinal surgery and its management have been well known, those after suboccipital craniectomy has been rarely described. A 32-year-old man was admitted to hospital for decreased consciousness level caused by acute brainstem and cerebellar infarctions with large amount of oedema. He was given emergent suboccipital craniectomy with duroplasty, and then his consciousness returned. However, he couldn’t get an active rehabilitation programme because of severe postural headache that was intractable to conservative management. He was given an epidural blood patch between L1-L2 level. Headache was significantly relieved after that procedure, but this immediate effect did not last more than 24 h. Persistent complete improvement of headache was accomplished 3 days after the second blood patch into the epidural space through T12-L1 interspinous level. Repeated epidural blood patches may be a more useful alternative treatment option than the reconstruction of the cranectomy site for postcraniectomy orthostatic headache.

Keywords: orthostatic headache, suboccipital craniectomy, epidural blood patch

H048
Zolmitriptan orally disintegrating tablet: improvement in disability and productivity in patients with migraine
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Background Migraine is a debilitating condition that impairs daily life and productivity.

Objective To assess the effect of zolmitriptan orally disintegrating tablet (ODT) 2.5 mg on improving disability and productivity.

Methods In this postmarketing study, patients with migraine and prescribed zolmitriptan ODT 2.5 mg for acute treatment were assessed at study entry and after 3 months.

Results Data were collected for 14 543 patients who were predominantly treated by general practitioners. Previous therapies for acute migraine were mainly analgesics (83% of patients). Patients rated baseline pain intensity as severe or moderate (59% and 39%) and daily activities as totally or moderately impaired (46% and 47%). The baseline mean MIDAS score was 28.5 (indicating a high level of disability). Following switching treatment to zolmitriptan ODT, headache pain improved in 35% of patients within 30 min, 80% within 1 h, and 94% within 2 h. Patients were also able to return quickly to daily activities (16% within 30 min, 51% within 1 h and 83% within 2 h). The mean MIDAS score was reduced to 11.4 (mild to moderate disability).
Zolmitriptan orally disintegrating tablet (ODT) demonstrates excellent patient and physician satisfaction in primary care migraine therapy

Andrew Dowson,1 Gary Shapero2, Jean-Pierre Lacoste3 & Per Almqvist4

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%).

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

Keywords: migraine, satisfaction, preference, zolmitriptan

Virtual medical advice to unknown patients by e-mail: an analysis of 219 cases of headache

D. Ezpeleta1,2,3

Objective To ascertain which people search for medical information and advice on headache on the internet and what they demand.

Methods From April 2000 to March 2003, patients or their close relatives or friends were able to make a consultation about any neurological problem on the author’s website. Communication, always in Spanish, was established by e-mail and a web forum. Free answers were always given by the author.

Results Among the 1237 requests for information or virtual neurological advice received, 219 (17.7%) were directly related to headache. Source of consultations: Spain (62.6%), Central and South America (32%), other (5.5%). Who consulted: patient (72.1%), relative (22.5%), friend (5%). Type of consultation: opinion about a clinical case (68.9%), information on a given headache or its treatment (29.7%), explicit or desperate request for help (14.2%), other (7.3%). Consultations on headaches were distributed as follows: migraine (25.1%), non-classified headache (20%), other headache (12.3%), tension headache (11.4%), chronic headache (9.1%), cluster headache (7.7%), post-traumatic headache (7.3%) and neuralgia (6.8%).

Conclusion Patients with headache search for medical information and advice on the internet. These data suggest the need for qualified virtual medical advisors who give guidance to patients using the internet as a source of neurological information.

Keywords: teleneurology, headache, virtual advice, e-mail, internet
Objective To compare patients’ preference for zolmitriptan orally disintegrating tablet (ODT) vs. eletriptan oral tablet, sumatriptan oral tablet and rizatriptan ODT.

Methods Three separate studies recruited patients diagnosed with migraine (IHS criteria). Patient preference for zolmitriptan 2.5 mg ODT was compared with that for eletriptan 20 mg oral tablet (study A; n = 64), sumatriptan 50 mg oral tablet (study B; n = 186) and rizatriptan 10 mg ODT (study C; n = 171).

Results Zolmitriptan ODT was preferred by >60% of patients in all three studies. Preference rates for zolmitriptan ODT were significantly higher than those for eletriptan (study A; 62.3% vs. 37.7%, P < 0.01), sumatriptan (study B; 60.1% vs. 39.9%, P = 0.013) and rizatriptan ODT (study C; 70.0% vs. 27.0%, P < 0.001). Reasons given for preferring zolmitriptan ODT included: better efficacy (studies A and B), fast relief (study A), convenience (studies B and C) and taste (study C). Over 90% of patients (study B) stated zolmitriptan ODT allowed migraine treatment any time and anywhere.

Conclusion Patients with migraine prefer zolmitriptan ODT to eletriptan, sumatriptan and rizatriptan ODT, citing fast and effective relief, convenience and taste as the key reasons.

Keywords: migraine, preference, zolmitriptan

H053

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.

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

Methods A cross-sectional, multicentre study in PCP settings was implemented in patients ≥18 years of age attending a health centre 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 k coefficient, and determination of sensitivity, specificity, and positive and negative predictive values.

Results 9670 patients [48.9 ± 17.2 years (mean ± SD); 61.9% females] were enrolled by 410 PC physicians. Migraine was presented in 24.7% of participants according to IHS criteria and in 22.6% according to MS-Q. Kappa coefficient ranged from 0.70 to 0.84 (P < 0.001). Sensitivity was 0.82 (95% CI 0.81, 0.84); specificity 0.97 (95% CI, 0.97, 0.97); positive predictive value 0.90 (95% CI 0.89, 0.91); and negative predictive value 0.94 (95% CI 0.94, 0.95).

Conclusion The MS-Q was found to be a valid screening tool for migraine headaches at the primary care practice level.

Keywords: migraine, primary care practice, MS-Q, screening, clinimetry

H054

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.

Objective To determine the level of undiagnosed migraine at the primary care level.

Methods This was a cross-sectional, multicentre study in PCP settings. Patients were male and female 18 years of age and older, attending the health centre for any reason, and able to understand healthcare questionnaires. Diagnosis of migraine was established by IHS criteria and by means of a five-question migraine-screening questionnaire (MS-Q). New diagnosis rates were calculated using both MS-Q and IHS criteria in patients without previous history of migraine related to the total sample.

Results 9670 patients [48.9 ± 17.2 years (mean ± SD); 61.9% females] were enrolled by 410 PC physicians. According to IHS criteria, migraine was present in 24.7% of all participants compared with 20.4% using MS-Q. New diagnosis based upon HIS criteria was presented in 7.8% of patients with no previous migraine and 6.1% of the total sample vs. 7.2% and 5.7%, respectively, using MS-Q. Significant differences were not found for new diagnosis rates.

Conclusion There is a proportion of migraine patients without adequate diagnosis at the PCP level. MS-Q may be a valid and easy screen tool for diagnosing new patients.

Keywords: migraine, primary care practice, MS-Q, new diagnosis, undiagnosed

H055

Headache and Japanese expression

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Objective The Japanese word ‘zukizuki’ is believed to stand for the condition of pulsating headache. But further interview sometimes revealed that headache with ‘zukizuki’ was not necessarily a pulsating one. In this study, we analysed the diagnostic value of ‘zukizuki’ for pulsating headache.

Methods We studied the experience of headache in workers in our hospital using questionnaires including ‘Whether your headache is/was pulsating or not?’ with detailed explanation about ‘pulsating’.

Results We interviewed 330 workers by this questionnaire and 293 (89%) of them responded. 207 workers had experienced headache, and 97 expressed their headache as ‘zukizuki’ in their own languages. Pulsating headache was
diagnosed in 48 of 97 (50%) with ‘zukizuki’ headache through further interview.

**Conclusion** Our study showed that ‘zukizuki’ was recognized in only half of patients with pulsating headache. The expression ‘zukizuki’ might have low diagnostic value for pulsating headache

**Keywords:** pulsating, ‘zukizuki’, headache, diagnosis, Japanese

**H057**

**Pulsating headache accompanied with left V1 trigeminal neuralgia in a patient with anterior dissection of basilar artery**

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A 77-year-old man who had previous history of basilar artery dissection at the middle pons level came to our hospital with pulsating headache accompanied by left V1 trigeminal neuralgia (TN). He also had a cerebral infarction in right paramedian area of pons 2 months previously. Brain CT at the onset of headache revealed the high density area (HDA) in the anterior wall of basilar artery. Drug treatment was administered. A month later the headache diminished, at the same time the HDA in arterial wall was resolved. We diagnosed the cause of HDA as the result of newly formed small dissection at basilar artery. Past reports show that half of headache cases caused by verteobasilar artery dissection have pulsating character and that 2% of TN is caused by direct compression of verteobasilar artery to trigeminal nerve. But it is very rare that pulsating headache and TN simultaneously accompany verteobasilar artery dissection. In referring to the recent knowledge of sensitization mechanism in migraine, our case might raise suggestions for the explanation of the relation between pulsating headache and cutaneous sensation.

**Keywords:** pulsating headache, trigeminal neuralgia, dissecting verteobasilar artery, migraine, sensitization

**H058**

**Functional and emotional impact of strict chronic migraine vs. probable chronic migraine in Framig 3 survey: importance of medication overuse**

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**Background** The 2004 revised International Headache Society (IHS) classification (ICHD-II) distinguishes chronic migraine (CM) and medication overuse headache (MOH). CM (IHS category 1.5.1) is a new entity defined without medication overuse (MO). The ICHD-II proposes a diagnosis of ‘probable CM’ (IHS category 1.6.5) should be assigned as temporary diagnosis if MO has not yet been withdrawn.

**Objective** To compare strict CM and probable CM in terms of functional impact by the Migraine Disability Assessment questionnaire (MIDAS), emotional status by the Hospital Anxiety and Depression Scale (HADS) and quality of life using the SF-12 scale (HRQoL).

**Methods** 262 CM subjects identified in the screening phase of FRAMIG 3 using a mailed questionnaire.

**Results** The prevalence of strict CM was 1.7% and that of probable CM 0.8% in the general French population. There were significantly more subjects with probable CM in grade IV (45.4%) and fewer in grades I and II. Probable CM was also associated with a trend towards greater emotional impact as assessed by the HADS. As regards HRQoL, subjects with probable CM reported significant decreases in all concepts of the SF-12 scale except Role-Emotional.

**Conclusion** Impact of the disease is more marked in subjects with probable CM, i.e. when medication overuse is present.

**Keywords:** chronic migraine, functional and emotional impact

**H059**

**Symptoms of anxiety and depression among Egyptian patients with chronic daily headache**

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**Objective** To study the prevalence of anxiety and depression in patients with chronic daily headache (CDH) compared with patients with chronic arthritis and controls.

**Methods** A detailed headache interview with emphasis on CDH was made; symptoms of anxiety and depression were recorded as well as Hamilton rating scales for anxiety and depression.

**Results** The study included 50 patients with CDH, 20 patients with chronic arthritis, and 20 controls; the three groups were matched for age and sex. Hamilton rating scale for depression was significantly higher in patients with CDH 13.03 ± 7.45, than chronic arthritis 5.59 ± 5.08, and controls 4.22 ± 4.48 (P < 0.01). Similarly, Hamilton anxiety rating scale was significantly higher in patients with CDH 9.42 ± 6.67, than patients with chronic arthritis 6.48 ± 3.38, and controls 5.85 ± 3.51 (P < 0.01). Depression was diagnosed in 48% of patients with CDH, 15% of patients with chronic arthritis and 5% of control subjects (P < 0.001). Anxiety disorders were diagnosed in 16% of patients with CDH and in one patient with chronic arthritis and none in controls. Patients with medication overuse and longer duration of headache were more likely to have depression.

**Conclusion** Patients with chronic daily headache are more likely to have depression and anxiety, thus requiring recognition and adequate treatment.

**Keywords:** chronic headache, depression, anxiety, migraine

**H060**

**Premonition symptoms in migraine without aura in Japanese patients**

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**Objective** Premonition symptoms are seen several hours to a day or two before in the description of ICHD-I. But many
Japanese cases of migraine without aura show such symptoms prior to attack about 1 h before, as different from ICHD-I.

**Patient and methods** We examined by interview 716 patients with migraine without aura.

**Results** Some kind of premonitory symptom was detected in 617 patients (86.2%) among 716 cases. The highest ratio of appearance was 86.8% in the fourth decade, and the lowest was 73.9% in the 7th decade. Symptoms among 617 cases were as follows: shoulder stiffness in 187 cases (30.3%), indefinite feeling in 149 (24.1%), repeated yawning in 104 (16.9%), head heaviness in 43 (7.0%), purblind in 32 (5.2%) and decreased concentration in 21 (3.4%). Onset of these symptoms was within 30 min in 147 cases (30.9%), between 30 and 60 min in 146 (30.7%), and between 60 and 120 min in 77 (16.2%) before headache attack. Some patients had two or more symptoms.

**Conclusion** Almost all of these patients can predict the appearance of a headache attack accurately. These findings are not reported in Western literature. This could be a characteristic difference in the clinical picture between Japanese and Western patients in migraine without aura.

**Keywords:** migraine without aura, premonition symptoms, shoulder stiffness, indefinite feeling, yawning

**H061**

**Stress and psychological factors in migraine: a time-based analysis**

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**Objective** The aim of this study was to discuss the correlation between the occurrence of migraine and psychosocial factors from a time-based analysis.

**Methods** The study was conducted on six migraine patients (all women, average age 35.3 years) who consented to participate in this study. Each subject kept a headache diary four times a day for 2 weeks. They evaluated the degree of stressful events, daily stress, anxiety and depression by VAS. Each day was classified into migraine days, premigraine days, buffer days and control days based on the intensity of the headaches, accompanying symptoms, and a comparative study was conducted for each factor in the migraine days, premigraine days and control days.

**Results** Migraine headaches were observed in five of the six subjects. Significantly higher values were exhibited for ‘stressful events’ on premigraine days, highest scores were also demonstrated for ‘number of daily stress’ on premigraine days, and those values were significantly higher. In addition, significantly higher levels of anxiety and depression were observed on premigraine days compared with control days.

**Conclusion** Psychosocial stress that precedes the onset of migraine by several days was suggested to play an important role in the occurrence of migraine.

**Keywords:** migraine, stressful event, daily stress, anxiety, depression

**H062**

**A study on drug therapy for migraine accompanied by tension-type headache-like symptoms**

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**Objective** In this study, we discussed drug therapy for migraine accompanied with tension-type headache-like symptoms, putting a focus on stiffness in the shoulders.

**Methods** The patients (age 34, average ±12) were categorized into two groups: Group A for 16 patients having no symptoms of stiffness in the shoulders, and Group B for 18 patients having such symptoms, to examine their conditions before and after the drug administration. Based on the report of Ferrari, rizatriptan was selected as a drug for migraine to be used for the study.

**Results** In the comparative study with Group A and Group B, significant improvement rates (P = 0.0059) were confirmed in Group A (100%) and Group B (61.1%); and improvement tendency was seen in the rates of complete pain relief (P = 0.0906) in Group A (56.3%) and Group B (27.8%), after administration of rizatriptan.

**Conclusion** In comparison of effect of the drug on patients having tension-type headache-like symptoms with those having no such symptoms, greater improvement was confirmed in the group of patients having no symptoms of stiffness in the shoulders.

**H063**

**Efficacy of the therapeutic intervention in headache units in patients with frequent headache. EFUNCE study**

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**Background** There are very few data confirming that the therapeutic intervention in headache units is superior to the attention received by patients in other levels of the health system.

**Objective** To evaluate the efficacy of the therapeutic intervention in headache units.

**Methods** We included patients seen in the headache unit during at least a year’s period who had a headache frequency of more than 15 days per month. We evaluated the clinical situation, treatment, degree of patient satisfaction, and incapacity and quality of life.

**Results** We presented the results of the first 30 patients. 26 were women and four men. In 86% of cases the frequency of headaches was reduced and drug abuse was corrected. 100% were unsatisfied or very unsatisfied at their arrival, while 92% of them were satisfied or very satisfied later. These clinical results were very related to improvement of quality of life and incapacity scales (MIDAS: 81–28).
Conclusion This study represents evidence that Headache Units are efficient in treatment of headache patients, even in difficult cases, as they offer a high degree of clinical improvement, patient satisfaction and important benefits regarding incapacity and quality of life.

Keywords: headache units, efficiency

H064
Symptomatological analysis of cluster headache in Japan
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Objective Symptomatological analysis of cluster headache in Japanese cases has been rare. We examined this and compared with Western cases.

Patients and methods Four hundred and forty-two cluster patients (male 358, female 84 cases) were examined symptomatologically.

Results Onset was from 12 to 80 years old, with a mean of 26.9 ± 10.9. Four hundred and thirty-two cases (97.7%) were episodic type, and 10 (2.3%) were chronic. The affected side was right in 209 cases (50.1%), left in 174 (41.7%) cases, 21 (5.0%) changed and 13 (3.2%) were bilateral. In the episodic type, the most frequent cluster period was less than once per year in 76.2%. The maximum duration of the cluster period was within 1 month in 61.5%. The most attacks per day was once in 40.8%. The most frequent duration of attacks was more than 1 h but less than 2 h in 47.6% of the cases.

Conclusion The characteristics of Japanese cluster headaches show that middle-age onset is rare, female cases number slightly more, chronic type are fewer, number of attacks per day is less, frequency of the cluster period is less, duration of cluster period is shorter and duration of attack is longer, compared with reports in Western literature.

Keywords: cluster headache, clinical statistics

H065
Clinical features of osmophobia in migraineurs
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In the clinical setting, osmophobia is commonly mentioned during migraine attacks and, anecdotally, odours are described as a trigger. We investigated the presence of osmophobia in a sample of patients recruited from our Headache Centre with diagnosis of migraine (MA with aura, n = 92; MoA without aura, n = 477). Intolerance to smell during the attacks is reported by 42% (241/569) of patients (43% of those with MoA and 39% of those with MA). Osmophobia is present from the first year of headache history in 91% of patients; it occurs in more than 5/10 attacks in 86% of patients; its duration is the same as the pain in 98%. As offending odour, perfumes are mentioned by 64% (more specifically, women’s perfumes by 20%, regardless of gender); food-related smell by 55%; cigarette smoke by 55%; other types of smell by 15%. The olfactory stimulus triggered the attack in 25% of the migraineurs with osmophobia; that is in 11% of the total sample of migraineurs, cigarette smoke (8%) and women’s perfumes (7%) being the smell more frequently the cause. In conclusion, osmophobia appears to be a relatively constant component of attacks in the history of migraineurs presenting this symptom.

H066
Advice alone vs. structured detoxification programmes for medication overuse headache (MOH): a prospective, randomized, open-label trial in transformed migraine patients with low medical needs
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The effectiveness in MOH of doctor’s advice alone, without adjunctive pharmacotherapy, has not yet been defined.

Aim To compare the effectiveness of intensive advice to withdraw the overused medication with the effectiveness of two different structured strategies for patient detoxification.

Methods 108 patients diagnosed with probable MOH plus migraine participated in the study. Exclusion criteria were: previous detoxification experiences, coexistent, significant and complicating medical indications, major depression, overuse of opioids, benzodiazepines and barbiturate-containing agents. The patients were randomized in equal numbers in three different treatment groups. Group A received only intensive advice to withdraw the overused medication. Group B underwent a standard out-patient detoxification programme. Group C underwent a standard in-patient withdrawal programme. Withdrawal therapy was considered successful if, after 2 months, the patient had reverted to an episodic pattern of headache and was taking fewer than 10 doses of medication per month.

Results Three patients were excluded because they showed no improvement following the withdrawal. Sixteen patients dropped out of the study (group A five, group B six, group C five, P > 0.05). Of the 89 subjects who completed the study the success rates were: group A 90%, group B 80%, group C 86.3% (P > 0.05).

Conclusion In patients with transformed migraine with low medical needs and no previous detoxification experience, effective drug withdrawal may be obtained through giving advice alone.

H067
Use of complementary and alternative medicine by patients with chronic tension-type headache (CTTH): results of a headache clinic survey
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The use of complementary and alternative medicine (CAM) in the treatment of headaches is a growing phenomenon about which little is known.

Aim This study was undertaken to evaluate the rates, pattern and presence of predictors of CAM use in a clinical population of patients with CTTH.
Methods One hundred and ten CTTH patients attending a headache clinic were submitted to a physician-administered structured interview designed to gather information on CAM use.

Results Past use of CAM therapies was reported by 40% of the patients surveyed. CTTH patients prefer CAM practitioner-administered physical treatments to self-treatments, the most frequently used being chiropractic (21.9%), acupuncture (17.8%) and massage (17.8%). Only 41.1% of the patients perceived CAM therapies to be beneficial. Most of the CTTH patients used CAM treatment as a specific intervention for their headache (77.3%). The patients who had used more CAM treatments were found to be those recording a higher lifetime number of visits to conventional medical doctors, those with a comorbid psychiatric disorder, those enjoying a higher income, and those who had never tried a preventive pharmacological treatment.

Conclusions Our findings suggest that headache clinic CTTH patients, in their need of and quest for care, seek and explore both conventional and CAM therapies.

H068
Fibromyalgia among migraine patients: common but does not affect the headache

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Background Fibromyalgia (FMS), mainly characterized by widespread pain and excessive tenderness on applying pressure to 11 of 18 specific muscle-tendon sites, affects 2% of female population. Headache is often considered a part of the syndrome.

Objective To assess the prevalence of FMS among migraine patients and to characterize the migraine FMS patients.

Methods Consecutive patients suffering from migraine with and without aura (according to IHS criteria) attending the Soroka medical centre headache clinic were evaluated using a structured interview and clinical examination of tender points.

Results Sixteen patients suffered from FMS out of 92 migraine patients evaluated. All of them were female. There was no difference in migraine characteristics, severity or impact between migraine female patients with FMS and without FMS.

Conclusions The prevalence of FMS among migraine patients in a tertiary headache clinic is much higher than in the general population. It is unclear whether this over-representation reflects a truly high incidence of FMS among patients with migraine or merely a result of high consumption of medical services among FMS patients. Migraine is not affected in any way by the comorbidity with FMS.

H069
Patient’s satisfaction and compliance with usual migraine treatment in Germany: The German Migraine Register

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Objective Patient’s satisfaction and compliance with migraine drug treatments in Germany.

Methods 937 patients from 157 German out-patient clinics were included at the moment of an out-patient contact, and a telephone interview was held after 90 days. Patients were diagnosed with migraine at least 1 year previously and had a minimum of one migraine attack/month. Treatment satisfaction was recorded on a 5-point scale (1 very good to 5 unsatisfactory).

Results Previous prescription: nearly all patients (about 98%) used unspecific NSAIDs, 2/3 have also experience with triptans and about 10% used ergotics. Satisfaction: 70.3% of patients were satisfied with their acute treatment (score = 2), 24.1% were indifferent (= 2.5 and = 4) and 5.6% were not satisfied (= 4.5). Considering groups of drugs, satisfaction was highest in the group of triptan users, followed by the group using triptans and NSAIDs and lowest in the group of NSAIDs.

Compliance 20% did not follow prescriptions, 1/2 because of lack of effect and/or adverse events or fear of adverse events and 1/4 because of not having migraine or only mild migraine. Compliance in patients prescribed triptans was higher than in patients prescribed NSAIDs.

Conclusion In migraine patients NSAIDs are nearly always used for migraine, either alone or combined with triptans. When triptans are used, satisfaction and compliance improve.

H070
‘Lille en Tête’: assessing the impact of a pilot phase of collaboration between pharmacists and GPs to reduce the burden of migraine in Lille (France)

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Background A majority of migraine patients remain undiagnosed and inadequately treated.

Aims To evaluate the impact of migraine screening and education campaign involving GPs and pharmacists on migraine patients’ quality of life and migraine management.

Methods 40 pharmacists in Lille were trained to screen headache patients’ ID Migraine and the French medico-economic committee (ANAES) four treatment satisfaction questions. Pharmacists had to recruit at least five participants screened positively for migraine and encouraged them to consult their GP. Their MIDAS score and treatment information were collected at recruitment and 3 months later.

Results Among the 114 participants recruited by pharmacists 72% sought medical advice. 95% were confirmed to have migraine. At baseline 68% of the migraine patients considered
Conclusions

These preliminary results are encouraging; pharmacists screening patients with ID Migraine and the ANAES treatment satisfaction questions and motivating them to consult their GP might improve migraineurs’ quality of life.

**H071**

**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 from 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.

**Conclusion**

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.

**Keywords:** migraine, tension-type headache, psychiatric comorbidity, epidemiology

**H072**

**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 was 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 significantly 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).

**Conclusion**

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.

**Keywords:** migraine, tension-type headache, psychiatric comorbidity, epidemiology

**H073**

**The role of nurses in headache clinic**

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**Objective**

We examined the role of nurses in a headache clinic.

**Methods**

A total of 32 cases of migraine and tension-type headaches were investigated in the present study. We recorded the interviews from the clinical examination between doctor and patient. The time was from 4 to 15 min, with a mean time of 5.5 ± 3.5 min. The qualitative analysis was then performed.

**Results**

Not a few patients’ findings could be skilfully communicated. When the doctor picked up such findings, the quality was greatly appreciated, especially for new patients. And in repeated patients, good advice for medical self-control also showed high quality.

**Conclusion**

From these interviews between doctor and patient, the nurse should tune in to the high-quality communications, and provide due support for patients in this regard, understanding this concept of chronic disease over the long term.

**Keywords:** headache clinic, nursing, qualitative analysis of interview
H074
The natural history of primary headaches in elderly: a clinically based prospective study

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Background Although it is thought that the prevalence of headache decreases with ageing, it has been seen that this decrease is not obvious as perceived in recent studies.

Objective To analyse the natural history of headache in elderly patients who had been followed in our headache department.

Methods Three hundred and forty-two patients were studied. Headache features were assessed with headache diaries. The natural history analyses were supported with regression and survival analyses as with descriptive statistics.

Results Among 342 patients, 257 (75.4%) were women, 84 (24.6%) were men with a mean age of 70.04 ± 4.97 years. According to the IHS-II criteria, 291 patients (85.3%) were diagnosed as primary headache and 50 patients (14.7%) were diagnosed as secondary headaches. Mean follow-up time was 14.9 ± 15.1 months (3–67 months). It has been seen that the patients with chronic tension-type headache accompanying another medical state had poor response to the treatment.

Conclusions In this study, the importance of detailed history in distinguishing the primary and secondary headaches from each other in elderly patients was emphasized. It has been seen that the treatment is quite difficult in primary headaches, especially accompanying another medical state or analgesic overuse.

Keywords: headache, ageing, elderly, natural history, chronic tension type headache

H075
Headache in patients with COPD; effects of chronic hypoxaemia

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Background The frequency and characteristics of headache in patients with chronic obstructive pulmonary disease (COPD) are clear and there are only a few studies which have assessed the relationship between chronic hypoxaemia and headache.

Objective To evaluate the frequency and characteristics of headache in COPD patients.

Methods In total 119 patients, with a mean age of 63.4 ± 8.2 years, diagnosed with moderate or severe stable COPD, were included in this study. The mean disease duration was 9.5 ± 7.9 years and they commonly reported a smoking history. All subjects underwent detailed clinical and laboratory examinations in order to evaluate headache subtypes and comorbid conditions.

Results Of all study patients, 35.6% reported headache with a frequently chronic tension-type headache, hynic headache, and idiopathic stabbing headache diagnosis. Only 17% of the study groups were female and 50% of them reported headache. Patients with reported headache commonly had some symptom of sleep disorders, especially obstructive sleep apnoea syndrome and restless leg syndrome.

Conclusion Possibly being a specific subtype of elderly headache, headache in patients with moderate or severe COPD was a common problem and they merit future studies to obtain more knowledge about their pathophysiological and clinical basis.

Keywords: chronic obstructive pulmonary disease, headache, chronic hypoxaemia, sleep disorders, sleep apnoea syndrome

H076
A 6-month longitudinal study of migraineurs treated at a Specialist Headache Clinic in Singapore: clinical outcomes and patient satisfaction

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Background A previous prospective study by Siow et al. demonstrated improved clinical outcomes and satisfaction for migraineurs treated at a headache clinic for 3 months. The same cohort (still under specialist care) was re-evaluated at 6 months to determine if the results were sustained.

Method Data were collected via telephone interview with the same questionnaire used at 3 months.

Results At 6 months, 54.5% of patients felt ‘somewhat better’, compared with 73.7% at 3 months and 42.9% when treated by community physicians (at study entry). Treatment satisfaction rate was higher (78.8%) than at entry (62.8%). SF-36 individual parameter scores were better than or comparable to 3 months, and better than at entry. Composite scores were both higher (PCS = 47.7; MCS = 49.2) than at 3 months (PCS = 47.7; MCS = 46.9) and at entry. The mean MIDAS was 5.1, compared with 4.9 at 3 months and 31.6 at entry. The mean headache days in the last 3-month period (16.5) was comparable to 3 months (14), but lower than at entry (35).

Conclusion This longitudinal study shows that positive clinical outcomes and satisfaction are maintained when migraineurs are treated by headache specialists in the Singapore context.

H077
The influence of the assessment of more than one type of headache on the overall prevalence of migraine and tension-type headache in a population study

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Objective Little is known about the frequency of headache, migraine or tension-type headache in the general population in Germany. Aim of this study was to assess the prevalence of different types of headache according to their single or
combined occurrence and to evaluate the influence of the latter on the overall prevalence.

**Methods** Between September 2003 and July 2004 the Dortmund Health Study recruited 1312 participants for personal interviews in Dortmund, Germany. Participants were randomly selected from the city registration office and were between 25 and 75 years of age. The new criteria (1) of the International Headache Society (IHS) were applied to classify the type of headache and sociodemographic variables and risk factors assessed.

**Results** The 12-month headache prevalence among the 1312 study participants was 52.8%. In 8.7% of the participants headache was classified as migraine, in 11.1% as tension-type headache and in 0.9% as medication-induced headache. Prevalence of all types of headache was significantly higher in women than in men. 14.4% of the study participants reported to have more than one type of headache. The type-specific prevalences of the second headache were 0.08% for migraine, 4.5% for tension-type headache and 0.15% for medication-induced headache.

**Conclusion** Correcting the overall prevalences for the frequency of the second headache type only slightly changed the prevalence for migraine, but increased the 12-month prevalences of tension-type headache relatively by 40% and of medication-induced headache by 16%.

**Keywords**: headache, migraine, tension-type headache, prevalence

**Acknowledgements**

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**Reference**


H079

Clinical analysis of idiopathic thunderclap headache

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**Objective** The aim of the study is to clarify the clinical features of idiopathic thunderclap headache.

**Methods** We analysed backgrounds and clinical symptoms of 37 patients with idiopathic thunderclap headache (44.6 ± 17.6 years old; mean ± SD) during past 3 years that did not show any abnormalities in CT scanning and lumbar puncture. They were divided into III groups based on characteristic of headache; non-pulsating (N) group (11 cases), pulsating (P) group (14 cases) and exploding (E) group (12 cases). Their clinical features were compared among three groups.

**Results** (1) The gender ratio (female: male) was 7 : 4 in group N, 9 : 5 in group P and 11 : 1 in group E. (2) Duration was 2.3 ± 1.2, 2.9 ± 2.1, 4.7 ± 3.3 days, respectively. It was significantly longer in group E compared with group N (P < 0.05). (3) Attacks of headache during sleep were seen in one case (9%) of group N, 0 case (0%) of group P and four cases (33%) of group E.

**Conclusion** In exploding group, the ratio of female to male was higher, duration was longer, and frequency of headache attacks during sleep was higher than the other two groups.

**Keywords**: thunderclap headache, non-pulsating headache, pulsating headache, exploding headache

H080

Cephalalgia phobia: a new specific phobia of illness

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**Background** Migraine comorbidity is one of the main issues in migraine management. Psychiatric comorbidity is very common in chronic migraine (CM) and medication overuse. Anxiety and mood disorders are the most important diagnosis. Phobias are common in migraine patients, found in up to 50% of chronic migraineurs. Specific phobia of illness makes
its appearance in DSM-IV as a new diagnostic subtype, separate from hypochondriasis. Illness phobia appears to be a significant problem; it is prevalent in the general population and is associated with distress and impairment, including interference with medical care. Headache or migraine phobia has never been described.

**Objective**
To describe a new type of specific phobia of illness: cephalalgiaiphobia.

**Methods/results**
We describe 10 migraine patients with a particular phobic behaviour related to their headache attacks, characterized as a specific phobia of illness, coined cephalalgiaiphobia. Patients presented either phobia of a headache attack during a pain-free state or phobia of worsening the headache when having a mild headache. Patients overused acute medication because of the phobic behaviour.

**Conclusion**
Cephalalgiaiphobia is a new specific phobia of illness, possibly linked to acute medication overdose headache. Further studies are necessary to evaluate its epidemiology and clinical implications.

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**H081**

Some clinical phenomena suggestive for migraine and its diagnostic value: analysis of 88 cases

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**Objective**
To study additional phenomena (AP) and their role in the differential diagnosis between probable migraine (PM) and tension-type headache (TTH).

**Methods**
We studied some clinical phenomena such as familial antecedents of headache, disease onset in the second decade of life, preferring a recumbent position during the attack, etc., which were traditionally considered more suggestive for migraine. We have compared the frequency of these phenomena in three groups of patients: 60 patients with certain headache (CM), 18 with PM, 27 with TTH.

**Results**
Familial antecedents of migraine were observed 3.6 times more frequently in patients with CM and 1.4 times more frequently in patients with PM vs. TTH. Onset of disease in the second decade of life, the preferred recumbent position during the attack were seen twice as often in patients with CM and 1.2 times in patients with PM. The average number of AP is 4.25 for CM, 2.5 for PM and 2.0 for TTH. In both groups of patients with migraine the results were statistically significantly different from those with TTH.

**Conclusions**
In probable migraine cases and especially in difficult differential diagnosis between migraine and TTH, the use of additional criteria may be of great diagnostic value.

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**H082**

The headache and sleep diary

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**Background**
Headaches and sleep disorders are related in several ways. Sleep disorders can cause headaches, and headaches can cause sleep disruption. Headaches and sleep disorders may be part of the same syndrome or have a common secondary cause. Collecting prospective data is critical for the management of both disorders. A combined headache and sleep diary would ideally be the best tool for those patients.

**Objectives**
To propose a headache and sleep diary for clinical practice and reasearch.

**Methods/results**
Sleep variables were inserted into a headache diary model. Columns containing date, hours (24 columns, one for each hour), medication, total sleep time, time to sleep onset, are crossed with rows (one for each day). Patients are instructed to fill out the hour column with a x to xxxxx symbol, according to the headache intensity. Time patient goes to bed, falls asleep, and awakes are marked in the specific hour column (00:00 h format).

**Conclusion**
The headache and sleep diary is an excellent tool for following up patients with headache and sleep disorders. It can also be used for clinical trials looking at the effect of sleep medications in headaches, and headache prevents in sleep variables.

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**H083**

Chronic migraine: the frequency of cutaneous allodynia

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**Objective**
To study the clinical manifestations and frequency of cutaneous cephalic and extracephalic allodynia in patients with chronic migraine (CM) vs. patients with episodic migraine (EM).

**Methods**
We studied 37 patients with migraine: 19 with CM and 18 with EM, accordingly the IHS criteria (2004). A special original questionnaire for cutaneous allodynia (CA) assessment was performed.

**Results**
Manifestations of CA such as unpleasant sensation or pain during the following activities: combing the hair, make up, shaving, wearing a tie or jewels around the neck or taking a shower with the water falling above during or right before a headache attack have been described more frequently in cases of CM vs. EM (49% vs. 16%). CA was located mostly on dermatomes V1, V2 and C3–C4. Cutaneous extracephalic allodynia has been noted in nine patients with CM: 4 on superior limbs, 4 on the trunk, 1 on inferior limbs.

**Conclusions**
Cephalic CA is more frequent among patients with CM, extracephalic allodynia being observed only among them, which is suggestive for its relationship with pathogenic mechanisms of central sensitization. CA could be a marker of an eventual drug resistance in abortive migraine attack treatment.
Temporal arteritis with reversible proptosis: a case report

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Background Temporal arteritis is more common among people of Northern Europe than African-Americans, and is rare in Asians. However, there are various clinical presentations, especially for Asians. Here, we report a case of TA with persistent visual impairment, ophthalmoplegia and rarely reversible proptosis.

Objective To report a rare clinical picture of TA.

Methods To make differential diagnosis and check ESR, brain MRI, biopsy of temporal artery.

Results A 74-year-old male with underlying diabetes and hypertension developed a new, subacute onset headache, which interrupted his daily activity for 1 month and was of a progressive course. The persistent headache localized over bilateral temporal and occipital area. Besides, he also suffered from visual impairment, ipsilateral proptosis, right temporal scalp tenderness at the same time. Erythrocyte sedimentation rate (ESR) was 140. Brain MRI study excluded the space-occupying lesion. Temporal artery biopsy disclosed findings consistent with temporal arteritis. Pulse therapy of steroid was prescribed, and proptosis subsided. However, visual impairment and ophthalmoplegia remained unchanged.

Conclusion Temporal arteritis presents with different ocular symptoms, including double vision, intermittent blurred vision and complete vision loss. This was an unusual case of TA because the manifested ocular sign was reversible proptosis, and the steroid may be an effective therapy in this setting.

Keywords: temporal arteritis, ophthalmoplegia, reversible proptosis

Hypnic headache: an actigraphic and polysomnographic study

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Background Hypnic Headache (HH) is a primary headache characterized by a close relation to sleep. HH is a rare disorder. Polysomnographic studies report contrasting findings; most authors describe a close association with REM sleep.

Objective To study sleep pattern (macro- and microstructure of sleep) in patients with HH.

Methods We studied three patients, two women and a man, fulfilling the criteria for HH. Each patient underwent a sleep study including actigraphy and three polysomnographic recordings, before and after treatment.

Results Actigraphy revealed that motor activity during sleep was reduced during the nights with headache episodes compared with the nights without attacks. Polysomnographic studies showed that the headache episodes occurred during REM sleep; the amount of REM sleep was below normal values, and increased after pharmacological treatment. Sleep microstructure analysis, performed according to the Cyclic Alternating Pattern model, showed an increase in sleep instability after the treatment of the headache attacks. Sporadic obstructive apnoeas and hypopnoeas were observed; these events could trigger headache attacks, even though we observed a striking clinical improvement following drug treatment without any modification of the respiratory pattern.

Conclusion Our data support the hypothesis of hypoarousal as a pathogenetic mechanism for hypnic headache.

Accuracy of web-based information related to headache

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Purpose To determine the relation between credibility features and content accuracy of websites that provided information on headache health topics.

Methods Websites were identified by searching (meta)search engines. We selected English language websites. We assessed the credibility features of the websites: evidence hierarchy, source and currency as well as accuracy of contents. Relation between features of website credibility and level of accuracy of contents was expressed by cross tabulation. The strength of association was assessed with Kendall’s rank correlation, which adjusts for tied ranks in the data. Confidence intervals (CI) and significance levels were calculated for α = 0.0025.

Results In selected cases, 50% (CI 29.9, 70.1) websites described currency, 55% (CI 34.2, 74.2) source and 25% (CI 11.2, 46.9) evidence of hierarchy. Kendall’s rank correlations were 0.13, 0.20, and 0.19 for the source, currency, and evidence hierarchy, respectively, without significance level.

Conclusions Features of website credibility have moderate correlation with accuracy of information in headache health topics. Websites with description of credibility features tended to have higher levels of accuracy of contents, but this relationship was not strong. Thus, apparently credible websites may not necessarily provide higher levels of accurate health information.

Keywords: internet, headache, information, accuracy

Factors contributing to headache-related disability in chronic tension-type headache

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Objective To evaluate the impact of headache variables, such as frequency, intensity, duration of attack episode and demographics on functional disability in chronic tension-type headache patients (CTTH).

Background Reduction of headache-related disability is one of the main treatment goals in the management of headaches. Therefore, it is essential to understand which headache characteristics contribute to headache-related disability.
Methods Data from patients with chronic tension-type headache (n = 109) were used to evaluate the relationship between headache variables and headache-related functional disability. The patients were divided into different groups based on each variable. Headache-related functional disability was assessed as scores on the activity interference scale of three aspects of daily living and missing days due to headache.

Results In this study, higher average pain intensity was significantly associated with more severe headache-related disability. Although there was a tendency for patients with the higher frequency, longer duration attack of headache to show severe disability, this was not statistically significant. Multiple regression analysis revealed that average pain intensity is only significant predictor of headache-related disability.

Conclusions For chronic tension-type headache, headache intensity appears to be a major determinant of headache-related disability. According to our findings, headache attacks with severe intensity should not be underestimated and controlled before they reach high intensity to reduce headache-related disability even if they are infrequent.

Keywords: chronic tension-type headache, pain intensity, frequency, disability

**H088**

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 no 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 a 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.

Conclusion FAME is a useful tool to choose the most suitable triptan formulation, although we have not yet finished all of our trials. We expect FAME can contribute to early intervention of triptan and improvement of QOL of migraine patients.

Keywords: triptan, patient satisfaction, formulation, supporting tool

**H089**

Migraine aura without headache: diagnosis and treatment

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Background Migraine aura without headache is sometimes misdiagnosed as visual hallucination or psychiatric events because of the absence of headache. We recently experienced three patients with migraine aura without headache.

Objective To show what kind of scenery they see and to suggest the potential therapeutic medication.

Results Suddenly the lightening small object appears in the patient’s visual field between the object and the eye. The lightening object becomes bigger as time passes and becomes like lightening or scintillation which occupies the patient’s visual field. Finally, these phenomena disappear from the patient’s visual field about 10–15 min after onset. We tried to prescribe the lomerizine hydrochloride 10 mg/day in one of three patients and the drug was effective in ameliorating the attack. The remaining patients do not want to take the medication.

Conclusion Migraine aura without headache is a unique entity of migraine headache and romeridine hydrochloride is a useful therapeutic medication for these patients.

Keywords: migraine aura, diagnosis, treatment

**H090**

Headache in orthopaedic clinic

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Background It is well known that headache is one of the most important complications of orthopaedic disorders and traumatic injuries. However, there are few reports concerning headache subtypes. We investigated out-patients in an orthopaedic clinic in order to evaluate the subtypes of headache.

Objective and methods Patients who complained of headache and were referred to neurologists were prospectively registered from April 2004 to February 2005. Medical records of the patients were reviewed, and the subtypes of headache were classified according to ICHD-II.

Results 71 patients (29 males, 50 ± 20 years) were included in this study. Tension-type headache was the most frequent (37 cases 52%). Eight patients (11%) had migraine. Five patients (7%) were classified as headache attributable to cranial or cervical vascular disorders. All five patients were diagnosed to have vertebral artery dissection (three definite cases and two probable cases). Subarachnoid haemorrhage was not noted in these cases. Liquorrhoeic headache was found only in one case (1%) in this series.

Conclusion Major headache in patients who visit the orthopaedic clinic appears to be tension-type. Attention, however, should be paid to the fact that headache may be attributable to vertebral artery dissection in some cases.
Keywords: orthopaedic clinic, headache, subtypes, vertebral artery, arterial dissection

H091

The frequency of cerebral artery dissection in ischaemic stroke; a single study in a university hospital

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Background Cerebral artery dissection is one of the causes of ischaemic stroke and headache.

Objective We investigated frequency of cerebral artery dissection (CAD) in all patients with acute ischaemic stroke, and we compared the characteristics of CAD with other types of ischaemic stroke.

Methods We retrospectively collected the cases of ischaemic stroke admitted to our institute from January 2001 to December 2004. We examined frequency of CAD, headache, Wallenberg syndrome, cardiovascular risk factors such as hypertension, hyperlipidaemia, diabetes mellitus from medical records.

Results CAD was detected in nine of 537 total patients (1.68%). The mean age of CAD patients (54.2 ± 15.1 years) was significantly younger than the other patients (69.5 ± 11.5 years). In risk factor there was no difference in both groups. Seven of nine CAD patients had headache and four of nine had Wallenberg syndrome. The site of arterial dissection were vertebral artery (five patients), vertebrobasilar artery (one patient), basilar artery (one patient), internal carotid artery (one patient), and posterior cerebral artery (one patient).

Conclusion In this study from a single institution, a characteristic of CAD is more frequent in younger age and in posterior circulation.

Keywords: headache, cerebral artery dissection, ischaemic stroke, posterior circulation

H092

Triptan is effective for migraine with aura headache associated with moyamoya disease: two case reports

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Patient 1. A 32-year-old woman had a 14-year history of migraine with aura. Usually headache was preceded by fortification spectrum. Her neurological examination was normal. Brain CT was normal. She was diagnosed as suffering from typical aura with migraine headache. Her headache reacted well to the treatment with eletriptan. MRI of the brain showed no abnormality, but MRA showed severe right-sided narrowing of the internal carotid artery in the supraclinoid portion and extensive parenchymal vascular collaterals. She was diagnosed as having moyamoya disease.

Patient 2. A 30-year-old woman was seen presenting with a 2-month history of severe migraine-like headache that occurred every 2 weeks and was preceded by scotoma. She had past history of migraine from 7 years old. Zolmitriptan was effective in her headache. MRI of the brain was normal, but MRA showed vascular occlusions in the supraclinoid portion of right side internal carotid artery, which were consistent with the diagnosis of moyamoya disease.

Conclusion The physician treating patients with migraine is now able to choose from some triptans. In any case of typical aura with migraine headache, a detailed investigation should be kept in mind to detect an underlying vascular disease such as moyamoya disease.

Keywords: moyamoya disease, triptan, cerebrovascular disease

H093

Migraine disability awareness campaign in Asia: Migraine Assessment for Prophylaxis (MAP)

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Objective A multinational survey of the headache diagnoses and consequences in Asia among out-patients attending neurological services.

Methods This survey recruited patients who consulted neurologists for the first time with a chief complaint of headache. Patients suffering from headache ≥15 days/month were excluded. Patients answered a self-administered questionnaire, and their physicians independently completed another questionnaire.

Results Preliminary results are available from 546 patients (384 F/162 M; mean age 40.0 ± 15.0 years). On average, they had 4.2 severe headaches/month, and 51.5% of them missed school, work or household chores. Migraine was diagnosed in 38.5% prior to the consultation. From the physicians’ survey, 57.3% of the patients were diagnosed to have migraine. Most (77.8%) of the patients were taking medications for acute headache treatment; among them, 12.9% overused medications. Emergency room attendance was used in 22.4% of the patients. Only 14.3% were on prophylactic medications. Among patients not on prophylactic treatment, the neurologists would recommend pharmacological prophylaxis in 48.0% of them.

Conclusions The study is on-going and targets at 6000 patients in Asia. The preliminary results show that migraine is the most common headache diagnosis in neurological services. A majority of the patients have migraine-related disability. Migraine remains under-diagnosed and under-treated in this region.

Keywords: migraine, neurological clinic, prevalence, prophylaxis, disability
A self reporting questionnaire on the burden of migraine (BURMIG): development, reliability and validity

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Background In Europe pronounced cultural and linguistic differences exist. There are few questionnaires validated for different languages to measure the individual and socioeconomic impact of migraine in different linguistic groups.

Objective To validate a self-reporting questionnaire on the impact of migraine in patients in French, Portuguese, German and English.

Methods The questionnaire obtains information on different aspects of headache (diagnosis, treatment, satisfaction), social impact and comorbidity, partly using questions from validated tools, such as ID-migraine, WHODAS, MIDAS and PF19. All unvalidated questions were translated using a forward-backward method with to different translators. Face-, content- and language-validity, test–retest-reliability, and internal consistency were assessed.

Results 130 subjects filled in the questionnaire and 91 filled in the same questionnaire a second time at 1-month intervals. In the test–retest analysis, the κ coefficient for qualitative questions was 0.6–1.0, the intraclass correlation coefficient for quantitative answers was 0.7–1.0. The Cronbach’s α of already validated tools was 0.26 (ID-migraine) and between 0.74 and 0.91 for other questions from validated tools.

Conclusion Reliability and consistency of the new questionnaire are comparable to previous questionnaires, resulting in a validated tool in four languages to evaluate the impact of migraine on the individual sufferer and on society.

Keywords: migraine, questionnaire, burden, validation, multilingual

Impact of an educational intervention on care of patients with migraine headache: pilot testing an innovative measurement instrument

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Background The American Headache Society (AHS) has developed a continuing medical education (CME) programme for providers managing headache patients. Measuring outcomes of CMEs is challenging. Traditional measurement approaches have questionable validity, and limited ability to assess effect on patient care.

Objective Our objective was to assess the feasibility of an innovative approach using a standardized patient (SP) to measure the impact of the AHS-CME on patient care.

Methods We compared performance of eight CME attendees and eight non-attendees, through an unannounced SP visit, who portrayed a typical migraine case, and competed a checklist, satisfaction survey, and submitted all prescriptions after the visit.

Results 50% of invited physicians (n = 32) consented to an SP visit. The attendees: exhibited better history-taking skills, managed patients more appropriately, communicated better with the patient, had better patient satisfaction, and required less time.

Conclusion The SP instrument had construct validity, was acceptable, and could be utilized despite practical barriers. However, it was expensive, labour-intensive, and entailed volunteer bias. Considering the resources spent on CMEs, their outcomes should be evaluated regarding the impact they have on patient care. Our study demonstrates that the SP instrument can be utilized as a valid evaluation instrument.

Keywords: headache, migraine, CME, outcomes, standardized patient

Headache in multiple sclerosis—pilot study

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Background To investigate headache in multiple sclerosis (MS).

Objective To investigate primary headaches fulfilling International Headache Society (IHS) criteria in patient with definitive diagnosis of MS fulfilling McDonald criteria.

Methods 55 patients (41 women, 14 men), mean age 36 years (standard deviation 6.3; median age 36) with definitive diagnosis of MS (mean EDSS 2.5) were included in the trial. 37 patients were treated with interferon beta or copaxone together with other immunosuppressive therapy (prednisone, methylprednisolone, azathioprine), 18 patients were treated only with other immunosuppressive therapy (prednisone, methylprednisolone, azathioprine). 4 patients had secondary progressive MS (SPMS) and 5 patients had relapsing–remitting MS (RRMS).

Results Primary efficacy outcome included type of headache, start of headache, headache severity and MIDAS. 34% patients had headache. 16 patients suffered from migraine without aura, three patients had migraine with aura, six patients had tension-type headache, six patients had chronic migraine and three patients had combination of migraine and tension-type headache. Average of headache/patient/month was 4.1, average of headache severity/patient/month was 1.1. Mean of MIDAS score was 1.4. Headache began before diagnosis of MS in 26 patients.

Conclusion This pilot study demonstrated that headache is a common diagnosis in MS. Start of headache is more often before diagnosis of MS.

Keywords: headache, migraine, multiple sclerosis
Valproate withdrawal migraine, seizures have gone and headache starts

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Background There have been considerable clinical insights into the migraine–epilepsy relationship over the past years. In addition, valproate is effective to treat both migraine and epilepsy. The migraine attacks after discontinuing valproate have not well been documented.

Objective To report the valproate withdrawal migraine.

Methods Case study of three patients.

Results Three patients were identified who developed migraine attacks after discontinuing the valproate therapy for their epilepsy. Patient 1: she was a 26-year-old woman who has had generalized tonic clonic seizures. After the seizure-free period of 14 years, valproate was discontinued. In 2 weeks, she started to have migraine attacks. Patient 2: she had several febrile seizures at the age of 3. She developed absence seizures at the age of 10, and valproate was started. After the 5-year seizure-free period, valproate was discontinued to find that she has migraine attacks. Patient 3: she was a 25-year-old woman whose medication was switched from valproate to carbamazepine for poor control of her secondary generalized seizures. After switching the medication, her seizures had been completely eliminated but she started to have frequent migraine attacks.

Conclusion Withdrawal of the valproate treatment can precipitate migraine attacks even after the long seizure-free period in patients with epilepsy.

Keywords: migraine, valproate, epilepsy, seizure

Migraine-QUEST to screen non-treated headache patients effectively in daily medical practice

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Objective The objective of this study was to develop and evaluate Migraine-QUEST tool, which can screen non-treated headache patients (migraine/tension-type headache) who need appropriate treatment through the daily medical practice of primary care physicians.

Methods This study was conducted in out-patients aged from 16 to 60 to assess the usefulness of Migraine-QUEST for primary care physicians as the screening tool of headache treatment.

Results In this study, 117 patients among 649 patients visiting six GPs were identified as severe headache patients who needed appropriate treatment. The consistency rate between Migraine-QUEST screening results and definite diagnoses by the physicians was 86% for migraine and 92% for tension-type headache, respectively. Also, the evaluation of Migraine-QUEST was high among all physicians as a tool to screen non-treated headache patients who need appropriate treatment.

Conclusion Based on the results, it is proved that Migraine-QUEST can effectively detect non-treated migraine/tension-type headache patients who need appropriate treatment through their secondary complaints as part of holistic medicine. Thus, it can contribute to the improvement of headache treatment if this tool is widely used among primary care physicians.

Keywords: Migraine-QUEST, non-treated headache patients, migraine, tension-type headache, screening tool, headache treatments

A case of SUNCT syndrome successfully treated with intravenous lidocaine

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Introduction SUNCT syndrome is a short-lasting unilateral neuralgiform headache attack with conjunctival injection and tearing. In this report, we describe a patient with SUNCT syndrome whose pain was successfully treated with intravenous lidocaine.

Patient A 56-year-old male patient presented with a chief complaint of burning pain in the right fronto-temporal region. He had a past history of trigeminal neuralgia and traumatic epidural haematoma. Pain attacks lasted several tens of seconds and occurred at intervals of 1–5 min. These attacks were accompanied by autonomic symptoms of conjunctival injection, tearing, nasal secretion and miosis, and tended to be induced by movement such as standing, walking and mastication. His referring physician performed stellate ganglion block and provided treatment with oral carbamazepine. Because of the lack of pain relief, the patient was referred to our hospital.

Treatment We provided nerve block therapy including stellate ganglion block, supraorbital nerve block, auriculotemporal nerve block, and trigger point block without symptomatic improvement. Pharmacotherapy consisted of four different oral triptan formulations (suma, nara, riza, zolomi), sumatriptan injection (i.m.), carbamazepine, amitriptyline, indomethacin, baclofen and prednisolone. Oxygen inhalation was added to these therapies, none of which showed satisfactory efficacy. Previously, we had successfully used intravenous lidocaine to treat migraine, cluster headache and trigeminal neuralgia. This patient also responded to intravenous infusion of lidocaine with pain relief.

Conclusions This case suggests that intravenous administration of lidocaine may be effective for the treatment of SUNCT syndrome refractory to multiple treatments.
H101
Which headache lets company workers visit a company doctor?

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Background and objective Although a big company has a clinic in the office, most company workers with primary headache do not consult company medical staff for headache. This study presents which headache types cause workers to visit a company doctor.

Method Diagnosis of headache was based on the 2004 IHS criteria.

Results In 1 year, 100 patients visited the company doctors because of headache during their working time. Among 100 patients, 51 had migraine, eight had migraine and tension-type headache, 17 had tension-type headache, one had cluster headache and 12 had C2 neuralgia. 71 patients visited the doctors during headache. Among 71 patients, 35 visited during their migraine attacks, seven had chronic tension-type headache, seven during episodic tension-type headache and 11 with C2 neuralgia. Of 29 patients visiting the doctors during the interictal period, 18 suffered from migraine, four had migraine and tension-type headache, one had chronic tension-type headache and one had cluster headache.

Conclusion This study suggests that if company workers have a headache during working time, they visit a company doctor, and a half of these headaches will be migraine.

Keywords: company workers, company doctor, primary headache

H102
Migraine and weather in eastern Austria: a diary study in 327 patients

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Background Weather is frequently related to migraine, but prospective studies are sparse.

Objectives To evaluate the relation between headache, objective meteorological parameters and individual weather perception in migraineurs.

Methods A total of 327 patients with migraine (86.5% females) filled in a comprehensive diary for 3 months. Statistical analysis comprised 29 objective and five subjective meteorological parameters. We applied univariate and stepwise multivariate Cox regression analyses to evaluate the influence of the objective parameters on the risk of headache and we calculated separate logistic regression analyses to elucidate the relation between the objective parameters and the patients’ perception.

Results The risk of headache was increased by a ridge of high pressure (RHP, hazard ratio 1.19, \( P = 0.014 \)) and decreased by a weak pressure gradient (WPG, hazard ratio 0.76, \( P = 0.009 \)) as well as by a maximum atmospheric pressure > 1000.1 hPa (hazard ratio 0.92, \( P = 0.01 \)). During RHP the patients’ perception of too warm weather and annoying sun glare was increased, whereas during WPG the perception of annoying weather conditions was decreased.

Conclusion The risk of migraine may be increased as well as decreased by certain weather conditions. The patients’ subjective perception agrees at least in part with objective meteorological parameters.

Keywords: migraine, weather, objective meteorological parameters, subjective perception

H103
Migraine recurrence after treatment with oral sumatriptan is not related with anxiety or depression

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Objectives Since mood disorders have been recognized as migraine exaggerating factors, we aimed to explore the plausible causative relation of anxiety and depression symptoms with migraine recurrence.

Methods 160 migraineurs were randomized to either sumatriptan (50 mg orally) or placebo in a double-blind, cross-over design to treat six migraine attacks. The mean outcome measure was recurrence ratio in relation to scores of Hamilton rating scales for both anxiety and depression. Secondary measurements included scales for functioning and general health (SCL 90R). Statistical analysis was based on an intension-to-treat design.

Results A total of 131 randomized patients completed the study protocol (18 males and 113 females, mean age 39.6 ± 10.1 years) and 739 migraine attacks were treated. Sumatriptan 50 mg showed a 2-h pain free ratio of 44.9% vs. 30% for placebo (\( P < 0.001 \)). The recurrence ratio was 13% and 13.6%, respectively. Migraine recurrence was not correlated with the Hamilton rating scale scores for anxiety and depression, nor with the SCL 90R scores.

Conclusion Migraine recurrence after treatment with oral sumatriptan is not related to anxiety or depression symptoms.

Keywords: migraine recurrence, sumatriptan, anxiety, depression

H104
Migraine occurring in the work environment

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Background Migraine attacks in workplaces reduce productivity and increase indirect costs. Little is known about how employees spontaneously treat migraine attacks at work.

Objective To address migraine occurring during work activities.

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Methods Voluntees suffering from 1988 IHS migraine from six different work environments were invited to participate and fulfilled headache diaries during 60 days. Data on clinical and therapeutic aspects were collected and analysed.

Results A total of 59 patients recorded 243 attacks. Considering intensity, 30.7% were mild, 40.7% moderate, 21.6% intense and 7.1% excruciating. Only 69.7% of the attacks were treated, which lasted 7.56 ± 8.9 h. OTC medication was largely preferred. Only two individuals took sumatriptan. No patient was under prophylactic treatment. The average time from headache onset to medication was 03.35 h. Moderate pain was treated relatively earlier, after 02.77 h. Attacks with highest intensity were not treated earlier (03.71 h). Seventy attacks were treated within 1 h. Among patients who did not improve, 11.7% took medicines within 1 h, in contrast with 88.3% that improve ($P = 0.07$). The time required for improvement following medication was 02.58 h.

Conclusion Workers do not treat migraine adequately. Educational campaigns in different companies may reduce headache, improve productivity and help reducing costs.

Keywords: migraine, burden, treatment, productivity

H105

The associations Helicobacter pylori infection and migraine
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Background Previous studies have reported a high prevalence of *Helicobacter pylori* (HP) infection in patients with migraine.

Objective The purpose of this study is to investigate whether HP infection is strongly associated with migraine.

Methods We compared the prevalence of HP infection in 17 patients with migraine (two males, 15 females; mean age 38.4 ± 6.25 years) with that in 50 age-matched patients (20 males, 30 females; mean age 38.4 ± 6.25 years) and 123 patients not age matched (65 males, 58 females; mean age 56.8 ± 16.0 years) with gastrointestinal symptoms, and with that in asymptomatic patients reported in Japan. HP infection was diagnosed by 13C-urea breath test.

Results HP infection was recognized in 10 (58.8%) among patients with migraine, in 34 (68.0%) among age-matched patients, and in 102 (82.9%) among patients not age matched. The prevalence in patients with migraine was higher than that in asymptomatic patients but was significantly lower than in patients not age matched ($P < 0.05$). There were no significant differences between patients with migraine and age-matched ones with gastrointestinal symptoms.

Conclusion This study suggested that HP infection might be associated with migraine and the prevalence rate in patients with migraine was similar to that in age-matched patients with gastrointestinal symptoms.

Keywords: *Helicobacter pylori* infection, migraine, prevalence

H106

Carotidynia: always secondary to organic lesions?
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Background Carotidynia is described as neck pain with tenderness to palpation over the carotid bifurcation. There are some doubts about its existence as a primary headache.

Case report A 32-year-old woman, with no previous medical problems, developed a rapidly progressive right anterolateral continuum throbbing neck pain, which irradiated to the ipsilateral hemibrainum. The pain worsened with cervical palpation, hyperextension and swallowing. CT scan and two MRIs were performed and were unremarkable. A third high resolution (3 T) MRI was performed the 15th day and revealed a small dissection of the right internal carotid artery. The control MRI performed 1 month later was normal.

Discussion Controversy exists whether to consider carotidynia as an independent entity or a symptom associated with different pathologies in the carotid region. Because of this, carotidynia has been removed from the main classification to the appendix of the ICHD. Our patient could be classified as carotidynia on a clinical and neuroimaging base, but a microdissection was found in a 3-T MRI.

Conclusions Carotidynia is a clinical syndrome which is probably always secondary to structural lesions in the carotid and pericarotid area. The diagnosis in many cases depends on an exhaustive neuroimaging study.

H107

Chronic daily headache and medication overuse: comparison between in- and out-patient management
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Introduction Chronic daily headache (CDH) is an invalidating pathology affecting 4–5% of the population. Most patients overuse acute medication.

Objective To compare the efficacy of a detoxification scheme in two populations: a group was hospitalized while the second group was admitted to Day Hospital daily.

Methods We studied two groups, each of 10 patients, affected by CDH with medication overuse, without psychiatric comorbidity or opioid/barbiturate overuse. Patients underwent a 10-day treatment scheme consisting of: withdrawal of the overused drugs and administration of dexamethasone and amitriptyline. Subsequently, drugs were tapered and a prophylactic treatment commenced. Outcome measures were: number of days with headache during treatment, headache index (number of days with headache/total number of days) at 1 and 3 months and analgesic intake in the 3 months following detoxification.

Results Headache index and analgesic intake were significantly lower at follow-up compared with the month before treatment. There were no other 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 CDH with medication overuse, in the absence of conditions requiring hospitalization, is a valid therapeutic option. Hospitalization represents a stressful event for patients; it can be avoided and management costs can be reduced.

H108
ID migraine and migraine score equation for Thais:
preliminary study
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Background We designed a self-administered migraine screener for headache patients to help physicians in approaching the most common headache syndrome efficiently.

Methods A total of 243 patients presenting with headache were enrolled to complete the eight diagnostic screening questions which were designed related to previous 22-item Suandok-Migraine-Questionaires. Clinical diagnosis were made by neurologists following IHS criteria. Factors with P-values < 0.05 were selected and reapplied to SPSSV11.5 programme to get Migraine Score Equation (MSE).

Results Of eight diagnostic screening questions, 5-item subsets per se were female sex (SEX), pulsatile headache, nausea/vomiting: photophobia and improvement with anti-migraine medication. Migraine Score Equation (MSE) with a reliability coefficient of 0.55* was 1.271 (Sex) + 1.586 (pulsatile) + 1.652 (N/V) + 1.932 (Photophobia) + 1.70 (improvement with drug). Score migraine ranged from 1.83 to 8.27 whereas non-migraine score ranged from 0 to 8.27. Mean score for migraine was 6.57, SD = 1.70, whereas mean for non-migraine was 2.7, SD = 1.84. Cut point for migraine was more than 4 (sensitivity = 90.0%, specificity = 75.3%).

Conclusion ID Migraine screening questions have been designed to develop Migraine Score Equation to help primary physician in migraine diagnosis.

Keywords: Suandok Migraine Score, Migraine Score Equation, Headache Questionnaire, International Headache Society (IHS) criteria, migraine, tension-type headache

*The P-value was calculated by paired t-test. The reliability coefficient was calculated by α (Cronbach) model.

H109
Correlation between migraine disability assessment (MIDAS) questionnaire and headache diary; the experience from double-blind, randomized, placebo-controlled trial
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Background MIDAS questionnaire is a brief, self-administered questionnaire, designed to quantify headache-related disability over a 3-month period; nevertheless, use of MIDAS questionnaire in randomized controlled trial still needs to be validated.

Methods We validated the pre- and post-treatment MIDAS questionnaires with patient diary by using the database from DIMWAP (Dysport in migraine without aura prophylaxis) study.

Results Of a total of 128 patients, there were 121 who completed the MIDAS questionnaires and patient’s diary. For duration of headache assessment, pre- and post-treatment number of days from MIDAS questionnaire had relatively low correlation with number of days from patient’s diary (Pearson correlation = 0.313; P = 0.01 and 0.202; P = 0.02, respectively). MIDAS question A had better correlation with number of days from patient’s diary, both pre- and post-treatment (Pearson correlation = 0.437; P < 0.001 and 0.602; P < 0.001, respectively). Pre- and post-treatment MIDAS question B also had low correlation with total intensity score from patient’s diary (Pearson correlation = 0.352; P < 0.001 and 0.385; P < 0.001, respectively).

Conclusions MIDAS questionnaire had low correlation with patient’s diary, whereas patient’s diary was a more sensitive measurement than MIDAS questionnaires in disability assessment in this double-blind, randomized, placebo-controlled trial.

H110
Headaches in multiple sclerosis patients
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Objective To evaluate the occurrence and characteristics (types) of headaches in multiple sclerosis (MS) patients in the early course of the disease and after the initiation of interferons.

Methods Semi-structured questionnaire was answered by 90 patients with clinically definite MS (58 female and 32 male) aged 19–45 years, with EDSS range between 3.0 and 6.5. The diagnosis of primary headaches was made according to IHS criteria.
Results: Fifteen (16.6%) out of 90 patients reported headaches as follows: migraine eight (seven female/one male), tension-type headache five (three female/two male) and one male cluster headache patient. One patient reported headaches as initial symptom. There was no significant occurrence of headache after initiation of interferon.

Conclusion: Migraine was the most common primary headache in our MS patients group (female patients). Only one patient reported headache as initial symptom of the disease.

Keywords: headache, multiple sclerosis

Surgical treatment of trigeminal neuralgia

I001

Usefulness of magnetic resonance cisternography for trigeminal neuralgia surgery

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Background: It is useful that surgeons estimate the location of the V nerve and vessel before the microvascular decompression for the trigeminal neuralgia (TGN). Magnetic resonance (MR) cisternography shows nerves and vessels in a single view, and enables surgeons to suppose the location of the V nerve and the vessel.

Objective: The usefulness of MR cisternography as the preoperative imaging was examined.

Methods: A 62-year-old man underwent the microvascular decompression because of left-sided TGN. Authors examined the findings of this patient’s preoperative MR cisternogram and the intraoperative view.

Results: The preoperative MR cisternogram showed that a vessel touched the left V nerve. A vessel touched the VII/VIII nerve complex in another section. This patient did not suffer from hemifacial spasm. In the surgical view, a small artery touched the left V nerve and the indentation on the V nerve was seen. Another small artery touched the left VII/VIII nerve complex.

Conclusion: The MR cisternography simultaneously shows the location of not only the V nerve and vessel but also the VII/VIII nerve complex and vessel. Such findings provide useful information for safe surgery.

Keywords: MR cisternography, trigeminal neuralgia, preoperative imaging

I002

Trigeminal neuralgia due to vertebrobasilar dolichoectasia (two case reports)

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Aim: Vertebrobasilar dolichoectasia (VBD) is an uncommon vasculopathy of unclear aetiology affecting the arterial wall of vertebral and/or basilar arteries. Trigeminal neuralgia (TN) is occasionally observed associated with VBD. Invasive procedures are contraindicated due to increased morbidity. We report two cases of TN due to VBD to discuss pain control in these specific cases.

Cases: Case 1 was a 68-year-old lady who was diagnosed left V3 TN. Case 2 was a 78-year-old gentleman with right V3 TN. VBD was diagnosed by routine screening with MRI in both patients. They were soon referred to a neurosurgeon for future indication of neurosurgery and gamma-knife. However, the neurosurgeon only suggested contraindication of the operation. In the former case, the patient is currently taking 200 mg of carbamazepine (CBZ). In the latter case, the patient was prescribed CBZ and baclofen, but consequently became resistant to them. He preferred nerve block for pain relief, although gamma-knife was a preferable procedure. V3 block was successfully performed and he currently feels no pain.

Conclusion: Life expectancy for 5 years in patients with VBD is less than patients without VBD. We have to make a difficult decision to treat them. The best resolution for such patients is controversial.

Keywords: vertebrobasilar dolichoectasia, trigeminal neuralgia, nerve block, gamma-knife

Oriental approach to headache

J001

Efficacy of goshuyuto, the representative Kampo (Japanese herbal) medicine for headache, in chronic headache: a responder-limited, randomized, double-blind, placebo-controlled trial

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Objective: We examined the efficacy of goshuyuto, the representative Kampo medicine for headache, in chronic headache.

Methods: This study was conducted in two stages. In the first stage, each patient consumed goshuyuto or the placebo for 4 weeks. Only the patients who responded to the drug went on to the second stage. In the second stage, a randomized, double-blind, placebo-controlled trial was carried out, in which each subject consumed goshuyuto or the placebo for 12 weeks.

Results: Forty-two patients were enrolled in this study. Thirty patients were assessed as responders and 27 of them went on to the second stage. The number of days in which headache episodes were experienced during the last 4 weeks significantly decreased in the goshuyuto group (from 12.9 to 10.3, \( P = 0.01 \)) but not in the placebo group (from 9.5 to 9.1, \( P = 0.72 \)). The number of times the reliever medication was consumed also significantly decreased in the goshuyuto group (from 12.5 to 8.7, \( P = 0.01 \)) but not in the placebo group (from 5.8 to 5.5, \( P = 0.89 \)).

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Conclusion Goshuyuto can be a candidate as a controller of chronic headache. Using this study design, other Kampo medicines are also expected to be evaluated.

Keywords: goshuyuto, Kampo medicine, headache, responder-limited, RCT

J002
Useful method to confirm tender points of primary headache, the corresponding points of Koryo Hand Acupuncture Therapy

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Purpose We can not allot enough time to do physical examination without gain. We need to develop an objective method to decide the location of tender points in patients with headache. We compared corresponding points of Korean Hand Therapy (KHT) with tender points on the head.

Subjects and methods 600 patients with primary headache were included. We used headache questionnaire with special physical examination, we palpated head and middle finger together. We decided the right or left side and sites of one side. On the middle finger we pressed KHT points such as Urinary Bladder and Gallbladder micromeridian using pressure and or roller stimulator.

Results Among 400 migraineurs, 48 had pain-sensitive points on the both sides of head and middle finger, 196 on the right side and 156 on the left side. Among 200 patients with tension-type headache, 67 had sensitive points on the right side along midline from forehead to neck, 105 had sensitive points on the left side and 28 had sensitive points on both sides.

Conclusion We accurately localize the side and sites that trigger primary headache. Migraine headache is considered to relate to Gall Bladder Meridian only or Urinary Bladder Meridian combined, tension-type headache is related to mainly Urinary Bladder Meridian.

J004
Comparison of the effects of tianma Chinese recipes in treating patients with episodic tension-type headache

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Objective To evaluate the clinical effects of five kinds of tianma Chinese herbs products on episodic tension-type headache.

Methods According to the diagnostic criteria of the International Headache Society, 287 patients with episodic tension-type headache were randomly divided into six groups. The patients of five tianma Chinese herb groups were given pure natural tianma capsule, tianmatoufengying, tianmashouwu tablet, tianmaduzhong capsule, and tianma pilula, respectively, for 2 months, while the patients in control group were given naoliqing pilula. The degree of severity, the frequency of attacks and the duration of headache were observed and recorded.

Results 225 patients were administrated tianma Chinese herbs. The total effectiveness rate was 81.8%, which was significantly higher than that of control group, and 41 patients showed no response to tianma Chinese herbs. No adverse reaction was seen in any patients. There is a significant difference among the effects of five tianma Chinese herb products on the symptoms of episodic tension-type headache.

Conclusion Tianma Chinese herb is a safe and effective drug in treating patients with episodic tension-type headache. There is significant difference in the therapeutic effects of tianma Chinese herbs on tension-type headache compared with the control group. A moderate difference was found between the five tianma groups.

Keywords: tianma, tension-type headache, multicentre study, Chinese herbs, clinical effects

J005
Usefulness of Toki-Shigyaku-Ka-Goshuyu-Shokyo-To for prevention of migraine attack

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Objective Toki-Shigyaku-Ka-Goshuyu-Shokyo-To (TSKGST), one of the traditional oriental prescriptions, has the actions
as following: warming the middle-energizer, the meridians and invigorating ‘qi’ to dispel cold, nourishing blood and promoting blood circulation. This study estimated the usefulness of TSKGST for the prevention of migraine attack.

**Methods** TSKGST 5.0–7.5 g/day was prescribed to the outpatient suffering from migraine with tension headache like aura. The effectiveness was estimated by decrease of the attack frequency.

**Results** 23 patients (thirteen men, twenty women, mean age 34.0 years) have taken TSKGST. Follow-up period ranged between 35 months ± mean 7.9 months. In 18 patients, the attack frequency decreased 50% and more. In 10 patients, the attack was completely prevented.

**Conclusion** TSKGST showed good prevention effect against migraine attack.

**Keywords:** migraine, oriental medicine, Toki-Shigyaku-Ka-Goshuyuto-Shokyo-To

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**J006**

The relationship of carotid, vertebral and radial arteries before and after Koryo Hand Therapy in migraineurs

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**Background** The migraine may be related to any change of cerebral blood flow, therefore it can be controlled with acupuncture. The definition of health of Koryo Hand Therapy (KHT) is harmonized state of cerebral blood flow, the well-balanced state of anterior and posterior circulation in the brain. This study was done to certify the relations of anterior and posterior circulation in migraineurs.

**Subjects and methods** 30 migraineurs were included. Blood flow velocity was measured at three points such as on radial artery, the distal part of common carotid artery and vertebral artery using EME TCD with newly developed multiprobe frame before and after KHT acupuncture on H-2, E-38, I-38 and H-2 on the hand of KHT. The blood velocity of the radial, vertebral and carotid arteries was checked in 30 migraineurs. The comparison of blood velocities of three arteries was done right or left side, respectively.

**Results** In migraineurs, there were changes of blood velocity after management. The increased velocity of the vertebral artery accompanied the increased velocity of the radial artery on the same side as positive feedback. The decreased velocity of the carotid artery accompanied the increase velocity of the radial artery, which showed reverse seesaw-like relationship.

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**J007**

The effect of acupuncture on cortical excitability in migraineurs as measured by transmagnetic stimulation

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**Background** Acupuncture is considered an alternative form of treatment for migraine. Transmagnetic stimulation (TMS) has been used to show increased cortical excitability in migraineurs. This threshold increases after treating migraine patients with preventive medications. We intend to use this to study the effect of acupuncture on migraine patients.

**Objective** To determine the effect of acupuncture on the phosphen threshold by TMS and also headache symptoms as experienced by migraine patients.

**Methods** 10 headache patients were recruited into the study. They underwent 10 acupuncture sessions with TMS performed before the first, sixth and last session. A headache diary was used to follow changes in migraine frequency before and during treatment.

**Results** Seven patients with migraine without aura were recruited. There were two male and five female patients. Six patients had an increase in their phosphen threshold at their third TMS session compared with the initial. One patient had increased thresholds initially but this decreased by 6% at third TMS. Headaches improved in four patients after acupuncture and were unchanged in the rest.

**Conclusion** Acupuncture is shown to be effective in reducing cortical excitability in migraineurs as reflected by decreased phosphen thresholds and an improvement in migraine attacks in this study.

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**J008**

Goshuyuto vs. lomerizine hydrochloride in the preventive treatment of migraine headaches: a cross-over open trial

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**Background** Goshuyuto extract (GE) is a Chinese herbal medicine that has long been used in Japan to treat migraine headaches. Lomerizine hydrochlorid (LH) is a first-line medicine for preventing migraine headaches in Japan.

**Objective** To confirm the efficacy of GE vs. LH in preventing migraine headaches.

**Methods** Fourteen migraine patients were randomly divided into two groups (groups 1 and 2), each with seven patients. Group 1 received 10 mg/day of LH for 28 days and thereafter underwent a 2-week withdrawal, after which they received 7.5 g/day of GE for 28 days. Group 2 was subjected to an opposite protocol. Abortive administrations of triptans were allowed for migrainous attacks during the withdrawal period. The frequency and intensity of migrainous attacks were assessed using the headache diary and the visual analogue scale before treatment and at weeks 2, 4, 6 and 8 of the study.

**Results** The administrated compliance of the GE was 74% against 94% for LH. However, GE significantly alleviated the frequency and intensity of the migrainous attacks. Moreover, GE significantly reduced concurrent symptoms such as nausea, vomiting, dizziness and irritability.

**Conclusion** The efficacy of GE for preventing migraine headaches has been established.

**Keywords:** goshuyuto, lomerizine hydrochlorid, migraine

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J009

‘Hair-wash headache’, an unusual trigger for migraine in India—observations from 94 patients

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Objective This study was undertaken to document ‘hair-wash’ or ‘head-bath’ as an unusual trigger for migraine in India. The impact of migraine prophylaxis on this trigger link was also evaluated.

Methods Out of 1500 IHS migraine patients who attended our Headache Clinic, 94 patients who complained of ‘hair-wash’ triggering of their headache were included in the study. Patients were grouped differently according to whether this trigger occurred in isolation or in combination with other triggers. Group I included those in whom ‘hair-wash’ was the only trigger, Group II included those in whom ‘hair-wash’ was an isolated trigger but other trigger factors were present, and Group III included those in whom ‘hair-wash’ was a trigger but was simultaneously intermixed with another trigger. The frequency and severity of ‘hair-wash’-related headache before and after episodic and chronic migraine prophylactic treatment were studied.

Results There were 11 patients in Group I, 45 in Group II, 38 patients in Group III. 85% improved with episodic prophylaxis and 68% with chronic prophylaxis.

Conclusion ‘Hair-wash’ is an unusual trigger factor for migraine in Indian patients. The underlying scientific basis is not yet known but it is important to remember this regional trigger in the treatment plan.

Keywords: hair-wash headache, migraine, trigger, India

J010

Asian Headache Foundation (AHF)—launch of a new headache organization

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Background Neurologists with a special interest in headaches from eight countries in the Asia Pacific (AP) region came together initially to do a survey project on Migraine Assessment for Prophylaxis. During the discussions it was felt that there was a shortage of headache specialists and a lack of awareness of the need for headache management in this region. Hence, they decided to establish an Asia Pacific Headache Society named Asian Headache Foundation (AHF).

Objective The main aim of AHF will be to encourage headache management in a scientific manner, to stimulate headache research, to train specialists and to provide a forum for exchange of data and for support to headache sufferers.

Methods Committee members were elected by ballot and AHF was formalized. Singapore was chosen to register AHF. Representatives in each of the eight countries would be responsible for recruitment of local members. Headache centres will be set up across the AP to train potential headache specialists.

Results AHF will be launched at the IHC 2005 in Kyoto. Thereafter, scientific meetings are planned to be held biennially.

Conclusions Like other regional headache organizations, it is hoped that AHF will in future grow in strength and contribute significantly to world headache literature.

Keywords: Asia Pacific, headache, specialist, society, organization

J011

Effectiveness of Kampo medicines for primary headaches. Ten years’ experience at the Oriental Medicine Research Centre, Kitasato Institute

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Objective This study evaluated the effectiveness of Kampo (oriental) medicines for primary headache.

Methods Primary headache out-patients at our Centre from July 1995 to March 2005 were prescribed Kampo medicines (decoction or extract granule) at least 1 month. We investigated the effectiveness of three types of Kampo.

Results There were 113 patients (24 men, 89 women, mean age 42 ± 15.1 years: migraine 64, tension-type headache (TTT) 45, cluster headache 4). The total effectiveness was 64.6% (73/113). The effectiveness for migraine, TTT and cluster headache was 70.3% (45/64), 57.8% (26/45) and 50% (2/4), respectively.

Migraine patients were prescribed 15 kinds of Kampo medicine. The most frequently prescribed medicine was goshuyu-to, its effectiveness was 73.9%. The effectiveness was observed from 1 to 2 weeks, 80% of responders of migraine patients improved within 1 month. The effective group of migraine had a slightly higher rate of menstrual pain than non-effective group. TTT patients were prescribed 20 kinds of Kampo. The most frequent prescriptions was chuto-san, its effectiveness was 57.1%.

Conclusion Kampo medicine showed a high effectiveness in the treatment of primary headaches. The effect of Kampo was shown to be greater for menstrual migraine.

Keywords: Kampo medicines, primary headache, migraine, tension-type headache, goshuyu-to
The effect of acupuncture on tension-type headache

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Objective We examined the effectiveness of acupuncture treatment for the most frequent headache type, tension-type headache, in Japanese patients.

Methods The patients were referred by another department to receive acupuncture treatment. The efficiency and degree of satisfaction and also the background factors in the acupuncture treatments of the patients with tension-type headache were analysed.

Results A total of 96 patients (23 men, 73 women, mean age 54 years). 64% of the patients were referred by the Department of Neurology and 24% were in-patients. The headaches were related to cervical vertebra disease and stroke. Also, the related symptom was shoulder stiffness, which was shown in 70% of patients. The efficiency of acupuncture treatment was 82%. There was a positive correlation between shoulder stiffness improvement rate and satisfaction with the degree of efficiency. However, there was not a significant relation between the sickness period and the number of acupuncture treatments.

Conclusion The above data showed that acupuncture treatments are effective in the treatment of tension-type headache. Furthermore, the result of the satisfaction rate was as expected. We would like to stress the usefulness of acupuncture in the field of headache treatment.

Keywords: acupuncture, tension-type headache, shoulder stiffness, background

The efficacy of acupuncture on headache and shoulder stiffness of VDT workers

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Objective Many VDT workers suffer from shoulder stiffness or headache and these symptoms seem to affect work ability and their QOL. This prospective study presents the efficacy of the treatment of the symptoms by using acupuncture and its influence on QOL and work ability.

Methods We used the PYONEX 0.9 mm acupuncture. After informed consent to this study, the company workers at one of the computer companies were given the acupuncture treatment to the neck and shoulder once a week for 4 weeks. We used visual analogue scale (VAS) for the evaluation of neck and shoulder stiffness and headache and evaluated their QOL by SF-36 and work ability before and after treatment.

Results A total of 35 workers (24 men, nine women, mean age 37 years) finished the study. The VAS of neck from 67 to 32 and shoulder stiffness from 71 to 34 significantly improved after 4 weeks’ treatment ($P < 0.01$). The VAS declined from 66 to 12 with two patients’ chronic tension-type headache. The body pain in SF-36 also improved ($P < 0.1$).

Conclusion Acupuncture treatment is effective on neck and shoulder symptoms of VDT workers and this treatment is safe and improves the work ability and QOL of VDT workers.

Keywords: acupuncture treatment, VDT worker, headache, SF-36, work ability

The neck and headache

K001

An observational study of musculoskeletal symptoms in migraine patients between attacks

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Background It is unclear in many clinical settings whether head pain arises from the neck, or whether neck pain emanates from primary headaches. This precludes ready identification and classification of headache type.

Objective A retrospective chart analysis of 810 records was conducted to determine the degree to which migraine sufferers exhibit tenderness to palpation or palpable muscle spasm on examination between acute migraine attacks.

Methods Exclusion criteria included any trauma history, or a diagnosis of temporomandibular dysfunction or bruxism. This yielded 536 records with IHS migraine 1.1, 1.2, 1.5.1 or 1.6. Of these, 423 had findings on physical exam between migraine attacks when presenting to a community-based headache clinic. The acute and chronic migraine groups were analysed for tenderness and spasm in 18 anatomic regions.

Results The acute migraine group consisted of 296 subjects, of whom 227 exhibited symptoms interictally; in the 240-subject chronic migraine group, 196 showed symptoms. Only 23% of the acute group and 18% of the chronic group experienced no neck pain or tenderness between attacks. Minor difference was seen in symptom distribution in the non-migraine headache group.

Conclusion Further study with a non-headache control group is recommended for further understanding of headache classification.

Keywords: migraine, neck pain, muscle spasm

K002

Lower cervical disc prolapse can lead to headache: prospective study in patients undergoing surgery and controls

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Background Until now it has not been known whether compression of lower cervical roots can lead to headache.

Objective This monocentre, prospective trial investigated the presence and characteristics of headache in patients with
lower cervical root compression prior to and 1 week and 3 months following surgery. Patients with lumbar disc prolapse undergoing surgery were used as controls.

Methods
50 patients each with cervical or lumbar disc prolapse were asked with a structured interview about past and present headache and neck pain. The interviews were repeated 1 week and 3 months after surgery of the disc prolapse.

Results
12/50 patients with cervical disc prolapse reported new headache in close temporal relationship to the time of disc prolapse. Seven patients fulfilled the Sjaastad criteria and seven the IHS criteria for cervicogenic headache (three patients fulfilled both criteria). 2/50 patients with lumbar disc prolapse reported new headache which did not fulfil criteria for cervicogenic headache. One week after surgery of the cervical disc 8/12 patients had no more headache, one patient had improved and three patients were unchanged. After 3 months, seven patients were pain free, three had an improvement of >50% and two patients had unchanged headache.

Conclusion
This prospective study shows that lower cervical disc prolapse can lead to headache and neck pain fulfilling criteria for cervicogenic headache. The pain improves in most patients following surgery.

K004
Headache and spontaneous cervical artery dissections: time course and follow-up
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Background
Headache is very common at the acute phase of cervical artery dissection (CAD). However, the relationship between these two conditions is complex and the course of headache in patients with CAD is not well known.

Objective
The aim of this study was to evaluate the course of various types of headache in patients who had had spontaneous CAD.

Methods
We conducted a telephone interview with a structured questionnaire about headache in all consecutive patients hospitalized for spontaneous CAD in our stroke unit between 1998 and 2001, confirmed by a mural haematoma on MRI.

Results
42 patients had had a spontaneous CAD during this period. Twenty-two had had headache in the past: nine migraine without aura, five migraine with aura and eight with episodic tension-type headache. Twenty-one (95.5%) improved their headache after the spontaneous CAD. Of 14 patients who were migrainers, 13 (92%) had fewer migraine attacks after the CAD. Only seven patients without previous headache developed new headache after CAD: three migraine without aura, three episodic tension-type headache and one chronic tension-type headache.

Conclusion
Most patients improve their pre-existing headache after spontaneous CAD. A few patients only developed new headache after CAD.

Keywords: cervical artery dissection, migraine, tension-type headache

K005
Brainstem and cervical spinal cord Fos immunoreactivity evoked by nerve growth factor injection into neck muscles in mice
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Background
Although myofascial tenderness is thought to play a key role in the pathophysiology of tension-type headache, very few studies have addressed neck muscle nociception.

Objective
The Fos immunohistochemistry study addressed the neuronal activation pattern due to local nerve growth factor (NGF) administration into semispinal neck muscles in anaesthetized mice.

Methods
In order to differentiate between the effects of NGF administration on Fos expression and the effects of surgical preparation, needle insertion and intramuscular injection, the experiments were conducted in three groups. In the sham group (n = 7) cannula needles were only inserted without any injection. In the saline (n = 7) and NGF groups (n = 7) 0.9% NGF was injected.
physiological saline solution or 0.8 μM NGF solution were injected in both muscles, respectively.

**Results** In comparison with sham and saline conditions, NGF administration induced significantly stronger Fos immunoreactivity in the mesencephalic periaqueductal grey (PAG), the medullary lateral reticular nucleus (LRN), and superficial layers I and II of cervical spinal dorsal horns C1, C2, and C3.

**Conclusion** This activation pattern corresponds very well to central nervous system processing of deep noxious input. Knowledge of the central anatomical representation of neck muscle pain is an essential prerequisite for the investigation of neck muscle nociception in order to develop a future model of tension-type headache.

**Keywords:** brainstem, tension-type headache, muscle, neck, nociception

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**K006**

Diagnostic block of cervical spinal nerve ganglion and root in patients with cervicogenic headache due to growth hormone-producing pituitary tumour

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**Background** Headache associated with growth hormone-producing pituitary tumours is believed to be attributable to compression by irreversible thickening of ligaments around dorsal roots and ganglions of spinal nerve. We diagnostically conducted C2 ganglion and C3 dorsal root block before the surgical decompression.

**Case 1** A 42-year-old woman with growth hormone-producing pituitary tumour had begun to complain of acromegaly and severe headache at the age of 24. In spite of tumour resection at the age of 26, she had been suffering from persistent headache and visual disturbance. Slight lower cervical canal stenosis on MRI and muscular atrophy of the splenius suggested C2 compression neuropathy. C2 ganglion and C3 root block showed 80% headache reduction, which was followed by surgical decompression in success.

**Case 2** A 27-year-old woman with growth hormone-producing pituitary tumour experienced severe headache, hyperprolactaemia and visual field defect from 23 years old. She underwent partial excision by trans-sphenoidal approach age of 24, but headache did not disappear. C2 ganglion and C3 root block showed 70% reduction of headache, which was followed by effective surgical decompression.

**Conclusion** This diagnostic nerve block is thought to be useful in determining the indication of decompression surgery in patients with cervicogenic headache.

**Keywords:** spinal nerve ganglion block, spinal nerve root block, cervicogenic headache, growth hormone-producing pituitary tumour, decompression surgery

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**K007**

Trigger point injection method with small dose botulinum toxin-A in cervical-associated headache. Experience of 242 cases over a 2-year period

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**Background** The cervical-associated headache (CAH) met all the characteristic diagnostic criteria of a CH, with the exception of confirmation by an anaesthetic block. We have frequently experienced that most CAH have myofascial trigger points (MFTPs) in the painful areas. The ‘integrated hypothesis’ of formation of MFTPs suggests excessive acetylcholine release as the main pathogenic mechanism.

**Object** To verify the effectiveness of the trigger point injection (TPI) method with small dose BTX-A in CAH patients.

**Methods** 242 CAH patients were enrolled in this study. One or two injection sites were chosen by palpation, corresponding to one of the most tender cervical muscular trigger points. Each trigger point received 10 U of BTX-A (Dysport®). The subjective improvement was evaluated, using the global clinical improvement (GCI) index, in each patient.

**Results** For all patients, the mean GCI score was 2.9 points (SD = 1.1) after 4 weeks. The most common side-effect was local pain in the injected area (24%).

**Conclusions** The TPI method with BTX-A is effective for the treatment of CAH. Furthermore, the results suggest BTX-A doses that are far lower than those generally recommended for the muscular relaxation could yield significant pain relief.

**Keywords:** botulinum toxin, cervical-associated headache

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**K008**

Expression of Fos in the trigeminocervical complex of rat following stimulation of occipital afferents

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**Background** Stimulation of the GON produces excitation of second order neurons in the trigeminocervical complex (TCC). Convergent excitation may play a role in pain referral from cervical structures.

**Objective** To examine the distribution of second order neurons in the TCC receiving GON input, and the role of glutamate NMDA receptor activation.

**Methods** Sprague-Dawley rats were anaesthetized (pentobarbitone 60 mg/kg) and the occipital muscles exposed. Rats were allocated into five groups: surgery only (S), mineral oil injection into occipital muscles (O, 30 μl), mustard oil injection (MO, 30 μl), MO injection plus i.v. MK801 (3 mg/kg), O injection plus i.v. MK801. Fos expression was determined in the TCC, trigeminal nucleus caudalis, and the dorsal horns at the C1 and C2 spinal level. Data are expressed as medians (quartile range).

**Results** Fos expression in the TCC was significantly altered by MO and O ($\chi^2 = 31.3, P < 0.001, \text{Kruskal–Wallis}$). Baseline expression was 11 (4, 17) fos positive cells in the TCC, with
MO producing 23 (17, 33) and O 19 (15, 25). Both MO and O effects were reversed by MK-801.

Conclusions This study introduces a model for examining TCC activity after occipital afferent stimulation in the rat, and demonstrates involvement of glutamate NMDA receptors.

K009
Cervicogenic headache is a common preoperative symptom with good prognosis in patients operated with anterior cervical decompression and fusion (ACDF)

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Objective This is a prospective study searching for cervicogenic headache before and after neck surgery in patients referred to the Department of Neurosurgery. Cervical radiculopathy is an indication for this surgery and headache is not.

Methods The frequency, duration and intensity of headache were registered before the operation and 3 months postoperatively. The operation procedure was anterior cervical decompression and fusion (ACDF) and ‘cages’ and anterior plating were used. The patients needed only a few days in a stiff neck collar. The result is a decompression of the root as well as fixation of the actual movement level. Most operations were performed at a level C5-C6 and C6-C7.

Results More than half (57%) of 72 patients had headache before the operation. 34% of the headache patients were totally headache free after the operation, in 37% there was no improvement, while the remaining patients had a similar headache with lower intensity and frequency.

Conclusion Cervicogenic headache often accompanies neck pain and radiculopathy in patients with lower neck pathology in need of operation. The operation reduces the headache as well as the other symptoms. The anterior approach operation does not seem to be a risk for postoperative headache.

Keywords: headache, cervicogenic headache, neck, surgery

K010
Lower volume injection at lumbar level causes failure of epidural blood patch in patient with intracranial hypotension

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Objective Epidural blood patch (EBP) is an effective treatment for CSF leak. Patients with intracranial hypotension often receive EBP at lumbar level. We investigated the spread of solution in lumbar region.

Methods Subjects were 22 patients with actual site of the CSF leaks. The 30 ml blood with contrast medium was injected at lumbar level. If the patient complained of pain, injection was stopped. Epidurograms were obtained at each injected volume (10 ml, 20 ml and maximal volume). The spread of solution and amounts of injected volume were recorded and analysed. Moreover, we compared radiographic spreads with CSF leak site.

Results The mean total injected volume was 27 ± 5.0 ml. Although unilateral spread was seen in seven (32%) at 10 ml, no patient had unilateral spread at 20 ml. The sites of CSF leaks were the following: 15 in lumbar region and seven in thoraco-lumbar region. Success rate of EBP was 45% at 10 ml, 86% at 20 ml and 95% at maximal volume. No solution reached above T6 level.

Conclusion Less than 20 ml may cause failure of EBP due to unilateral and lack of spread. Additional puncture in thoracic region is recommended if CSF leak is wide and at thoracic level.

Keywords: intracranial hypotension, cerebrospinal fluid leak, epidural blood patch, epidurography, spread

K011
Increase of cranial and global pressure pain sensitivity due to acute whiplash injury

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Background Most of the patients complain about cervical pain after whiplash injury. In recent studies transient increases of cervical muscle pressure painfulness could be observed using computer-aided pressure algesimetry (Stude 2004, Nebel 2005).

Objective The goal of this study was a prospective investigation of alterations of pressure-painfulness of areas distant to the trauma-related structures of the neck.

Methods For this purpose 23 patients (QTF I + II) were investigated four times after whiplash injury (<2, at 3, 4 and 6 weeks) and compared with 24 healthy controls. Pressure painfulness was measured using a pressure-algometer (1310 kPa, 400 g) at the vertex and at the dorsal side of the left index finger for 180 s. The resulting time-pain-intensity function was analysed by means of ANOVA and posthoc t-tests.

Results Patients in the acute stage (≤7 days) showed increased pressure-painfulness in almost all parameters at both investigated sites. This increase completely receded within the next 3–4 weeks.

Conclusion Post-traumatic complaints after whiplash injury are accompanied by an increased pressure-painfulness at the vertex and also at the index finger distant to the trauma. This increase was transient and normalized within the first 4 weeks. The results suggest a transient post-traumatic sensitization of central pain-related structures.

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K012

Headache with C5 cervical radiculopathy: remember giant cell arteritis?

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Background Giant cell arteritis and C5 radiculopathy are both neurological conditions seen more commonly in older adults.

Case report A 72-year-old female presented with a month’s history of new onset headache and diplopia. Five days before presentation the patient awoke with weakness of the right arm and inability to abduct both shoulders. Detailed clinical examination showed a bilateral radicular pattern of weakness involving C5 and C6 predominantly on the right. The ESR and CRP were raised at 113 mm/h and 105 mg/l, respectively. A chest radiograph showed a raised right hemidiaphragm. Brain and cervical spine MRI, echocardiogram, electrocardiograph, lumbar puncture, electrophysiology and blood screening were otherwise unremarkable. Temporal artery biopsy showed histological findings consistent with giant cell arteritis. Both headache and neurological impairment improved rapidly with steroid therapy with full recovery.

Conclusion The combination of new onset C5 radiculopathy with headache is a rare but important presentation of giant cell arteritis and highlights the need for urgent assessment and treatment. We present an unusual case, suggest mechanisms and review the literature on four previous cases that highlight this important association.

Keywords: giant cell arteritis, radiculopathy

K013

Hangover headache in Japanese male workers

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Background Our previous study showed a positive association between inactive heterozygous aldehyde dehydrogenase-2 (ALDH2) and hangover susceptibility in Japanese workers, suggesting an aetiological role of acetaldehyde in the development of hangover.

Methods Associations between hangover headache, drinking, and ALDH2 genotype were examined for 139 Japanese male workers.

Results Inactive ALDH2 heterozygotes drank less alcohol than active ALDH2 homozygotes (P < 0.0001), but the frequency of hangover did not significantly differ between the two groups. Among 87 men who experienced hangover during the last year, 56 experienced headache as a hangover symptom. Sites of the headache were entire areas in 39% of the 56 patients and partial area(s) in 45% (occipital 29%; temporal 23%; frontal 18%; parietal 9%; and occular 6%). Throbbing headache was reported in 45% of them, and 61% felt heavy-headed. The frequency, sites and types of hangover headache did not differ between active and inactive heterozygous ALDH2 men who experienced hangover in the last year. Among 87 men who experienced hangover, the proportion of those who experienced hangover headache decreased significantly with increased daily alcohol consumption (P = 0.005).

Conclusion A major determinant for susceptibility to hangover headache was daily alcohol consumption, suggesting a link between tolerance to alcohol and susceptibility to hangover headache.

Keywords: alcohol, aldehyde dehydrogenase-2, hangover, delayed alcohol-induced headache, hangover headache

K014

Connective tissue abnormalities in Japanese patients with spontaneous cervical artery dissection

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Background In Western population the association of spontaneous cervical artery dissection (SCAD) with ultrastructural abnormalities of the dural connective tissue was pointed out.

Objective In Japanese to assess the association of SCAD with ultrastructural abnormalities of the dural connective tissue.

Methods Skin biopsies of three Japanese patients with SCAD without other clinical manifestations of a connective tissue disease like Marfan syndrome and one healthy relative were analysed. Case 1. A 41-year-old male had extracranial internal carotid artery dissection and extracranial vertebral artery dissection. Case 2. A 54-year-old male had extracranial vertebral artery dissection. Case 3. A 44-year-old male had extracranial vertebral artery dissection. The ultrastructural morphology of the dural connective tissue components was assessed by electron microscopy.

Results The collagen fibres of all three patients contained fibrils with highly variable diameters. All three patients had ultrastructural aberrations, including flower-like fibrils, enlarged diameters of the composite fibrils.

Conclusion This result indicated that Japanese and/or Asian patients with SCAD may have connective tissue abnormality as good as Western patients.

Keywords: spontaneous cervical artery dissection, skin biopsy, collagen fibre, Japanese

K015

Orthostatic headaches caused by spontaneous cerebrospinal fluid leak

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Background More patients with spontaneous intracranial hypotension are being diagnosed, and it is realized that most cases result from spontaneous cerebrospinal fluid (CSF) leak. The exact cause of CSF leak often remains unclear. When we examined patients with orthostatic headache, some of them had suffered from spontaneous CSF leak after a whiplash
Injury. According to our observation, a whiplash injury is likely to be one of the main causes of spontaneous CSF leak. The present study aims to present the diagnosis and treatment of 26 patients with orthostatic headache associated with CSF leak.

**Subjects and results** We examined 36 patients with spontaneous CSF leak. The mean age of the 13 female patients and 13 male patients was 35 ± 10 years. Fifteen patients (57.7%) had a medical history of neck and head trauma. The most common clinical manifestation was orthostatic headache. They presented other symptoms such as diplopia, dizziness, tinnitus, dysphasia and general fatigue. The CSF leak was documented with radioisotope (RI) cisternography for 20 patients (76.9%). Nineteen patients (73.1%) underwent epidural blood patches (EBPs) more than once because the success rate with each EBP is approximately 30%. In six patients EBPs and DIV combination therapy were more effective than single EBPs.

**Conclusion** It is possible that a weakening of the dural sac and neck and head traumas might lead to the occurrence of spontaneous CSF leak.

**K016**

**Massive volume injection for epidural blood patch in patients with intracranial hypotension**

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**Objective** Epidural blood patch (EBP) is a treatment for CSF leak. The efficacy of EBP in patients with intracranial hypotension (IH) is much lower than that with post dural puncture headache. We proposed a new technique with massive volume EBP for IH and evaluated the efficacy and complications.

**Methods** Subjects were 37 patients with CSF leaks confirmed by RI cisternography. More than 40 ml autologous blood with contrast medium was injected to fill up the thoracic and lumbar epidural space under fluoroscopic guidance. After epidurograms were obtained, the spread of solution, amounts of injected volume and complication were recorded and analysed.

**Results** 81 EBPs were performed and the mean EBP was 2.1 times. The mean injected volume was 40 ml. Of 81 EBPs, 25 were cancelled due to injection pain and low back pain lasting over 3 days was seen in six. There was no severe complication such as spinal cord compression or epidural abscess. The efficacy of EBP was the following: good in 31 cases (84%), poor in six cases.

**Conclusion** Massive volume EBP is a safe and effective treatment in patients with intracranial hypotension.

**Keywords:** intracranial hypotension, cerebrospinal fluid leak, epidural blood patch, massive injection, epidurography

**L001**

**Estimation of the risk factors of headache and TMD in relation to sleep quality**

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**Background** Poor sleep quality is a common clinical complaint in patients with headache and TMD. Evaluation of sleep quality may be an important consideration in the management of patients with headache and TMD.

**Objective** To explore the prevalence of headache and TMD and to analyse the potential risk factors of headache and TMD in relation to sleep quality.

**Methods** 76 female students, average 21 years old, participated in this survey, in which structured self-report questionnaires contained items designed to gain information on the sleep quality and habits as well as on headache and TMD complaints. This survey was done the day after vacation ended and during the semester. To explore the independent predictors of headache and TMD, symptoms related to sleep disturbance were sought. The odds ratio (OR) and 95% confidence interval (CI) for the different variables were calculated by stepwise logistic regression analysis.
Results The results of the logistic regression analysis revealed that both tension-type headache and masticatory muscle disorder could be predicted by a greater tendency to wake up more than four times during the night. The tendency is more prominent during the semester than the day after vacation ended.

Keywords: headache, TMD, sleep quality, odds ratio, step-wise logistic regression analysis

Botulinum toxin

M001

Effect of botulinum toxin type A (BoNTA) on capsaicin-evoked pain, flare, and secondary hyperalgesia in an experimental human model of trigeminal sensitization

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Background The trigeminal system is involved in migraine. Efficacy of Botulinum toxin A (BoNT-A) in migraine has been reported in some clinical studies while its mechanism of action in such pain conditions remained unexplored. It is proposed that BoNTA inhibits peripheral sensitization of nociceptive fibres (by neuropeptide release inhibition) and indirectly reduces central sensitization.

Objective Examine the effect of intramuscular BoNTA (BOTOX®, Allergan, Inc.) in an experimental human model of trigeminal sensitization to evaluate suppression of the capsaicin-induced pain intensity, flare, and secondary hyperalgesia.

Methods BoNTA or saline were injected intramuscularly to 32 healthy male volunteers in a double-blind, randomized manner. Intradermal capsaicin injections to the forehead were obtained before and 1, 4 and 8 weeks after study treatment to induce pain, flare and secondary hyperalgesia.

Results BoNTA significantly reduced capsaicin effects throughout the study. The strongest suppressive BoNTA effects on capsaicin-induced flare (70.38%), pain (47.16%) and secondary hyperalgesic area (78.02%) were observed as early as week 1.

Conclusion BoNTA presented suppressive effects on the trigeminal nociceptive system activated by intradermal injection of capsaicin, which suggests a local peripheral effect of BoNTA on cutaneous nociceptors.

Keywords: botulinum toxin A, capsaicin, hyperalgesia, trigeminal sensitization

M002

Botulinum toxin A for the treatment of greater occipital neuralgia and trigeminal neuralgia. A case report with pathophysiological considerations

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Objective To report a patient with refractory greater occipital neuralgia (GON), trigeminal neuralgia (TN) and chronic daily headache (CDH) with medication overuse headache (MOH), in whom the GON and TN treatment with botulinum toxin type-A (BTX-A) resulted in complete relief of neuralgic pain, reduction in CDH frequency, and MOH cessation.

Results This is a 44-year-old white male patient who had a history of episodic migraine with and without aura since the age of 12, temporomandibular dysfunction and TN since age 22, CDH since age 40 [probably secondary to aspirin/acetaminophen/caffeine (AAP) overuse], and GON since age 42. Due to side-locked right GON, persistent left TN and MOH, the patient was given a right occipital nerve and left mandibular injection of 15 units and 7.5 units of BTX-A, respectively, with complete pain relief for 4 months. The injections were repeated at the end of the fourth and seventh month of follow-up, with complete relief of pain for the following 10 months.

Conclusions We report a case where BTX-A was effective in the treatment of GON, TN and CDH with MOH. This study expands our knowledge regarding the local analgesic effects of BTX-A. This case also highlights the importance of other chronic pain syndromes in the development of CDH.

M003

Botulinum toxin type A (BoNT-A) for migraine prophylaxis in the Japanese population: an open-label prospective trial

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Background Botulinum toxin type A (BoNT-A) has been used as migraine prophylaxis. No prospective study has yet been conducted in the Japanese population.

Objective To evaluate the efficacy and tolerability of BoNT-A for migraine prophylaxis.

Methods Nineteen Japanese adult patients (50 ± 10 years old), who met the ICHD-II criteria for migraine and had at least five migraines a month, were enrolled in this open-label prospective study. BoNT-A (50 units) was injected in 19 fixed sites of muscles including procerus, corrugator, frontalis, temporalis and occipitalis. All participants stopped taking preventive medicine from 1 month before and during the treatment. MIDAS, migraine questionnaire and headache diary were used for the evaluation of efficacy. Six patients
received the second injection of the same dosage combined with prophylactic medication.

**Result** MIDAS score of 24.1 (preinjection) reduced significantly to 15.6 after 2 months and 15.7 after 3 months of injection ($P<0.05$). Eighteen patients stated subjective improvement following injection. Mean headache frequency showed a tendency to decrease following injection. The amount of analgesics consumption did not change after BoNT-A injection. No serious adverse event was reported. The second BoNT-A injection after 3 months was also effective.

**Conclusion** Botulinum toxin A was an effective and safe treatment for migraine prophylaxis among Japanese population.

**Keywords:** botulinum toxin type A, MIDAS, migraine

**M004**

**Botulinum toxin treatment in nummular headache**

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**Background** Nummular headache (NH) has been recently described as a primary disorder, which is characterized by head pain, exclusively felt in a small rounded area, typically 2–6 cm in diameter.

**Objectives** To evaluate the effectiveness of botulinum toxin-A (BTX-A) on NH.

**Methods** Over a period of 1 year we have experienced 18 patients with NH. Of these 18 patients, four who had abnormal findings on neurological and neuroimaging examinations were excluded. We treated 14 out of 18 patients with BTX-A. Each local pain area received 10 U of BTX-A (Dysport®). The subjective pain assessment for the headaches was used, based on a visual analogue scale (VAS). The pre- and post-injection pain scores were statistically analysed.

**Results** The mean age at the onset was 38 years (range 13–72). The locations of the symptomatic area were mostly parietal ($n=7$) or temporal ($n=5$), but also frontal ($n=1$) and occipital ($n=1$). For all patients, the mean pre- and post-injection pain scores were 6.2 (SD = 1.0) and 3.1 (SD = 0.8), respectively ($P<0.01$).

**Conclusion** The present study demonstrated that botulinum toxin was effective in the treatment of nummular headaches.

**Keywords:** nummular headache, botulinum toxin

**M005**

**A pilot study of botulinum toxin A as part of the treatment of chronic post-whiplash cervicogenic headache**

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**Background** Chronic cervicogenic headache (CEH) after whiplash is connected with reduced range of motion in the neck and local pain on stretching the muscles. Recent fine wire EMG studies of the semispinalis capitis muscles have shown abnormalities in whiplash patients. Botulinum toxin A paralyses the muscles by inducing a permanent blockade of neurotransmission at the motor end plate. It is reversible as the paralysed muscles recover their function as new nerve terminals develop.

**Objective** To investigate whether botulinum toxin A is effective as part of the treatment of CEH.

**Methods** Five patients with daily CEH of at least 1 year’s duration were included. A total of 100 units of botulinum toxin A were injected. The patients were given a neck mobilizing programme.

**Results** Four patients were headache free after the first injection; their headaches returned at larger intervals and three were headache free at 18 months. One had only intermittent reduction of pain intensity.

**Conclusion** Botulinum toxin A seems to be useful in the treatment of cervicogenic headache. The headache relief extends the typical duration of 8–12 weeks of symptom relief seen in other botulinum toxin A studies.

**Keywords:** headache, cervicogenic headache, botulinum toxin A, Botox

**M006**

**Outstanding efficacy of botulinum toxin A for cluster headaches**

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**Objective** The efficacy of botulinum toxin A for episodic and chronic cluster headaches was examined.

**Patients and methods** Twenty-nine cluster headache patients, 25 males and four females, 22 with episodic type and seven with chronic type, were injected with 30 units of Botox at 15 points on the head bilaterally. Episodic types were within 2 weeks from onset of this cluster period. We evaluated the changes in severity, frequency and duration of attacks.

**Results** Eighteen cases (81.8%) showed a frequency below one-third of episodic type, and four cases (57.1%) of chronic type. Less than one-third the severity was shown by 17 episodic cases (77.3%) and four chronic cases (57.1%), while one-third the duration was found in 17 episodic cases (77.3%) and three chronic cases (42.9%), respectively. The cases showing efficacy for more than one item were 21 episodic cases (95.5%) and six chronic cases (85.7%), respectively. Efficacy appeared from the 2nd to the 10th day in the episodic type. In the chronic type, the 2nd month was the most favourable. The cluster period was shorter than the previous cluster period in all but one episodic case. In the chronic type, the average efficacy time was 7.3 ± 3.8 months.

**Conclusion** Botulinum toxin proved to be effective for both types. For episodic type, the efficacy was surprisingly outstanding, and should be the treatment of choice for cluster headaches, and we must progress this therapy throughout the world.

**Keywords:** cluster headache, botulinum toxin
M007
The effect of botulinum toxin type A on headache-related disability in migraine sufferers: a double-blind, randomized, placebo-controlled study

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Objective To evaluate the effect of botulinum toxin type A (BoNTA) on headache-related disability (MIDAS) in migraine sufferers.

Methods A double-blind, randomized, placebo-controlled study involving 79 patients with disabling migraine with or without aura. Migraine disability (MIDAS) was evaluated at baseline and 3 months after study injections using a modified follow-the-pain injection strategy. Injection sites and dose per site were standardized. Patients received between 25 and 100 units of BoNTA.

Results No significant difference (95% CI –14, –19) was demonstrated between the mean baseline and 12-week MIDAS scores in the BoNTA group (45 and 24) compared with the placebo group (46 and 22). No significant differences were demonstrated in secondary endpoints including headache frequency, headache severity, headache impact, or migraine-specific quality of life at any time point. Seven patients withdrawd from the study (1 BoNTA/5 placebo). Adverse events were mild to moderate. BoNTA was well tolerated.

Conclusions Botulinum toxin type A was not superior to placebo in reducing migraine-related disability as measured by MIDAS.

M008
Constellation of symptoms identifying migraine trigger sites

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Background Botulinum toxin (Botox®) injections for migraines have been shown to be effective. Identifying common trigger sites by their location and associated symptoms will lead to an accurate injection pattern, and eliminate overuse of Botox®.

Objective To identify symptoms associated with migraine, which improve after injection of Botox®.

Methods Each patient answered a questionnaire. Based on the location of the pain, 12.5 units of Botox was injected into the frontal, temporal, or occipital trigger sites, bilaterally. The same questionnaire was answered 4–6 weeks after injection.

Results Regardless of injection site, sparkling lights, blurred vision, and lightheadedness (P = 0.0441, < 0.01, 0.02) improved. The resolution of unique symptoms was associated with specific trigger sites. Occipital symptoms include retro-orbital pain, weakness and runny nose (OR = 1.29, 1.24, 1.59). Temporal symptoms include temple pain, ptosis and puffy eyes (OR = 1.25, 1.23, 1.22). Frontal symptoms include pain above the eyebrow (OR = 1.59).

Conclusion A combination of site-specific symptoms and location of pain provides the best identification of the trigger points for injection.

Keywords: migraine, Botox A

M009
Botulinum toxin effects on pain in cervical dystonia

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Background It has not been clarified whether botulinum toxin effects on pain in cervical dystonia are secondary to decreases in muscle tonus or via direct effects on the sensory system. In this study, we investigated botulinum toxin effects on pain in patients with cervical dystonia.

Objects Subjects included 76 patients with cervical dystonia (age range 18–74 years, duration of the illness 2 months to 37 years).

Methods Botulinum toxin type A (BTA) was initiated 40–60 mouth units and gradually increased at an interval of 3 months. Cervical/cephalic pain was evaluated in addition to the severity of dystonia before and after BTA therapy.

Results Pain was complicated in 54 patients (71%), but was not correlated with duration of the illness or severity of cervical dystonia. Both pain and cervical dystonia were alleviated in 25 patients (46%), but only pain was alleviated in five patients (9%) even at a low dose of BTA.

Conclusion BTA effects on pain in cervical dystonia are thought to be via direct effects on the sensory system, especially nociceptive nerve endings, and secondary to decrease in muscle tonus. BTA is expected to be clinically useful not only for tension-type headache but also for migraine.

Keywords: botulinum toxin, cervical dystonia, pain, nociceptive nerve endings, headache

M010
Botulinum toxin type A in migraine without aura prophylaxis; a 12-week prospective, multicentre, double-blind, randomized, placebo-controlled trial

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Background Botulinum toxin type A had been investigated in mixed migraine with and without aura prophylaxis by vehicle-controlled trial; nevertheless, a well-designed, multicentre, double-blind, randomized, placebo-controlled trial has not been conducted in patients with migraine without aura.

Methods This 12-week prospective, multicentre, double-blind, randomized, placebo-controlled trial was conducted in Thai migraineurs by using 120 units, 240 units of botulinum...
toxin type A (Dysport), or placebo for six sites pericranial subcutaneous/intramuscular injection.

**Results** Out of a total of 128 patients who participated, 119 patients completed the protocol. There was no significant difference in the baseline data amongst the three groups. At week 4, in the treatment group with 240 units of botulinum toxin A there was a significant reduction in both mean change from baseline of total headache score (\( P = 0.03 \)) and duration of moderate to severe pain during migraine attack (\( P = 0.03 \)) compared with placebo. Doctor’s and patient’s global assessment change from the 4th to 12th week was significantly improved in 240-unit group (\( P = 0.01 \) and \( P = 0.03 \), respectively). Side-effect composed of decreased wrinkle, mild ptosis and dizziness.

**Conclusions** Botulinum toxin type A 240 units was proven to be safe and efficacious in migraine without aura prophylaxis.

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**M011**

**Botulinum toxin in refractory chronic daily headache**

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**Background** There are few reports about botulinum toxin (BT) in chronic daily headache (CDH).

**Objective** Describe patients and outcome after BT injection in refractory CDH.

**Methods** We offered BT injection to CDH patients refractory to usual preventive treatment. They were considered refractory after four preventives had failed. In Spain BT is not approved for headache, so patients had to sign an informed consent and then remitted to authorities for its approval as compassionate use. We administered 150–200 BT units (Dysport) at 10 pericranial points. We analyse headache subtypes, patient characteristics and results: negative or positive (more than 50% subjective improvement in visual analogue scale).

**Results** Nine patients included. Mean age 40.56 years (22–66), 8 : 1 female: male. 21.67 (4–40) years suffering headache. All had CDH, eight of them chronic or episodic migraine according to IHS criteria; five medication overuse headache criteria, five chronic tension-type headache and two new-daily persistent headache criteria. 5 patients (55.56%) had positive response. 18 BT injection in total, 67% positive response. No adverse events either than little bleeding at some injection points.

**Conclusion** In very refractory CDH patients, BT injection may be an alternative to ameliorate their continuous pain, but just half of patients tend to respond.

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**M012**

**Botulinum toxin type A: reduction in the use of acute pain medication in patients with transformed migraine (TM)**

Ninan T. Mathew MD, Frederick G. Freitag DO, Ronald DeGryse MA, MS & Catherine Turkel PharmD

**Background** Studies have shown that transformed migraine is often associated with the overuse of headache pain medications. Medication overuse is not only associated with increased frequency of headaches but adds to the economic burden and quality of life of the patients.

**Objective** Evaluation of botulinum toxin type A (BoNTA, BOTOX®; Allergan, Inc., Irvine, CA) on the use of acute pain medications in patients with TM.

**Methods** A subgroup analysis of 177/355 patients with ≥15 headache days (≥75% of which were migraine/probable migraine days) and ≥4 headaches during 30-day baseline in a randomized, double-blind, placebo-controlled study. Patients received 110–260 U of BoNTA or placebo for three treatment cycles.

**Results** A greater reduction in the number of days for which acute medications were used was observed for BoNTA than placebo at all time points, reaching statistical significance at day 180 (BoNTA = –7.8, placebo = –4.2; \( P = 0.035 \)). Similarly, greater reduction in the use of acute medications was observed for BoNTA than placebo at all time points, with a maximum between-group difference of 5.6 uses at day 210 (\( P = 0.036 \)).

**Conclusions** BoNTA was safe, well tolerated and effective in reducing the use of acute headache medications in patients with TM.

**Keywords:** botulinum toxin, transformed migraine, acute medications, headache, prophylaxis

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**M013**

**Botulinum toxin type A as stand-alone headache prophylaxis of transformed migraine (TM)**

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**Background** Several open-label and small placebo-controlled trials suggest that botulinum toxin type A (BoNTA, BOTOX®; Allergan, Inc., Irvine, CA) may be effective as prophylactic headache treatment in various headache populations. Concomitant prophylactic headache medications may be a confounding factor in a clinical trial designed to evaluate the effectiveness of a prophylactic treatment.

**Objective** Evaluate BoNTA for the prophylaxis of transformed migraine (TM).

**Methods** A subgroup analysis of 177/355 patients with TM and frequent headache (≥4 per month during baseline) not using concomitant headache prophylaxis in a randomized, double-blind, placebo-controlled study. Patients received 110–260 U of BoNTA or placebo up to three treatment cycles.
M014

Botulinum toxin type A: reduction in the frequency of migraine/probable migraine (M/PM) episodes in patients with transformed migraine

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Background Several open-label and small placebo-controlled trials suggest that botulinum toxin type A (BoNTA; BOTOX®; Allergan, Inc., Irvine, CA) may be effective as prophylactic treatment in various headache populations and in various headache types.

Objective Evaluation of BoNTA as headache prophylaxis for transformed migraine patients.

Methods A subgroup analysis of 177/355 patients with ≥15 headache days (≥50% of which were migraine/probable migraine days) and ≥24 headaches per month during baseline and overusing acute pain medications in a randomized, double-blind, placebo-controlled study. Patients received 110–260 U of BoNTA or placebo for up to three treatment cycles.

Results Significant reduction in migraine/probable migraine (M/PM) frequency favouring BoNTA at several time points was observed, with a maximum difference between treatment groups of 4.3 M/PM (P = 0.010). From day 150 through day 270, 60–65.5% of BoNTA patients had ≥50% reduction in M/PM frequency, compared with 33.3–50.0% with placebo. Four patients discontinued due to adverse events.

Conclusions BoNTA was safe, well-tolerated, and effective in reducing the frequency of headaches in a subset of patients with TM and overusing acute pain medications.

Keywords: botulinum toxin, transformed migraine, prophylaxis

M015

Botulinum toxin type A: reduction in headache frequency in patients with transformed migraine (TM) overusing acute pain medications

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Background Studies have shown that transformed migraine (TM) is often associated with the overuse of headache pain medications. Medication overuse is not only associated with increased frequency of headaches but adds to the economic burden and quality of life of the patients.

Objective Evaluation of botulinum toxin type A (BoNTA, BOTOX®; Allergan, Inc., Irvine, CA) on headache frequency in patients with TM and overusing acute pain medications.

Methods Subgroup analysis of 77/355 patients with ≥15 headache days (≥50% of which were migraine/probable migraine days) and ≥24 headaches per month during baseline and overusing acute pain medications in a randomized, double-blind, placebo-controlled study. Patients received 110–260 U of BoNTA or placebo for three treatment cycles, with no concomitant headache prophylaxis.

Results Greater reduction in headache frequency favouring BoNTA at all, and reaching statistical significance at most, time points was observed, with maximum between-treatment group difference of 7.1 headaches (day 210, P = 0.047, n = 22). Few patients discontinued due to adverse events.

Conclusions BoNTA was safe, well-tolerated, and appeared effective in reducing the frequency of headaches in a subset of patients with TM and overusing acute pain medications.

Keywords: botulinum toxin, transformed migraine, over users, headache, prophylaxis

M016

A randomized, double-blind comparison of botulinum toxin type A (Botox) and divalproex sodium (Depakote) for the prophylactic treatment of episodic migraine headaches: a pilot study

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Background There is a need for effective, well-tolerated prophylactic migraine treatments.

Objective To assess and compare the safety, tolerability and efficacy of botulinum toxin type A (BoNTA) and divalproex sodium (DVPX) in the prophylaxis of headache in patients suffering from episodic migraines.

Methods A randomized, double-blind pilot study comparing a single injection of BoNTA (200 U) and DVPX (250–500 mg b.i.d.). The number of headache-free days per month, HIT-6, and adverse events were assessed every 30 days for 3 months.

Results Forty-four patients (n = 22 each group; mean age 43 years, 90.9% female) were enrolled. Both BoNTA and DVPX treatments resulted in statistically significant mean improvements from baseline in the number of headache-free days at all assessments (P ≤ 0.0189), with no between-group
Management of headache in pregnancy

N001

Idiopathic cerebrospinal fluid rhinorrhea in a pregnant woman—successful treatment of pneumocephalosis and a meningitis conservatively, and natural childbirth was possible. A case report

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Case A 31-year-old woman, gravid 28 weeks with no remarkable medical history.

Chief complaint Cephalalgia/pyrexia.

Clinical history She had cold symptoms from 18 February 2004. Cephalalgia developed from 21 February and she also noticed a large quantity of nasal dripping. She visited our department on 23 February.

Symptoms Body temperature 36.6 °C. Slight nuchal rigidity was shown.

Result of examinations Glucose qualitative test was positive in pituita. After permission, we performed cranial CT and found severe pneumocephalosis. Examination of cerebrospinal fluid findings: cell count 624 (N 49%, P 51%); protein 101 mg/day; glucose 21 mg/day.

Clinical course We diagnosed idiopathic cerebrospinal fluid rhinorrhea complicating with pneumocephalosis and meningitis and started CTX (8 g/day), ABPC (12 g/day). Liquor findings were normalized on 8 March. On 9 March, liquor rhoea eliminated and we stopped antibiotics on 10 March. Free air in the skull disappeared on 18 March and she left the hospital on 3 April. Afterwards, she delivered a 3374-g baby under painless epidural anaesthesia on 38 weeks of pregnancy on 29 April. There was no post partum recurrence either.

Conclusion There is no report of idiopathic cerebrospinal fluid rhinorrhea in pregnancy. We thought this case was valuable in that normal delivery was possible after successful conservative treatment of pneumocephalosis and meningitis without recurrence.

Keywords: idiopathic cerebrospinal fluid rhinorrhea, cephalalgia, pregnancy
artery was clearly visible. The artery was preconstricted of drugs, respectively. The skull was drilled until a dural lar vein were cannulated for ventilation and administration

Background Activation of trigeminal nerves is thought to play a pivotal role in migraine pathophysiology. They innervate the dura mater and activation leads to the release of neuropeptides, including calcitonin gene-related peptide (CGRP).

Objective This study was undertaken to establish a model of trigeminovascular activation using intravital microscopy on a closed cranial window.

Methods Mice were anaesthetized and the trachea and jugular vein were cannulated for ventilation and administration of drugs, respectively. The skull was drilled until a dural artery was clearly visible. The artery was preconstricted (~70% of baseline) with endothelin-1 followed by perivascular electrical stimulation (ES), exogenous CGRP (10 μg/kg) or capsaicin (30 μg/kg) in the absence or presence of BIBN4096BS (100 μg/kg).

Results ES dilated the dural artery voltage-dependently, with a maximum increase of 114 ± 38% of preconstriction. CGRP and capsaicin increased the vessel diameter by 157 ± 36% and 119 ± 18%, respectively. The increased vessel diameter was significantly attenuated with BIBN4096BS in all the study groups.

Conclusion The data suggest that this model can be used for studies on the mechanism of anti-migraine drugs as previously demonstrated in rats. This mouse model offers the advantage of studying transgenic animals.

Keywords: migraine, mouse, intravital microscopy, perivascular stimulation, CGRP

Classification of headache

P001

Tension-type headaches: an integrated model

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Background It seems that the underlying pain mechanisms in TTH vary in their presentation. Current studies seem to support the existence of three main types of TTH patients including: (I) myofascial subgroup, (II) psychosocial subgroup, and (III) mild migraine subgroup.

Methods A model was developed from the current literature which seems to support the existence of several subgroups of tension-type headache.

Findings
(I) Myofascial subgroup. These patients are currently characterized as TTH with pericranial tenderness under the current IHS classification.
(II) Psychosocial subgroups. Patients in this subgroup may have a poorly functioning descending pain modulating system, possibly as a result of poor coping mechanisms.
(III) Mild migraine subgroup. Alternatively, patients in the mild migraine subgroups may have a well-functioning pain modulation system accompanied by well-developed adaptive coping skills. These patients may be able to prevent a progression of migraine and experience this headache episode as only a TTH.

Conclusions This proposed model stresses the importance of differentiating the subgroups of tension-type headache.

P002

Is diagnosis of cervicogenic headache (CH) specific enough to separate from migraine headache (MH)?

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The diagnostic criterion for CH appears to include characteristic of MH.

Purpose To determine if proposed criteria were specific enough to separate CH from MH.

Methods A prospective evaluation of headache location, associated symptoms (nausea, vomiting) early (with the start of headache) or late (>2 h after headache started), photophobia and phonophobia (early and late), pain radiation, and neck mobility done in CH patients (Sjaastad criteria + diagnostic blocks) in comparison with age-matched MH without aura.

Results Thirty CH patients, mean age 28 (range 18–47), n = 23 women and n = 7 men. Mean age for MH was 26 (range 18–45), n = 25 women and n = 5 men. Side-locked headaches in n = 26 CH compared with n = 2 MH, P < 0.0001. CH was occipitotemporal n = 20, early frontal radiation n = 6, late frontal radiation n = 15. MH was frontal n = 25, temporopariental n = 5, early occipital radiation n = 5, late radiation n = 18, P < 0.05. Persistent headache between severe episodes CH n = 23, MH n = 3, P < 0.001. Late nausea n = 20 and early n = 2 in CH, where as in MH very early nausea n = 28, P < 0.0001. Vomiting reported in n = 11 MH, none in CH. Early photophobia and phonophobia n = 2, late photophobia and phonophobia n = 8 in CH, n = 25 MH early photophobia and phonophobia, P < 0.001. N = 28 CH and one MH had neck stiffness and reduced motion P < 0.0001.

Conclusion CH can mimic MH. CH can be differentiated from MH on the proposed diagnostic criteria with attention to associated symptoms, particularly the time of their onset in relation to headache.

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Validation of a simple semiobjective methodology for headache classification.

Keywords: Headache Disorders.

discuss the problem of 2nd International Classification of Headache Disorders, included the chronic ones.


closely related by many authors. While many authors discuss these, they were thought to be coincidental. This discrepancy may be due to diagnostic difficulty of migraine. Epidemiological incidence of epilepsy in migrainers is significantly great. Patients with epilepsy are more likely to develop migraine. These findings support close association of migraine and epilepsy. Migrainers often have increased driving response, represent cortical hyperexcitability. Migralepsy and epilepsy are extremely rare. Migralepsy was first described by Lennox in 1960. It is known as common in children, however, the reported cases of migralepsy are extremely rare.

Objective We report our own experience of patients with migralepsy.

Results Migralepsy is not rare, even in adults. History taking is essential for differential diagnosis. Appropriate medication resulted in good control.

Conclusion Migraine and epilepsy were thought to be closely related by many authors. While many authors discussed these, they were thought to be coincidental. This discrepancy may be due to diagnostic difficulty of migraine. Epidemiological incidence of epilepsy in migrainers is significantly great. Patients with epilepsy are more likely to develop migraine. These findings support close association of migraine and epilepsy. Migrainers often have increased driving response, represent cortical hyperexcitability. Migralepsy should be differentiated from post-seizure headache, epileptic migraine, or benign occipital epilepsy of childhood. We will discuss the problem of 2nd International Classification of Headache Disorders.

Keywords: aura, epilepsy, headache, migralepsy, migraine

P004

Validation of a simple semiobjective methodology for headache classification.

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Objective Aim of the study was to control the reliability between the IHS Classification 1988 and a semiobjective methodology for headache classification.

Methods and results—I A 5-item (Yes or No) questionnaire was completed by pharmacological challenges, hyperalgesia/alldynia measurements, neurobiological makers. A randomized sequence of HIS ‘88 and semiobjective classification was administered to 80 headache sufferers, university students balanced for sex. Reliability between the two classifications was controlled by the Cronbach’s α(0.7).

Methods and results—II In 3445 subsequent sufferers (2094 females, mean age 36.4 ± 3.2 SD) observed during 8 years, results indicate a high internal consistency of the semiobjective methodology. Regarding validity, because of the known lack of gold standard, we used the alternative approach of identifying symptom clusters, biological markers, treatment response. The 8-year study outlines the design and validation of an instrument which can be used by briefly (1 h) trained non-specialists. The semiobjective methodology ascertained 100% of migraine and tension-type headache (100% sensitivity). Instrument was independent of the knowledge—patient and operator—of migraine and tension-type headache. Concerning generalizability, the semiobjective classification can be successfully applied to the milder as well as to the severest forms of headache, included the chronic ones.

Keywords: headache, classification, validation, internal consistency

P005

Premonitory and resolution symptoms in migraine: a prospective study in 100 unslected patients

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Objectives To analyse premonitory (PS) and resolution (RS) symptoms in migraine.

Methods 100 unslected migraine patients filled in, for three attacks, a PS and RS questionnaire containing 28 symptoms (referring to the days before and after the beginning and resolution of migraine headache) and a headache questionnaire with the IHS items for migraine diagnosis. True RS or PS were those experienced the day before (or the day after) the headache had started only if these were not present in a headache-free questionnaire.

Results True PS and RS were experienced by a total of 84 and 78 subjects for the first attack. The mean and range (per patient) of PS and RS were 6.8 and 0–20 and 4.6 and 0–15, respectively. The most common individual PS were anxiety (46%), phonophobia (42%), irritability (42%) and unhappiness (30%). The most common PS were asthenia (55%), tiredness (46%), somnolence (29%) and concentration difficulties (28%). Mean PS and RS consistencies in at least two out of three attacks were 63 and 61%, respectively.

Conclusions Around 80% of standard migraineurs experience true RS and PS. Neuropsychiatric (82% of subjects) and general (69%) symptoms are, respectively, the most frequent PS and RS.

Keywords: migraine, premonitory symptoms, resolution symptoms

P006

Influence of demographic and clinical variables on premonitory and resolution migraine symptoms

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Objectives To analyse the influence of demographic and clinical variables on premonitory (PS) and resolution (RS) migraine symptoms.

Methods 100 unslected patients filled in, for three attacks, a PS and RS questionnaire containing 28 symptoms and a headache questionnaire with the IHS items for migraine diagnosis. True RS or PS were those experienced the day before (or the day after) the headache had started only if these were not present in a headache-free questionnaire.
Results The frequency and distribution of PS and RS did not differ in males vs. females or in migraineurs over vs. under 40. Both PS and RS were numerically more frequent in migraine with aura compared with without aura. There was also a tendency for PS and RS to be more frequent in patients with severe pain compared with those with slight–moderate pain. This tendency was not seen for the MIDAS scores. Interestingly, PS and RS were statistically and numerically (respectively) less frequent in those patients on preventatives compared with those not on preventatives.

Conclusions Migraine with aura and severe pain are risk factors for PS and RS, while the use of preventatives seems to be protective, especially for PS.

Keywords: migraine, premonitory symptoms, resolution symptoms

P007

Headache as an initial symptom in multiple sclerosis

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Objective In order to examine the association between multiple sclerosis (MS) and headache, we analysed the patients who presented headache as one of the initial symptoms of MS.

Methods We reviewed the records of 107 patients who had been admitted to our hospital with a diagnosis of MS from 1988 to 2004. Patients who experienced headache as one of first symptoms of MS attack were classified as the headache group, and the other patients as the non-headache group. Patients with pain due to optic neuritis or trigeminal neuralgia were classified as the non-headache group.

Results The headache group was composed of eight patients (7%) (seven experienced headache resembling tension-type headache and one migraine). Female/male ratio was 3.0 and 1.9 for the headache and the non-headache groups, respectively. Age of MS onset and all the laboratory data were similar between both groups. In the headache group, MRI showed plaques in the thalamus (13%), brainstem (25%) and cervical spinal cord (13%). In one patient headache recurred at the MS relapse. There were patients whose initial symptom of MS was only headache.

Conclusion MS should be included as one of the differential diagnoses when patients seek medical attention due to headache.

Keywords: multiple sclerosis, initial symptom, headache, MRI

P008

Spike and wave headache

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500 cases of chronic headache were analysed in 2 years (1998–2000). Out of this 500 cases, 175 cases of chronic headache have epileptic background. None of the (175/500 cases) has symptoms of seizures (loss of consciousness/ altered senso-rium or tonic and clonic moments). Headache is the only symptom of presentation. Headache as part of seizures or postical is not taken into consideration. Three subgroups are noticed in these 175 (35%) cases. (1) Calcified granulamases are commonly seen in India in large population; of the 175 cases of chronic headache (epileptic background) 61 cases (35%) have calcified granulamas. All of these case have EEG done and showed either spike wave discharge or sharp wave discharge—none of these patients has seizures before or during headache. (2) Chronic headache in 35 cases out 175 cases (20%) gave history of febrile seizures up to 5 years; all these 35 cases are above 15 years—no fresh episodes of seizures during headache. (3) 79 cases of chronic headache out of 175 cases gave positive family H/O seizures (siblings/cousins on treatment for seizures), EEG showing interictal, sharp wave/ slow wave discharge.

Conclusion Spike and wave headache (hemicrania epileptica) forms significant percentage (2–3%) of general population. It needs to be included in the one of the major groups in primary or secondary headache classification.

P009

Probable migraine in nurses—Hallym University migraine in nurses study

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Background and objectives According to IHS criteria, probable migraine missed one of features needed to fulfil all criteria for migraine. There were several reports on prevalence and clinical characteristics of migraine in Korean population but no reports on probable migraine. We assessed the prevalence, clinical features of migraine and probable migraine in Korean nurses.

Method We sent a 72-item questionnaire to all 1501 nurses working at Hallym Medical Centre. The completed questionnaires were analysed for migraine and probable migraine.

Results 1340 nurses completed the questionnaire. All nurses were female with a mean age of 27.49 ± 5.70. 13.4% were classified as having probable migraine. Mean attack frequency for probable migraine was 3.86 ± 5.29 per month. Mean MIDAS score for probable migraine 4.65 ± 9.08. 17.5% of them were noted as having migraine. Mean attack frequency for migraine was 4.25 ± 5.87 per month. Mean MIDAS score for migraine was 4.73 ± 7.52. Pulsating quality, aggravation by routine physical activity, association of nausea of vomiting, severe headache intensity and photophobia were less common in probable migraine than migraine.

Conclusion Both migraine and probable migraine were common headache disorders in Korean nurses. Probable migraine showed somewhat different clinical characteristics from those of migraine.

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P010

Diagnostic criteria of trigeminal neuralgia and persistent idiopathic facial pain

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Background Recurrent or chronic facial pain may be a diagnostic challenge. Applying the diagnostic criteria of ICHD-II leaves a considerable number of patients unclassifiable.

Objectives To establish and evaluate revised criteria of trigeminal neuralgia and persistent idiopathic facial pain.

Methods Based on the diagnostic value of 12 features of trigeminal neuralgia and 15 features of persistent idiopathic facial pain in 97 patients, we established the following revised criteria for persistent idiopathic facial pain (abbreviated): A. Persistent pain in the face. B. At least four of the following: 1. At onset confined to a limited area. 2. Deep and poorly localized. 3. Moderate or severe intensity. 4. No paroxysms. 5. No precipitation. C. No autonomic symptoms and no sensory loss. D. No relevant abnormality in laboratory investigations. In addition, we established criteria for probable trigeminal neuralgia and probable idiopathic facial pain.

Results Applying the newly proposed criteria reduced the number of patients with facial pain not classifiable by more than 50%. The new criteria improved the sensitivity, particularly in idiopathic facial pain, and did not cause a relevant decrease in specificity compared with ICHD-II.

Conclusion This study suggests that amendments to the ICHD-II criteria improve the diagnostic classification of facial pain.

Keywords: ICHD-II, diagnostic criteria, trigeminal neuralgia, persistent idiopathic facial pain

P011

Review of International Classification of Headache Disorders (ICHD-II) diagnoses of 50 consecutive patients with chronic daily headache

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Background Transformed migraine (TM), as defined by Silberstein and Lipton (1) is not included in ICHD-II (2). This study explored the possibility that many of these patients satisfy criteria for chronic migraine (CM).

Methods The charts of 50 consecutive patients with chronic daily headache (CDH) in an academic headache clinic were examined with particular attention to criteria for CM. Of these, 41 were initially diagnosed as TM, four as CTH, one as hemicrania continua (HC) and four as new daily persistent headache (NDPH). If chart notting was insufficient, patients were further interviewed by phone.

Results Of the 50 CDH cases reviewed, 42 were found to fulfil all ICHD-II criteria for CM or probable CM (84%). Four were found to fulfil the criteria for CTH (8%), one for HC, and three for NDPH. None had symptoms, signs, or testing results consistent with secondary headache.

Conclusion Surprisingly high numbers of cases of CDH were found to fulfil ICHD-II criteria for CM (84%). All TM patients met criteria for CM. While TM is not classified by ICHD-II, CM criteria seem to capture most of these.

Keywords: chronic daily headache, transformed migraine, chronic migraine

References


P012

A grouping issue of 3417 patients with headache at our ‘Headache Clinic’ arising from the new IHS classification

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Objective Based on the new IHS classification, 3417 patients diagnosed by our clinic were estimated into a total 18 types consisting of the primary headaches as Part 1 into four groups, the secondary headaches as Part 2 into 12 groups, and other headaches as Part 3 into two groups.

Methods For 1 year and 10 months from the starting business, 5167 patients attended. Of all patients, 3417 patients (66%) (male:female 1013 : 2404, mean age 42.8 years) complained of a headache and/or head dullness. These patients were diagnosed by a past and family history, present illness, physiological and neurological findings, and head MR imaging including paranasal sinuses and cervical spine (performed in 80% patients).

Results The primary headache was classified into 975 migraines (29%), 2260 tension-type headaches (66.2%), 38 cluster headaches, and three other primary headaches. The secondary headache was grouped into 14 cases in Group 5, five cases (four SAHs, one ICH) in six, 14 cases including 10 brain tumours in seven, 27 cases including medicine-overuse headache in eight, no case attributed to infection in nine, five cases in 10, 61 cases including 55 patients including rhinosinusitis in 11, nine cases including four due to somatization disorder in 12. Part 3 was classified into six cases in 13, one case in 14.

Conclusion The new IHS classification was very useful for a diagnostic material for the treatment of headache.

Keywords: ICHD-II, headache, migraine, tension-type headache, MRI
P013
Comparison between taste temperaments of patients with migraine without aura type headaches 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 complicated diseases as chronic headache.

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 were 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 behaviour to some distinct tastes, while temperaments in headache patients had different patterns as three groups detected as sweet-sour temperament with distinct phobic behaviour 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 \( r \approx 0.02, \ P \approx 0.10 \).

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

Keywords: taste temperaments, chronic headaches, migraine without aura

P014
Primary stabbing headache; clinical aspects and outcome in a 2-year follow-up study
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Background Primary stabbing headache (PSH) is a quite unknown disorder.

Objective There has been no report about the prognosis of PSH and factors influencing it.

Methods Between February 2001 and December 2001, 107 patients were recruited consecutively and prospectively. These patients derived from a total 1756 patients visiting our Headache Clinic during the same period. We tried to make contact with and interview them by telephone in December 2003. Overall recurrence rate and factors influencing it were investigated.

Results The interview was successful in 80 patients (mean age 46 years, range 12–80 years; 55 women and 25 men). Mean duration of follow-up was 807.2 ± 137.4 days. Twenty-nine of 80 patients (36%) suffered recurrence. The recurrence rates were significantly higher in males \( (P = 0.048) \). Precipitating factors for recurrence were reported by 18 patients (62%). The most frequently reported precipitants were fatigue and stress.

Conclusion Although PSH are self-remitted in virtually all cases, recurrence could be expected in more than one-third within 2 years. Recurrence rate may be higher in males than in females. Fatigue and stress are most common precipitants of recurrence.

Keywords: Primary stabbing headache, recurrence

P015
Headache after whiplash is likely to represent stress-induced primary headache
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Background Acute and chronic headache attributed to whiplash injury are new diagnoses in the ICHD-2.

Objective To assess the validity of these nosological entities by studying the headache pattern in exposed individuals in Lithuania where negative expectations and secondary financial gain are almost non-existent.

Methods An inception cohort study in which 200 rear-end car accident victims answered headache questionnaires after 2 weeks, 2 months and 1 year, and 193 matched controls at inclusion and after 1 year.

Results Of 75 accident victims developing headache within 7 days, 37 did and 38 did not accord with criteria for acute whiplash headache (i.e. concomitant neck pain). Migraine and tension-type headache occurred in similar proportions, and the long-term prognosis was also similar. Pre-existing headache was a strong prognostic factor for both acute and chronic pain. Compared with the control group, the 1-year incidence of new or worsened headache, or of headache improvement, was similar.

Conclusion Acute whiplash headaches seem to represent episodes of a primary headache, probably precipitated by stress. The nosological validity of both acute and chronic whiplash headache is poor since headaches fulfilling the criteria lack distinguishing clinical features and have the same prognosis as headaches in a control group.

Keywords: whiplash, headache, cohort, Lithuania, validity

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P016

Presence of low CSF pressure headache due to dehydration

Jun Teramoto
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Objective Low CSF pressure headache was reported to only be due to loss CSF, but the dehydration could cause the same headache due to low CSF. To resolve these problems, we observed patients who consulted my clinic with complaints of dehydration in summer.

Patients and methods Seventeen patients (five male and 12 female, from 23 to 78 years old) who consulted my clinic with complaints of headache, dizziness and nausea from June to August in 2004. Headaches were not pulsatile and were shown bilaterally in all patients. Headache and dizziness decrease when lying down or with the Valsalva manoeuvre. Lumber puncture was not performed for humane reasons. The average blood pressure was 83.3 ± 4.7 mmHg. Drip infusion of 500 ml was done.

Results After infusions, headaches completely decreased in nine cases (52.9%) and moderately in eight (47.1%). Dizziness and nausea showed almost the same results. The average blood pressure increased to 88.6 ± 2.5 mmHg. After this therapy, patients were instructed to drink much more water with salt, and the prognosis was favourable.

Conclusion A low CSF state is the suspected aetiology of the headache in these patients. We must appreciate the possibility of headache due to low CSF such as dehydration.

Keywords: low CSF pressure headache, dehydration, drip infusion, low product of CSF

P017

Aircraft headache

Jun Teramoto
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Objective Sunaga et al. (Japan) were the first to report a severe headache when landing an aircraft in 1997. We experienced eight such cases.

Patients Eight patients visited my clinic with the complaints of severe headache when boarding an aircraft. The age was from 28 to 47 years old with a mean of 33.4 ± 6.3. Four cases were male and four were female. All cases developed severe headache when the altitude was decreasing for landing. The nature of the pain was all non-pulsating. Five cases were bilateral and three were hemilateral. Nausea was seen in one case. The appearance of the headache was always in five cases and sometimes in three cases. The headache naturally disappeared within 1 h after arrival in seven cases. One case continued for about 12 h. Two cases who took indomethacin on the flight showed a lighter headache compared with a usual flight.

Conclusion Almost any headache clinic doctor has experienced such patients in Japan. In ICHD-II, a headache of 13.10 external compression headache is confirmed, but the increase of air pressure in an aircraft when landing is about 10%. Thus, we propose that this type of headache should be classified as a new clinical entity.

Keywords: aircraft headache, external compression headache

P018

Headaches from wearing eyeglasses

Jun Teramoto
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Objective External compression headache is induced by strong pressure to the head. Apart from this, experienced severe headache due to smaller power with the use of eye glasses.

Patients (Case 1) For 3 months, a 64-year-old female developed severe bilateral non-vascular headache when using eye glasses. When removed, the headache decreased rapidly. (Case 2) A 62-year-old female developed right-left non-vascular severe headache recently when using eye glasses. After removal, her headache continued 5 h. Several years ago, she had experienced this in the same period. (Case 3) Migraines in a 48-year-old female. Over the past 15 years when using sunglasses, severe bilateral headaches have occurred and recovered by removal of the glasses. (Case 4) The daughter of case 3, 21 years old, except for migraine, when using eye glasses developed the same headache as her mother for 1 year. (Case 5) A 37-year-old male developed a severe headache when using eye glasses for 7 years. The headache appeared within 2 min and disappeared within 3 min by their removal.

Conclusion These five patients developed severe headaches from the use of eyeglasses and by their removal the headache recovered. The pressure of an eyedglass string is not tight compared with a Swim-goggle headache. These headaches were induced by small power, so they should be confirmed as a new subgroup of external compression headaches.

Keywords: eyeglass headache, external compression headache

P019

Headache during extracranial endovascular procedures

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Headaches attributed to carotid angioplasty, endovascular procedures or angiography feature in the Revised 2004 International Classification of Headache Disorders in more detail. In this study presence and characteristics of headaches during or after endovascular procedures applied in patients with carotid stenosis more than 70% are investigated. Preliminary results of 40 patients (13 women, 27 men) are presented. Among 40 patients 11 (27.5%) described momentary, burning pain during angiography, especially during administration of contrast material. Mean age of patients with headache during angiography was lower than patients without pain (57.7 ± 12.9 vs. 65.1 ± 8.33 years). A group of 12 patients (30%) defined ipsilateral, burning headache, lasting < 10 min during or after stent procedure. Mean age of group with headache after stent procedure was lower than group without headache as in angiography group (58.8 ± 10.5 vs. 65.9 ± 10.3 years). Number of neurologically asymptomatic patients was also
higher among patients without headache than with headache. Difference of risk factors (hypertension, diabetes mellitus, hyperlipidaemia and smoking) or presence of primary headache is not detected in both groups. Presence of lesser degree of headache during or after endovascular procedures among older and neurologically asymptomatic patients led to impression of possible association between colateral circulation and headache.

P020
Clinical analysis of occipital neuralgia
Jun Teramoto
Teramoto Neurology Clinic, Japan

Objective The classification of occipital neuralgia described in ICHD-II is too simple. There are three main neuralgias: greater occipital (GO), minor occipital (MO) and major auricular (MA) neuralgias. We examined symptomatically these neuralgias in Japanese cases.

Patients and methods A total of 797 cases (304 male and 493 females) were investigated clinically. The age ranged from 11 to 85 years with a mean age of 49.9 ± 16.8.

Results Diagnosis was 599 cases (75.1%) with GO neuralgia, 93 cases (11.7%) with MO, 50 cases (6.3%) with GA, and 35 cases (6.9%) of combined neuralgias. Distribution of combined neuralgia was 20 cases of GO + MO, 18 cases of GO + GA, 11 cases in GA + GA and four cases in GO + MO + GA. The affected side was bilateral in 43 cases (5.6%), right in 346 cases (45.2%) and left in 376 cases (49.2%). However in males, slightly right-sided cases were more numerous. Age of onset, the 6th decade was the most frequent time of onset. Seasonal appearance was in spring, autumn, summer and winter in that order. The ratio occipital neuralgia vs. migraine was 1 : 3.9 in our clinic.

Conclusion There are few detailed reports on occipital neuralgia. In the present study, the outline of Japanese occipital neuralgia cases was clarified. The classification must be made in more detail, because these patients are seen much in Japanese headache clinics.

Keywords: clinical analysis, greater occipital neuralgia, minor occipital neuralgia, major auricular neuralgia

P021
Osmophobia as a criterion for the diagnosis of migraine
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Intolerance to smell is often reported by migraine patients; despite this, the relationship between osmophobia and migraine has not been investigated in depth. This study evaluates osmophobia in connection with the diagnosis of migraine and tension-type headache. We recruited from our Headache Centre patients with diagnosis of migraine with (MA) and without aura (MoA), and episodic tension-type headache (ETTH); patients with two or more forms of primary headaches were excluded. 704 patients entered the study (545 females, 159 males; age 37 ±12); of them, 477 were MoA, 92 MA, 135 TTH. Among migraine patients, 43% with MoA (205/477) and 39% with MA (36/92) reported osmophobia during the attacks; none, among the 135 TTH patients, suffered this symptom. A greater percentage of females than males had osmophobia (45% vs. 33%). In the appendix of the second edition of the International Headache Society Classification (IHS, 2004), osmophobia has been proposed in the associated symptoms category of the criteria for the diagnosis of migraine. We conclude that osmophobia has a low sensitivity; but is a very specific marker to discriminate adequately between migraine (MoA and MA) and ETTH; therefore, it should be considered as a new criterion for the diagnosis of migraine.

P022
Application of ICHD 2nd edition criteria of chronic headaches with the aid of a computerized, structured medical record
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Introduction We recently developed a computerized, structured medical record based exclusively on the ICHD 2nd edition classification system for primary headaches.

Methods We tested the computerized structured record by entering and analysing 200 consecutive clinical sheets of primary chronic headaches and the corresponding output diagnoses.

Results The diagnosis of chronic migraine (CM) could be obtained for 36 patients (18%), that of probable CM (PCM) + probable medication-overuse headache (PMOH) for 45 (22.5%). Chronic tension-type headache (CTTH) and probable CTTH + probable MOH were diagnosed in 18 (9%) and 21 (10.5%) patients, respectively. In 38 cases (19%) diagnoses of CM or CTTH, and in 42 cases (21%) diagnoses of PCM or CTTH and PMOH, did not obtain an output diagnoses of headache, mainly because not enough criteria were fulfilled for the diagnosis of migraine without aura and tension-type headache, respectively.

Conclusion In the present study, ICHD-II classification does not allow the diagnoses of CM or CTTH or probable forms, in the case of medication overuse in about 40% of patients because the mandatory criteria for the diagnosis are too stringent and do not reflect modification of headache pattern in relation to its chronization.

Keywords: ICHD-II, chronic headaches, computerized system
P023
Chronic headache attributed to CSF hypovolaemia (broadening of CSF hypotension syndrome)
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Background Spontaneous intracranial hypotension (SIH) is characterized by orthostatic headache, low CSF pressure and diffuse dural enhancement in MRI. Recently cases of SIH without orthostatic headache or low CSF pressure or diffuse dural enhancement were reported. Mokri mentioned that pathophysiology of SIH was not CSF hypotension but CSF hypovolaemia. Many cases of SIH must be misdiagnosed.
Objective Clinical and neuroradiological evaluation of CSF hypovolaemia was performed.
Method Cases of suspected CSF hypovolaemia were evaluated with RI cisternography and cranial MRI. All cases were treated by epidural blood patch.
Results Of 668 cases with CSF hypovolaemia, 312 cases were associated with whiplash injury and no cause was detected in 240 cases. Most prominent symptom was chronic headache. Other symptoms were neck pain, photophobia, dizziness, insomnia, memory disturbance and fatigue, etc. Mean CSF pressure was 12.5 cm H2O. RI cisternography showed positive findings in 80% and positive MRI findings rate was 60%. Outcome was excellent 22%, good 40%, fair 27%, poor 8%.
Conclusion Many cases of CSF hypovolaemia were not compatible with ICHD-II. Broadening of CSF hypotension syndrome is proposed.
Keywords: CSF, hypovolaemia, spontaneous intracranial hypotension, epidural blood patch, RI cisternography

P024
Paroxysmal stabbing headache appearing on the multiple nerve dermatomes: a variant of primary stabbing headache or occipital neuralgia?
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Objectives Paroxysmal stabbing or icepick-like headache in the multiple nerve dermatomes, especially involving both trigeminal and cervical nerves, is not fully explained or classified by the recent International Headache Classification II.
Methods Among patients attending Hallym University Medical Centre because of acute-onset paroxysmal stabbing headache during last 3 years, 28 consecutive subjects in whom stabbing symptoms involved multiple dermatomes at initial presentation or during the courses, were prospectively enrolled.
Results All patients were neurologically and otorologically free. There was coincidental involvement of both trigeminal and cervical nerve dermatomes in seven cases, initially trigeminal and then cervical nerves in six, cervical nerves and then trigeminal nerves in five, and multiple cervical nerve branches (lesser occipital, greater occipital, greater auricular) in the rest of patients. The nature of pain was very short-lasting and previous history of headache of same nature was reported in 13 cases. Preceding symptoms of infection and physical and/or mental stresses were in seven and six subjects, respectively. All had a self-limited benign course recovering completely in 2–30 days.
Conclusion Paroxysmal stabbing headache appearing on multiple dermatomes can be explained by spread and referral of pain, and considered to be a variant of primary stabbing headache or occipital neuralgia.

P025
Prevalence of migraine among medical students in Sri Lanka
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Background Prevalence of migraine among medical students (MS) in Sri Lanka is unknown.
Objectives Find the prevalence and common precipitating factors of migraine among MS.
Methods Self-administered pretested questionnaire was given to consented MS in Faculty of Medicine, Galle. The data collected were age, gender, whether suffering from longstanding headache, duration, onset, site, nature, severity, associations, precipitating factors and details of aura. Prevalence was calculated according to IHS 2004 criteria.
Results Of 622 MS who consented, 188 (30.22%) suffered from longstanding headache and 47 (7.6%) fulfilled IHS criteria for migraine. Age range was 19–29 years; 16 (34%) were males and 31 (66%) were females. Of them, 18 (38.3%) had aura, 29 (61.7%) had no aura. Eleven (61.1%) had visual aura, three (16.67%) had sensory aura and one (5.55%) had both. Common associated symptoms identified were phonophobia 31 (12.77%), photophobia 27 (65.96%), nausea 21 (57.45%), vertigo six 12.77%. Common precipitating factors were being in the sun 37 (78.72%), travelling 25 (53.19%), sleep deprivation 25 (53.19%), hunger 22 (46.81%), continuous physical activity such as walking, climbing stairs, etc. 15 (31.91%) and food nine (19.15%).
Conclusion Headache is a common health problem among medical students. 7.6% fulfilled the criteria for migraine. Two thirds were females. Being in the sun, travelling, sleep deprivation and hunger were identified as common precipitating factors.
Keywords: migraine, medical students, prevalence, precipitating factors, Sri Lanka

P026
Tension or migraine—clear-cut differentiating features
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Objective To document clear-cut features to differentiate tension headaches from migraine.
Method 1022 patients were prospectively studied. All were diagnosed as ETTH or just tension headaches in the past [bilateral, non-throbbing, continued with routine activities, phonophobia alone (782), photophobia alone (240)]. All common and known triggers (except tension anxiety), family
history of migraine, activity affected or not, autonomic symptoms, how headache got aborted and migraine trait symptoms were recorded. Diagnosis of migraine: 877 patients had one of the common migraine triggers in our region precipitating these headaches. 807 had one of the family members with migraine pain. All of them continued with their activities. 783 reported that only sleeping off aborted their headaches and 239 had to lie down after completing their activities to get rid of their head pain. 307 reported either dizzy spells or motion sickness (present or past) associated with one of the common migraine triggers.

**Conclusion** Common migraine triggers precipitating headache, family history of migraine, sleeping off or lying down to abort the headache and migraine trait symptoms will definitely differentiate most of the tension as migraine.

**P027**

**Motion sickness and dysmenorrhoea with autonomic symptoms and vertigo—are they periodic syndromes?**

M. V. Francis

**Headache and Migraine Centre, Cherthala, Kerala, South India**

**Objective** Cyclical vomiting, abdominal migraine and benign paroxysmal vertigo are precursors of paediatric migraine. This study is to show that motion sickness and dysmenorrhoea with autonomic symptoms and vertigo are similar entities.

**Methods** 142 patients with past history of motion sickness (multiple vomiting episodes while travelling by bus) presented with IHS 1.1, 1.2 while bus travelling, were included in this study. 19 female migraineurs (1.1 and 1.2) who complained of severe dysmenorrhoea with autonomic symptoms and vertigo while trying to get up from bed were also included. Three female patients with same dysmenorrheic symptoms but without migraine headaches were included as their children were getting short duration migraine attacks with vomiting.

**Conclusion** This study shows that motion sickness is a precursor of migraine headache and to be considered as a periodic syndrome. Severe dysmenorrhoea with autonomic symptoms and vertigo also to be considered as another periodic syndrome in adolescents and adult female migraineurs as it helps in diagnosing early migraine or migraine trait in their children.

**P028**

**Comparing a novel probability and IHS diagnostic models for menstrual migraine**

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**Background** A new IHS research criteria for menstrual migraine has been proposed, however, these criteria need to be validated before included in the main classification system.

**Objective** To compare menstrual migraine diagnosis using IHS criteria and a new probability model using prospective, daily diary data.

**Methods** 62 women aged 19–45 reporting increased migraines with menses were recruited through advertisements. For 3 consecutive months, subjects recorded headache severity four times daily and occurrence of menses. Headache diagnoses were assigned using IHS research criteria and a novel probability model. The probability model, based on a binomial distribution, was used to determine whether migraine reports represented a statistically significant menstrual pattern or random occurrence.

**Results** The IHS criteria and probability model gave significantly different results ($P < 0.001$). Perfect agreement occurred for IHS true menstrual migraine (five cases) and non-menstrual migraine (24 cases), but only 62% for the 33 IHS menstrually related migraine cases. Significant increases in headache index ($P = 0.02$) and somatic and emotional symptoms ($P = 0.003$) during the menstrual days were more likely to occur in women with menstrual migraine identified by the probability method compared with classification using the IHS criteria.

**Conclusion** A probability diagnostic model more accurately identified menstrual migraine than the proposed IHS criteria.

**Keywords:** IHS diagnosis, menstrual migraines, probability model

**P029**

**Characterization of headache presenting to a tertiary allergy clinic**

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**Background** Migraine and allergy are common disorders of childhood. Many adults with migraine are misdiagnosed with sinusitis and referred to allergist. Proper headache diagnosis is essential to effective treatment.

**Objective** Assess the frequency of headache in a tertiary allergy clinic and determine the headache diagnosis.

**Methods** 133 consecutive patients (mean age 8.2 ± 3.4; M:F 74 : 59) completed a detailed headache questionnaire, the Children’s Health Survey for Asthma (CHSA) and PADQLQ as part of their routine allergy assessment. Independent diagnosis of headache was established.

**Results** 61 (45.9%) patients reported having recurrent headache [mean frequency –5.8 ± 8.1 h; mean duration –3.1 ± 4.8 h; mean severity 5.6 ± 2.3 (0–10 point scale)]. Headache was a reason for referral in nine. PedMIDAS score was 20.2 ± 34.4. Using independent measures (CHSA and PADQLQ), 42.5% and 54.4% (controls 22.9%) reported headache. 63.9% headache patients had a diagnosis of migraine or migrainous headache. Photophobia (17) and phonophobia (17) were the most common associated symptoms.

**Conclusion** Headache is more common in allergy patients than controls. The majority of these headaches are migrainous. The complementation of three independent assessments and the high occurrence of migraine emphasize the
importance of migraine recognition in patients presenting with allergies.

**Keywords:** migraine, headache, paediatric, allergy, diagnosis

**P030**

**Is there an effect of a 2-month drug-free period in patients with probable medication-overuse headache?**

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**Background** Primarily based on expert opinion, ICHD-II introduced specific diagnostic criteria for medication-overuse headache. Data are needed to obtain evidence-based criteria.

**Objective** To investigate the development in headache frequency (days/month) for patients with probable medication-overuse headache (pMOH), following a 2-month drug-free period.

**Methods** Case records for patients discharged from Danish Headache Centre in 2002 and 2003 were evaluated and headache frequencies, before and after medication withdrawal, were established for patients with pMOH.

**Results** Out of 1326 patients, 337 had pMOH. Eligible were 216 who had completed withdrawal. Median age 48 years, male/female ratio 1:2.7. The relative reduction in headache frequency was highly skewed. Overall, 53% of the patients had no reduction. The median reduction in migraine was 67%, in tension type (TTH) 0% and in migraine + TTH (MT) 37%. Comparing medication groups, ergot- and triptan-overusers had the best outcome. Comparing diagnostic groups, the reduction in headache frequency differed significantly between migraine and TTH (P < 0.01) and between MT and TTH (P < 0.01). Excluding ergot- and triptan-overusers neutralized these differences.

**Conclusion** Using headache frequency as effect outcome, half of the patients with pMOH do not benefit from complete medication withdrawal. Ergot- and triptan-overusers seem to have the best outcome.

**Keywords:** medication-overuse headache, medication withdrawal, treatment outcome, secondary headaches

**Patent foramen ovale (PFO) in migraine**

**Q001**

**Patent foramen ovale closure and migraine headache**

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**Objectives** The purpose of this study was to determine the impact of percutaneous patent foramen ovale (PFO) closure on migraine headache frequency.

**Methods** Patients with a PFO associated with atrial septal aneurysm who had a cryptogenic brain infarct (BI) and who underwent a percutaneous closure in our centre were included in this study. A questionnaire was composed to diagnose migraine with or without aura (MA+ and MA−) according to the criteria of the International Headache Society. We focused on three periods: 1 year before BI, after BI but before percutaneous closure, and after PFO closure.

**Results** Thirty-eight patients (mean age 45 years, sex ratio 1) were included in this study. Migraine was present in 15 of 38 patients before BI. Five (13.2%) had MA+, and 10 (26.2%) had MA−. After BI, the prevalence of migraine decreased to 32.5% (P = 0.45 vs. before BI) and to 21.6% after PFO closure (P = 0.025 vs. before BI). We noted no reduction of non-migraine headaches after BI and PFO closure.

**Discussion** We found a high rate of migraine in cryptogenic stroke patients with PFO (39.5%) and documented a decrease in migraine frequency after BI and PFO closure. However, the improvement noted after PFO closure could be due to the natural evolution of migraine after BI.

**Conclusion** More prospective trials are needed to evaluate PFO closure as a prophylaxis treatment of migraine attacks.

**Q002**

**Shunt-associated migraine improves only after atrial septal repair: a case–control study**

G. P. Anzola, E. Morandi, F. Casilli & E. Onorato

**Objective** To compare prospectively the course of migraine in symptomatic (for cerebrovascular disease, CS) and asymptomatic (CA) patients undergoing PFO closure and in patients with PFO treated medically (Ctrl).

**Methods** 20 CS and 24 asymptomatic CA migraineurs underwent PFO closure. Eighteen Ctrl were followed up medically. The severity of migraine was assessed at baseline and in the second 6 months after closure with a numeric scale (score range 0–10).

**Results** Baseline severity of migraine did not differ between groups (6.4, 6.3 and 6.4 in CS, CA and Ctrl groups, respectively). At 1 year the score was 2.1 in CS, 3.5 in CA and 6.8 in Ctrl (P < 0.001 on ANOVA). All Ctrl patients but only 6% of CS and 25% of CA still had aura at the end of follow-up (P = 0.0012 on Fisher’s exact test). Multiple regression analysis showed that only treatment was significant (P < 0.0001).

**Conclusions** Compared with medical treatment, closure of PFO brings about a significant improvement in migraine irrespective of migraine type and of prior cerebrovascular disease. In migraine with aura the occurrence of aura is dramatically reduced.

**Q003**

**Is patent foramen ovale associated with atypical features of migraine aura?**

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Recent reports suggest an increased prevalence of patent foramen ovale (PFO) in migraine with aura (MA) patients and
show that PFO closure reduces attack frequency. Transcranial Doppler (TCD) is a very sensitive tool for detecting microembolic signals in brain circulation after injection of saline solution mixed with air in cases of right-to-left shunt. We set out to evaluate whether PFO is more prevalent among patients with atypical aura features (prolonged aura/interictal aura).

All MA patients referred to a headache unit in the last year underwent contrast-enhanced TCD. Their MA had been diagnosed in accordance with the revised International Headache Society criteria (ICHD-II). We studied 65 subjects (48 females; 17 males; mean age 35.7 ± 10.8). Forty-one (63.1%) of these patients fulfilled the criteria for typical aura and 24 (39.9%) for atypical aura. PFO was more prevalent in the subjects with atypical aura features than in those presenting typical aura (79.17% vs. 46.3%; OR 4.4, CI 1.4, 14.0). These findings were also considered in relation to patient history data and cardiovascular risk factors. Our preliminary results underline the need to look for PFO particularly in subjects with atypical aura, but the underlying pathophysiology is not clear.

Q004
Right to left shunt and subclinical brain lesions in migraine with aura

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Background Aim of our study has been to evaluate the relationship between migraine with aura, right-to-left shunt (RLS) on transcranial Doppler and subclinical brain lesion occurrence.

Subjects and methods 84 patients with migraine with typical aura (mean age 41 years) underwent a structured interview to assess: family history of migraine and/or cerebrovascular diseases, migraine characteristics, use of vasoconstrictor migraine agents, known cerebrovascular risk factors. Laboratory analyses were performed and included serum homocysteine concentration and coagulation panel. All participants underwent a standard neurological examination, contrast transcranial Doppler ultrasonography (c-TCD) recordings, and brain MRI. Brain magnetic resonance images were evaluated for infarcts, by location and vascular supply territory, and for white matter lesions.

Results 38 subjects (45%) were found to have RLS. MRI was abnormal in 24 migraineurs (28%) and normal findings were found in 60 migraineurs. We did not find any significant relationship between RLS and subclinical brain lesions. Hypertension, years of disease and hyperhomocisteinaemia were prevalent among subjects with migraine associated with subclinical brain lesions.

Conclusions According with previous studies, RLS is frequently associated with migraine with aura. The subclinical brain lesions observed in this cohort of migraineurs do not seem related to the occurrence of RLS non-invasively evaluated by mean of TCD.

Keywords: migraine with aura, transcranial Doppler, right-to-left shunt, silent brain lesions

Q005
Atrial septal defect and migraine with aura

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Background Possible associations between migraine with aura and patent foramen ovale (PFO) were demonstrated (1). Complete remission or reduction in migraine frequency and intensity after closure of PFO has been observed by independent research groups (1, 2). In contrast to these reports, exacerbation and new appearance of migraine attacks with aura (MA) after transcatheter closure of atrial septal defects (ASD) have been described (3, 4).

Objective An analogous case history of a patient with MA and ASD will be presented.

Methods Case history.

Results A 27-year-old woman suffered of migraine with aura since age 13 years with mostly two attacks per year. After transcatheter closure of a secundum atrial septum defect she suffered from almost daily recurring migraine attacks with prolonged aura symptoms (hemianoptic visual disturbances and brachiofacial dysesthesias). Six weeks after the intervention, migraine attacks with aura spontaneously decreased to twice per week. The reason for this change in pattern is currently not known.

Conclusion Transcatheter closure of ASDs can be complicated by increase in frequency or new appearance of migraine attacks with aura. We suggest that patients scheduled for transcatheter ASD closure should be screened for migraine and offered neurological follow-up.

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Trigeminal autonomic cephalalgias

R001

Autonomic tests in episodic cluster headache: a comparison between active and remission periods
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Background Cranial autonomic involvement in episodic cluster headache (ECH) is known and well documented. Less is known about systemic autonomic impairment. Moreover, few authors have studied the differences between active and remission phase

Objective To study autonomic nervous system, in particular cardiovascular function, in ECH, either during cluster periods and during remission phases.

Methods 17 ECH patients during active and silent period were studied with: (1) cutaneous sympathetic reflex (CSR) measured on four limbs, (2) measurement of R–R interval during Valsalva manoeuvre (VM), lying to standing test (LS) and deep breathing test (DB). Values were compared with normal, age- and sex-matched controls.

Results CSR, a marker of sympathetic activity, showed no difference either between the active and the silent period or between ECH and normal controls. On the contrary, we found a significant (P < 0.01) difference in VM, LS and DB, tests that explore parasympathetic function: the R–R ratio was lower than in normal controls, either in cluster and in remission period.

Conclusion As previously described, our findings confirm a systemic autonomic involvement, which seems to be ‘chronic’, as it persists beyond the active period. These data are in favour of a parasympathetic more than a sympathetic dysfunction.

Keywords: cluster headache, autonomic system, autonomic tests

R002

Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA). A case report
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Objectives To describe a patient with short-lasting, unilateral, neuralgiform headache attacks with cranial autonomic symptoms, with cranial autonomic symptoms (SUNA). To our knowledge this is the first report of SUNA.

Methods Case report.

Results We present an 11-year-old girl with extremely severe, sharp, unilateral, side-locked headaches of 7 months’ dura-

tion. Pain is located in the back of left eye, with occasional radiation to the ipsilateral temple. It lasts from 40 to 80 s (occasionally 15–30 min). Since its start, the patient has had from 20 to 30 attacks per day. Between attacks she is completely symptom-free. She denies any premonitory features or auras. The attacks are extremely disabling and are associated with profuse tearing strictly on the ipsilateral eye, without conjunctival injection. She does not have other autonomic features. Her disability score, as assessed by the Headache Impact Test (HIT-6), is 63 (severe disability). All probable secondary causes were ruled out. The treatments with indomethacin 25 mg t.i.d., for 2 months (3 mg/kg/day) amitriptyline 50 mg hs (2 mg/kg/day), valproic acid 125 mg t.i.d. (15 mg/kg/day), aspirin plus caffeine, acetaminophen, ibuprofen and mefenamic acid, and gabapentin have been unsuccessful.

Conclusions TACs are an uncommon, often poorly recognized group of primary headaches disorders.

R003

Somatosensory impairment in cluster headache
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Background Cluster headache is characterized by attacks of peri-orbital pain. It is unclear whether somatosensory processing in the trigeminal system is altered due to repetitive pain attacks.

Objective The psychophysical and electrophysiological study addressed the hypothesis that trigeminal somatosensory processing is impaired in patients with cluster headache.

Methods Trigeminal somatosensory processing was assessed by quantitative sensory testing (QST) and laser-evoked cortical potentials (LEP) in 34 healthy human volunteers and 12 patients suffering from episodic (n = 7) or chronic (n = 5) cluster headache. In QST thermal and mechanical detection and pain thresholds were determined on either side. Noxious heat stimuli of an infrared laser stimulator evoked middle and late cortical potentials in vertex and temporal EEG leads.

Results All cluster patients showed somatosensory impairment in various tests in comparison with healthy controls. In six patients warm detection threshold increased. In five patients each cold, mechanical, and deep pain thresholds increased. In four patients each heat pain and mechanical detection thresholds were raised. In six patients LEP components were altered.

Conclusion The majority of psychophysical thresholds increased, indicating a suppression of trigeminal somatosensory processing on the site of cluster headache attacks. This impairment may be a cause for or a result of cluster headache.

Keywords: cluster headache, laser, psychophysics, somatosensory, trigeminal
R004

Occurrence of cluster headache in a nationwide sample of 31 192 Swedish twins
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Background Cluster headache (CH) is commonly held to affect 1 per 1000 individuals of the general population. However, epidemiological data on CH are sparse.

Objective To study the occurrence of CH in a large, unselected sample of twins.

Methods Twins born 1935–1958 were recruited from a national register of twin births in Sweden as part of the Screening Across the Lifetime of Twins (SALT) study. Ascertainment of CH was made through (i) structured and computerized lay telephone interviews using two main screening criteria, namely, a minimum number of key features and self-report of CH (N = 31 192), and (ii) follow-up telephone interviews of screen-positives conducted by two of us (EW & KE) using the updated IHS criteria (n = 256).

Results So far, 46 cases of CH (39 M, seven F) out of 192 screen-positives have been found. Their zygodity distribution was typical and the crude lifetime prevalence 0.15% (1 per 678). Cases had obtained previous diagnoses of CH via neurologists (20), general practitioners (16) and self-ascertainment (3), while four cases were newly diagnosed.

Conclusion CH is a rare condition, although the occurrence appears to be twofold higher than previously thought. In Sweden, headache clinic populations provide only part of the full spectrum of patterns of disease.

Keywords: cluster headache, epidemiology

R005

Cardiac autonomic control in cluster headache: analysis by continuous wavelet transform
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Background The underlying mechanism of cluster headache is unknown, but autonomic symptoms predominate.

Objective To evaluate the sympathetic and parasympathetic activity in males with cluster headache compared with healthy controls.

Methods We examined cardiac autonomic function in 12 male subjects during the headache period (CH) and 10 subjects during the pain-free period (PF). Control group consisted of nine healthy males. Participants rested supine for 30 min before performing an active stand. We used a time frequency analysis of the heart rate (HR) and blood pressure (BP) using a modified continuous wavelet transform (CWT).

Results No differences were observed between groups in HR or BP during rest, or while standing. Low-frequency (LF) fluctuations in BP were similar between groups at all times. At rest, there were no differences in LF or high-frequency (HF) modulations of HR between the groups, and between PF and controls at any point. During stand, CH displayed significantly greater reductions in HF fluctuations of HR than the other groups (P < 0.04) and a trend towards higher LF/HF ratio.

Conclusions Our findings indicate that CH patients have a significant reduction in parasympathetic activity during standing than PF or controls.

R006

Pituitary adenoma presenting with headache and trigeminal autonomic signs: evidenced by side concordance
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Background Different types of symptomatic trigeminal autonomic cephalalgias (TAC) were reported in patients with pituitary adenoma.

Objective To analyse the patterns of headache and trigeminal autonomic signs (TAS) in patients with pituitary adenoma.

Methods We reviewed patients with headache and MRI-confirmed pituitary adenoma from 1998 to 2004. Headache profile, the presence or absence of TAS, the locations and size of pituitary adenoma, and treatment efficacy were recorded. TAS was defined as ≥ 1 ICHD-II TAC autonomic sign.

Results Twenty-seven patients (21 F/6 M) with pituitary adenoma were collected, including 17 with TSA and 10 without. Twelve (71%) patients with TAS and six (60%) without TAS reported daily persistent headache. In the TAS group, the tumour locations (left, right or bilateral) were significantly correlated to the sides of headache (κ = 0.47, P = 0.006) and those of TAS (κ = 0.64, P < 0.001). Moreover, the latter two were also concordant with each other (κ = 0.64, P < 0.001). In contrast, the agreement was poor in those without TAS. Only three out of 11 patients with TAS reported headache improvement after trans-sphenoidal surgery.

Conclusion Our study provided evidence that pituitary adenoma was related to chronic headache with TAS. The side concordance analysis suggested a mechanical effect.

Keywords: pituitary adenoma, trigeminal autonomic signs

R007

Trigeminal neuralgia resulting from linear pontine trigeminal root lesion
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Background Various lesions affecting the trigeminal nerve entry zone may produce trigeminal neuralgia, and include tortuous vessels, aneurysms, arteriovenous malformations and tumours. However, pontine infarction or pontine multiple sclerosis (MS) lesion have not been well recognized as a cause of trigeminal neuralgia. Here we report two patients with a pontine lesion (ischaemic or demyelinating) transecting the trigeminal pathways resulting with trigeminal
neuralgia. These are very rare cases of unusual causes of trigeminal neuralgia.

**Case** A 55-year-old man presented with severe lacinating pain in the right V2 and V3 distributions. Magnetic resonance imaging of the brain demonstrated a small linear infarct at the root entry zone of the right trigeminal nerve in the pons. The other 30-year-old woman developed electric shock-like pain in the same distribution as a symptom of MS. Brain MRI showed multiple patchy cerebral lesions including right lateral portion of the pons.

**Conclusion** The mechanism for the trigeminal neuralgia due to pontine lesion may be increased neuronal activity in the trigeminal fascicles and nucleus. Our patients illustrate that the differential diagnosis of trigeminal neuralgia should include pontine infarction or pontine MS lesion.

**Keywords:** Infarction, ischaemia, multiple sclerosis, pons, trigeminal neuralgia

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**R008**

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, two women), with an IHS diagnosis of episodic ECH, mean age of 32 years (range 18–48), and mean illness duration 3.6 years (range 1–12) completed the translated form of MIDAS questionnaire, a 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.

**Conclusion** 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.

**Keywords:** Cluster headache, functional disability, questionnaire

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**R009**

Warfarin as a therapeutic option in the control of chronic cluster headache. Report of two cases

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**Background** Chronic cluster headache remains refractory to medical therapy in at least 30% of who suffer it. Based on a serendipitous previous report, we gave oral anticoagulants to three patients with chronic cluster headache.

**Objective** To confirm the effectiveness and safety of sodium warfarin as a therapeutic option for treating chronic and refractory cluster headache.

**Methods** Inclusion criteria followed IHS definition for chronic cluster headache. Exclusion criteria consisted of blood dyscrasia and inability to comply. Sodium warfarin was titrated as usual. Concomitant therapy was withdrawn upon improvement. The protocol was approved by the local regulatory agency, and all the patients read and signed an informed consent form before inclusion.

**Results** Three patients were included. In all of them, chronic cluster headache abated after the introduction of warfarin. In one patient, warfarin could be discontinued without recurrence. The two other patients remain cluster headache-free for 3–6 months while taking warfarin. Two of the patients had evidence of a right-to-left shunt.

**Conclusion** Warfarin seems to be safe and effective for treating chronic and refractory cluster headache. Its effectiveness may point the new lines of research.

**Keywords:** Cluster headache, chronic cluster headache, trigeminal autonomic cephalalgias, oral anticoagulants, warfarin

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**R010**

Onset of cluster headache (CH) triggered by emotional impact: a case report

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**Background** CH is a strictly unilateral headache that occurs in association with autonomic symptoms. Stress is a recognized precipitant of migraine but not CH.

**Objective** We describe the case of a patient suffering from migraine in who extreme emotional stress triggered CH.

**Case report** A 51-year-old male suffered from migraine without aura from the age of 13. The attacks responded to subcutaneous sumatriptan 6 mg. After 10 years of marriage, he had gone through a difficult divorce, and subsequently struggled to maintain contact with his three children. He remarried and his son had been living with him. Unexpectedly, his son had announced to move back with his mother, the patient’s ex-wife. He described this to have been the worst moment of the last years. In the early evening of the same day, a new type of headache started, with a frequency of two attacks per day. This pain was strictly left temporo-parietal and accompanied by lacrimation, conjunctival injection and restlessness. He...
always treated it with subcutaneous sumatriptan, with benefit. An MRI was normal. CH was diagnosed and we started a course of prednisolone and introduced methysergide, with good headache control.

**Conclusion** Extreme emotional stress can be a trigger of CH.

**R011**

A case report: autonomic headache with autonomic seizures

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**Background** Although it has some common pathophysiological basis, there are restricted data about autonomic headache associated with autonomic seizures.

**Objective and methods** A 19-year-old male patient with a history of complex partial seizures beginning at the age of 4 was admitted with the complaints of tachycardia, left hemiranal headache, flushing, epigastric discomfort and left palmar hyperhidrosis which were followed by watching television for 2 years. The frequency of this pressine type headache was 2–4/day and 20 days/month and lasted for a few hours, especially being clustered at noon time. The attacks were not fullfiling the criteria for the diagnosis of trigeminal autonomic cephalalgias. Brain MRI showed no abnormality and EEG revealed epileptic activity in right hemispheric areas. The frequency and the severity of seizures with autonomic features and following headache decreased with valproic acid.

**Results and conclusion** In epileptic headache, pressing type pain is felt over the forehead for several minutes to a few hours and convulsions sometimes follow the headache, which occurs contralateral to the focus. Anti-epileptic drugs is a choice in such a case and headache as well as seizure disappears. It was suggested that the headache could be a non-trigeminal autonomic headache instead of epileptic headache.

**R012**

Subcutaneous sumatriptan and verapamil in cluster headache: modalities of prescription and delivery in private practice

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**Objective** Epidemiological surveys suggest that prevalence of cluster headache (CH) could be 1 per 500. Misdiagnosis, diagnosis delays and mismanagement are frequent. Our objective was to study the modalities of prescriptions in private practice of attack treatment [subcutaneous injection of sumatriptan (SCS)], and prophylactic treatment (verapamil), in the population of south-west of France.

**Methods** This study has been performed in collaboration with the National Health Insurance of south-west of France. We have determined during 2 consecutive years (2002 and 2003) the modalities of private practice prescriptions of SCS and verapamil.

**Results** 353 patients had at least one prescription of SCS during the 2 consecutive years. There were 259 men and 94 women. The mean age was 42.6. 152 patients had the association subcutaneous sumatriptan and verapamil. 56% of precriptions of SCS were done by a general practitioner. 39% of patients had at least one prescription of SCS done by a neurologist. The mean daily dose of verapamil was 248 mg and 318 mg when prescribed by general practitioners and neurologists, respectively.

**Conclusion** Physicians’ education and patients’ information about CH and their treatments have to improve.

**R013**

Intravenous lidocaine for the treatment of trigeminal autonomic cephalalgia (TAC): report of three cases

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**Background** We report three TAC patients who were poor responders to triptans successfully treated with intravenous lidocaine.

**Objective** Case 1: A 31-year-old female cluster headache patient. Though eletriptan and inhalation oxygen was effective, sometime headache was not sufficiently controlled. Unfortunately, subcutaneous injection of sumatriptan was not as effective as abortive drug. Case 2: A 42-year-old male cluster headache patient. Sumatriptan and inhalation oxygen was effective but not sufficiently so. Case 3: A 56-year-old male SUNCT syndrome patient. Nerve block therapy, triptans, oxygen inhalation were not able to relieve his headache satisfactorily.

**Methods** These patients were applied 2–3 mg/kg lidocaine diluted with 100 ml saline intravenously for 30–60 min.

**Results** During the application of lidocaine, no changes of blood pressure, ECG, SpO2 were observed. Within 30 min, the symptoms complete disappeared and showed satisfactory efficacy in all patients.

**Conclusion** Lidocaine is used as one of the effective drugs for neuropathic pain systemically and peripherally due to suppression of the abnormal neurogenic activities. Some clinical studies suggested that neurogenic inflammation in trigeminal region might be linked with TAC. This result suggested that systemic lidocaine might suppress the abnormal neurogenic activities and be an effective abortive method.

**Keywords:** trigeminal autonomic cephalalgia, neurogenic inflammation, lidocaine, abortive

**R014**

Persistent partial Horner syndrome due to SUNCT: second case from Turkey

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SUNCT syndrome characteristics are well recognized at present. Its diagnostic criteria have also been identified.
However, new features of SUNCT syndrome are being encountered every day. A 43-year-old male suffered from headache triggered by stress and exhaustion. Initial site of pain was left infraorbital area, spreading to eyebrow region, maxillary and nasal base area. On neurological examination immediately after the attack, left conjunctival hyperaemia, myosis and minimal ptosis were detected, without sweating. These findings, suggestive of partial Horner syndrome, were related to the attack. Gabapentin was administered 900 mg daily and attacks were controlled. After full recovery, the case was re-evaluated. Partial Horner syndrome was still present. Blood tests and radiological examinations were normal. Our case is noteworthy since it is the second persistent Horner case due to SUNCT syndrome in the literature. In the first case, it was put forward that it might be due to continuous carotid vasodilation during headache attacks which causes cumulative traumatic effect on the sympathetic fibres. Although cumulative effect was considered as a causative factor, it is never seen in frequent or status-form SUNCT cases. For this reason, it is still not simple to interpret the persistence of autonomic symptoms.

R015

Treatment of cluster headache attacks with less than 6 mg subcutaneous sumatriptan

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Objective 6 mg subcutaneous sumatriptan has been shown to be effective in the treatment of cluster headache attacks. Some patients report an efficacy even of doses of <6 mg. We performed an open, prospective trial on the efficacy of 3 mg and 2 mg sumatriptan.

Methods 81 consecutive patients with cluster headache were enrolled (mean age 43 years; 12 female; 30 with chronic cluster headache). Patients were advised to treat their next cluster headache attacks with 6 mg, 3 mg and 2 mg sumatriptan.

Results 98% were responders to 6 mg sumatriptan. 74% were responders to 3 mg sumatriptan. 41% were responders to 2 mg sumatriptan. In total, preference rates were 98% for 6 mg, 74% for 3 mg, and 41% for 2 mg sumatriptan. The most side-effects were reported for 6 mg sumatriptan (79% of the patients).

Conclusion This study suggests that doses of sumatriptan <6 mg are effective in aborting cluster headache attacks. Patients with cluster headache should also try doses < 6 mg sumatriptan.

Keywords: cluster headache, sumatriptan, attack treatment

Neuro-ophthalmology

S001

Glaucomatic visual field defects in migraine and tension-type headache

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Background Migraine and glaucomatos visual field defects were investigated in various studies. Glaucomatic visual field defects have been found in patients with migraine.

Objective In this study, we investigated the relation between glaucomatos visual field defects and migraine and tension-type headache.

Methods Twenty-five migraine and 25 tension-type headache patients were included in this study. All of the patients were evaluated by the same ophthalmologist and the same neurologist. Visual field analysis (threshold 30-2 and blue yellow) was performed in all patients.

Results Intraocular pressure levels and cup/disc ratio were within normal limits in all patients. Eight migraine patients (32%) had glaucomatos visual field defects. Two patients with tension-type headache (%) had glaucomatos visual field defects.

Conclusion This study shows that migraine patients may represent normal-tension glaucoma and glaucomatos visual field defects.

Keywords: migraine, tension-type headache, glaucoma

S002

Painful ophthalmoplegia (Tolosa–Hunt syndrome): steroid treatment and neuroimaging correlations in five cases

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Objective To evaluate correlations between clinical evolution, neuroimaging and steroid treatment in patients affected by Tolosa–Hunt syndrome (THS).

Methods We report five patients (three male, two female, age range 35–65 years) affected by THS.

Results In three patients laboratory data and neuroimaging were normal at the onset of symptoms; high-dose steroid therapy was started (dexamethasone 16 mg b.i.d. i.m. tapered in 4 weeks) within 5 days from onset of symptoms. Pain disappeared within 60 h, and oculoral palsies within 5 days from onset therapy. Two other patients had cavernous enhanced soft-tissue mass at brain MRI and lightly increased sedimentation rate. Mass biopsy was performed in one case showing non-specific inflammatory abnormalities. These two patients underwent high-dose steroid therapy only after 1 month from the onset of symptoms and showed slow improvement with complete recovery within 2 months. Mass disappeared after 6 months on brain MRI. All patients did not show any clinical relapse during follow-up (from 3 to 10 years, mean 6 years).
Conclusions Our report confirms that steroid treatment has to be started early to obtain a more rapid recovery possibly preventing anatomical damage. MRI could have a positive prognostic value in predicting steroid efficacy and clinical outcome.

S003
Parasympathetic reflex abnormalities can prelude chronic migraine
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Background Pattern and time course of pupillary light reflex is determined by successive activation of parasympathetic and sympathetic innervation of the iris sphincter muscle. Recovery time is mainly under sympathetic control.

Objective The aim was to identify a prelude symptom of chronic migraine.

Methods In a prospective study carried out on 105 patients (65 females, 35.5 ± 5.2 years SD) with 4–7 attacks A2–A3/month as well as in 43 matched healthy controls (35.5 ± 4.2 years SD), we evaluated the parameters of light reflex in five sessions, in headache-free period, during 2 years by using a pupillometry provided to evaluate reflexes in darkness before and after flashes (green 565 nm wavelength).

Results Controls and migraine sufferers have similar baseline pupillary diameters (mm 6.3 ± 3.6 SD vs. 6.5 ± 2.8 SD). Parameters studied were miotic reaction, latency, velocity of constriction, recovery time. Analyses of variance indicated a significant difference regarding velocity of constriction that reached a peak of 1230 ± 380.4 msc. In who will become chronic migraine sufferer (n = 24) during the 3 months following, the result contrasts with the values of 80 ± 40.5 SD msc. and 85.6 ± 50.2 SD (P > 0.0001), respectively, gained by controls and migraine sufferers who remained episodic.

Conclusion Seemingly a dysfunction of parasympathetic reflexes preludes the stemming of chronic migraine.

Keywords: chronic migraine, iris, light reflex, parasympathetic system

S004
Headache in carotid cavernous fistula
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Objective To characterize the clinical features of headache in patients with carotid cavernous fistula (CCF).

Methods We retrospectively obtained clinical data of 12 consecutive patients with CCF (mean age 65; nine men and three women, Barron’s classification: type A in two; type B in one; type C in one; type D in eight patients).

Results Nine (75%) of 12 patients had experienced headache or orbital pain during their clinical course. There were no differences in age, sex or type of Barron’s classification between these two groups with/without headache. Tinnitus or orbital bruit was complicated in three patients. The characteristics of headache were mild in four, severe in one, pulsate in one and tight in three patients. The location of their headache was orbit in three, temporal region in two, all around their head in four. Their headache occurred gradually in six patients and suddenly in one. Headache was the only initial symptom in three patients, whose diagnosis of CCF was made by other symptoms or MR angiography 1–6 months after the onset.

Conclusion Headache associated with CCF was various and did not have any distinctive features. Headache occasionally might be the one and only symptom related to CCF.

Keywords: carotid cavernous fistula, dural arteriovenous fistula

S005
Photophobia in Korean patients with migraine
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Background Although photophobia is a main component of migraine classification and ID migraine, previous literature reported a lower incidence rate (about 40%) in Korean patients with migraine than international studies with caucasian patients.

Objective This study was performed to compare the photophobia incidence rate detected by simple interview in Korean migraineurs with that detected by a specific photophobia questionnaire.

Methods Seventy-four migraine patients with mean age of 39.8 ± 17.36 years were enrolled in this study. After simple interview by a headache specialist, patients were asked to report the questionnaire, which is comprised of eight items. Seven items are questions about various symptoms, avoidance and as a triggering factor related to light during migraine attacks, and one item is a question if the symptom occurs during interictal period.

Results A total of 40 (54.1%) patients noted photophobia through the simple interview, and all of them reported ‘yes’ to at least one item in the questionnaire. Fifty-three (85.1%) patients were revealed as having photophobia by the questionnaire. Of these 53 patients, 23 had same symptoms in photophobia incidence rate detected by simple interview in Korean migraineurs with that detected by a specific photophobia questionnaire.

Conclusion Similar photophobia incidence with caucasian migraine was revealed by the questionnaire. The questionnaire may be used as sensitive method to help detect photophobia in Koreans.

Keywords: photophobia, questionnaire, migraine, Korean, light
S006
A review of painful ophthalmoplegia: the Tolosa–Hunt syndrome

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Background The Tolosa–Hunt syndrome consists of painful ophthalmoplegia caused by cavernous sinus inflammation, which is responsive to steroid therapy. Also, other infectious disease, tumour, pseudotumour, and vascular disease in cavernous sinus, superior orbital fissure and orbital apex are similar symptoms and response to steroids.

Objective We attempt to review the clinical features and magnetic resonance imaging (MRI) scans of 15 cases of painful ophthalmoplegia in Wonkwang University Hospital from 1997 to 2004.

Methods 19 patients with painful ophthalmoplegia who attended Wonkwang University Hospital from 1997 to 2004. We exclude two patients diagnosed with aneurysm of posterior communication artery and two patients diagnosed with brainstem infarction.

Results There were eight men and seven women, and mean age was 57.9. Involved side was right in eight and left in seven. All patients complained of painful ophthalmoplegia and suffered from ocular motor nerve palsies. Twelve patients had only one attack and three had recurrences. All these cases showed similar pain nature except one case, steroid response time to pain and time for recovery of cranial nerves. Recurrent cases were treated with steroid again and response was good.

Conclusion Although the aetiology of Tolosa–Hunt syndrome is unknown, from a practical clinical standpoint it can be regarded as a distinct entity which may be simulated by various other disorders. We think that patients with painful ophthalmoplegia must be considered the THS and should be educated to evaluate painful ophthalmoplegia for the public.

Keywords: painful ophthalmoplegia, Tolosa–Hunt syndrome

S007
Oculomotor nerve neuroma presenting as ophthalmoplegic migraine

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Background In many cases of ophthalmoplegic migraine, signs of inflammation of the affected nerve have been found on gadolinium-enhanced MRI scans.

Objectives Case presentation of a 14-year-old girl with a history of episodic right oculomotor nerve lesions with ptosis and pupillary dilatation with headaches with complete remissions between episodes since age 2.

Methods An MRI scan was done during an acute episode and 4 months after remission. A former MRI scan done at age 4 was also reviewed.

Results A neuroma type lesion of 7 mm of diameter was identified on the part in the prepontine cistern of the right oculomotor nerve. Retrospectively this lesion was also visible with a similar size on the MRI scan done at age 4. During the acute phase the lesion strongly enhanced with gadolinium, whereas 4 months after complete clinical remission this enhancement was less marked.

Conclusion This is a rare case of a 3rd nerve neuroma presenting as ophthalmoplegic migraine in a child. The stronger gadolinium enhancement of the lesion during the acute phase compared with a few months after complete clinical remission suggests an inflammatory mechanism.

S009
Evidence for precortical, potentially retinal-based, abnormalities of the visual system in migraine

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Background In the retina, light is absorbed by the L-, M- and S-cone photoreceptors. Studies have shown that people with migraine perform worse than controls in experiments that assess sensitivity to S-cone stimuli. It is unclear whether these differences arise from dysfunction at cortical or precortical sites.

Objective To localize the source of this abnormality, we took advantage of an experimental paradigm called transient tritanopia, in which observers exposed to a long wave-length adapting display experience a paradoxical reduction in sensitivity to short wave-length stimuli. There is strong evidence to suggest that this phenomenon is precortical/retinal in origin.

Methods Participants with migraine and age-matched controls were tested to determine S-cone detection thresholds using a 4AFC procedure both before and after adaptation to (1) a long-wavelength (yellow) display, and (2) a control (grey) display.

Results In both groups, adaptation to a long-wavelength display increased subsequent detection thresholds to S-cone stimuli. This loss of sensitivity was significantly greater in the migraine group. Loss of sensitivity following adaptation to a neutral display was minimal, and did not differ between groups.

Conclusion Abnormalities in precortical sites may contribute to a loss of sensitivity in the detection of short-wavelength stimuli in migraine.

Keywords: migraine, vision, tritan, precortical, threshold

S010
 Intracranial hypertension associated with Crohn’s disease

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Background Benign intracranial hypertension (ICH) is a relatively rare condition occurring mostly in young obese women. Its aetiology is unknown.

Objective To report a patient with ICH associated with Crohn’s disease.

Methods A 35-year-old non-obese woman with a 10-year history of Crohn’s disease underwent surgery due to small bowel perforation. A few days postsurgery, she complained of headache and shortly after of visual obscurations.
**S011**

**Visual adaptation in migraine and non-headache control groups: local and global motion aftereffects (MAE) are pronounced in migraine, and both exhibit storage**

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**Background** A class of visual illusions known as aftereffects are enhanced in migraine, such that the tilt aftereffect is greater and the MAE lasts longer than for headache-free control participants (Shepherd, 2001).

**Objective** The earlier studies used simple stimuli (gratings, stationary random dots) in which the aftereffects reflect activity in early visual cortex. This study extended the display types to engage extrastriate cortex, and assessed effects of delayed recovery from adaptation.

**Methods** 50 migraine, 50 control participants adapted to a moving display before viewing a stationary or dynamic (random motion) test, which, consequently, appeared to move in the opposite direction. Half of the trials included a delay between the adaptation ending and the test.

**Results** These results replicate and extend Shepherd (2001): MAEs lasted longer in migraine for stationary and dynamic tests. Dynamic MAEs survived delays completely for both groups, whereas stationary MAEs were reduced to a greater extent in migraine.

**Conclusion** Static and dynamic MAEs are pronounced in migraine, which contradicts other reports that global motion perception is impaired. The effects on the recovery of the MAE following a delay suggest cellular fatigue-type mechanisms differ, between migraine and control groups, for early but not later visual cortical areas.

**Keywords:** migraine, adaptation, motion, aftereffect

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**S012**

**Recurrent headpains with neuro-ophthal manifestations—benign or ominous?**

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**Objective** To document benign neuro-ophthal manifestations which mimics ominous intracranial lesions in patients with recurrent headpain of migraine origin.

**Methods** 27 patients were studied over a period of 10 years. Age 10–50 years. All were diagnosed as IHS 1.1, 1.2, 1.6 and IHS R or brief migraine attacks of <1 h duration. 14 of them were investigated (CT, MRI and MRA) in other centres for various intracranial lesions.

**Results** The benign conditions associated with recurrent migraine headpains were Duane’s retraction syndromes (3), superior oblique tendon sheath syndrome (Brown’s syndrome) (2), superior oblique myokymia (1), double elevator palsy (2), Alice in Wonderland syndrome (3), tonic pupil or Adies syndrome (2), physiologic and traumatic anisocorias (4), ischaemic (microvascular) third (pupil sparing) and sixth nerve palsies in above 40 age (4), congenital nystagmus (2), end point (physiological) nystagmus (1) and pseudopapilloedema (3).

**Conclusion** A sound knowledge of various benign neuro-ophthal manifestations avoids expensive investigations and unnecessary treatment. This study highlights the simple diagnostic features including FAT scan (family album tomography for headtilt) of these benign manifestations in patients with recurrent headpains.

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**S013**

**Impairment in colour perception in migraine with and without aura**

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**Background** Visual perception abnormalities are a common feature in migraine patients suffering from migraine with and without aura, also outside attacks.

**Methods** We performed luminance and colour central perimetry in 40 patients with migraine with aura (MA), 40 with migraine without aura (MoA) (all studied when headache-free) and 40 controls.

**Results** Luminance perimetry was similar in patients and controls. Colour perimetry revealed a reduced perception of red, more pronounced in MA ($P < 0.001$) than in MoA ($P < 0.05$), which correlated with the degree of photophobia recorded during testing only in MoA. A subgroup of MoA patients who had a migraine attack shortly after being tested also displayed a marked impairment in the perception of blue. These patients had a statistically significant ($P < 0.001$) lower perception of blue than those who had a migraine attack after a longer time interval than in either MA patients or controls.

**Conclusion** The reduced perception of red may be explained by a specific impairment in the perception of this colour, more marked in patients with MA, but also present in those with MoA. The reduced perception of blue seems to occur only in a subgroup of MoA patients in the premonitory phase of migraine attacks, probably though mechanisms that involve dopaminergic function.

**Keywords:** migraine, colour perception, perimetry

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**S014**

**Migraine, visual field defects and intraocular pressure**

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**Background** There are a few data, still unexplained, that some migraine patients have visual field disturbances typical for glaucoma.

**Objective** The study was to evaluate visual field and intraocular pressure in a group of migraine patients, the frequency of headaches, primarily of migraine type, in patients with glaucoma, and relations between successful treatment of glaucoma and frequency of headaches.

**Methods** Visual field in 22 patients with migraine was evaluated by kinetic perimeter, while intraocular pressure was examined by air-puff tonometer. A questionnaire regarding headaches was given to 54 patients with glaucoma.

**Results** In four migraine patients (18%) the intraocular pressure happened to be increased. Visual field defects in the nasal peripheral area were found in eight out of 22 patients with migraine (36%) (in six cases also in the temporal area) but only two of them (25%) had also the intraocular pressure increased. In the group of glaucoma patients headaches were reported by 29 of them (54%) and, among the later, nine patients (17%) had migraine. After successful treatment of glaucoma, 16 patients (55%) felt relief in their headaches.

**Conclusion** The results of the study confirm common visual field defects in migraine and also suggest certain correlations between headaches and increased intraocular pressure.

**Keywords:** headache, migraine, vision field, glaucoma

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**Secondary headache**

**T001**

**Ependymal cyst in cerebral convexity. Case report**

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Ependymal cysts are benign developmental cysts. Their primary locations are within cerebral parenchyma and often have communication with the ventricles or basal cisterns. Cerebral convexity is very rare site for ependymal cyst. We report one case with ependymal cyst in right fronto-temporo-parietal convexity without any communication to ventricle. A 23-year-old woman presented with the complaints of headache, nausea, vomiting, and evidence of increased intracranial pressure. In her neurological examination we found slight weakness in left extremity. Computed tomography revealed a huge low-density area in the left fronto-temporo-parietal convexity that was isolated from the ventricles. Magnetic resonance imaging revealed a large cystic lesion in cerebral convexity associated with midline shift. The patient was prepared for the operation with a large craniotomy. At operation a smooth-walled cyst with an ependymal type lining was found. Cyst fluid was watery clear and protein and sugar contents were 15 mg/dl and 58 mg/dl, respectively. Partial removal of the cyst wall was performed and pathological examination of resected tissue showed a single layer of cuboid cells that resembled an ependymal structure. Her postoperative course was uneventful and symptoms improved gradually.

**Keywords:** ependymal cyst, cerebral, convexity

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**T002**

**Prevalence of migraine in patients with multiple sclerosis**

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**Background** Few studies have investigated the prevalence of migraine, diagnosed according to the diagnostic criteria of the International Headache Society, in patients with multiple sclerosis (MS).

**Objective** To determine the prevalence and the characteristics of migraine in patients with MS.

**Methods** The prevalence and characteristics of migraine were studied prospectively in 132 subjects affected by MS and in 130 age- and sex-matched controls. An ad hoc questionnaire based on the International Classification of Headache Disorders, 2nd Edition was used in a face-to-face interview.

**Results** Migraine was diagnosed in 46 (34.8%) patients with MS and in 20 (15.4%) controls ($P < 0.001$). A typical visual aura was present in seven (5.3%) patients with MS and in six (4.6%) controls ($P = NS$). The clinical characteristics of migraine in MS patients and controls were similar. There were no differences between MS patients who were affected by migraine and those who were not, as regards disease type, disease duration and disability. Only three (2.3%) patients reported a simultaneous onset of migraine and MS symptoms. In 31 (67.4%) patients migraine preceded and in 12 (26.1%) followed MS symptom onset.

**Conclusion** This case–control study confirms that the prevalence of migraine in patients with MS is higher than in the general population.

**Keywords:** multiple sclerosis, migraine, prevalence, case–control study

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**T003**

**Orthostatic headache by spontaneous cervical CSF leak treated with lumbar epidural blood patch**

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**Objective** To evaluate the efficacy of lumbar epidural blood patch (EBP) in the treatment of spontaneous cervical CSF leakage (SCCSFL).

**Methods** We report one case of SCCSFL (among the 24 with spontaneous CSF leak evaluated between 1992 and 2004).

**Results** A 31-year-old woman presented sudden, gravitative occipito-nucal-frontal orthostatic headache (OH), nausea, vomiting, tinnitus, mild neck stiffness, and bilateral upper limb numbness. Brain MRI showed diffuse pachymeningeal enhancement. After 2 months of bed rest OH and tinnitus were still present. CT myelography showed
contrast extravation at C2–C3 level. CSF pressure was unmeasurable. The patient was treated with autologous EBP (20 ml) at L1–L2 level. After injection, she remained in Trendelemburg position approximately 30° for 24 h. She was asymptomatic within 24 h after EBP and at 6 months' follow-up.

Conclusions We hypothesize that recovery is due to the fact that EBP, injected at the level of lumbar spine, may move upward reaching the cervical segments, possibly favoured by prolonged Trendelemburg position. Alternatively, EBP may determine an increase in intracranial pressure, which would favour the seal of extruding borders of the dural hole. Thus, EBP at the cervical level, where the procedure is hard to be attempted, may not be necessary.

T004

Epidural blood patch in the treatment of 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).

Methods Among 24 patients with SCSFL we report six patients (four women and two men with age range 31–66 years, mean 44 years) treated with EBP. Follow-up ranged from 6 months to 2 years. All patients had received autologous EBP in lumbar side, using 15–30 ml (mean 23 ml).

Results All patients had orthostatic headache as primary symptom. Spinal taps were performed in four patients. The level of the leak was determined in four patients. All six patients failed an initial conservative treatment, bed rest and hydration (ranged from 2 months to 13 months). With first EBP five patients (83%) became asymptomatic; one patient responded only to a third EBP. EBP had been given at the level of the leak (lumbar) in three patients, at a different level in one patient (cervical CSF leak). ‘Blind’ lumbar EBP was performed in two patients. All patients after injection remained in Trendelemburg position approximately 30° for 24 h. Headache relief was obtained immediately.

Conclusions Our data confirm the efficacy of EBP and of Trendelemburg position post-EBP in SCSFL.

T005

Headache in cerebral venous thrombosis; incidence, pattern and location in 200 consecutive patients

Mohammad Wasay, George Bobustuc, Suleman Kojan, Zubair Sheikh, Alper Dai & Zahid Cheema

Objective To analyse the incidence, pattern and location of headache in a large cohort of patients with diagnosis of CVT.

Methods We retrospectively reviewed consecutive 200 patients with proven diagnosis of CVT at 10 centres in the USA.

Results Age range was 8–82 years (mean 37). Headache was present in 136 (68%) patients. 22% of these patients had previous history of headache including migraine, tension headache and cluster headache. Duration of headache ranged from 1 day to 6 months (mean 3 days). The pattern of headache was only reported in 72 patients (55%). The pattern of headache reported was throbbing, 12; diffuse, 28; localized (temporal or occipital), 25; thunderclap, 1; cluster like, 1; and worst headache of life, 5. 43 (32%) patients had normal neurological examination. There was no correlation to presence of haemorrhage. 49 (37%) patients had intracerebral haemorrhage. There was no correlation between localization of headache and sinus thrombosis except sigmoid sinus thrombosis, where almost all patients had pain in posterior auricular and occipital region.

Conclusion Headache was the most common presenting feature in patients with CVT. Headache did not correlate to presence of intracerebral haemorrhage or location of CVT except sigmoid sinus thrombosis.

T006

Evaluation of headache in Iranian patients with multiple sclerosis (MS)

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Background MS has a significant prevalence in Iran, especially in Isfahan. Headache is one of the manifestations of acute MS attacks. This study investigates the relative incidence of headache in MS according to sex, age, type of treatment and drugs and presence of depression.

Methods and materials This descriptive cross-sectional study was performed in Neurologic Clinic in Alzahra Hospital, Isfahan, Iran. A questionnaire according to IHS criteria was completed on 100 patients with MS, including past history of headache, intensity change of headache before and after MS. The relation between headache and MS based on age, sex and various clinical headache types, drug use and presence of depression was evaluated.

Results Of 100 patients (75 female, 24 male), 66 patients had headache with MS. 4% had headache during the course of MS, among these cases 24% presented with headache, in 11% headache was one of the primary manifestations of MS (but no first presentation), and 10% had headache only in acute attack of MS. In this study of 100 patients with MS, 51 cases (76.1%) had depression with MS.

Conclusion Headache was a presenting symptom and one of the clinical manifestations of acute attacks. No statistical differences in intensity of headache before and after MS, nor relation between headache and MS based on age, sex and various clinical type of headache in MS, were recorded. Depression may play a role in presentation of headache in MS.
CSF hypovolaemia as a cause of chronic headache attributed to whiplash injury

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Background WAD (whiplash associated disorders) is a common disease but its pathophysiology remains uncertain and effective treatment is not established. Chronic headache is a main symptom of WAD. Symptoms of WAD are similar to SIH (spontaneous intracranial hypotension).

Objective This paper shows neuroradiological findings and the outcome after blood patch in patients with WAD.

Methods 312 cases with WAD were evaluated by RI cisternography and gadolinium-enhanced cranial MRI. All patients were treated with epidural blood patch.

Results RI cisternography performed. 101 patients revealed early accumulation of RI in the bladder in 84 cases and CSF leak in 58 cases. Gadolinium-enhanced cranial MRI showed venous dilation, subdural fluid accumulation, downward displacement of the cerebellar tonsil and dural enhancement. Outcome was excellent: recovery 66 cases, good 120, fair 70, poor 28.

Conclusion CSF hypovolaemia is one cause of WAD. The epidural blood patch is very effective for chronic headache attributed to whiplash injury.

Keywords: CSF hypovolaemia, spontaneous intracranial hypotension, whiplash injury, chronic headache, epidural blood patch

Headache after acute and mild head injury

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Objective The milder head injury with the stronger headache has been reported. To check this paradox, patients with acute but mild trauma were studied on severity of trauma, age, gender, and duration of headache.

Methods 171 acute cases with mild head injury were analysed. Forty-seven cases (concussive group) lost their consciousness for 30 min or less. Another 124 patients were alert after the accidents. Statistical difference was evaluated by χ² test with Yate’s correction.

Results Sixty patients (35.1%) experienced PTH out of 171. Among the young group (age < 60), 52 cases (45.6%) out of 114 had PTH, while only 8/57 (14%) had PTH in the group > 60 years old (P < 0.001). Difference by gender was not evident. Incidence of PTH in concussive group was 17/47 (36%), and 43/124 (34.7%) in the alert group. PTH of 44/60 patients relieved within 30 days. So, only 12 cases out of 171 (7%) remained to complain of PTH.

Conclusion Incidence of acute PTH was lower in the aged group. Loss of consciousness by trauma had no effect on PTH incidence. Only 7% of the whole head-injured cases became patients with chronic PTH.

Keywords: Post-traumatic headache, paradox, incidence, acute case

The clinical presentation and affective disorders in burning mouth syndrome

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According to IHS classification, burning mouth syndrome (BMS) is an intra-oral burning sensation without obvious medical or dental cause. Diagnostic criteria of the disorder include the presence of burning oral sensation during most of the day without obvious changes of oral mucosa. Local and systemic causes have to be excluded by appropriate diagnostic procedures. Subjective feeling of dry mouth, paraesthesias and taste changes could be associated symptoms. The BMS is of unknown pathophysiology. The aim of the study was to analyse the clinical and affective parameters in BMS. We examined 51 patients fulfilling the diagnostic criteria for primary BMS. The average age was 65.5 ± 11.2 years, with female:male ratio 2 : 1. The disorder lasted more than 12 months in 62.7% of patients. The burning sensations were distributed over the whole oral cavity in 39.2%, on tongue or lips in 29.4%, while in the other patients the sensation involved part of the oral cavity. In all patients the affective status was evaluated. High scores were obtained on Hamilton Depression Rating Scale (16.5 ± 4.5), Beck Depression Inventory (17.4 ± 8.2) and Hamilton Anxiety Rating Scale (20.6 ± 5.6). As in other chronic pain conditions, BMS is strongly associated with anxiety and depression.

Keywords: burning mouth syndrome, clinical presentation, affective disorders

Headache of foramen magnum syndrome

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Objective We revised our cases with reference to the literature to determine why the diagnosis of extradural tumours around the great foramen is still difficult to make despite amazing progress in imaging diagnosis in recent years.

Subjects and methods We reviewed five patients, one man and four women, who presented extradural tumours involving the great foramen. The average age was 47.

Results (1) Only slight symptoms are seen despite the presence of large tumours; (2) symptoms greatly fluctuate or change (in 20% of our patients); (3) few symptoms are site-specific; (4) false localizing signs which do not parallel with the lesion level are seen; and (5) this condition constitutes a pitfall in diagnosis since it is on the borderline between areas covered by image diagnosis and those covered by conventional diagnostic techniques in different departments.

Conclusion In order to increase the rate of accurate diagnosis it is recommended that sagittal section images be routinely acquired in MRI, including the great foramen in patients with...
initial symptoms of great foramen syndrome (such as pain in the occipital region or posterior region of the neck and peripheral paraesthesia in the upper limbs).

**T011**

Rathke's cleft cyst as a cause of secondary headache of pituitary origin

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**Background** Rathke's cleft cyst (RCC) is a common pituitary lesion occurring in ~20% of individuals at autopsy. Because RCC is usually asymptomatic and detected incidentally, it is not recognized as a cause of headache.

**Objective** To examine incidence of headache, effect of transsphenoidal drainage surgery, and correlation between headache and gender, cyst size or endocrine abnormality.

**Methods** We carried out headache survey in 102 RCC patients (78 women, 24 men). The cyst size was determined on MRI and pituitary functions evaluated with provocation tests. Change in headache was studied in 28 operated and eight non-operated patients with headache.

**Results** The prevalence of headache was 35%, while those of visual disturbance and hormonal symptoms were 13% and 25%, respectively. Headache was variable in characteristics and distribution. There was no statistical difference in the proportion of women, large cyst >1 cm, hormonal abnormality, or visual disturbance between two groups with and without headache. Within 2 weeks after operation, headache disappeared in 93% and diminished remarkably in 7% of operated patients, whereas it persisted in all non-operated cases.

**Conclusion** RCC is an important cause of secondary headache of pituitary origin. The underlying mechanism does not appear to involve either cyst size or hormonal abnormality.

**Keywords:** Rathke's cleft cyst, pituitary

**T012**

Cold-stimulus headache of progressive systemic sclerosis with CNS vasculitis

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**Case report** Involvement of the central nervous system is uncommon in progressive systemic sclerosis (PSS). We describe a patient with repeated cold-stimulus headache of PSS with CNS vasculitis. A 63-year-old woman with a 7-year history of PSS was admitted because of severe headache in December 2002. The severe headaches were induced by repeated cold stimuli. The patient's blood pressure was 162/92 mmHg. The neurological examination was normal. MRI scan of the head disclosed haemorrhagic infarction in the left occipital lesion. Cerebral angiography showed localized severe stenosis and poststenotic dilation, a string of beads appearance in left posterior parietal artery. We attributed the abnormal angiogram findings to arterial spasm or vasculitis. Treatment was started with cyclosporin A. We believe that our patient's vasospasm in the cerebral circulation might have caused haemorrhagic infarction. Spasm is difficult to demonstrate. We consider that vasospasm has been implicated as the primary mechanism underlying Raynaud's phenomenon with PSS. It can also occur as a result of platelet aggregation, leading to the release of serotonin damaged vessels.

**Keywords:** cold-stimulus headache, progressive systemic sclerosis, CNS vasculitis

**T013**

Compensation issue may produce a paradox of post-traumatic headache

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**Objective** When compared with the severely head-injured group with grave sequelae, persistent headache, paradoxically, is complained of more in the mildly injured group.

**Methods** All labourers injured on duty can claim compensation, if disabled. Two post-traumatic samples for the official evaluation of disability were studied. First, sequelae of 34 severe head injury cases (17 diffuse axonal injury, 13 focal contusion, four intracranial haematomas) were checked in detail. They lost consciousness over 6 h, and had neurological or neuropsychological deficit. Then, complaints of 87 mildly head-injured patients (alert around the time of accident but claiming compensation) were investigated.

**Results** In the severe cases, disabilities were dementia, aphasias, frontal-lobe dysfunction, personality change, paresis, ataxia, and cranial nerve deficits. Nine cases were accompanied by headache (26.5%). In the mildly injured sample, 64 patients (73.6%) had headache (29 cases intractable). Other 23 cases without headache complained of hypaesthesia, neurotic symptoms, tinnitus, diziness, neck pain, or others.

**Conclusion** A quarter of severely injured cases complicated with headache. As the incidence of acute traumatic headache was low when investigated at emergency facility, high rate of headache after mild injury may relate to compensation issue.

**Keywords:** post-traumatic headache, paradox, severe head injury, compensation

**T014**

A comparative study of opening pressure of lumbar tap in patients with spontaneous intracranial hypotension and traumatic cerebrospinal fluid hypovolaemia

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**Background** The opening pressure (op) of spontaneous intracranial hypotension (SIH) and traumatic cerebrospinal fluid (CSF) hypovolaemia is thought to be low.

**Objective** This study compared op of patients with SIH and traumatic CSF hypovolaemia (TCSFH) before and after treatment.
Methods The op in patients suspected of having SIH and TCSFH were measured in lateral recumbent position at the time of indium cisternography.

Results The op was measured over 140 times in 100 patients (50 male, 50 female, mean age 41.7). The results of cisternography in 11 patients with suspected SIH showed CSF leak in seven and no leak in four and mean op, except one with 0 cmH2O, was 14.8 and 14.9 cmH2O, respectively. In 89 patients with TCSFH suspected, CSF leak was recognized in 78 and no leak in 11, and mean op was 12.9 and 12.6 cmH2O, respectively. In total, mean op in no leak patients at diagnosis was 13.4, and 13.4 cmH2O in leak patients. The mean op was 13.6 cmH2O after confirmation of CSF leak discontinuance in 26 patients.

Conclusion The opening pressure was normal through entire clinical course in all patients with CSF leak except one in acute phase.

Keywords: spontaneous intracranial hypotension, traumatic cerebrospinal fluid hypovolaemia, opening pressure, cisternography

T015
Acute symptomatic headache caused by sphenoid sinusitis
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Objective Diagnosis of sphenoid sinusitis is sometimes difficult, if headache only is complained of. To find effective factors to diagnose this condition at primary care site, a retrospective check-up was performed on these rather silent but dangerous cases.

Clinical cases and results Seven afebrile patients (male:female 4:3, mean age 29.9 years, range 23–34) visited the author’s clinic with non-specific headache continuing for 1–7 days. Neither nasal obstruction nor running nose was reported. Three cases out of seven experienced increased pain at shaking heads or sudden flexion of the neck. Five cases underwent CRP test, complete blood count and blood smear. Mean CRP was 1.6, and four cases out of five showed abnormally high values. Increased white blood count was found in only one case. Neutrophil component was not increased. Headache in all cases improved within a few days by administration of antibiotics and anti-inflammatory drug. Cranial CT confirmed the final diagnosis.

Conclusion The sphenoid sinusitis pain may increase when the head is shaken. CRP test is also helpful. But cranial CT is strongly recommended to confirm diagnosis.

Keywords: acute symptomatic headache, sphenoid sinus, CRP, pain at head shaking

T016
Obstructive sleep apnoea syndrome (OSAs) associated with refractory chronic headache
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Objectives To investigate the comorbidity of chronic and refractory headache with obstructive sleep apnoea syndrome (OSAs).

Methods Seventy-two patients (51 women and 21 men) with chronic and refractory headache were scanned by polysomnography. In case the OSAs was diagnosed (RDI > 10) continuous positive airway pressure (C-PAP) treatment was suggested and patients were followed up for 6 months at least.

Results Twenty-one cases (29.6% of all, 13.7% of women and 66.6% of men) of OSAs were identified. Headaches were classified into several primary syndromes including cluster headache, but in most cases medication overuse was reported. In only one case (1.4% of all, 4.7% of men) the criteria for hypnic headache were fulfilled. Age, gender and body mass index were associated with OSAs. C-PAP treatment improved both sleep apnoea and headache only in one-third of cases. Preventive headache pharmacotherapy was necessary for all OSAs patients.

Conclusions Patients suffering from chronic refractory headache, those in particular who are overweight men of middle age and overuse medications, should be considered for polysomnography. C-PAP treatment may improve headache.

Keywords: obstructive sleep apnoea syndrome, headache, polysomnography

T017
Lupus and recurrent headache in patients with MRI positive and MRI negative cases
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In this study, our goal was to find out whether cerebral lesions in SLE patients have any relation to headache. Forty-five cases with SLE (diagnoses based on the revised criteria of the American College of Rheumatology) were included in the study. Neurological diagnoses were done according to 2004 IHS criteria, following face-to-face interview and detailed neurological examination. They were divided into two groups as MR-positive and MR-negative patients. As well as the type of headache, data were also collected on age at onset, triggering or aggravating factors, location, frequency of the attacks. Forty-three patients were female and two were male. The mean age was 34.6 (18–60), the mean disease period was 84.5 months and the mean headache period was 90.2 months. MR revealed positive findings in 40% of all patients. Of these,
24.4% had positive neurological findings. In 28.9% of all patients, migraine without aura and in 26.7% of all patients infrequent episodic tension-type headache diagnoses were established. No relationship of location of pain, duration of pain, triggering or aggravating factors, frequency and severity of the attacks was determined in MR-positive group. Statistically significant relationship with the duration of SLE and positive lesions on MR was found.
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