Cephalalgia
An International Journal of Headache
International Headache Society

Cephalalgia
2016, Vol. 36(1S) 1–185

DOI: 10.1177/0333102416670318
cep.sagepub.com
SAGE

EHMTIC 2016 – INVITED SPEAKER ABSTRACTS

EHMTC-0433
TEACHING COURSE IV: CLUSTER HEADACHE
EPIDEMIOLOGY

J.P. Monteiro[1]

[1]*Instituto de Investigação e Inovação em Saúde, Centro de Genética Preditiva e Preventiva, Porto, Portugal*

EHMTIC 2016 – Cluster Headache Teaching Course

Cluster Headache: epidemiology

JM Pereira Monteiro, MD, PhD

Chair of Headache and Facial Pain Unit, Hospital CUF Porto, Portugal
Clinical Researcher on Primary Headache Disorders, CGPP/IBMC/I3S, Porto University
Emeritus Professor of Neurology, Porto University

This lecture is an overview on the published data on the available epidemiological studies about a headache disorder known by several different names and definitions through the last four decades but now known as Cluster Headache and described on the ICHD-3 beta (2014) as composed by attacks of severe, strictly unilateral pain which is orbital, supraorbital, temporal or in any combination of these sites, lasting 15–180 minutes and occurring from once every other day to eight times a day. The pain is associated with ipsilateral conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhea, eyelid edema, forehead and facial flushing and/or sweating, miosis and/or ptosis, and a sense of restlessness or agitation. Symptoms and signs suggesting, at least, an episodic disequilibrium between the sympathetic and parasympathetic local autonomic control, preceded by ipsilateral hypothalamic activation however of unknown etiology.

A summary of the available Cluster Headache incidence and prevalence studies of general or selected populations samples, in developed and developing countries are presented and commented on. The epidemiological data available on age and gender distribution as well as pain location and clinical profile including predisposing and trigger factors are analyzed and also commented on.

The lecture will finish with a Cluster Headache epidemiological summary that includes the most relevant and confident data and some proposals for future studies to get answers to the Cluster Headache epidemiological features still unknown.

EHMTC-0436
TEACHING COURSE IV: CLUSTER HEADACHE
PATHOPHYSIOLOGY

A. May[1]

[1]*Hamburg, Germany*

Trigemino-autonomic Cephalalgias: Pathophysiology and neuroimaging

Arne May, MD

Department of Systems Neuroscience
University Clinic of Hamburg
e-mail: a.may@uke.de

Trigeminal autonomic cephalalgia (TAC) is a relatively new term, first proposed by Goadsby and Lipton for a group of primary headaches with pain and autonomic involvement in the facial area of the trigeminal nerve. Although the headache syndromes of this group, namely cluster headache, paroxysmal hemicrania, and SUNCT/SUNA, clearly share typical clinical features, in most cases a sub-classification is possible and reasonable as therapeutical regimen and response differ. Functional imaging showed that all of these syndromes share a specific activation pattern during the attacks. A case report suggests that even in patients who are suffering from excruciating trigemino-autonomic headache attacks, in whom frequency, duration and therapeutic response allowed no clear-cut classification to one of the subtypes of trigeminal autonomic cephalalgia, the cerebral activation pattern was similar- although not

identical to those previously observed in cluster headache and SUNCT with a prominent activation in the hypothalamic grey matter. This case study underlines the conceptual value of the term "TAC" for the group of headaches focusing around the trigeminal-autonomic reflex and moreover emphasizes the importance of the hypothalamus as a key region in the pathophysiological process of this entity.

Hemicrania continua is a strictly unilateral, continuous headache of moderate intensity, with superimposed exacerbations of severe intensity that are accompanied by trigeminal autonomic features and migrainous symptoms. The syndrome is exquisitely responsive to indomethacin. In seven patients with hemicrania continua a significant activation of the contralateral posterior hypothalamus and ipsilateral dorsal rostral pons in association with the headache was described. This study demonstrated nicely that the neuroimaging markers of trigeminal autonomic headaches and migrainous syndromes are demonstrated in hemicrania continua, mirroring the clinical phenotype, which in fact exhibits a certain overlap with trigeminal autonomic headaches and migraine. Taken together, just as in the case of an atypical trigemino-autonomic headache, the functional imaging data in hemicrania continua and paroxysmal hemicrania impressively emphasizes that primary headache syndromes can be distinguished on a functional neuroanatomic basis by areas of activation specific to the clinical presentation.

Recently, the sphenopalatine ganglion came to the fore, based on the observation that functionally blocking this ganglion stops cluster headache attacks and may even have a preventative effect. This lecture will focus on the pathophysiological basis of the TAC focussing on cluster headache and will delineate the central and peripheral aspects of this puzzle.

References

1. Goadsby PJ and Lipton RB. A review of paroxysmal hemicranias, SUNCT syndrome and other short-lasting headaches with autonomic feature, including new cases. *Brain* 1997; 120(Pt 1): 193–209.
2. May A. Cluster headache: pathogenesis, diagnosis, and management. *Lancet* 2005; 366(9488): 843–55.
3. Sprenger T, Boecker H, Tolle TR, Bussone G, May A and Leone M. Specific hypothalamic activation during a spontaneous cluster headache attack. *Neurology* 2004; 62(3): 516–7.
4. May A, Bahra A, Büchel C, Frackowiak R and Goadsby P. Cerebral activation in cluster headache in and outside the bout: a PET study. *Europ J Neurol* 1998; 5(3): 7–8.
5. May A, Bahra A, Buchel C, Turner R and Goadsby PJ. Functional magnetic resonance imaging in spontaneous attacks of SUNCT: short-lasting neuralgiform headache with conjunctival injection and tearing. *Ann Neurol* 1999; 46(5): 791–4.
6. Sprenger T, Valet M, Hammes M, Erhard P, Berthele A, Conrad B, et al. Hypothalamic activation in trigeminal autonomic cephalgia: functional imaging of an atypical case. *Cephalalgia* 2004; 24(9): 753–757.
7. Cohen AS, Matharu MS, Kalisch R, Friston K and Goadsby PJ. Functional MRI in SUNCT shows differential hypothalamic activation with increasing pain. *Cephalalgia* 2004; 24: 1098–1099.
8. Matharu MS, Cohen AS, Frackowiak RS and Goadsby PJ. Posterior hypothalamic activation in paroxysmal hemicrania. *Ann Neurol* 2006; 59(3): 535–45.
9. May A, Ashburner J, Buchel C, McGonigle DJ, Friston KJ, Frackowiak RS, et al. Correlation between structural and functional changes in brain in an idiopathic headache syndrome. *Nat Med* 1999; 5(7): 836–8.
10. May A, Bahra A, Büchel C, Frackowiak RSJ and Goadsby PJ. Hypothalamic Activation in Cluster Headache Attacks. *Lancet* 1998; 352: 275–278.
11. May A and Goadsby PJ. The trigeminovascular system in humans: pathophysiological implications for primary headache syndromes of the neural influences of the cerebral circulation. *J Cereb Blood Flow Metab* 1999; 19: 115–127.
12. May A, Buchel C, Turner R and Goadsby PJ. Magnetic resonance angiography in facial and other pain: neurovascular mechanisms of trigeminal sensation. *J Cereb Blood Flow Metab* 2001; 21(10): 1171–6.
13. Schoenen J, Jensen R, Lantéri-Minet, Láinez M, Gaul C, Godman A, Caparso A, May A., Stimulation of the sphenopalatine ganglion (SPG and) for cluster headache treatment. Pathway CH-1: A randomized, sham-controlled study. *Cephalalgia* 2013 Jul; 33(10): 816–30.

EHMTC-0431
TEACHING COURSE IV: CLUSTER HEADACHE
EVIDENCE-BASED TREATMENTS

R. Jensen[1]

[1]*Copenhagen, Denmark*

Cluster headache is highly disabling due to the very severe pain attacks and hampered by decreased quality of life both during and outside the bouts. Patient with the episodic forms are the most frequent in the general population but in most countries they are underdiagnosed and heavily undertreated. In most specialized clinics the patients with the chronic subforms may dominate and they can be extremely difficult to treat. They may also suffer from significant comorbidities, including other primary and secondary headaches and psychiatric diseases.

Despite efforts, the precise nature of the disease mechanisms remain obscured and yet there are no specific treatment. A better understanding of this relation may lead to more effective therapeutic regimes for patients suffering

from this debilitating disease. The severe pain intensity and the periodic nature of cluster attacks require very careful management for both the acute attack and prevention but the right combination can really make a significant difference for the patient and their families. This teaching course aims to evaluate the latest acute and preventive pharmacological and neuromodulatory therapies with several case presentations in addition to an interactive discussion with the audience.

EHMTC-0417
TEACHING COURSE III: BASH PRIMARY CARE

MIGRAINE IN CHILDREN

D. Kernick[1]

[1]*United Kingdom*

Migraine affects over 10% of children and the needs of this group are largely overlooked. GPs find difficulty in diagnosis and management in this age group, resulting in high levels of unnecessary referral. This session will deal with simple guidelines to diagnose and manage headache in children and warning signs of potential underlying pathology.

EHMTC-0429
TEACHING COURSE V: PEDIATRICS/ ADOLESCENT

HEADACHE IN UNDER 7S

R. Howells[1]

[1]*Royal Devon + Exeter Hospitals NHS Foundation Trust, Children's and Women's Health, Exeter, United Kingdom*

This teaching course focuses on headaches in young children (under 7 years)

Headaches in very young children are less common than in adolescence. They can cause anxiety amongst families and health professionals alike due to concern that brain tumours are the cause. However, most headaches in young children are primary in origin. The objectives of this session on headaches in young children are

- to show how clinical examination can be used to distinguish between primary and secondary headache
- to analyse how primary headache such as migraine presents in early childhood
- to determine a pragmatic approach to primary headache in young children where the evidence base is poor

The author intends this to be an interactive session where the experience of the participants can be shared.

EHMTC-0430
TEACHING COURSE III: BASH PRIMARY CARE

MEDICATION OVERUSE HEADACHE

D. Watson[1]

[1]*United Kingdom*

MEDICATION OVERUSE HEADACHE, ABSTRACT EHMTIC 2016

Dr David PB Watson, Hamilton Medical Group and Department of Neurology, Aberdeen Royal Infirmary, Aberdeen, Scotland.

david.watson@nhs.net
tel 01224562888, 07545697233

ICHD 3- beta definition
8.2 Medication-overuse headache (MOH)

Headache occurring on 15 or more days per month developing as a consequence of regular overuse of acute or symptomatic headache medication for more than 3 months. It usually, but not invariably, resolves after the overuse is stopped.

What is overuse?
Simple Analgesics 15 days a month
Opiate e.g. codeine 10 days a month
Triptans 10 days a month

What headache phenotypes can get MOH?
Migraine or Tension-type headache mainly

Risk factors for progression from episodic to chronic migraine
Management of MOH

Abrupt withdrawal of overused symptomatic medication has been shown to be effective (single cohort and cohort studies)

More effective for triptans (and ergots), than opioids and combination analgesics

Less effective if complicating co-morbidities including significant medical illness, mood, anxiety, eating or substance misuse disorder

Do prophylactic medications work in MOH?

- No Evidence for β blockers, tricyclics, pizotifen, valproate, gabapentin

Prognosis after successful withdrawal
Relapse rate

Katsarava et al. Cephalalgia. 2004; 25:*12–15*, 45% relapse rate after follow up for 4 years (94% year 1)
Rossi et al. Cephalalgia. 2008; 28:1196–1200, 20.5% relapse rate after follow-up for 1 year in patients with "low medical needs"

EHMTC-0426
PLENARY SESSION I

INFLUENCE OF SEX HORMONES ON CEREBRAL VESSELS AND TRIGEMINAL GANGLION: POSSIBLE RELEVANCE FOR MENSTRUAL MIGRAINE

D. Krause[1]

[1]*University of California- Irvine, Pharmacology, Irvine, USA*

Migraine is more prevalent in women, and headache onset often varies with changes in ovarian hormone levels, such as occur in puberty, menstrual cycles, pregnancy, and menopause. Despite these well-known observations, the underlying processes that link hormones and headache are not understood. To better treat conditions such as menstrual migraine, we need to know how sex hormones affect migraine mechanisms. Our research has shown that two tissues considered important in migraine, cerebral blood vessels and the trigeminal ganglion, are directly regulated by ovarian hormones. Using rodent models, we have shown that cerebrovascular function is altered by changes in circulating estrogen and progesterone, either assessed over the estrus cycle or by using ovariectomy and hormone replacement. Estrogen enhances vasodilation, either by influencing expression of endothelial substances, such as nitric oxide and prostaglandins, or by direct vasodilator action on smooth muscle. Cerebral arteries are particularly sensitive to the latter effect compared with peripheral arteries. In addition, estrogen suppresses and progesterone enhances inflammatory responses of the cerebral vessels. We have shown that estrogen receptors are expressed in both the endothelium and smooth muscle of cerebral vessels, with ERalpha being the most predominant receptor subtype in vessels of young adult females. Cerebrovascular levels of ERalpha are influenced by circulating levels of estrogen. In addition, we are investigating possible regulation of sensory innervation by sex hormones. Recently we found that ERalpha is expressed in human trigeminal ganglia, suggesting that sensory processing also is directly modulated by estrogen and thus sensitive to hormonal fluctuations.

EHMTC-0414
PLENARY SESSION I

NEUROPATHIC PAIN IN THE FACE: MECHANISMS LEAD TO SUCCESSFUL TREATMENT

R. Baron[1]

[1]*Universitätsklinikum Schleswig-Holstein, Division of Neurological Pain Research, Campus Kiel, Germany*

Neuropathic pain in the face: mechanisms lead to successful treatment

Prof. Dr. Ralf Baron

Division of Neurological Pain Research and Therapy, Department of Neurology, University Hospital, Kiel, Germany

Neuropathic pain represents a major medical problem and treatment has been unsatisfactory. Therefore, a new hypothetical concept was proposed in which pain is analyzed on the basis of underlying mechanisms and sensory abnormalities rather than on the basis of the causing etiology. If a systematic clinical examination of the pain patient and a precise phenotypic characterization is combined with a selection of drugs acting at those particular mechanisms, it should ultimately be possible to design optimal treatments for the individual patient.

To achieve these goals several international consortia German Research Network on Neuropathic Pain, IMI-Europain, Neuropain) established a large data-base that includes epidemiological and clinical data as well as a standardized symptom questionnaires and quantitative sensory testing. Using a subgroup analysis, in all neuropathic etiologies three different somatosensory profiles could be identified. Three distinct subgroups with characteristic sensory profiles were identified and replicated: Subgroup 1 (sensory loss) showed a loss of small and large fiber function in combination with paradoxical heat sensations. Subgroup 2 (thermal hyperalgesia) was characterized by preserved sensory functions in combination with heat and cold hyperalgesia and mild dynamic mechanical allodynia. Subgroup 3 (mechanical hyperalgesia) was characterized by a loss of small fiber function in combination with pinprick hyperalgesia and dynamic mechanical allodynia. Patients with trigeminal neuralgia mainly fall into subgroup 2 (56%) which reflects the fact that in many patients the cutaneous innervation is normal. On the other hand, 50% of patients with an idiopathic trigeminal neuralgia demonstrate subtle afferent negative signs in the skin.

Several recent clinical trials using QST-based classification techniques could already identify a differential treatment effect in subgroups of patients. In a study with topical 8% capsaicin patches in patients with peripheral neuropathic pain, responders could be retrospectively distinguished based on the presence of cold- and pin-prick hyperalgesia, a profile which corresponds to subgroup 2. A recent study in patients with peripheral neuropathic pain revealed that the presence or severity of allodynia as well as limited thermal deficits, again a profile similar to subgroup 2, predicts the response to intracutaneous botulinum toxin treatment. The sodium channel blocker oxcarbazepine was evaluated in patients with peripheral neuropathic pain who were prospectively stratified into two groups. Patients in the first group correspond to the "thermal hyperalgesia" subgroup 2. Patients in the second group (non-irritable nociceptor) were similar to the "sensory loss" subgroup 1. The number needed to treat to obtain one patient with more than 50% pain relief was 6.9 in the total sample, 3.9 in the irritable, and 13 in the non-irritable nociceptor phenotype.

In summary, data exist that patients with different sensory profiles will respond differently to treatment. Consequently, cohorts in clinical trials should be stratified and potentially enriched with patients who likely respond to the study drug based on the sensory profile rather than on the underlying etiology. This approach has the potential to minimize pathophysiological heterogeneity within the groups under study and to increase the power to detect a positive treatment result.

Conflict of interest
Disclosure statement:
Ralf Baron has received grants/research support from Pfizer, Genzyme GmbH, Grünenthal GmbH, Mundipharma. He is a member of the EU Project No 633491: DOLOR-isk. A member of the IMI "Europain" collaboration and industry members of this are: Astra Zeneca, Pfizer, Esteve, UCB-Pharma, Sanofi Aventis, Grünenthal GmbH, Eli Lilly and Boehringer Ingelheim Pharma GmbH&Co.KG.

German Federal Ministry of Education and Research (BMBF): Member of the ERA_NET NEU-RON/IM-PAIN Project. German Research Net-work on Neuropathic Pain, NoPain system biolo-gy. German Research Foundation (DFG). He has received speaking fees from Pfizer, Genzyme GmbH, Grünenthal GmbH, Mundipharma, Sanofi Pasteur, Medtronic Inc. Neuromodulation, Eisai Co.Ltd., Lilly GmbH, Boehringer Ingelheim Pharma GmbH&Co.KG, Astellas, Desitin, Teva Pharma, Bayer-Schering, MSD GmbH, bioCSL. He has been a consultant for Pfizer, Genzyme GmbH, Grünenthal GmbH, Mundipharma, Allergan, Sanofi Pasteur, Medtronic Inc. Neuromodulation, Eisai Co.Ltd., Lilly GmbH, Boehringer Ingelheim Pharma GmbH&Co.KG, Astellas, Novartis, Bristol-Myers-Squibb, Biogenidec, AstraZeneca, Merck, Abbvie, Daiichi Sankyo, Glenmark Pharmaceuticals, bioCSL, Teva Pharma an Genentech.

References

1. Baron R, Förster M and Binder A. Subgrouping of patients with neuropathic pain according to pain-related sensory abnormalities: a first step to a stratified treatment approach. *Lancet Neurol* 2012; 11: 999–1005.
2. Demant DT, Lund K, Vollert J, Maier C, Segerdahl M, Finnerup NB, Jensen TS and Sindrup SH. The effect of oxcarbazepine in peripheral neuropathic pain depends on pain phenotype: A randomised, double-blind, placebo-controlled phenotype-stratified study. *Pain* 2014 Nov; 155(11): 2263–73.
3. Maier C, Baron R, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): Somatosensory abnormalities in 1236 patients with different neuropathic pain syndromes. *Pain* 2010; 150: 439–50.

EHMTC-0424
INTERNATIONAL FORUM FOR HEADACHE NURSES (IFHN) HEADACHE EDUCATION

HOW TO ESTABLISH A HEADACHED CLINIC? EXPIRIENCES FROM ESTONIA

K. Tamela[1]

[1]*Estonia*

How to establish a Headache Clinic? Experiences from Estonia

According to the revised data of Statistics Estonia, 1,315,944 persons lived in Estonia on 1 January 2016. There is two Headche Clinics in Estonia. One is in South-Estonia: Tartu University Hospital and the second one is in North-Estonia: East Tallinn Central Hospital.

I work as a headache nurse in Tartu University Hospital. Headache Clinic started work in april 2014. We have two headache specialist/neurology and two headache nurse. Headache Clinic is once a week. Headache nurse counseling is two days a week.

EHMTC-0422
INTERNATIONAL FORUM FOR HEADACHE NURSES (IFHN) HEADACHE EDUCATION

MEDICATION OVERUSE HEADACHE: HOW TO INCREASE AWARENESS IN GENERAL PUBLIC?

L.N. Carlsen[1]

[1]*Danish Headache Center, Neurology Department, Glostrup, Denmark*

Medication-overuse headache – How can we increase awareness in the general public?

Medication-overuse plays a major role in the chronification of episodic headache. Chronic headache combined with medication-overuse is a very disabling condition. According to the Global Burden of Disease, approximately 63 million people worldwide suffer from medication-overuse headache. This contributes to significant socioeconomic costs and increased awareness is needed.

Thus, overuse of medication can be treated, and much better – prevented. However, prevention of too high intake of painkillers requires information in the general public. One way to spread information is to put up a national information campaign with a simple message, e.g. maximum use of painkillers two times a week in average. Also, it is important to reach health-care professionals in first line, like general practitioners and pharmacists. This presentation will present an example of how to spread the message of medication-overuse headache.

EHMTC-0420
INTERNATIONAL FORUM FOR HEADACHE NURSES (IFHN) HEADACHE EDUCATION

HEADACHE SERVICE QUALITY REGISTER – WHY? PRELIMINARY RESULTS AND EXPIRIENCES WITH A NORWEGIAN REGISTER FOR SEVERE PRIMARY HEADACHES (THE TACs)

G.B. Gravdahl[1]

[1]*Norway*

Background: Among the neurological conditions, headache disorders result in the greatest overall functional impairment (disability) in the population as a whole, according to the Global Burden of Disease 2013 study. Patients with severe headaches also constitute a significant proportion of patients treated at neurological departments. The quality and extent of the services offered in different hospitals in Norway is unknown. Norwegian health authorities wishes medical quality registers for evaluating and improving quality of care for a variety of medical conditions. It is impossible to have all headache sufferers in a register therefor we decided to include only relatively rare but very serious headaches (the trigemino-autonomic cephalalgias, TACs). New costly and invasive procedures for treating these patients also require monitoring of treatment results through a register. We conducted a pilot study from St. Olav's Hospital in Trondheim in 2015

Method: A local consent-based quality register is established at St. Olav's Hospital from 01.01.2015. In accordance with published quality indicators for headache services the register was designed to monitor whether patients with TACs have equal access to health services and that the quality of diagnosis, treatment and follow-up are adequate and whether the treatment was of benefit to the patients. The register shall also facilitate research.

Results: During the first year we registered 24 patients, 9 men and 15 women, recruited by 8 different neurologists. Only one patient declined to be included in the register. The initial registration took about 20 minutes. There were 23 with cluster headache (two with probable cluster headache), and 1 with likely hemicrania continua. 11 of the cluster headache patients had the chronic form. 3 had never tried sumatriptan inj, 8 had not tried O2, and 8 had not been attempting preventive treatment. 9 had been offered other types of treatment (blockades, stimulator etc). 22 had an MRI scan of the head.

Conclusion: The inclusion in a registry seems to be well accepted by patient group. Even in a group with many chronic patients, there were several who had not been offered an adequate treatment, such as sumatriptan inj, oxygen or preventive treatment. The register may be even more useful when it is established as a national register, but require further development in order to capture patient satisfaction with care, and also effect of treatment.

EHMTC-0418
SLEEP & HEADACHE

BASIC MECHANISMS LINKING SLEEP AND HEADACHE

P. Holland[1]

[1]*London, United Kingdom*

There is a clear association between headache and sleep in the clinical setting. Disrupted sleep-wake patterns may predispose individuals to migraine attacks and increase the risk of chronification. In contrast, sleep is one of the most commonly reported abortive strategies for migraine.

As such migraine may be both caused and relieved by sleep marking a complex interaction.

Sleep is governed by both circadian mechanisms and increasing sleep pressure that accumulates during the day and abates during sleep. The clearest link between our internal "body clocks" and headache is observed in cluster headache, with its striking circadian and circannual periodicity.

Our current preclinical understanding of the pathophysiology, pharmacology and genetics linking headache and sleep disorders will be discussed. Focussing on discrete neural networks and underlying shared anatomical processes we will review the basic mechanisms linking sleep and headache to address if the potential shared aetiology represents a novel therapeutic strategy?

EHMTC-0428
EFIC/EHF SYMPOSIUM: CGRP, PAIN AND HEADACHE

CGRP AND CGRP RECEPTOR IN THE TRIGEMINOVASCULAR SYSTEM AND CNS

S. Eftekhari[1]

[1]*University of California- Los Angeles, Neurology, Los Angeles, USA*

Migraine is a chronic disorder that affects more than 10% of the general population. The disorder is characterized by attacks of severe headache and accompanied by a wide variety of associated symptoms that can occur before, during or after the headache. Although the exact cause of migraines is still not fully understood, the neuropeptide calcitonin gene-related peptide (CGRP) has been shown to have a prominent role in the pathophysiology of migraine and is associated with activation of the trigeminovascular system. This system includes the trigeminal ganglion, intracranial vasculature, dura mater and parts of the brainstem.

CGRP receptor antagonists and monoclonal anti-CGRP/anti-CGRP receptor antibodies have been developed that display clinical efficacy. Therefore, it is of great importance to identify where the CGRP receptor is expressed and to reveal the potential sites of action for these drugs.

The expression of CGRP and its receptor within the trigeminovascular system and parts of the CNS has been demonstrated suggesting that several regions such as the dura mater, trigeminal ganglion, the cerebellum and the brainstem to be involved in migraine pathophysiology. Recent data show that CGRP can act at more than one receptor, where expression and functionality of two CGRP receptor candidates in the sensory trigeminal system has been demonstrated. Functional data suggest that CGRP may be involved in neurogenic inflammation, light aversion, calcium signaling in the trigeminal ganglion and cortical spreading depression (CSD).

Further it has been suggested that current CGRP receptor antagonists cannot pass the blood-brain barrier (BBB) (or only to a low degree). The recently developed monoclonal anti-CGRP and anti-CGRP receptor antibodies will not likely cross the BBB due to their large size. It is therefore important to clarify which sites can be reached and may therefore contribute to the clinical efficacy. The trigeminal ganglion and some areas in the brainstem are not protected by the BBB and CGRP receptor antagonists and antibodies may act in these regions to block the CGRP signaling regardless of the molecules ability to cross BBB.

EHMTC-0435
MIGRAINE TRUST LECTURE

THE INITIATION OF MIGRAINE ATTACKS – REVISITING THE BRAINSTEM

A. May[1]

[1]*Hamburg, Germany*

The initiation of migraine attacks – revisiting the brainstem

Arne May
University Clinic of Hamburg
Dept. of Systems Neuroscience
a.may@uke.de

Migraine has a complex pathophysiology. This lecture will focus on the newest findings which render more precisely what role the brainstem and midbrain play in the attack initiation of migraine.

Due to the clinical picture and also based on early imaging data (Weiller et al., 1995), the brainstem and midbrain structures have been intensely discussed as possible driving or generating structures in migraine. The fact that the brainstem activation persisted after treatment (Weiller et al., 1995; Bahra et al., 2001) makes it unlikely that this activation was only due to increased activity of the endogenous anti-nociceptive system. It was consequently (and somewhat simplifying) coined the "migraine generator". Since then several studies have focussed on this region when investigating episodic (Afridi et al., 2005), but also chronic migraine (Matharu et al., 2004). Denuelle et al were the first to not only demonstrate significant activations in the midbrain and pons but also in the hypothalamus, which, just like the brainstem activation in the first

study, persisted after headache relief with sumatriptan (Denuelle et al., 2007).

Expanding these studies into f-MRI studies, refined the involvement of rostral parts of the pons in acute migraine attacks. Interestingly, this area only showed higher activation during the attack and not between attacks and not shortly before an attack. This was unlike the activation in spinal trigeminal nuclei, in response to nociceptive stimulation which showed a cycling behaviour over the migraine interval. While interictal (i.e. outside of attack) migraine patients revealed lower activations in the spinal trigeminal nuclei compared to controls, pre-ictal (i.e. shortly before attack) patients showed activity similar to controls, which demonstrates that the trigeminal activation level increases over the pain-free migraine interval (Stankewitz et al., 2011). The question arises whether other structures may operate as modulators of neuronal activity in the spinal trigeminal nuclei, such as the hypothalamus or the endogenous pain control system, e.g. the PAG or the raphe nuclei. Evidence for deficient inhibition comes from a study reporting hypo-functional structures in the midbrain in migraineurs (Moulton et al., 2008).

Given that the brainstem was not specifically activated in the pre-ictal state and given the clinical progression of the migraine cycle, it is tempting to consider oscillating impulse generators in the limbic system, perhaps including the hypothalamus, which may have (indirect) modulating effects on the activation level of the Pons and trigeminal nuclei towards an attack, which is succeeded by a specific activation of the rostral parts of the pons in the actual headache attack. Given, that one of the key features in migraine is the cycling behaviour of attacks, a recent report on a migraine patient who went into the scanner every day for 30 days including 3 complete, untreated migraine attacks, adds certainly another piece to the puzzle (Schulte et al., 2016). This study clearly suggests the hypothalamus to be the primary motor of migraine attacks as it is indeed activated before the attack and exhibits significant phase-specific interactions with the brainstem. The chapter of the "migraine generator" is certainly not closed, but we should broaden our view and focus also on other structures than the brainstem alone.

References

1. Afridi SK, Matharu MS, Lee L, Kaube H, Friston KJ, Frackowiak RS, et al. A PET study exploring the laterality of brainstem activation in migraine using glyceryl trinitrate. *Brain* 2005; 128: 932–9.
2. Bahra A, Matharu MS, Büchel C, Frackowiak RSJ and Goadsby PJ. Brainstem activation specific to migraine headache. *Lancet* 2001; 357: 1016–1017.
3. Denuelle M, Fabre N, Payoux P, Chollet F and Geraud G. Hypothalamic activation in sponatneous migraine attacks. *Headache* 2007; 47: 1418–1426.
4. Matharu MS, Bartsch T, Ward N, Frackowiak RS, Weiner R and Goadsby PJ. Central neuromodulation in chronic migraine patients with suboccipital stimulators: a PET study. *Brain* 2004; 127: 220–30.
5. May A. New insights into headache: an update on functional and structural imaging findings. *Nat Rev Neurol* 2009; 5: 199–209.
6. Moulton EA, Burstein R, Tully S, Hargreaves R, Becerra L and Borsook D. Interictal dysfunction of a brainstem descending modulatory center in migraine patients. *PLoS One* 2008; 3: e3799.
7. Stankewitz A, Aderjan D, Eippert F and May A. Trigeminal nociceptive transmission in migraineurs predicts migraine attacks. *J Neurosci* 2011; 31: 1937–43.
8. Schulte L, May, A.; The migraine generator revisited: Continuous scanning of the migraine cycle over 30 days and 3 spontaneous attacks; BRAIN (2016); 139(Pt 7): 1987–93.
9. Weiller C, May A, Limmroth V, Jüptner M, Kaube H, Schayck RV, et al. Brain stem activation in spontaneous human migraine attacks. *Nature Medicine* 1995; 1: 658–660.

EHMTC-0419
ENDOCRINE DISORDERS AND HEADACHE

PITUITARY DISORDERS AND HEADACHE

M. Levy[1]

[1]*University Hospitals of Leicester, Endocrinology, Leicester, United Kingdom*

There are numerous reasons why patients with pituitary tumours might present with headache. Pituitary incidentalomas are common, occurring in as much as 10% of brain imaging reports. In many cases, the presence of a reported pituitary lesion is truly incidental to the headache presentation; in others the clinician must be alert to the possibility that management of the pituitary lesion might lead to an improvement in symptoms. This session gives a clinical overview of the potential pitfalls and management dilemmas that may occur in this clinical situation. The pathophysiology and treatment of pituitary tumour-associated headache is discussed using real-life case scenarios as examples.

EHMTC-0427
PLENARY SESSION II

HIGH ALTITUDE HEADACHE: TRACKING DOWN THE BIOCHEMICAL PATHWAYS OF THE PLACEBO/NOCEBO RESPONSE

F. Benedetti[1]

[1]*Turin, Italy*

High altitude headache: tracking down the biochemical pathways of the placebo/nocebo response

Fabrizio Benedetti
University of Turin & Plateau Rosà Labs, Italy/Switzerland

High altitude, or hypobaric hypoxia, headache has recently emerged as an excellent model to understand the biological and psychological mechanisms of the placebo and nocebo response. Indeed, placebos and nocebos have been found to modulate the cyclooxygenase pathway and prostaglandins synthesis in hypoxic conditions, along with headache pain. Likewise, placebos have been found to affect hyperventilation-induced alkalosis, a typical compensatory response to hypoxia that leads to headache pain. Overall, these mechanisms help understand both the biological underpinnings of placebo/nocebo responses and the pathophysiology of hypobaric hypoxia headache.

EHMTC-0416
VESTIBULAR MIGRAINE

WHAT IS VESTIBULAR MIGRAINE?

M. von Brevern[1]

[1]*Germany*

During the last decades a new vestibular syndrome has emerged that is now termed vestibular migraine (MV). The main body of evidence for VM is provided by epidemiologic data demonstrating a strong association between migraine and vestibular symptoms. Today, VM is recognised as one of the most common causes of episodic vertigo. The clinical presentation of VM is heterogeneous in terms of vestibular symptoms, duration of episodes and association with migrainous accompaniments. Many patients experience attacks both with and without headache. Quite frequently, patients have an attenuated headache with their vertigo as compared to their usual migraine. In some patients, vertigo and headache never occur together. Similar to migraine, there is no clinical or laboratory confirmation for VM and the diagnosis relies on the history and the exclusion of other disorders. Recently, diagnostic criteria for MV have been elaborated jointly by the International Headache Society and the Bárány Society. Clinical examination of patients with acute VM has clarified that the vast majority of patients with VM suffer from transient central vestibular dysfunction. Findings in the interval may yield mild signs of damage to both the central vestibular and ocular motor system and to the inner ear. How migraine affects the vestibular system is still a matter of speculation.

EHMTC-0421
GETTING IT RIGHT: MEASURING AND MANAGING HEADACHE

INTERICTAL BURDEN OF HEADACHE: RESULTS FROM THE EUROLIGHT STUDY

C. Lampl[1], H. Thomas[2], L.J. Stovner[2], C. Tassorelli[3], Z. Katsarava[4], J.M. Laínez[5], M. Lantéri-Minet[6], D. Rastenyte[7], C. Andrée[8], T.J. Steiner[2]

[1]*Hospital Sisters of Charity Linz, Headache Medical Center Seilerstaette, Linz, Austria*
[2]*Norwegian University of Science and Technology- Trondheim- Norway, Department of Neuroscience, Trondheim, Norway*
[3]*C Mondino National Neurological Institute- Pavia- Italy, Headache Science Centre, Pavia, Italy*
[4]*University of Duisberg-Essen- Essen- Germany, Department of Neurology, Essen, Germany*
[5]*Hospital Clinico Universitario- University of Valencia- Valencia- Spain, Department of Neurology, Valencia, Spain*
[6]*Centre Hospitalo-Universitaire de Nice- Nice- France, Departement d'Evaluation et Traitement de la Douleur, Nice, France*
[7]*Lithuanian University of Health Sciences- Kaunas- Lithuania, Department of Health Sciences, Kaunas, Lithuania*
[8]*Luxembourg Institute of Health- Luxembourg, Department of Population Health, Luxembourg, Luxembourg*

Background: Most estimates of the heavy disability burden attributed to headache derive from epidemiological data focused on episodic migraine and tension-type headache (TTH). These disorders give rise directly, but intermittently, to symptom burden, but People with

them may not be entirely symptom-free between attacks. We analysed the Eurolight dataset for interictal burden.

Methods: Eurolight was a cross-sectional survey using modified cluster sampling from the adult population (18–65 years) in 10 countries of the European Union. We used data from nine. The questionnaire included headache-diagnostic questions based on ICHD-II and several question sets addressing impact, including interictal and cumulative burdens.

Results: There were 6,455 participants (male 2,444 [37.9%]) with headache. Interictal symptoms were reported by 26.0% of those with migraine and 18.9% with TTH: interictal anxiety by 10.6% with migraine, avoidance (lifestyle compromise) by 14.8%, both much more common than in TTH (3.1% [OR 3.8] and 4.7% [OR 3.5] respectively). Mean time spent in the interictal state was 317 days/year for migraine, 331 days/year for TTH. Those who were "rarely" or "never" in control of their headaches (migraine 15.2%, TTH 9.6%) had significantly raised odds of interictal anxiety, avoidance and other interictal symptoms. Among those with migraine, interictal anxiety increased markedly with headache intensity and frequency, avoidance less so but still significantly. Lost productive time was associated with high odds (OR up to 5.3) of anxiety and avoidance.

Discussion: Interictal burden in those with episodic headache is common, more so in migraine than TTH. Some elements have the potential to be profoundly consequential.

EHMTC-0432
GETTING IT RIGHT: MEASURING AND MANAGING HEADACHE

SERVICE QUALITY IN HEADACHE CARE: A STUDY IN 14 SPECIALIZED CENTRES IN EUROPE

S. Schramm[1], D. Uluduz[2], R. Gil Gouveia[3], R. Jensen[4], A. Siva[2], U. Uygunoglu[2], G. Gvantsa[5], M. Maka[5], M. Braschinsky[6], E. Filatova[7,8], N. Latysheva[7,8], V. Osipova[8,9], K. Skorobogatykh[9], J. Azimova[9], A. Straube[10], O. Emre Eren[10], P. Martelletti[11], V. De Angelis[11], A. Negro[11], M. Linde[12,13], K. Hagen[12,13], A. Radojicic[14], J. Zidverc-Trajkovic[14], A. Podgorac[15], K. Paemeleire[16], A. De Pue[16], C. Lampl[17], T.J. Steiner[18,12], Z. Katsarava[19,20]

[1]*Institute of Epidemiology- Biometry and Statistics, University of Duisburg-Essen, Essen, Germany*
[2]*Department of Neurology, Cerrahpasa School of Medicine, Istanbul University, Turkey*
[3]*Hospital da Luz Headache Centre, Neurology Department, Hospital da Luz, Lisbon, Portugal*
[4]*Danish Headache Centre, Department of Neurology, University of Copenhagen, Rigshospitalet-Glostrup, Denmark*
[5]*Department of Neurology, Aversi Clinic, Tbilisi, Georgia*
[6]*Department of Neurology, Tartu University Clinics, Tartu, Estonia*
[7]*Alexander Vein Headache Clinic, Moscow, Russian Federation*
[8]*First Sechenov Moscow State Medical University, Moscow, Russian Federation*
[9]*University Headache Clinic, Moscow, Russian Federation*
[10]*Department of Neurology, Ludwig-Maximilians-University Munich, Klinikum Großhadern, Munich, Germany*
[11]*Department of Clinical and Molecular Medicine, Sapienza University of Rome, Regional Referral Headache Centre, Sant'Andrea Hospital, Rome, Italy*
[12]*Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway*
[13]*Norwegian Advisory Unit on Headaches, St Olavs University Hospital, Trondheim, Norway*
[14]*Neurology Clinic Clinical Centre of Serbia, Belgrade, Serbia*
[15]*Faculty of Medicine, University of Belgrade, Serbia*
[16]*Department of Neurology, Ghent University Hospital, Ghent, Belgium*
[17]*Headache Medical Center Linz Seilerstätte, Linz, Austria*
[18]*Division of Brain Sciences, Imperial College London, London, UK*
[19]*Department of Neurology, Evangelical Hospital Unna, Germany*
[20]*Medical Faculty, University of Duisburg-Essen, Germany*

The study was a collaboration between Lifting The Burden (LTB) and the European Headache Federation (EHF). Its aim was to evaluate the implementation of quality

indicators for headache care Europe-wide in specialist headache centres (level-3 according to the EHF/LTB standard). Employing previously-developed instruments in 14 such centres, we made enquiries, in each, of health-care providers (doctors, nurses, psychologists, physiotherapists) and 50 patients, and analysed the medical records of 50 other patients. Enquiries were in 9 domains: diagnostic accuracy, individualized management, referral pathways, patient's education and reassurance, convenience and comfort, patient's satisfaction, equity and efficiency of the headache care, outcome assessment and safety. Our study showed that highly experienced headache centres treated their patients in general very well. The centres were content with their work and their patients were content with their treatment. Including disability and quality-of-life evaluations in clinical assessments, and protocols regarding safety, proved problematic: better standards for these are needed. Some centres had problems with follow-up: many specialised centres operated in one-touch systems, without possibility of controlling long-term management or the success of treatments dependent on this. This first Europe-wide quality study showed that the quality indicators were workable in specialist care. They demonstrated common trends, producing evidence of what is majority practice. They also uncovered deficits that might be remedied in order to improve quality. They offer the means of setting benchmarks against which service quality may be judged. The next step is to take the evaluation process into non-specialist care (EHF/LTB levels 1 and 2).

EHMTC-0425
ENRICO GREPPI AWARD

EXPRESSION OF MESSENGER MOLECULES AND RECEPTORS IN RAT AND HUMAN SPHENOPALATINE GANGLION

A. Steinberg[1], S.D. Frederiksen[2], F.W. Blixt[2], K. Warfvinge[2], L. Edvinssom[2]

[1]*Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden*
[2]*Division of Experimental Vascular Research- Lund University, Department of Clinical Sciences, Lund, Sweden*

Background: Migraine and Cluster Headache (CH) are two primary headaches with severe disease burden. The disease expression and the mechanisms involved are poorly known. In some attacks of migraine and in most attacks of CH, there is a release of vasoactive intestinal peptide (VIP) originating from parasympathetic cranial ganglia such as the sphenopalatine ganglion (SPG). Patients suffering from these diseases are often deprived of effective drugs. The aim of the study was to examine the localization of the botulinum toxin receptor element synaptic vesicle glycoprotein 2A (SV-2A) and the vesicular docking protein synaptosomal-associated protein 25 (SNAP25) in human and rat SPG. Additionally the expression of the neurotransmitters pituitary adenylate cyclase activating polypeptide (PACAP-38), nitric oxide synthase (nNOS), VIP and 5-hydroxttryptamine subtype receptors (5-$HT_{1B,1D,1F}$) were examined.

Methods: SPG from adult male rats and from humans, the later removed at autopsy, were prepared for immunohistochemistry using specific antibodies against neurotransmitters, 5-$HT_{1B,1D,1F}$ receptors, and botulinum toxin receptor elements.

Results: We found that the selected neurotransmitters and 5-HT receptors were expressed in rat and human SPG. In addition, we found SV2-A and SNAP25 expression in both rat and human SPG. We report that all three 5-HT receptors studied occur in neurons and satellite glial cells (SGCs) of the SPG. 5-HT_{1B} receptors were in addition found in the walls of intraganglionic blood vessels.

Conclusions: Recent focus on the SPG has emphasized the role of parasympathetic mechanisms in the pathophysiology of mainly CH. The development of next generation's drugs and treatment of cranial parasympathetic symptoms, mediated through the SPG, can be modulated by treatment with BoNT-A and 5-HT receptor agonists.

EHMTIC 2016 – POSTER ABSTRACTS

EHMTC-0325
POSTER SESSION A

HULL PROSPECTIVE ANALYSIS OF ONABOTULINUMTOXINA IN THE TREATMENT OF CHRONIC MIGRAINE; REAL LIFE DATA IN 536 PATIENTS; AN UPDATE

F. Ahmed[1], M. Khalil[1], A. Buture[1], R. Nimeri[1]

[1]*Hull York Medical School, Department of Neurosciences, Hull, United Kingdom*

Objectives: To evaluate the efficacy and safety of OnabotulinumtoxinA in adult patients with Chronic Migraine (CM) in real-life settings.

Methods: Adult patients with CM attending the Hull Migraine Clinic were treated with OnabotulinumtoxinA based on clinical needs. Patients were treated as per PREEMPT protocol. Patients were asked to maintain a headache diary for at least 30 days prior to and

continuously after treatment. Patients with medication overuse were included based on the expert opinion. Data were extracted for headache days, migraine days, crystal clear days (headache-free) as primary outcome; also analgesic consumption, adverse events and quality of life using HIT-6. Responder was defined as per Hull criteria (50% reduction in either headache or migraine days or increment on headache free days twice the baseline) for treatment in the first cycle.

Results: Of a series of 610 patients (July 2010 – December 2015) full data were available on 536 patients (100 male, median age 48 years; range 19–77 years, 436 female, median age 45 years; range 18–91 years). A total of 2596 cycles were given. 521 (97.2%) had failed three preventive treatments. 274 (51.1%) patients were overusing analgesics. Patients had CM for a median of 4 years (Range 0.5–67 years). 313 (58.4%) responded based on Hull Criteria and reported improved health related quality of life outcome. 80 (15%) reported adverse events mainly stiffness in the neck with 48 (9%) reporting mild ptosis.

Conclusion: OnabotulinumtoxinA is a safe and effective preventive treatment in adults with CM in a real-life setting.

Conflict of interest
Disclosure statement:
Fayyaz Ahmed has served on the Allergan advisory board and conducted training session for which he received honorarium paid to the British Association for the Study of Headache and the Migraine Trust.

Modar Khalil has received honorarium from Allergan for delivering presentations at the Expert Master class.

EHMTC-0340
POSTER SESSION A

DOES MEDICATION OVERUSE MATTER? RESPONSE TO ONABOTULINUMTOXINA IN CHRONIC MIGRAINE (CM) WITH OR WITHOUT MEDICATION OVERUSE; UPDATE FROM REAL-LIFE DATA

F. Ahmed[1], A. BUTURE[2], R. NIMERI[2], M. KHALIL[2]

[1]*United Kingdom*
[2]*HULL YORK MEDICAL SCHOOL, DEPARTMENT OF NEUROSCIENCES, HULL, United Kingdom*

Introduction: CM affects 2% of the general population with substantial impact on quality of life. Medication overuse in CM is seen in around two third of patients in specialist headache clinics. There is lack of consensus on whether preventive treatment be initiated before or after the analgesic withdrawal. We analysed the response to OnabotulinumtoxinA in patients with CM with or without analgesic overuse treated at the Hull Migraine Clinic.

Objectives: To compare the efficacy of OnabotulinumtoxinA in adults with Chronic Migraine with or without medication overuse.

Methods: Adult patients with CM were offered OnabotulinumtoxinA based on clinical need and were injected based on the PREEMPT treatment paradigm. Headache diaries were maintained for 30 days prior to and continuously after treatment. Data were extracted for headache, migraine and headache-free days and responders were defined based on Hull Criteria (50% reduction of either headache or migraine days or increment in headache free days twice that of the baseline).

Results: Of 610 patients, full data for the first cycle was available on 536 patients [274 (51.1%) with analgesic overuse and 252 (48.9%) without overuse]. The responder rate based on Hull criteria was 61.4% in patients with analgesic overuse compared to 56.4% in patients without overuse. There was significant reduction in days with analgesic consumption in both groups.

Conclusion: Patients with CM respond equally well to OnabotulinumtoxinA irrespective of analgesic consumption at baseline.

Conflict of interest
Disclosure statement:
Fayyaz Ahmed has received honorarium from Allergan, eneura and electrocore paid to the British Association for the Study of Headache and the Migraine Trust for running training workshop and being on their advisory board.

Modar Khalil has received honorarium to present in the chronic migraine masterclass from Allergan

EHMTC-0412
POSTER SESSION A

MAINTENANCE OF CLINICAL RESPONSE TO ERENUMAB (AMG334) IN EPISODIC MIGRAINE: COMPLETE ONE YEAR RESULTS FROM AN ONGOING OPEN-LABEL EXTENSION STUDY

M. Ashina[1], D. Dodick[2], P.J. Goadsby[3], U. Reuter[4], S. Silberstein[5], F. Zhang[6], S. Cheng[6], D. Mikol[6], R.A. Lenz[6]

[1]*Dept. of Neurology, Danish Headache Center, Rigshospitalet Glostrup, University of Copenhagen, Copenhagen, Denmark*
[2]*Dept. of Neurology, Mayo Clinic, Scottsdale, AZ, USA*
[3]*NIHR-Wellcome Trust King's Clinical Research Facility, Kings College London, UK*
[4]*Dept. of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany*
[5]*Jefferson Headache Center, Thomas Jefferson University, Philadelphia, PA, USA*
[6]*Amgen Inc., Thousand Oaks, CA, USA*

Introduction and Objectives: To assess long-term efficacy and safety of erenumab (AMG334), a fully human anti-CGRP receptor antibody, in patients with migraine.

Methods: One year analysis from an ongoing 5-year open-label extension (OLE) of 70 mg erenumab every four weeks in adult patients with episodic migraine (4–14 migraine days and <15 headache days/month) who completed a 12-week double-blind, placebo-controlled phase 2 study (NCT01952574) of erenumab (7, 21, or 70 mg). Outcomes at week 64 (OLE week 52) included change in monthly migraine days (MMD), ≥50% reduction in MMD, and several patient-reported outcomes. Safety was assessed by monitoring adverse events.

Results: Of 383 patients in the OLE, 273 (71%) were continuing open-label 70 mg erenumab at week 64. Mean monthly migraine days, which were significantly lower for erenumab (70 mg) than placebo at week 12, remained comparably low for all patients over weeks 16–64, irrespective of initial treatment allocation. Patients experienced a mean (SD) 5.0 (4.2) fewer MMD at week 64 than baseline (8.8 (2.6) days). At week 64, 65%, 42% and 26% of patients experienced a ≥50%, ≥75% and 100% response, respectively. Twenty-one patients reported serious adverse events (SAEs). No SAE occurred in >2 patients. Nine of 382 subjects (2.4%) were positive for neutralizing antibodies against erenumab at some time; of these, only one was persistent (positive result at last time point).

Conclusion: Sustained efficacy was observed with erenumab during the 1-year OLE. Safety results were consistent with previous erenumab studies and no new safety concerns were identified.

Conflict of interest
Yes This study was funded by Amgen Inc.
Messoud Ashina is a consultant or scientific advisor for Allergan, Amgen, Alder, ATI and Eli Lilly, primary investigator for Amgen and GM-11 gamma-Core-R trials, and reports grants from Lundbeck Foundation, Research Foundation of the Capital Region of Copenhagen, Danish Council for Independent Research-Medical Sciences and Novo Nordisk Foundation during the conduct of the study.

David Dodick Consulting fees: Amgen, Alder, Allergan, Eli Lilly, eNeura, Boston Scientific, Teva, Novartis, Autonomic Technologies, Scion Neurostim, Tonix, Trigemina, Supernus, Xenon, GBS, Xalan. Honoraria Sage Publishing, Wiley, UpToDate. Royalties: Oxford University Press, Cambridge University Press.

Peter J Goadsby and Stephen Silberstein Consulting fees – Amgen Inc.

Uwe Reuter Consulting fees, speaking/teaching fees, and/or research grants – Allergan, Amgen Inc., Autonomic Technologies, CoLucid, Electrocore, and Pharm Allergan.

Feng Zhang, Sunfa Cheng, Daniel Mikol, and Rob Lenz Employees and stock/stock options – Amgen Inc.

EHMTC-0397
POSTER SESSION A

A MULTIPLE-DOSE, PHASE I PLACEBO-CONTROLLED, RANDOMIZED STUDY OF ALD403, AN ANTI-CGRP ANTIBODY, ADMINISTERED EVERY 3-MONTHS VIA IV, SC, OR IM

B. Baker[1], B. Schaeffler[2], S. Jeff[2]

[1]*Alder Biopharmaceuticals Inc, Bothell, USA*
[2]*Alder Biopharmaceuticals Inc, Translational Medicine, Bothell, USA*

Background: CGRP is involved in the pathophysiology of migraine. We evaluated the pharmacokinetics and pharmacodynamics of ALD403, a humanized anti-CGRP antibody, administered once every 3-months via IV, SC, or IM routes in healthy subjects.

Methods: The trial was approved by the Ethics Committee and conducted in accordance with applicable ICH GCP guidelines. All subjects signed a written informed consent. Five groups of 12 participants each were scheduled to receive three different injections via IV, SC, or IM routes

on study days 1 and 84, with up to one injection containing either 100 mg (IV, SC, or IM) or 300 mg (IM) ALD403, and the remaining injections as placebo. Plasma samples were analyzed for free ALD403 concentrations and pharmacokinetic results were generated according to standard non-compartmental methods. Pharmacodynamic effects following ALD403 administration were investigated by evaluating the inhibition of vasodilation induced by topically applied capsaicin solution to the forearm.

Results: Following dose 1, the T_{max} was observed at 0.05, 6.0, 5.0, or 4.5 days, with corresponding mean C_{max} values of 36.0, 11.0, 16.7 or 47.3 μg/mL ALD403, in the groups receiving 100 mg IV, SC, IM, or 300 mg IM, respectively. The half-life for ALD403 ranged from 30.2 to 35.7 days. Subjects receiving ALD403 via all routes were observed with reductions in capsaicin induced dermal perfusion relative to placebo that persisted for greater than 3-months.

Conclusions: The pharmacokinetic and pharmacodynamic results support 100 mg ALD403 intravenous or extravascular (SC, IM) administration, or 300 mg IM administration, once every 3-months in future clinical trials.

Conflict of interest
Disclosure statement:
I am an employee and stock owner for Alder BioPharmaceuticals.

EHMTC-0188
POSTER SESSION A

CHARACTERIZATION OF SLEEP DISTURBANCES IN HEADACHE CLINIC PATIENTS WITH MIGRAINE-LIKE HEADACHES

O. Begasse de Dhaem[1], E.K. Seng[2], M.T. Minen[3]

[1]*NYU School of Medicine, Internal Medicine, New York, USA*
[2]*Ferkauf Graduate School of Psychology- Yeshiva University. Saul R. Korey. Albert Einstein College of Medicine., Neurology, New York, USA*
[3]*NYU Langone Medical Center, Neurology, New York, USA*

Objectives: Sleep disorders may contribute to migraine onset and chronification. We sought to assess the relationship between migraine characteristics and comorbidities and the Insomnia Severity Index (ISI) to identify the characteristics that would prompt referral for Cognitive Behavioral Therapy for Insomnia (CBT I).

Methods: This is a retrospective study of the headache characteristics and comorbidities of the new patients with suspected migraines who presented to our clinic from 8/15/2015 to 10/28/2015. Our predictors were headache severity and frequency, associated symptoms, Patient Health Questionnaire (PHQ-9), and General Anxiety Disorder (GAD-7). Our outcome variable was the ISI score. The relationships between our predictors and the ISI score were evaluated with two tailed t-tests and ANOVA.

Results: Out of the 61 patients, 75.4% were women, the mean age was 41.5, and the mean headache days/month was 11.6. 49.2% had clinical insomnia (ISI $\geq$ 15). There were no statistically significant differences in ISI between moderate (4–6/10) and severe headache pain (7–10/10), between episodic ($<$15 days per month) and chronic headache ($\geq$15 days per month). The mean ISI scores were higher for the patients with PHQ-9 scores of $\geq$10 (moderate depression) (22.4 vs 14.4, $p = 0.02$) and for the patients with General Anxiety Disorder (GAD-7) scores of $\geq$5 (mild anxiety) (18.28 vs. 13.4, 2 $p = 0.01$).

Conclusion: Migraine patients with comorbid depression and/or anxiety may be at higher risk for clinical insomnia and may hence benefit from referral for CBT-I regardless of their headache frequency.

EHMTC-0233
POSTER SESSION A

PERIPHERAL NERVE STIMULATION FOR CHRONIC DRUG-RESISTANT CRANIAL NEURALGIAS

P. Bermejo[1], C. del Pozo[2]

[1]*Hospital Puerta de Hierro, Majadahonda, Spain*
[2]*Hospital Puerta de Hierro, Pain Unit, Majadahonda, Spain*

Introduction: Cranial neuralgias are a group of treatable syndromes which comprise one of the possible causes of facial pain. Although some preventive medications and techniques have been proposed, there are still many refractory patients and other therapeutic options are warranted. Peripheral nerve stimulation (PNS) has been proposed as a promising therapy for these patients. Aim: The aim of this study is to evaluate the efficacy, tolerability and safety of PNS for the treatment of refractory cranial neuralgias. Methods: Fifteen patients (5 men, 10 women, average age 51.3 $\pm$ 11.9) suffering from different drug-resistant cranial neuralgia were enrolled and implanted with a neurostimulation device. Seven suffered from occipital neuralgia, 4 had postherpetic neuralgia and 4 had trigeminal neuralgia. Average follow-up period was 3.7 $\pm$ 1.8 years. The primary endpoint was the reduction in Analogical Visual Scale (AVS). Patient satisfaction, side effects and reasons for discontinuation were also studied. Significance level was set at $P < 0.05$. Results: Pain severity

according to the AVS was reduced from 8.7 ± 0.8 before PNS to 4.8 ± 2.9 after treatment initiation. 59% of treated patients were satisfied or very satisfied with the procedure. The most common adverse event was persistent implant site pain and three patients required to be explanted due to inefficacy. There were not differences between different subgroups. Conclusions: PNS has been explored as a possible treatment option in selective drug-resistant cranial neuralgias and, according to our results, this technique may be effective, safe and well tolerated in treating them. More studies are warranted to confirm these results.

EHMTC-0267
POSTER SESSION A

OCCIPITAL NERVE STIMULATION FOR REFRACTORY CHRONIC MIGRAINE: RESULTS OF A LONG-TERM PROSPECTIVE STUDY

P. Bermejo[1], D. Rodrigo[2], P. Azín[3]

[1]*Hospital Puerta de Hierro, Majadahonda, Spain*
[2]*Hospital Lozano Blesa, Pain Unit, Zaragoza, Spain*
[3]*Hospital Royo Villanova, Pain Unit, Zaragoza, Spain*

Introduction: Occipital Nerve Stimulation (ONS) refers to the electric stimulation of the distal branches of greater and lesser occipital nerves and has been proposed as a preventive treatment for chronic migraine.

The aim of this study is to evaluate the long-term efficacy and tolerability of ONS for medically intractable chronic migraine.

Methods: 35 patients who met the IHS criteria for chronic migraine received the implantation of an ONS system after a positive psychological evaluation and a positive response to a a preliminary occipital nerve blockage. After the surgery, they were thoroughly evaluated annually using different scales: analogical visual scale, number of migraine attacks, sleep quality, functionality, reduction in pain medication, satisfaction, tolerability and reasons for termination. The average follow-up was 9.4 ± 6.1 years, and 31 patients completed a 7-year follow-up period.

Results: Substantial pain reduction was obtained in most patients, and the AVS decreased 4.9 ± 2.0 points. These results remained stable over the follow-up period. Five patients were free from migraine attacks at their last visit, whereas the pain severity decreased 3.8 ± 2.5 (according to the AVS) in the remaining patients. Seven devices were removed: 2 because of treatment inefficacy, and 5 because the patients were asymptomatic. Systemic side effects were not observed.

Discussion: ONS may provide long-term benefits for chronic migraine. These results are slightly better than previous reports, and our results were maintained over the 7- year follow-up period. An accurate selection of patients, realization of diagnostic occipital nerve blocks, psychological evaluations, rigorous surgical technique and appropriate parameter programming helped us to obtain these results.

EHMTC-0305
POSTER SESSION A

LONG TERM OCCIPITAL NERVE STIMULATION FOR DRUG-RESISTANT CHRONIC MIGRAINE

P. Bermejo[1], C. del Pozo[2]

[1]*Hospital Puerta de Hierro, Majadahonda, Spain*
[2]*Hospital Puerta de Hierro, Pain Unit, Madrid, Spain*

Introduction: Although some preventive medications have been proposed to treat chronic migraine (CM) there are still many refractory patients and other treatments are warranted. Occipital nerve stimulation (ONS) is a promising therapy although long term studies are needed.

Aim: The aim of this study is to evaluate the efficacy and tolerability of ONS in the long term for the treatment of refractory CM. Methods: Twenty three patients (10 men, 13 women, average age 53.9 ± 11.7) meeting the IHS criteria for refractory CM were enrolled in this study and implanted with a neurostimulation device near the occipital nerves. The primary endpoint was the reduction in Analogical Visual Scale (AVS). Patient satisfaction, migraine frequency, side effects and reasons for discontinuation were also studied. Follow-up period was 4.8 ± 1.1 years.

Results: Headache severity according to the AVS was reduced from 8.5 ± 0.6 before ONS to 3.3 ± 2.8 after treatment initiation and these results remained stable after the follow-up period. There was also a significant difference in reduction of number of headache days and 80% of the patients were satisfied or very satisfied with the procedure. The most common adverse event was persistent implant site pain and only one patient required to be explanted due to inefficacy.

Conclusions: ONS has been explored as a possible treatment option in selective drug-resistant primary headache disorders and, according to our results, this technique may be effective, safe and well tolerated in the long term. An increasing experience and a more routine use of these techniques can be forecasted in the near future.

EHMTC-0218
POSTER SESSION A

MIGRAINE PROPHYLAXIS USING A NOVEL CALORIC VESTIBULAR STIMULATION DEVICE

R. Black[1]

[1]*Scion NeuroStim, none, Raleigh, USA*

A solid-state device has been developed that enables extended CVS therapy in a home setting. This device has been used in a prophylactic randomized controlled trial (RCT) for patients with episodic migraine (NCT01899040), demonstrating statistically significant reductions in migraine headache days. A second RCT has been undertaken so as to augment the dataset from the first and also explore factors affecting titration, optimal duration of therapy and the potential for durable gains past the end of therapy.

In a small pilot study, the effects of prolonged caloric vestibular stimulation on cerebral blood flow physiology and autonomic tone were studied. Preliminary results suggest that time-varying CVS thermal waveforms may entrain a pontine-based pacing center that subserves autoregulation. Also, CVS-induced changes in heart rate variability were seen. The viability of various non-invasive metrics in the context of personalized "biomarkers" for titrating CVS migraine therapy will be discussed.

We will present an overview of the CVS neuromodulation approach and review clinical study results to date and ongoing plans for migraine headache trials. CVS efficacy for migraine suggests a mechanism of action that may help to inform theories of migraine pathogenesis. We will also provide an overview of the rich literature background on vestibular pathways and argue that the vestibular system is an ideal candidate for facilitating non-invasive neuromodulation for treating CNS disease.

Conflict of interest
Disclosure statement:
I am an executive with Scion NeuroStim

EHMTC-0328
POSTER SESSION A

LONG TERM OUTCOME FOR ONABOTULINUMTOXINA IN CHRONIC MIGRAINE; TWO YEAR FOLLOW UP OF 302 PATIENTS FROM THE HULL MIGRAINE CLINIC

A. BUTURE[1], R. NIMERI[1], M. KHALIL[1], F. AHMED[1]

[1]*HULL YORK MEDICAL SCHOOL, DEPARTMENT OF NEUROSCIENCES, HULL, United Kingdom*

Introduction: The long-term outcome for patients with CM treated with OnabotulinumtoxinA remains uncertain. The National Institute for Health and Care Excellence (NICE) recommends discontinuing treatment if there is no response to two consecutive cycles (negative stopping rule) or when the migraine becomes episodic (positive stopping rule). However, this is based on consensus only.

Objectives: To determine the long term outcome of patients with CM treated with OnabotulinumtoxinA.

Methods: All patients treated with OnabotulinumtoxinA at the Hull Migraine Clinic were prospectively followed. Treatment was delivered as per the PREEMPT paradigm. Responders were defined as per NICE or Hull criteria. Treatment was stopped if there was no response to two consecutive cycles or until the headache days were less than 10 for three consecutive months (modified positive stopping rule).

Results: Of a series of 610 patients treated between July 2010 and January 2014 and received 2596 cycles, full data was available on 536 patients. Treatment data for at least two years (range 24–42 months) was available on 302. 175 (58%) patients fulfilled either NICE (48%) or Hull criteria for responder at cycle 2 and continued treatment. 127 patients (42%) stopped treatment at cycle two. Of the 175 patients 84 (48%) patients continued treatment for two years or more and 91 (52%) were able to stop the treatment within two years; 17/91 (18.6%) relapsed after stopping, 11/91 (12.08%) got resistant after initial response and 56/91 (61.53%) remained episodic.

Conclusion: At two years, 48% of initial cohort of responders will still require therapy with OnabotulinumtoxinA.

Conflict of interest
Disclosure statement:
Fayyaz Ahmed has received honorarium from Allergan to run workshops and advisory board which is paid to the British Association for the Study of Headache and the Migraine Trust

Modar Khalil has received honorarium to deliver presentation in the Expert Masterclass

EHMTC-0343
POSTER SESSION A

ANALYSIS OF PATTERNS OF RESPONSE TO ONABOTULINUMTOXINA IN CHRONIC MIGRAINE IN PREDICTING LONG TERM OUTCOME

A. BUTURE[1], M. KHALIL[1], R. NIMERI[1], A. RAMAN[1], F. AHMED[1]

[1]*HULL YORK MEDICAL SCHOOL, DEPARTMENT OF NEUROSCIENCES, HULL, United Kingdom*

Introduction: The efficacy of OnabotulinumtoxinA for Chronic Migraine (CM) is established; however, long term outcome data is limited and need for ongoing treatment remains uncertain.

Objectives: The study aims to identify patterns of response to OnabotulinumtoxinA that predict successful conversion to episodic migraine.

Methods: Adult patients receiving OnabotulinumtoxinA for CM at the Hull Migraine Clinic were prospectively followed. All patients maintained headache diary continuously during treatment. Data was extracted on headache and migraine days to identify patterns of response and need for ongoing treatment at two years.

Results: Of 302 patients initiating OnabotulinumtoxinA treatment 175 fulfilled NICE or Hull Criteria for responder and continued treatment beyond cycle 2. Of the 175 responders, 140 patients were still obtaining positive response at year 2 (84) or had successfully converted to episodic migraine (56). Others were either lost to follow up, became resistant or stopped treatment for other reasons. Our study analysed patterns of response and outcome in the cohort of 140 responders. We found two distinct patterns of response with 78 (55.7%) patients having a fluctuating 'wearing off' pattern with an increase in headache frequency prior to their next treatment; 62 (44.28%) having a steady decline on headache days without significant fluctuation between treatments. We found that the 'wearing off' pattern predicted those patients who would remain in chronic migraine with only 8/78 (10.25) patients converting to episodic migraine compared to 48/62 (77.4%) with stable non-fluctuating response.

Conclusion: We observed two distinct patterns of response that help to predict long-term outcome.

Conflict of interest
Disclosure statement:
Fayyaz Ahmed has received honorarium paid to the British Association for the Study of Headache and the Migraine Trust from Allergan, eneura, electrocore as an advisory board member and running training workshops.

Modar Khalil has received honorarium to lecture in the Chronic Migraine Expert Masterclass organised by Allergan.

EHMTC-0092
POSTER SESSION A

ONABOTULINUMTOXIN A AS ONE OF THE PREVENTIVE TREATMENTS FOR CHRONIC MIGRAINE IN KOREAN ADOLESCENTS

Y. Choi[1], C. Bae[2]

[1]*Presbyterian Medical Center, Department of Neurology, Jeonju, Republic of Korea*
[2]*Daegu Catholic University Hospital- Catholic University of Daegu- Daegu, Department of Neurology, Daegu, Republic of Korea*

Chronic migraine is a common, disabling primary headache disorder. The known preventive drugs have limited efficacies, adverse effects and unwanted outcomes. Also the adolescent migraineurs and their care-givers do not want to prescribe antiepileptics or antipsychotics in order to treat their headaches. Onaboulinumtoxin A, the established migraine preventive treatment in adults, could be one of the applicable therapies for adolescent migraine. We enrolled five adolescent patients aged 14–16 years with chronic migraine. The frequency, severity, nature, duration and accompanying symptoms were investigated on first visit day, 1 month, 3 month, and 1 year after first injection of onabotulinumtoxin A. The patients were underwent brain magnetic resonance imaging and routine laboratories. The patients were injected at 31 fixed sites with 155 IU fixed dose according to the approved scheme. The responder rate was 4/5 at three months after the first injection. On average number of headache days per month was reduced from 23.6 days to 5.8 days. The headache frequency was not elevated on 1 year after first injection. The headache severity measured with visual analog scales reduced from 8.6 to 3.4 on 3 month after first injection. All responders had allodynia as accompanying symptom of migraine. Nonresponder did not suffer this accompanying

symptom. Adverse effects did not occur in all patients. Onabotulinumtoxin A could be an effective and safe treatment in adolescent migraine. The important age-specific problems, such as weight gain, learning disability, and compliance amount do not matter with this therapeutic modality.

EHMTC-0358
POSTER SESSION A

PILOT STUDY OF SPHENOPALATINE INJECTION OF ONABOTULINUMTOXINA FOR THE TREATMENT OF INTRACTABLE CHRONIC MIGRAINE

D. Bratbak[1], S. Nordgård[2], L.J. Stovner[3], M. Linde[3], D.W. Dodick[4], I. Aschehoug[3], M. Folvik[5], J. Crespi Vidal[6], E. Tronvik[6]

[1]*Department for neuroscience, Neurosurgery, Trondheim, Norway*
[2]*Department for neuroscience, ENT, Trondheim, Norway*
[3]*Department for neuroscience, Neuroscience, Trondheim, Norway*
[4]*Neurology, Neurology, Phoenix, USA*
[5]*Department for neuroscience, Radiology, Trondheim, Norway*
[6]*Department for neuroscience, Neurology, Trondheim, Norway*

Objective: The main objective of this pilot study was to investigate the safety of administering onabotulinumtoxinA towards the sphenopalatine ganglion in ten patients with intractable chronic migraine with an open, uncontrolled design. We also collected efficacy data to provide indication on whether future placebo-controlled studies should be performed.

Method: In a prospective, open-label, uncontrolled study, after one-month baseline, we performed bilateral injections of 25 IU onabotulinumtoxinA (total dose 50 IU) towards the sphenopalatine ganglion in a single outpatient session in ten patients with intractable migraine with a follow-up of 12 weeks. The primary outcome was adverse events and the main efficacy outcome was frequency of moderate and severe headache days in month 2 post-treatment compared to baseline.

Results: All ten patients experienced a total of 25 adverse events. The majority of these were different types of local discomfort in the face and jaw, and none were classified as serious. In an intention-to-treat analysis of the main efficacy outcome, a statistically significant reduction of moderate and severe headache days in baseline versus month 2 was observed (16.3 ± 6.2 days baseline versus 7.6 ± 7.6 days month 2, $p = 0.009$). Eight out of ten patients experienced an at least 50% reduction of moderate and severe headache days compared to baseline.

Conclusion: The result warrants randomized, placebo-controlled studies to establish both safety and efficacy of this potential novel treatment of chronic migraine.

EHMTC-0208
POSTER SESSION A

IDENTIFICATION OF 'PROTECTORS' AGAINST MIGRAINE ATTACKS USING A DIGITAL PLATFORM

S. Donoghue[1], A. Mian[2], M. Albert[3], G. Boucher[4], F. Peris[5], C. Wöber[6]

[1]*Curelator Inc., Clinical Research, Skipton, United Kingdom*
[2]*Curelator Inc., CEO, Cambridge, USA*
[3]*Curelator Inc., Design, Barcelona, Spain*
[4]*Curelator Inc., Project Management, Montreal, Canada*
[5]*Curelator Inc., Statistics, Barcelona, Spain*
[6]*Medical University of Vienna, Neurology, Vienna, Austria*

Background and Methods: Curelator Headache(TM) is a digital platform which identifies factors associated with increased risk of attacks (potential triggers)(1,2). The analysis also identifies factors associated with reduced risk of attacks: potential 'protectors'. We analysed for potential 'protectors' in individuals with migraine who used Curelator Headache for 90 days, recording daily information about a list of factors which those previous research indicates could affect attack occurrence and all headaches. Telephone interviews were conducted with about 100 consenting participants after providing them with their processed data (Trigger and Protector MapsTM). Results: Of 284 individuals, 87% had at least one 'potential protector' (range 0–11): most commonly reported were:

Potential Protector	% Curelator Users with the 'protector'
Travel	7.7
Alcohol	7.0
Stress	4.9
Bright Lights	3.2
Odours	3.2
Neck Pain	3.2

Interviews revealed interesting insights into why some of these 'protectors' appeared. For example when 'neck pain' (a possible premonitory symptom) occurred some said they had neck massage, did stretching or used heat pads: this intervention may be the 'true' protector. Similarly 'travel' was for some a time to relax: again this may be the 'true' protector. Conclusion: Identifying "protectors"

may be a useful strategy in migraine management. However it is important to guide individuals to think about their behaviours and self-analyse why and in what context such factors may affect their condition.

(1) Donoghue S et al. Presentations at AHS 2016
(2) Peris F et al. Cephalalgia 2016 (In press)

Conflict of interest
Disclosure statement:
Drs Donoghue, Mian, Peris and Mr Albert and Mr Boucher are employees of Curelator Inc. Dr Wöber is a paid consultant to Curelator Inc.

EHMTC-0213
POSTER SESSION A

IDENTIFICATION OF INDIVIDUAL 'PROTECTORS' (FACTORS ASSOCIATED WITH REDUCED RISK OF MIGRAINE ATTACKS) IN THE PAMINA STUDY DATABASE

C. Wöber[1], S. Donoghue[2], A. Mian[3], M. Albert[4], G. Boucher[5], F. Peris[6]

[1]*Medical University of Vienna, Neurology, Vienna, Austria*
[2]*Curelator Inc., Clinical Research, Skipton, United Kingdom*
[3]*Curelator Inc., CEO, Cambridge, USA*
[4]*Curelator Inc., Design, Barcelona, Spain*
[5]*Curelator Inc., Project Management, Montreal, Canada*
[6]*Curelator Inc., Statistics, Barcelona, Spain*

Background: The PAMINA study analysed collectively factors increasing and decreasing the risk of migraine attacks in patients with migraine (1). Curelator Headache™ is a digital platform which identifies such factors individually in single patients (2, 3).

Methods: During analytical algorithm development we performed N = 1 analyses in 326 patients of the PAMINA study database to identify potential 'protectors' in two ways: 1) using *all* factor data including on days of attack start; 2) eliminating factor data on days of attack start to identify factors that appear protective in the days preceding attacks.

Results: In the PAMINA database we found 0 – 6 'protectors' per patient: 55% had at least one. The most common "protectors", present in at least 5% of the patients, were:

Potential Protector	% PAMINA patients All factor data	% PAMINA patients Excluding factors on day of attack start
Caffeine	15.3	5.2
Physical activity	9.8	3.1
Citrus fruit	7.4	3.7
Cheese	7.1	3.4
Nitrates in food	6.4	4.3
Chocolate	5.5	3.1
Artificial sweetener	5.2	3.7
Nicotine	5.2	1.2

Conclusion: Potential 'protectors' are frequently found in individuals with migraine. Further studies are required to differentiate 'true' protectors from factor avoidance or other action immediately before or during migraine attacks. In addition, it is necessary to examine separately for each potential 'protector' if it prevents attacks within a few hours,e.g. same day, or with longer latency, e.g the next day.

(1) Wöber C et al. Cephalalgia 2007
(2) Donoghue S et al. Presentations at AHS 2016
(3) Peris F et al. Cephalalgia 2016, in press

Conflict of interest
Disclosure statement:
Dr Wöber is a paid consultant to Curelator Inc. Drs Donoghue, Mian, Peris, Mr Albert and Mr Boucher are employees of Curelator Inc.

EHMTC-0260
POSTER SESSION A

MIGRAINEURS' SUSPECTED TRIGGERS VS ASSOCIATIONS STATISTICALLY DETERMINED USING A DIGITAL PLATFORM

S. Donoghue[1], P.R. Martin[2], G. Boucher[3], F. Peris[4], A. Mian[5]

[1]*Curelator Inc., Clinical Research, Skipton, United Kingdom*
[2]*Griffith University, School of Applied Psychology & Menzies Health Institute Queensland, Queensland, Australia*
[3]*Curelator Inc., Project Management, Montreal, Canada*
[4]*Curelator Inc., Statistics, Barcelona, Spain*
[5]*Curelator Inc., CEO, Cambridge, USA*

Introduction: Most migraineurs suspect certain factors as triggers, based on retrospective recall and hence subject to recall bias. In theory, successful identification of individuals' trigger-attack associations requires *daily entry of lifestyle data and statistical analysis of when a factor IS or IS NOT followed by an attack (1). Curelator Headache™ enables such daily* data collection, then statistically identifies factor-

attack associations (2) so confirming suspected triggers and identifying unsuspected potential triggers (or premonitory signs). Here we compare individuals' *suspected* triggers against those identified by Curelator Headache.

Methods: 284 Individuals with migraine registered with Curelator Headache and in an initial questionnaire answered questions about their *suspected* triggers. They then used Curelator Headache daily for 90 days entering all headache details and tracking a list factors that may affect migraine attack occurrence. Subsequently factors statistically significantly associated with attacks were determined (2).

Results: Each individual *suspected* between 1 and 42 different triggers. Commonly suspected triggers and the % in whom they were statistically confirmed were:

Suspected trigger (N=number of patients)	% patients in which statistically identified
Stress (262)	25
Dehydration (246)	16
Tiredness/fatigue (229)	25
Missed meals (224)	13
Neck pain/tension (215)	41
Bright lights (214)	35
Eyestrain (185)	27
Travel (184)	10
Menstruation (149)	23

For the group overall:

TOTAL no. suspected triggers (n = 284 individuals)	4341
Proportion of total suspected triggers identified statistically (%)	17
Average no. potential triggers statistically identified/individual	4.5 (95% CI = 0.37)
Average no. of statistically identified potential triggers previously suspected/individual	2.3 (95% CI = 0.27)
Average no. of unsuspected potential triggers identified/individual	2.2 (95% CI = 0.26)

Conclusions: Identification of personal triggers by individuals is often unreliable and may be improved by prospective data collection and statistical analysis of factor-attack associations. Increasing an individual's knowledge about their triggers may enable them to improve their condition by coping with their triggers differently (3).

(1) Spierings ELH et al. Curr Pain Headache Rep 2014; 18:455.
(2) Peris F et al. Cephalalgia 2016 (In press)
(3) Martin PR. Curr Headache Rep 2010; 14:221.

Conflict of interest
Disclosure statement:

Drs Donoghue, Peris, Mian and Mr Boucher are employees of Curelator Inc. Prof. Martin is a paid consultant to Curelator Inc.

EHMTC-0401
POSTER SESSION A

DIFFERENCES IN RESPONSE TO ONABOTULINUMTOXIN A TREATMENT ACCORDING TO THE HEADACHE DAYS SUFFERED PER MONTH

J.B. Gomez-Galvan[1]

[1]*HOSPITAL VALL D'HEBRON, Neurology, BARCELONA, Spain*

Objective: Describe and compare the response to preventive treatment with onabotulinumtoxinA in patients according to the headache days suffered per month.

Methods: We performed a prospective, observational study. Clinical data was collected before and after two treatments with onabotulinumtoxinA. Response was categorized as: no improvement, $<$50% or $\geq$50% improvement; for frequency, intensity, analgesics use, response to analgesics, disability (MIDAS) and global subjective improvement. Patients were divided into 3 groups: 10–14 headache days/month15–20 headache days/month and $\geq$21 headache days/month. Comparisons were made for each category of improvement and group.

Results: We included 106 patients (25.9% HFEM/13.0% CM15-20/61.1% CM $\geq$ 21), with a mean age of 46.2 $\pm$ 14.1 and 81.5% women. There were no differences in baseline characteristics, except for medication overuse (8(28.6%) HFEM/10(71.4%) CM15-20/48(72.7%) CM $\geq$ 21; $p < 0.001$). In table 1 we summarize the percentage of patients who improve in different domains (includes $<$50% and $>$50%, when appropriate) and the comparison p value.

Table 1.

Response outcomes	HFEM (10–14) - n(%)	CM 15–20 - n(%)	CM $\geq$ 21 - n(%)	p values
Frequency	20(71.4)	11(78.6)	55(83.3)	$<$0.001
Intensity	23(82.1)	10(71.4)	56(84.8)	0.202
Analgesics response	13(59.1)	7(58.3)	41(71.9)	0.236
Analgesics usage	20(71.4)	9(64.3)	56(84.8)	0.002
Disability (MIDAS)	7(43.8)	1(16.7)	15(44.1)	0.854
Subjective global improvement	25(89.3)	12(85.7)	61(92.4)	0.561

Conclusions: All the 3 groups showed improvement in the evaluated outcomes.

Even if the improvement in frequency and analgesic usage is significantly lower in High Frequency Episodic Migraine this finding was not reflected in the other outcomes of improvement. This supports the use of onabotulinumtoxinA in HFEM.

Conflict of interest
Disclosure statement:
Dr. Pozo-Rosich has received grants, honorarium and served as a consultant for Allergan.

EHMTC-0322
POSTER SESSION A

ONABOTULINUMTOXIN A FOR CHRONIC MIGRAINE: HOW TO IDENTIFY A RESPONDER?

R. Gooriah[1], A. Buture[1], R. Nimeri[1], M. Khalil[1], F. Ahmed[1]

[1]*Hull Royal Infirmary, Neuroscience, Hull, United Kingdom*

The efficacy of onabotulinumtoxinA (onaBoNTA) in chronic migraine (CM) is well-established. The Phase III REsearch Evaluating Migraine Prophylaxis Therapy trials was the largest clinical program to study the efficacy of onaBoNTA as a prophylactic treatment for CM using an established set of diagnostic criteria and specific clinically relevant outcome measures. The ability to pinpoint which subgroup of patients are more likely (or less likely) to respond is important for any treatment. With respect to onaBoNTA for CM, it is still debatable how long treatment should be continued for and what constitutes a responder. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) has devised its own criteria for patients receiving onaBoNTA. However, these criteria have some shortcomings. Strict application of its stopping rule would entail discontinuation of treatment for a patient with 14 days of headache while a patient with 16 days of headache would be allowed to continue. We proposed our own responder criteria (Hull criteria) which identified an additional 17% of patients (who would have previously been classified as non-responders under the NICE criteria and would have had to stop treatment) who improved with reduction in the number of headache and migraine days. We, hereby, discuss and compare the different available criteria for responder identification. We also highlight the need for a consensus agreement on how best to recognise a responder so that patients are not unfairly denied an effective treatment.

Conflict of interest

Disclosure statement:
Fayyaz Ahmed has received honorarium to deliver training workshops for Allergan paid to British Association for the Study of Headache (BASH) and to attend Allergan Advisory Board meetings. He is on the standing committee of the Headache Guidelines (CG150 Revision) for the National Institute of Clinical Excellence, a trustee of the Migraine Trust, and an educational officer for the BASH. The authors report no other conflicts of interest in this work.

EHMTC-0148
POSTER SESSION A

BOTULINUM A TOXIN FOR TREATMENT OF CHRONIC MIGRAINE WITH MEDICATION OVERUSE

L. Grazzi[1], D. D'Amico[2], A. Raggi[3], M. Leonardi[3], F. Andrasik[4]

[1]*Neurological Institute "C. Besta", Milano, Italy*
[2]*Neurological Institute C. Besta IRCCS, Headache Center, Milano, Italy*
[3]*Neurological Institute C. Besta IRCCS, Neurology- Public Health and Disability Unit, Milano, Italy*
[4]*University of Memphis, Dept. of Psychology, Memphis, USA*

Background: Chronic Migraine (CM) is common, debilitating and worsened when accompanied by medication Overuse (MO). Botulinum neurotoxin A (BoNT A) is approved for CM, but its effectiveness when MO is present is lesser known.

Objective: Report our clinical experience employing BoNT A as a primary treatment for patients experiencing CM-MO.

Method: Fifty-three patients, all diagnosed as above, after first being withdrawal from medications, were treated by BoNT A injection in multiple sites according to the PREEMPT protocol study, 155 U for 31 sites, every three months for one year. Medication intake and days of headache per month were recorded in a headache daily diary. Questionnaires for assessing disability, allodynia and quality of life (MIDAS, Allodynia Symptom Checklist-12 and HIT-6) were administered at every followup.

Results: Patients recorded a significant decrease of days of headache/month (19.9 ± 13.1 vs 13.2 ± 7.9 at the last session) and medication intake/month (17.4 ± 5.6 vs 12.2 ± 6.0 at the last session). MIDAS scores also decreased significantly (79.8 ± 57.9 vs 31.4 ± 31.3 at the last session). We noted a slight decrease with respect to allodynia but it was not statistically significant (5.8 ± 4.7 vs 3.7 ± 5.3 at the lasts session).

Conclusion: Our data confirm the effectiveness of BoNTA in CM suggesting its use in patients complicated by MO, who are often difficult to treat, also depending on their refractoriness to preventive medications and difficulties in adhering to daily treatments.

EHMTC-0149
POSTER SESSION A

MINDFULNESS VERSUS PREVENTATIVE MEDICATION TREATMENT FOR CHRONIC MIGRAINE (CM) WITH MEDICATION OVERUSE (MO): A PILOT INVESTIGATION WITH 1-YEAR FOLLOW UP

L. Grazzi[1], F. Andrasik[2], A. Raggi[3], E. Sansone[3], M. Leonardi[3], D. D'Amico[4]

[1]*Neurological Institute "C. Besta", Milano, Italy*
[2]*University of Memphis, Dept. of Psychology, Memphis, USA*
[3]*Neurological Institute "C. Besta", Neurology- Public Health and Disability Unit, Milano, Italy*
[4]*Neurological Institute "C. Besta", Headache Center, Milano, Italy*

Introduction: Chronic migraine (CM) is a disabling condition which arising from a complex mixture of interconnected biological, psychological and social factors and is worsened when associated with medication overuse (MO). Mindfulness is an emerging treatment for pain, but it has yet to be explored fully for CM-MO. We report preliminary findings from an on-going trial exploring the feasibility and utility of mindfulness as a primary treatment for CM-MO. Methods: Forty-four patients, diagnosed as CM-MO (IHS-3beta-2013-criteria), completed a standardized medication withdrawal in a day hospital setting. Patients were then assigned to 1 of 2 conditions: Prophylactic Medication Alone (Med) or Mindfulness Training alone (MT). MT was administered during 6 weekly sessions, each consisting of 30 minutes of guided mindfulness, with patients encouraged to engage in 7 minutes of daily home practice. Follow up evaluations were conducted 3, 6, 12 months after withdrawal. Daily pain diaries, measures of disability (MIDAS), quality of life (HIT-6), state and trait anxiety (STAI Y1-Y2) and depression (BDI) were measured before treatment and at every follow up. Results: At the 12-month assessment both groups reported significant decreases in key headache parameters and MIDAS values (but no changes for other measures): 45% improvement in HA Days/Month for each; and 42 vs. 53% improvement in Medication Consumption and 52 vs. 39% improvement in MIDAS Scores for Med and MT, respectively. Conclusions: Our results provide evidence of equivalent effects for MED and MT over a period of 12 months and warrant further exploration of this emerging nonpharmacological approach.

EHMTC-0187
POSTER SESSION A

EFFECTS OF PROPHYLACTIC LOW-DOSE TOPIRAMATE ON LANGUAGE DEVELOPMENT IN CHILDREN WITH MIGRAINE

S.A. Han[1], S.J. Kim[1]

[1]*Chonbuk National University Hospital, Pediatrics, Jeonju, Republic of Korea*

Purpose: Topiramate is one of the most frequently prescribed medicine for migraine prevention in children. However, this medicine can have a potential to language disturbance in pediatric epileptic patients with recommended dose. The purpose of this study was to verify the safety of low-dose topiramate on language development in pediatric migraine patients.

Patients and Methods: Twenty seven newly diagnosed pediatric migraine patients who needed topiramate were enrolled. All patients were assessed twice using standard language tests: the Test of Language Problem Solving Abilities (TOPs), a Korean version of the vocabulary test. Data were collected before and the treatment had been sustained at least 3 months. The average follow-up period was 4.30 ± 2.73 months. The mean dosage of topiramate was 0.89 mg/kg/day.

Results: The mean age of patients was 144.11 ± 42.34 months (male: female = 1:2). All of the language parameters of TOPs worsened after topiramate treatment: Determine cause, 15.15 ± 4.41 to 14.19 ± 4.62 ($P < 0.05$); Problem solving, 17.59 ± 5.70 to 16.52 ± 6.14 ($P < 0.05$); Predicting, 11.37 ± 4.60 to 10.96 ± 4.00 ($P > 0.05$); total test score, 44.11 ± 13.50 to 41.56 ± 12.96 ($P < 0.05$). Total Mean Length of Utterance in words during the test decreased, 53 ± 1.96 to 4.90 ± 1.45 ($P < 0.05$). However, vocabulary tests did not changed significantly: Receptive Vocabulary Test was 97.78 ± 22.12 to 96.31 ± 19.97 months; Expressive Vocabulary Test was 81.79 ± 23.40 to 82.29 ± 25.43 months ($P > 0.05$).

Conclusion: Our data suggests that even a low-dose topiramate has negative effects on the problem solving language ability without significant changes of vocabulary function. We recommend that topiramate should be use carefully in pediatric migraine patient even in low-dose.

EHMTC-0153
POSTER SESSION A

THE EFFECT OF METOPROLOL ON TRIGEMINAL PAIN

J.M. Hebestreit[1], A. May[1]

[1]*University Medical Center Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*

Introduction: Metoprolol is used as a first-choice preventive medication in migraine in daily clinical practice. Although very effective, little is known about how metoprolol exerts its therapeutic effect in migraine treatment.

Aims: The aim is to study central effects of metoprolol in healthy subjects as a basis for further investigations in migraineurs.

Methods: Using event-related fMRI we studied the effect of metoprolol on trigemino-nociceptive processing in 24 healthy subjects. In a within-subject, randomized, cross-over, placebo controlled design the participants received a 75 mg oral dose of metoprolol in one session and an inert substance in the other.

Results: There was no effect of medication on perceived painfulness and systole differences. A significant decrease of the pulse after metoprolol administration compared to placebo could be observed ($p < 0.05$). Imaging data reveals a slightly increased activation in the hypothalamus ($T(23) = 3.01$, $p < 0.01$ uncorrected) and the primary sensory cortex ($T(23) = 3.21$, $p < 0.01$ uncorrected) under metoprolol compared to placebo.

Conclusion: The current results point towards the hypothalamus being a possible central site for the effect of metoprolol and are in line with previous research emphasizing the central role of the hypothalamus in migraine. The results may serve as a reference for future clinical research on the central effect of metoprolol in the pathological system of migraine patients.

EHMTC-0197
POSTER SESSION A

EVALUATION OF CLINICAL DOSES FOR INHIBITION OF CAPSAICIN-INDUCED DERMAL BLOOD FLOW AND MIGRAINE PREVENTION BY THE CGRP NEUTRALIZING ANTIBODY LY2951742

K. Johnson[1], W. Kielbasa[1], Q. Zhang[1], J. Polzer[1], E. Raddad[1], E. Collins[1]

[1]*Eli Lilly and Company, Indianapolis- Indiana, USA*

Background: LY2951742 is a humanized monoclonal antibody that selectively binds CGRP and is being evaluated as a treatment for migraine prevention. Inhibition of capsaicin-induced dermal blood flow (DBF) measured by laser Doppler imaging is a biomarker for CGRP activity. The objective was to assess the clinical doses that inhibited capsaicin-induced DBF and reduced the number of migraine headache days (MHD) in a Ph2b trial.

Methods: A pharmacokinetic/pharmacodynamic model was developed to describe the relationship between serum concentrations and inhibition of capsaicin-induced DBF following administration of LY2951742 in healthy volunteers at single doses (1–600 mg), and at 150 mg every 2 weeks (Q2W). Model-based simulations were conducted to predict inhibition of capsaicin-induced DBF at Week 12 by LY2951742 at doses from 1–600 mg Q4W. A 12-week, Phase 2b trial was conducted at doses of 5, 50, 120, and 300 mg Q4W to assess whether LY2951742 was superior to placebo in reducing the number of MHD.

Results: Doses greater than 50 mg Q4W were predicted to have near maximum inhibition of capsaicin-induced DBF at Week 12. Doses of 120 mg Q4W and 300 mg Q4W, but not 5 mg Q4W or 50 mg Q4W, were superior to placebo in reducing the number of MHD across a 12-week period.

Conclusions: Capsaicin-induced DBF inhibition is a useful biomarker to aid in dose elimination for efficacy trials.

Conflict of interest
Disclosure statement:
Full-time employee and stockholder, Eli Lilly and Company

EHMTC-0138
POSTER SESSION A

A NURSE – LED SERVICE FOR THE TREATMENT OF CHRONIC MIGRAINE WITH BOTOX

S. Jones[1], A. Zermansky[1]

[1]*Salford Royal NHS Foundation Trust, Neurology, Manchester, United Kingdom*

Botox is a treatment for chronic migraine (CM). Administration of Botox has been consultant–led predominately. In recent years a number of nurse–led services have been introduced in the UK.

This audit aimed to explore whether a nurse–led service improved the treatment of patients with CM. The main outcomes assessed were the efficacy of treatment, including the reduction of headache days, and compliance with NICE and regional guidelines.

Additional aims were to identify whether a nurse–led service made a difference to the efficiency of the clinic and patient adherence (patients taking 'ownership' of their condition, such as recording their headache days and completing rating–scales).

Prior to the nurse led service, data was collected for 100 patients from their 1st treatment for 1 year. This was compared to data collected after implementation of the nurse–led service ($n = 80$). As the nurse–led service is relatively new, only 12 patients had treatment initiated by a nurse, many having been treated partly within the consultant-led service.

Early results demonstrate an improvement in the reduction of headache days (30% reduction in headache days from baseline after 2 treatment cycles), an improvement in data collection (compulsory completion of headache diaries, which was not previously adhered to, and more reliable adherence with NICE guidelines).

Full analysis is ongoing and will be available next year.

EHMTC-0189
POSTER SESSION A

RESULTS OF PERIPHERAL NERVE BLOCKS IN MIGRAINE PATIENTS DURING PREGNANCY AND BREASTFEEDING

A. Juanatey[1], M. Ruiz[1], L. Blanco[1], E. Martinez[1], M. De Lera[1], M. I. Pedraza[1], J. Barón[1], Á.L. Guerrero[1]

[1]*Hospital Clinico Universitario de Valladolid, Neurology, Valladolid, Spain*

Introduction: Peripheral nerve blocks seem to be effective in migraine treatment. During pregnancy, the risk of teratogenicity of blockades with anaesthetics is considered low, mainly when using lidocaine (Food and Drug Administration Category B).

Aim: To assess efficacy of peripheral nerve blocks used either as acute or as preventive migraine therapy during pregnancy and breastfeeding.

Methods: We considered patients attended from January 2009 to March 2016 in a headache outpatient office at a tertiary hospital. We injected both occipital nerves with lidocaine 1% in all cases; we added supraorbital nerve blockade when we found tenderness to palpation in that area. We used blocks as acute therapy during prolonged migraine attacks, or as preventive treatment in patients with chronic or high-frequency episodic migraine. We considered acute efficacy when total pain relief was achieved 2 hours after procedure and prophylactic response when the number of headache days decreased at least 50%.

Results: We included 23 patients (31.9 ± 5.5 years, range 16–39). We performed 51 procedures, 37 (72.5%) during pregnancy, and 14 (27.5%) during breastfeeding. In 4 out of 5 blocks performed during prolonged migraine we observed efficacy. Preventive response was obtained after 29 procedures (56.9%), lasting from two weeks to six months; preventive efficacy was comparable when performed during pregnancy or breastfeeding (54.1% vs 64.3%). No side effects were detected except one syncope with no obstetric consequences.

Conclusion: According to our experience, peripheral nerve blocks are a safe and effective acute and preventive therapy of migraine during pregnancy and breastfeeding.

EHMTC-0112
POSTER SESSION A

PHARMACOKINETIC AND PHARMACODYNAMIC MODELING OF LY2951742, A CALCITONIN GENE RELATED PEPTIDE ANTIBODY, IN MIGRAINE PATIENTS

W. Kielbasa[1], T. Quinlan[1], R. Bell[1], B. Miller[2], V. Skljarevski[3]

[1]*Eli Lilly and Company, Global PKPD, Indianapolis, USA*
[2]*Eli Lilly and Company, Neuroscience Tailoring, Indianapolis, USA*
[3]*Eli Lilly and Company, Medical, Indianapolis, USA*

Objective: To characterize the pharmacokinetics (PK) and pharmacodynamics (PD) of LY2951742 in migraine patients.

Methods: A phase 2b, randomized, double-blind, placebo-controlled, 12-week treatment phase study of LY2951742 in patients with episodic migraine was conducted at doses of 5 mg, 50 mg, 120 mg and 300 mg given subcutaneously every 28 days. Blood samples were collected to measure LY2951742 and CGRP concentrations. The change from baseline in the number of migraine headache days (MHD) over a 28-day period was assessed in placebo and LY2951742-treated patients.

Results: Interim data indicate LY2951742 concentrations increased linearly, but CGRP concentrations increased nonlinearly, with dose. Direct response PKPD models characterized the relationship of LY2951742 with CGRP and change in MHD. For PK, LY2951742 apparent clearance of 0.0099 L/h and apparent volume of distribution of 8 L was estimated using a 1-compartment model. For PD, baseline CGRP concentration of 0.009 nM, LY2951742 EC50 of 94 nM, CGRP Emax of 1.2 nM, and gamma of 0.8 were estimated using a sigmoidal Emax model. Maximum placebo effect of −3.5 MHD difference from baseline was estimated using an exponential decay model. Baseline MHD (prior to LY2951742 treatment) of 6 days per 28-day period, LY2951742 EC50 of 57 nM, and LY2951742 Emax of −1.25 MHD difference from placebo were estimated using an Emax model.

Conclusions: PKPD modeling characterized the relationship of LY2951742 with clinical response on the basis of CGRP (target engagement) and MHD (efficacy) and can be used to aid in dose selection for subsequent clinical trials.

EHMTC-0257
POSTER SESSION A

CLINICAL OUTCOME OF ENDOSCOPIC NERVE DECOMPRESSION FOR MIGRAINE TREATMENT

S.K. Kim[1], C.Y. Pak[2], N.C. Choi- [1], O.Y. Kwon[1], B.H. Lim[1], H.S. Gang[3]

[1]*Gyeongsang National University Hospital, Department of Neurology, Jinju, Republic of Korea*
[2]*Jinju Korea Hospital, Department of Neurology, Jinju, Republic of Korea*
[3]*Yeil Hospital, Department of Otolaryngology- Head and Neck Surgery, Changwon, Republic of Korea*

Background: Surgical decompression of various trigger sites has been shown to relieve migraine headaches. The purpose of this study was to evaluate the effectiveness of endoscopic decompression of multiple migraine trigger sites in a clinical practice setting.

Methods: A retrospective, descriptive analysis was performed on 20 consecutive migraine patients who had undergone endoscopic nerve decompression. All patients had been diagnosed with migraine headaches according to the International Classification of Headache Disorder(ICHD)-III criteria. Preoperative and 12-month or greater postoperative migraine frequency, duration, and intensity were analyzed.

Results: The number of migraines per month and the pain intensity of migraine headaches decreased significantly. Five patients (25%) had complete relief of their migraines, and 90% of patients (18 of 20) had at least a 75 % reduction in the frequency, duration, or intensity of migraines. 20% of patients have discontinued all migraine medications. Mean follow-up was 14 months (range, 6 to 34 months) after surgery.

Conclusions: Endoscopic nerve decompression was found to be successful at reducing or eliminating frontal migraine headache.

EHMTC-0282
POSTER SESSION A

HEALTHCARE RESOURCE UTILISATION WITH ONABOTULINUMTOXINA FOR THE SYMPTOMATIC TREATMENT OF CHRONIC MIGRAINE: REPOSE STUDY 12-MONTH INTERIM ANALYSIS

K. Kollewe[1], M. Oberling[2], M. Kiszka[3], O. Günther[4], A. Antonakakis[5], S. Brown[6]

[1]*Hannover Medical School, Department of Neurology, Hannover, Germany*
[2]*Regionales Schmerzzentrum DGS, N/A, Bad Camberg, Germany*
[3]*Neurologischen Praxis, N/A, Erfurt, Germany*
[4]*Regionales Schmerzzentrum DGS, N/A, Magedeburg, Germany*
[5]*Schmerzzentrum Rhein-Main Frankfurt, N/A, Frankfurt, Germany*
[6]*Allergan plc, Specialty Care- International, Buckinghamshire, United Kingdom*

Background: The REPOSE Study describes 2-year, real-life use of onabotulinumtoxinA for chronic migraine (CM) in Europe and its impact on healthcare resource utilisation (HRU). This analysis examines REPOSE Study HRU, with a focus on Germany, where physicians are less incentivised to treat with onabotulinumtoxinA because of the reimbursement structure.

Methods: This 12-month interim analysis compares HRU at baseline and each ~12-week onabotulinumtoxinA re-treatment visit in the overall European population and in the subset of patients enrolled at German study centres.

Results: Data were available from 405 patients (61 centres throughout Europe) and from 171 patients in the German subset. Proportions of patients admitted to a hospital or visiting a healthcare professional in the previous 3 months were reduced from baseline to all re-treatment visits (Table). In the German subset, the most frequently used health services for the 6 months before baseline were medical specialists and family doctors, with reduced use between each re-treatment and no notable differences among re-treatment visits (Table).

Conclusion: This 12-month interim analysis demonstrates that preventative treatment of CM with onabotulinumtoxinA in a real-world setting reduces headache-related HRU.

Funding: Allergan

Table. REPOSE Study Healthcare Resource Utilisation

Patients, n (%)*	Baseline (n=405)	FU1 (n=370)	FU2 (n=377)	FU3 (n=351)	FU4 (n=331)
Admitted to a hospital in last 3 months	21 (5.2)	5 (1.4)	5 (1.3)	4 (1.1)	6 (1.8)
Visited an HCP in last 3 months	193 (47.7)	73 (19.7)	61 (16.2)	57 (16.2)	53 (16.0)

German Analysis Set

Patients, n (%)*	Baseline (n=171)	FU1 (n=151)	FU2 (n=157)	FU3 (n=142)	FU4 (n=143)
Visited a medical specialist in last 3–6 months†	100 (58.5)	23 (15.2)	16 (10.2)	9 (6.3)	20 (14.0)
Visited a family doctor in last 3–6 months†	66 (38.6)	27 (17.9)	28 (17.8)	24 (16.9)	27 (18.9)

*Percentages are based on the number of patients (n) with the respective visit.
†Baseline: in the last 6 months; follow-up visits: since the last visit.
FU=follow-up re-treatment visit; HCP=healthcare professional.

Conflict of interest
Disclosure statement:
Katja Kollewe has received travel grants and honoraria for lectures from Allergan, Ipsen and Merz.
Dr. Oberling has no disclosures to report.
Dr. Kiszka has no disclosures to report.
Dr. Günther has no disclosures to report.
Dr. Antonakakis has no disclosures to report.
Stephanie Brown, MBBS, MRCS, MFPM, is an employee of Allergan plc.

EHMTC-0143
POSTER SESSION A

REAL-WORLD TREATMENT UTILIZATION AND SAFETY OF ONABOTULINUMTOXINA FOR CHRONIC MIGRAINE FROM AN OBSERVATIONAL STUDY IN THE EUROPEAN UNION

M. Matharu[1], J. Pascual[2], I. Nilsson Remahl[3], A. Straube[4], A. Lum[5], G. Davar[5], D. Odom[6], L. Bennett[6], C. Proctor[6], L. Gutierrez[7], E. Andrews[8], C. Johannes[9]

[1]*National Hospital for Neurology and Neurosurgery, Headache Group- Institute of Neurology, Queen Square, United Kingdom*
[2]*University Hospital Marques de Valdecilla, Department of Neurology, Santander, Spain*
[3]*Karolinska University Hospital Huddinge, Department of Clinical Neuroscience- Division of Neurology- Karolinska Institute, Stockholm, Sweden*
[4]*Klinikum Grosshadern, Department of Neurology, Munich, Germany*
[5]*Allergan plc, Clinical Development, Irvine, USA*
[6]*RTI Health Solutions, Biostatistics, Research Triangle Park, USA*
[7]*RTI Health Solutions, Pharmacoepidemiology and Risk Management, Barcelona, Spain*
[8]*RTI Health Solutions, Epidemiology, Research Triangle Park, USA*
[9]*RTI Health Solutions, Pharmacoepidemiology and Risk Management, Waltham, USA*

Objective: To evaluate treatment utilization and safety of onabotulinumtoxinA for chronic migraine (CM) in routine clinical practice.

Methods: This was a prospective, observational, post-authorization study in adults treated with onabotulinumtoxinA for CM(NCT01432379) conducted in UK, Germany, Spain, and Sweden. Data were collected at the first study injection and approximately every 3 months for $\leq$52 weeks for utilization or $\leq$64 weeks for safety data. Data are summarized using descriptive statistics.

Results: Eighty-five physicians (81% neurologists) were recruited at 58 practices and enrolled 1160 patients (average 46.6 years old [range = 19–79], 84.2% female, 97.8% Caucasian); 85.8% had diagnoses of CM/transformed migraine. At baseline, patients reported an average of 7.7 (SD = 6.9) headache-free days per usual month and 50.6% had used onabotulinumtoxinA for CM in the past. Of the 4071 total study treatments observed, the median number of injection sites (n = 31) and total dose (155U) were consistent across all treatment sessions with a median 13.7 weeks reported between sessions. Most patients (74.4%) indicated they were satisfied/extremely satisfied with onabotulinumtoxinA treatment for CM. 291 patients (25.1%) reported $\geq$1 treatment-related adverse event (AE); most frequently reported was neck pain (4.4%). One (0.1%) serious treatment-related AE was reported (worsening of migraine); there were no treatment-related deaths. Data were generally consistent between countries.

Conclusions: Patient demographics/characteristics are consistent with published data on the CM population. OnabotulinumtoxinA treatment utilization appears to be consistent with the Summary of Product Characteristics and published PREEMPT injection paradigm. No new safety signals were identified; data continue to support the favorable safety profile of onabotulinumtoxinA.

Conflict of interest
Disclosure statement:
MM received honoraria for the development of educational presentations and serving on the advisory board for Allergan, Inc. JP serves as an advisor for Allergan, Inc. INR led teaching courses on PREEMPT injection paradigm in Sweden, which was sponsored by Allergan, Inc. AS received honoraria for educational lectures and advisory boards from Allergan, Inc., Boehringer Ingelheim, Hormosan, EletroCore, and CerboMed CJ, DO, LG, LB, and EG are salaried employee of RTI Health Solutions, the organization responsible for the conduct of the study, which is sponsored by Allergan plc CP was formerly a full-time salaried employee of RTI Health Solutions, during the conduct of the study and preparation of the abstract. AL and GD are full-time employees of Allergan plc.

EHMTC-0159
POSTER SESSION A

EFFICACY AND SAFETY OF ONABOTULINUMTOXINA IN AN OPEN-LABEL STUDY FOR THE PROPHYLACTIC TREATMENT OF CHRONIC MIGRAINE IN ADULT PATIENTS: COMPEL

A. Blumenfeld[1], R. Stark[2], A. Manack Adams[3], A. Orejudos[4], S. Aurora[5]

[1]*The Neurology Center, Headache Center, Carlsbad, USA*
[2]*Monash University and Alfred Hospital, Department of Medicine, Melbourne, Australia*
[3]*Allergan plc, Medical Affairs, Irvine, USA*
[4]*Allergan plc, Biostatistics, Bridgewater, USA*
[5]*Stanford University, Medical Center, Stanford, USA*

Objective: This study evaluates the longer-term efficacy and safety of onabotulinumtoxinA for the treatment of chronic migraine (CM).

Methods: This is a multicenter, open-label study in adult CM patients treated with 155U onabotulinumtoxinA every 12 weeks (NCT01516892) using a fixed-site, fixed-dose injection paradigm. Change in frequency of headache days from baseline at 108 weeks (following 9 treatments) is the primary measure. Secondary/exploratory measures included Migraine Disability Assessment Questionnaire (MIDAS) and Migraine Specific Quality of Life Questionnaire (MSQ). Efficacy cohort includes patients who received $\geq$1 onabotulinumtoxinA treatment and $\geq$1 efficacy assessment. Safety cohort includes patients who received $\geq$1 onabotulinumtoxinA treatment.

Results: Enrolled patients (n = 716) were 18–73 years old, primarily female (n = 606, 84.8%) and Caucasian, (n = 581, 81.3%) with an average 22.0 (SD = 22.0) headache days per month at baseline. By 108 weeks, a significant reduction in number of headache days per month (−10.7 days, $p < .0001$; n = 715/716) was observed. Patients demonstrated significant improvements ($p < .0001$) from baseline at 108 weeks in MIDAS (34.8 point change; n = 489/715) and MSQ domain scores (+15.2, +22.3, and +22.1 point change in role function preventive, role function restrictive, and emotional function subscales, respectively; n = 489, 489, 487, respectively). 131 patients (18.3%) reported $\geq$1 treatment-related adverse event (TRAE); most frequently reported was neck pain (n = 29, 4.1%). One patient reported a serious TRAE (rash). No treatment-related deaths were reported.

Conclusions: Sequential improvements in efficacy were observed through 108 weeks with no new safety signals. Data from COMPEL supports the efficacy and safety of onabotulinumtoxinA for CM, up to 108 weeks (9 treatment cycles).

Conflict of interest
Disclosure statement:
Andrew Blumenfeld has served on advisory boards and/or has consulted for: Allergan, Depomed, Teva, Supernus, Pernix, Guidepointe, GLG, Avanir, Best Doctors, Keller labs, Verilogue, Zosano, Autodigest, Medlink and has received funding for travel, speaking, consulting and/or royalty payments from these companies.

Richard Stark has received lecture and/or consulting fees from Allergan, MSD, Abbvie and SciGen (Australia) and InVivo communications relating to a Pfizer sponsored project and holds stock/stock options in CSL

Aubrey Manack Adams and Amelia Orejudos are full-time employees of Allergan plc.

Sheena K. Aurora has received consulting fees/honoraria from Allergan, eNeura, Merck, and Teva and speaker's bureau participation for Allergan and is a full-time employee of Eli Lilly.

EHMTC-0231
POSTER SESSION A

ONABOTULINUMTOXINA IN CHRONIC MIGRAINE: LONG-TERM OUTCOME AND PREDICTORS OF EFFICACY IN A LARGE MULTICENTRE STUDY IN SPAIN

C. Dominguez[1], C. Jurado-Cobo[2], P. Pozo[3], M. Torres-Ferrus[3], C. Gonzalez Oria[4], M.J. Monzon[5], G. Latorre[6], J.A. Alhama[7], M. Huerta[8], A. Gago[9], M. Gallego de la Sacristana[9], V. Medrano[10], R. Belvis[11], R. Leira[1]

[1]*University Hospital Santiago de Compostela, Neurology, Santiago de Compostela, Spain*
[2]*University Hospital Reina Sofia, Neurology, Cordoba, Spain*
[3]*University Hospital Vall d'Hebron, Neurology, Barcelona, Spain*
[4]*University Hospital Virgen del Rocio, Neurology, Sevilla, Spain*
[5]*Hospital Royo Vilanova, Neurology, Zaragoza, Spain*
[6]*Hospital de Fuenlabrada, Neurology, Madrid, Spain*
[7]*Hospital de Bellvitge, Neurology, Barcelona, Spain*
[8]*Hopital Viladecans, Neurology, Barcelona, Spain*
[9]*University Hospital La Princesa, Neurology, Madrid, Spain*
[10]*Hospital de Elda, Neurology, Alicante, Spain*
[11]*Hospital Dexeus, Neurology, Barcelona, Spain*

Background: Long-term response to OnabotulinumtoxinA (OnabotA) in chronic migraine (CM) has been confirmed in large series. However no clinical predictors factors of efficacy has been found.

Aim: to analyse the experience with OnabotA in CM in a prospective multicentre study with focus on one year.

Patients and Methods: Prospective register of long-term outcome (12 months) in CM patients treated with OnabotA. We analysed several efficacy parameters at 3 and 12 months: reduction of headache, days of headache and migraine/month, number of analgesics and triptans/month, emergency admission, disability, HIT-6, and MIDAS. Register of adverse events at 3 and 12 month. Correlations between several clinical variables and efficacy at 3 and 12 months were made in order to find potentials efficacy predictors to OnabotA.

Results: 553 patients with CM (mean age 47.8 years; 478 women) were included in the study. Efficacy of OnabotA at 3 months was observed in 70.2% of patients), and at 12 months in 71.4% of patients. Significant reduction (at 3 and 12 months) were registered in consumption of analgesics (16.7 ± 8.9 vs 8.9 ± 6.1 vs8.9 ± 11.7), triptans (9.2 ± 5.9 vs

6.3 ± 4.7 vs 5.7 ± 6.8), emergency admission (1.4 ± 0.9 vs 1.1 ± 0.8 vs 0.8 ± 0.7), days with disability ((7.5 ± 4.3 vs 4.5 ± 6.1 vs 2.8 ± 3.9), HIT-6 (64.7 ± 7.2 vs 43.2 ± 24.2 vs 44.1 ± 21.7), and MIDAS (34.3 ± 36.7 vs 23.5 ± 26.1 vs 20.4 ± 27.5). Efficacy at 12 months was related with age (p = 0.025) and time of evolution of migraine (p = 0.003).

Conclusions: Our results confirm the long-term efficacy of OnabotA in more than 70% of CM patients and good safety and tolerability. Age and time of evolution of migraine were predictors of efficacy of OnabotA at 12 months.

Conflict of interest
Disclosure statement:
Grants and paid positions on advisory boards of Allergan

EHMTC-0363
POSTER SESSION A

A NURSING INTERVENTION IMPROVES HIT-6 SCORES: THE IMPACT PROJECT, A CONTROLLED TRIAL ON 200 MIGRAINEURS

E. Leroux[1], C. Lambert[2], L. Beaudet[2], M. Chagnon[3], G. Boudreau[4], L. Marchand[1], H. Pim[1]

[1]*Montreal University Health Center, Neurology, Montreal, Canada*
[2]*Montreal University Health Center, Nursing Sciences, Montreal, Canada*
[3]*University of Montreal, Mathematics and Statistics, Montreal, Canada*
[4]*Montreal University Health Center, Family Medicine, Montreal, Canada*

Introduction: Interdisciplinary approaches have been proposed for migraine management. A nursing intervention could improve patient outcomes.

Methods: we prospectively studied new patients referred to our tertiary headache center for migraine. The control group was followed by a physician, the active group was also followed a nurse with a personalized intervention including adaptation of the lifestyle.

Results: 200 patients (176 women and 24 men, mean age 40 years old) were included and stratified according to headache frequency. Each group was followed for 12 months with daily headache diaries. 162 completed the study. There were no significant differences between groups for the decrease in headache days, the percent of chronic patients reverting to episodic status or the cessation of medication overuse. Patients in the control group were more likely to find a successful prophylaxis (55,6% vs 27,7%, p = 0,002). Despite this, the mean decrease in HIT-6 scores at month 8 was −5,2 for the active group compared to −2,1 for the control group (p = 0,02, clinically significant difference of 3,1). HMSE scores, representing the feeling of self-efficacy, increased by 14,3 for the active group vs 4,7 in the control group (p = 0,002).

Conclusion: a nursing intervention can lower the impact of migraines on the patient's life. The improvement in the HIT-6 score in this study seems to correlate more with improvements in self-efficacy than with absolute changes in headache days.

Conflict of interest
Disclosure statement:
The IMPACT study is an investigator initiated protocol funded by Allergan. The principal investigator has received honoraria from Allergan as an advisory board member and speaker, and has participated in educational events funded by Allergan grants.

EHMTC-0133
POSTER SESSION A

TREATMENT PATTERNS IN MIGRAINE: A REAL-WORLD ANALYSIS IN A U.S. POPULATION

L. Lombard[1], J. Ford[2], J. Jackson[3], G. Milligan[3], S. Cotton[3], J. Ahl[4]

[1]*Eli Lilly and Company, GPORWE-ACE, Windlesham- Surrey, United Kingdom*
[2]*Eli Lilly and Company, GPORWE, Indianapolis- Indiana, USA*
[3]*Adelphi Real World, Adelphi Mill, Bollington- Cheshire, United Kingdom*
[4]*Eli Lilly and Company, Global Scientific Communications, Indianapolis- Indiana, USA*

Migraine is a disabling neurological disease that places an enormous burden on patients. The purpose of this study was to assess current treatment patterns for migraine headache in a U.S. population. Data were drawn from the Adelphi Migraine United States Disease Specific Programme; a cross-sectional point-in-time survey of physicians (N = 150) and their patients with migraine (N = 1500; index period, January to March 2014). Physicians completed a Patient Report Form on the next 10 consulting patients with migraine, and patients completed the Patient Self Completion form. Over 70% of the patients were female; 91% (n = 1350/1500) were episodic migraine sufferers; and 9% of patients had chronic migraine (n = 137). The majority of episodic and chronic patients were prescribed acute treatment (93% and 96%, respectively). Preventive treatment was currently prescribed for 52% (n = 701) of patients with episodic

migraine and for 81% (n = 111) of patients with chronic migraine. Prior preventive treatment was discontinued/switched at least once by 51% (n = 356/701) of patients with episodic migraine and by 66% (n = 73/111) of patients with chronic migraine. Of those patients who gave collective reasons for discontinuation/switching, over 70% selected lack of efficacy and tolerability/safety. The high percentage of patients who discontinue or switch migraine treatment suggests that there is still an unmet need for efficacious medications for migraine that are also tolerable and safe.

Conflict of interest
Disclosure statement:
Full-time employee and stockholder, Eli Lilly and Company

EHMTC-0221
POSTER SESSION A

MODELING AND SIMULATION-BASED STRATEGY FOR TEV 48125 IN PREVENTIVE TREATMENT OF CHRONIC AND HIGH FREQUENCY EPISODIC MIGRAINE

J. Fiedler-Kelly[1], J. Passarell[1], M. Denise[1], Y. Ronghua[2], Y. Ma[2], E. Aycardi[2], M.E. Bigal[2], O. Cohen-Barak[3]

[1]*Cognigen Corporation, a Simulations Plus Company, Buffalo NY, USA*
[2]*Teva Pharmaceutical Industries, Research and Development, Frazer PA, USA*
[3]*Teva Pharmaceutical Industries, Research and Development, Netanya, Israel*

Modeling and simulation (M&S) were implemented for TEV-48125 using Phase 1 and Phase 2b (patients with chronic migraines (CM) or high frequency episodic migraines (HFEM)) data. A population PK model, including patient covariate effects, was developed. Exposure-efficacy response (E-R) models were developed for monthly cumulative headache hours, migraine days, and moderate/severe headache days. Clinical trial simulations (CTS) were performed to explore efficacy in different dose paradigms.

A 2-compartment model with first-order absorption for subcutaneous TEV-48125 and zero-order process for intravenous administration, allometric weight scaling of linear clearance (CL) and volume of distribution (V), and both linear and nonlinear contribution to elimination adequately described the data. Separate parameters for CL and peripheral V were estimated based on administration route. Covariate effects of weight, sex, and race were identified, but deemed not to be clinically relevant.

E-R models for all endpoints were maximum pharmacologic effect (E_{max}) time-course models, including TEV-48125 C_{max} as either a linear or separate E_{max} function describing the E-R. For all models except moderate/severe headache days in CM, greater use of acute medications at baseline was predictive of higher baseline values of the endpoint. Model-based CTS showed a high likelihood of success (>93%) in differentiating efficacy response between TEV-48125 and placebo in the studied monthly and quarterly dose regimens at month 3.

Overall, a prospective M&S approach provided understanding of the E-R relationships for TEV-48125 to inform the design of future clinical trials.

Conflict of interest
Disclosure statement:
JF-K, JP, DM are employees of Cognigen which was contracted by Teva Pharmaceuticals to perform analyses included in this report. RY, YM, EA, MEB, and OC-B are employees of Teva Pharmaceuticals who sponsored the research of this report.

EHMTC-0318
POSTER SESSION A

AN ASSOCIATION OF FEVERFEW, MAGNESIUM AND COQ10 FOR PREVENTION OF HEADACHE: A PROSPECTIVE STUDY

A. Guilbot[1], M. Bangratz[1], S. Ait Abdellah[1], C. Lucas[2]

[1]*Laboratoire Pileje, 7 quai de Grenelle 75015, Paris, France*
[2]*CHRU Lille & Univ. Lille Nord-de-France – UDSL, Pain clinic, LILLE, France*

Feverfew, magnesium and Coenzyme 10 are 3 nutraceutical agents for migraine prophylaxis. Antemig® (Pileje) is composed with feverfew (100 mg), coenzyme Q10 (100 mg) and magnesium (112.5 mg).

The primary objective of this prospective open-label study was to evaluate the number of migraine headache days after three months of treatment with Antemig®.

Healthy adults migrainers were recruited by GPs. All participants had at least 2 migraine attacks in the previous month before recruitment (electronic diary). We excluded chronic migraine and patients with medication overuse.

This study was approved by French regulatory committees.

Three visits were planned: D0, D30 ± 10 and D120 ± 10. The assessment of the treatment's efficacy was defined as

the reduction in migraine headache days at D120. We also assessed the tolerance.

From Jan to Dec 2015, 62 subjects fulfilled the protocol. A large majority were women (91.1%) with a mean age of 43.9 y. At D120, the mean number of migraine headache days between during the 30 last days was 1.3 ± 1.5 *vs* 4.9 ± 2.6 at baseline, $p < 0.001$ and the proportion of patients with at least 50% reduction in migraine headache days was 75% [range 64.7–85.3]. At D120, 65.0% of patients were non anxious versus 38.1% at baseline, $p < 0.05$. Regarding depression, the proportion of patients in a depressive state evolve from 52.2% to 30.0 % at the end of the study, $p < 0.05$. The product was well tolerated. No serious adverse events have been reported during this study.

Antemig® seems to be efficacy and safe for prevention of migraine.

Conflict of interest
Disclosure statement:
I have received honorarium from Pileje as principal investigator of this study

EHMTC-0124
POSTER SESSION A

TRANSCUTANEOUS OCCIPITAL NERVE STIMULATION AND TRANSCRANIAL DIRECT CURRENT STIMULATION IN CHRONIC MIGRAINE: A PILOT COMPARISON OF THERAPEUTIC AND ELECTROPHYSIOLOGICAL EFFECTS

D. Magis[1], K. D'Ostilio[1], R. Baschi[1], A. Cosseddu[1], M. Lisicki[1], R. Nonis[1], S. Simona[1], J. Schoenen[1]

[1]*Headache Research Unit, University Department of Neurology CHR, Liege, Belgium*

Background: Management of chronic migraine (CM) is often challenging. There is a need for more effective and better-tolerated preventive therapies. Among non-invasive neurostimulation procedures, transcutaneous occipital nerve stimulation (tONS) would act via central pain modulation, while transcranial direct current stimulation (tDCS) would modify cortical excitability that is abnormal in CM.

Objectives: In this pilot trial we compared the clinical effects of tDCS and tONS in refractory CM and their ability to modify nociception and cortical responsiveness.

Methods: Forty-three CM patients (17 with history of drug overuse) applied either 2mA tDCS during 2 months ($N = 20$, cathode over visual cortex, anode over left DLPFC), or tONS during 3 months ($N = 23$, Cefaly Kit Arnold™), both in daily 20 min-sessions. Visual evoked potentials (VEP), nociceptive blink reflexes (nBR) and quantitative sensory testing were recorded before and after treatment.

Results: During the last stimulation month, total headache days decreased in both groups (−16.4% for tDCS, −17% for tONS, $p < 0.05$). Migraine days were reduced by 21.4% ($p = 0.06$) and 22% ($p < 0.05$) respectively, while 30% responder rates were 47% and 42%. Medication intake was significantly reduced after tONS (−43%). There was no significant change of nBR in either group. VEP habituation reversed to an episodic migraine pattern, i.e. a deficit, after tONS but not after tDCS.

Conclusion: tONS and inhibitory tDCS of the visual cortex are interesting non-invasive options for the treatment of CM, but these results have to be confirmed in a randomized controlled trial. tONS was able to induce recordable changes in visual cortex responsiveness.

Work supported by FP7-EUROHEADPAIN no.602633

EHMTC-0205
POSTER SESSION A

THE MIGRAINE PHYSICAL FUNCTION IMPACT DIARY (MPFID): USABILITY TESTING OF AN ELECTRONIC PATIENT ASSESSMENT TOOL

S. Shaffer[1], S. Eremenco[1], S. Hwang[2], C. Evans[2], S.M. Dallabrida[3], T. Mazac[2], M. Savalia[3], A. Hareendran[4], S. Sapra[5], P. Desai[5]

[1]*Evidera, Outcomes Research, Bethesda, USA*
[2]*Endpoint Outcomes, N/A, Boston, USA*
[3]*ERT, N/A, Boston, USA*
[4]*Evidera, Outcomes Research, London, United Kingdom*
[5]*Amgen, N/A, Thousand Oaks, USA*

Background: The Migraine Physical Function Impact Diary (MPFID) was developed to assess impact of migraine on physical function. The original MPFID was migrated, with minor modifications, to an electronic patient-reported outcome format for use in clinical studies. Equivalence between the two formats was assessed using methods recommended for minor changes: cognitive interviews and usability testing.

Aim: To evaluate usability of the electronic version of the MPFID and conceptual equivalence between the electronic and paper formats.

Method: Individuals with migraine completed the MPFID electronically and on paper. Participants were interviewed about the usability of the electronic version. Responses on each format were compared, and participants were questioned about differing responses.

Results: Ten migraineurs (50% male) with a mean age of 48 years (SD 10.6) were interviewed. Their feedback confirmed conceptual equivalence between the electronic and paper formats of the MPFID, including instructions, items, and response options. In most cases, the same response was selected for both formats (60% of patients). On probing, differing response selections were attributed to situational factors (reading the item for a second time may trigger patients to think about a particular experience and/or be more cognizant of the recall period) or more than one response option being appropriate for their experience, and not conceptual difference. Usability findings were positive, though a few subjects reported deficits in screen sensitivity (n = 2) and/or extended screen loading time (n = 5).

Conclusion: The electronic format of MPFID was equivalent to the paper format and met the requirements for use in a migraine population.

Conflict of interest
Disclosure statement:
The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or presentation of this abstract: Sandhya Sapra and Pooja Desai were employees of Amgen at the time this study was conducted and received financial support. Shannon Shaffer, Sonya Eremenco, and Asha Hareendran are employees of Evidera, who received financial support from Amgen in connection with the abstract/poster development. ERT (Susan Dallabrida & Manoj Savalia) and Endpoint Outcomes (Chris Evans, Steve Hwang, & Taylor Mazac) also received financial support from Amgen, in connection with the execution of the study.

EHMTC-0292
POSTER SESSION A

THE MIGRAINE PHYSICAL FUNCTION IMPACT DIARY: CONTENT VALIDITY OF A NEW INSTRUMENT TO EVALUATE THE BENEFIT OF PREVENTIVE MIGRAINE TREATMENTS

S. Mannix[1], H. Oko-osi[1], S. Gleeson[1], A. Skalicky[1], P. Desai[2], S. Sapra[2], M. Bayliss[3], D.C. Buse[4], A. Hareendran[5]

[1]*Evidera, Outcomes Research, Bethesda, USA*
[2]*Amgen, N/A, Thousand Oaks, USA*
[3]*Optum, N/A, Lincoln, USA*
[4]*Albert Einstein College of Medicine and Montefiore Medical Center, N/A, Bronx, USA*
[5]*Evidera, Outcomes Research, London, United Kingdom*

There is a dearth of patient reported outcomes instruments assessing the impact of migraine on an individual's physical functioning. The Migraine Physical Function Impact Diary (MPFID) was developed with input from patients with migraine to quantify the impacts of migraine on physical function and to evaluate outcomes of preventive treatments for migraine.

The objective of this study was to assess the content validity of the MPFID. Two rounds of in-person cognitive interviews were conducted with a total of seventeen subjects with migraine to assess comprehensiveness of the MPFID and the clarity of the items, instructions, and response options.

Subjects confirmed that the MPFID was comprehensive and that all items were relevant to their migraine experience. After Round 1 (n = 9), an interim analysis was conducted and the MPFID was revised with consultation from clinical experts. Modifications included refining the instructions to clarify the intent of the diary, updating three items to enhance specificity and clarity, and revising one item to include gender neutral language. Review by a translatability expert resulted in updated response options for one revised item. Round 2 interviews (n = 8) confirmed that the revisions were broadly acceptable, supporting the content validity of the new instrument.

The study results provide evidence supporting the content validity of the MPFID in patients with migraine. Additional studies to evaluate psychometric properties and clinically meaningful definitions of response for the MPFID are ongoing.

Conflict of interest
Disclosure statement:

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or presentation of this abstract: Sandhya Sapra, Pooja Desai, and Patricia Corey-Lisle were employees of Amgen at the time this study was conducted. Sally Mannix, Hafiz Okoosi, Sara Gleeson, Anne Skalicky, and Asha Hareendran are employees of Evidera. Evidera received financial support from Amgen in connection with the implementation of the study and abstract/poster development.

EHMTC-0052
POSTER SESSION A

PREVENTIVE TREATMENT WITH TOPIRAMATE FOR MORE THAN A YEAR AT A BUENOS AIRES' HOSPITAL

F. Martin Bertuzzi[1], D.E. Doctorovich[1], J. Matiasevich Leale[1], P.E. Seilikovich[1]

[1]*Hospital Italiano de Buenos Aires, Neurology, Ciudad Autónoma de Buenos Aires, Argentina*

Objective: To describe response and adverse reactions of patients evaluated in the past 5 years at the Neurology Department of the Hospital Italiano de Buenos Aires whom received preventive treatment with topiramate for 12 months or more.

Material and Methods: Electronic registers of patients with migraine that were evaluated at our Headache Center and completed a year of treatment with topiramate between 1/2010 and 12/2014 were review retrospectively. Migraine was diagnosed according to the ICHD II criteria.

Results: From 80 patients included, 92.5% were women with an average age of 46 years (95%CI ± 3.26). The 46.25% were MWOA, 13.75% MWA and 40% chronic migraine. Average time of use was 29.4 months (95%CI ± 4.24, range 12–107 months). More frequent dose was 100mg. An 81.25% (n = 65) reported sustained clinical improvement during treatment and only the 13.75% (n = 11) showed an adverse effect. The 20% of patients had depression and 20% anxiety as comorbidities, according to their medical records.

Conclusion: It is still controversial how long to keep prophylaxis treatment, in our patients, long term topiramate was beneficial and safe, with no significant adverse effects reported.

EHMTC-0261
POSTER SESSION A

BRAIN STATE MONITORING FOR THE PREDICTION OF MIGRAINE ATTACKS

P. Martins[1], M. Westerfield[2], M. Lopes[2], C. Maruta[3], R. Gil-da-Costa[2]

[1]*Faculty of Medicine- Univ Lisboa, Neurology, Lisboa, Portugal*
[2]*Neuroverse- Inc., Research and Development, San Diego-CA 92122, USA*
[3]*Faculty of Medicine- University o Lisbon, Clinical Neurosciences, Lisbon, Portugal*

Migraine attacks are unpredictable, precluding preemptive interventions and contributing to a lack of control over patients' lives. Although there are neurophysiological changes 24–48 hours before migraine attacks, it has been so far impossible to utilize this information in patient management. Current roadblocks include the lack of both an adequate monitoring system and reliable neural measures of these changes. This study evaluates the applicability and predictive value of daily "*at home*" electroencephalography records obtained with a new portable system for migraine patients.

Here, twenty five subjects with episodic migraine (>1 attack/month; 33 ± 9.6 years of age; 21 females; 20 without aura) fulfilling ICHD criteria and without prophylactic medication were instructed how to use a novel portable system from Neuroverse, Inc. (the BrainStation EEG device and BrainVitalsM tablet application) and asked to self-record their neural activity daily while resting at home, over approximately 14 days. Standard EEG spectral analysis methods were used and recordings were grouped by time from a migraine event (i.e., over 24 h before migraine; 24 h preceding migraine onset; migraine day; up to 48 h post-migraine).

Our results show a statistical significant modulation of relative power in the delta (decrease), beta and gamma (increase) frequency bands 24h before migraine symptoms onset. This study demonstrates that brain state monitoring, utilizing an easy-to-use portable EEG system, to track neural modulations *at home*, can identify physiological changes preceding a migraine attack, potentially enabling pre-symptoms prediction. Further studies will investigate how this information can best change patients' quality of life.

Conflict of interest
Disclosure statement:
Isabel Pavão Martins has shares of Neuroverse,Inc. and has received financial support from Allergan for travelling. Ricardo Gil-da-Costa has shares of Neuroverse, Inc.

Carolina Maruta, Marissa Westerfield and Marco Lopes report no conflicts of Interest.

EHMTC-0156
POSTER SESSION A

THE IMPACT OF ONABOTULINUMTOXINA ON SEVERE HEADACHE DAYS: PREEMPT 24-WEEK POOLED ANALYSIS

M. Matharu[1], R. Halker[2], P. Pozo-Rosich[3], R. DeGryse[4], A. Manack Adams[5], S.K. Aurora[6]

[1]*Institute of Neurology, Headache Group, London, United Kingdom*
[2]*Mayo Clinic, Neurology, Phoenix, USA*
[3]*Institut de Recerca VHIR- Universitat Autònoma de Barcelona- Vall d'Hebron University Hospital, Headache and Pain Research Group- Neurology Department, Barcelona, Spain*
[4]*Allergan plc, Biostatistics, Irvine, USA*
[5]*Allergan plc, Global Medical Affairs, Irvine, USA*
[6]*Stanford University, Department of Neurology, Stanford, USA*

Background: The PREEMPT trials established the efficacy of onabotulinumtoxinA for chronic migraine (CM) based on reduced headache-day frequency. This analysis of PREEMPT study data reports the benefits of onabotulinumtoxinA on headache-day severity.

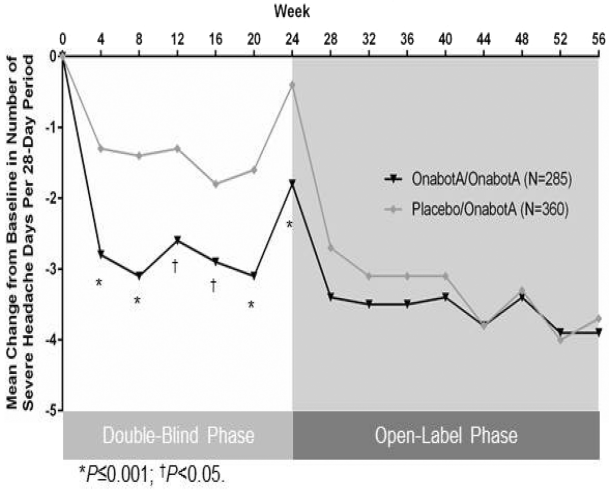
Methods: In this pooled analysis of 2 multicenter, phase 3, double-blind, parallel-group, placebo-controlled studies, patients with CM (≥15 headache-days/month) received two 12-week treatment cycles of onabotulinumtoxinA (155U–195U) or placebo. Headache-day severity was assessed at baseline and 24 weeks.

Results: 1384 patients received onabotulinumtoxinA (n = 688) or placebo (n = 696). Among those with <50% reduction from baseline in headache-day frequency at week 24 ("nonresponders"), reduction in the number of severe headache days per 28-day period was better for onabotulinumtoxinA than placebo ($P = 0.001$; Figure 1), as was the proportion of severe headache days pooled across all nonresponders ($P < 0.001$; Figure 2). A greater proportion of nonresponders receiving onabotulinumtoxinA vs placebo had ≥1-grade improvement in severity (41.1% vs 31.4%; $P = 0.01$); those with improved severity also showed improvement in HIT-6 (≥5 points; 62.2% vs 43.5%; $P < 0.001$).

Conclusion: This analysis demonstrates reduced headache-day severity among patients without headache-day frequency reduction, suggesting that patients with CM experience relief from daily headache intensity from onabotulinumtoxinA.

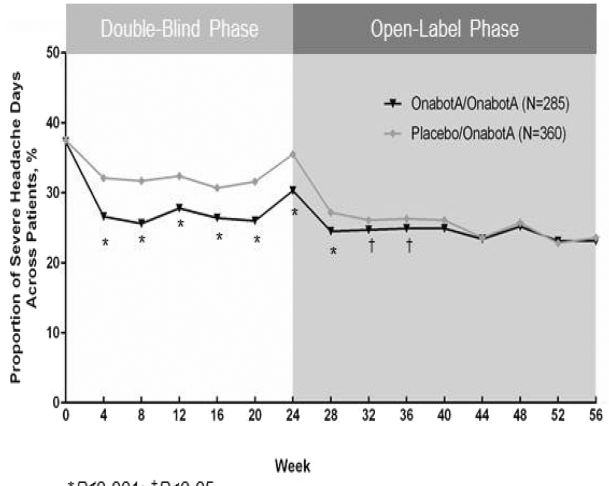
Funding: Allergan

Figure 1. Mean Change from Baseline in Number of Severe Headache Days Per 28-Day Period Among Patients With <50% Decrease from Baseline in Headache-Day Frequency



*$P \leq 0.001$; †$P < 0.05$.

Figure 2. Proportion of Severe Headache Days Across All Patients With <50% Decrease from Baseline in Headache-Day Frequency



*$P \leq 0.001$; †$P < 0.05$.

Conflict of interest
Disclosure statement:
Manjit Matharu has received consulting fees/honoraria from Allergan, St Jude Medical, Medtronic and electroCore.

Rashmi Halker has received honoraria from Medlink Neurology, NEJM Journal Watch Neurology, and Current Neurology and Neuroscience Reports.

Patricia Pozo-Rosich has received consulting fees/honoraria from Allergan.

Ronald DeGryse is an employee of Allergan plc, and has stock in the company.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc, and owns stock in the company.

Sheena K. Aurora has received consulting fees/honoraria from Allergan, eNeura, Merck, and Teva and speaker's bureau participation for Allergan.

EHMTC-0290
POSTER SESSION A

SUBCUTANEOUS BOTULINUM TOXIN TYPE A TREATMENT FOR PROPHYLAXIS OF HEADACHES IN CHRONIC MIGRAINE: A NEW THERAPEUTIC STRATEGY

M.R. Mazza[1], G. Ferrigno[1], B. Vescio[2], A. Quattrone[1], F. Bono[1]

[1]*Institute of Neurology, Headache Group. Department of Medical and Surgical Science, Catanzaro, Italy*
[2]*Institute of Bioimaging and Molecular Physiology- National Research Council- Germaneto, Neuroimaging Research Unit, Catanzaro, Italy*

Background: A meaningful proportion of patients with chronic migraine (CM) are non-responders to repeated intramuscular botulinum toxin type A (BoNTA) treatments.

Aim: To test if two subcutaneous BoNTA treatments are effective for prophylaxis of headaches in patients with CM.

Method: Sixty-three consecutive non-responders patients with CM were assigned, according to area of maximum pain (trigeminal or occipital) and severity of cutaneous allodynia, to receive two subcutaneous administrations of BoNTA (which comprised several injections up to 200 units) or placebo. During the follow up patients were evaluated at 30, 60 and 90 days. Primary end-point was change >50% in number of monthly headache days.

Results: According to area of maximum pain and severity of CA, patients were divided in 2 groups: Group 1, included 38 allodynic patients with trigeminal area of maximum pain, performed subcutaneous BoNTA injections in the cutaneous area innervated by first branch of trigeminal nerve; Group 2, 25 non allodynic patients with occipital area of maximum pain, performed subcutaneous injections in the cutaneous area innervated by greater and lesser occipital nerves. The subcutaneous BoNTA treatment decreased significantly the number of monthly headache days in 62% of patients in Group 1, and 43% of patients in Group 2. The efficacy lasted about 60 days. While, 34% of patients had a temporary response to false treatment.

Conclusion: Two subcutaneous administrations of BoNTA have a sustained efficacy for prophylaxis of headaches in patients with CM who do not respond to repeated intramuscular BoNTA injections.

EHMTC-0173
POSTER SESSION A

EVALUATION OF TREATMENT-EMERGENT ANTI-DRUG-ANTIBODIES (TE-ADA) FOLLOWING ADMINISTRATION OF LY2951742, A CALCITONIN GENE RELATED PEPTIDE (CGRP) ANTIBODY, TO PATIENTS WITH MIGRAINE

B. Miller[1], E. Collins[1], M. Hodsdon[1], A. Camporeale[1], H. Nguyen[1], T. Oakes[1], Q. Zhang[1], M. Ferguson[1], V. Skljarevski[1], J. Martinez[1], K. Johnson[1], A. Schacht[2], M. Due[1], K. William[1], Y. Jyun Yan[1]

[1]*Eli Lilly and Company, Indianapolis- Indiana, USA*
[2]*Eli Lilly and Company, Elanco Animal Health, Greenfield-Indiana, USA*

Objective: Evaluate the immunogenic potential of LY2951742 in patients with migraine.

Methods: In this study, patients with 4–14 migraine headache days per month received placebo (N = 136) or 1 of 4 LY2951742 doses (5, 50, 120, and 300 mg; N = 264) given subcutaneously once monthly for 3 months (double-blind treatment phase), followed by a 3-month post-treatment phase (ClinicalTrials.gov, NCT02163993). TE-ADA was defined as an ADA-negative result at baseline followed by an ADA-positive result post-baseline with a titer of ≥20, or an ADA-positive result at baseline followed by an ADA-positive result post-baseline with ≥4 fold increase in titer. The impact of TE-ADA on efficacy, safety, pharmacokinetics (PK), and CGRP concentration was assessed.

Results: Thirty patients (11.4%) in the LY2951742 groups and 5 (3.7%) in the placebo group had TE-ADA with low titers (1:20 to 1:160). Comparison against the apparent incidence of TE-ADA in patients receiving placebo is critical in order to account for random or other non-treatment associated increases in ADA. Among patients with

treatment-emergent adverse events of allergic reactions/hypersensitivity, none had TE-ADA. Efficacy, safety, and LY2951742 and CGRP concentration analyses did not show any association with TE-ADA status.

Conclusion: These data suggest that the presence of low titers of TE-ADA in 11.4% of LY2951742-treated patients had no apparent clinically meaningful effect on efficacy, safety, PK or antibody target-mediated binding. Larger, longer duration trials are needed to confirm these findings. The specific values reported here are only relevant for this assay, given that each assay has different characteristics.

Conflict of interest
Disclosure statement:
Full-time employee and stockholder, Eli Lilly and Company

EHMTC-0164
POSTER SESSION A

SYSTEMATIC LITERATURE REVIEW OF PATIENT REPORTED OUTCOMES IN STUDIES EXAMINING PROPHYLACTIC TREATMENTS IN PATIENTS WITH EPISODIC OR CHRONIC MIGRAINE

A. Earley[1], P. Desai[2], E. Bergrath[1], P. Guyot[1], N. Miller[1], S. Sapra[2], C. Makin[1]

[1]*Mapi USA Inc, RWSA, Boston, USA*
[2]*Amgen, Health Economics, Thousand Oaks, USA*

Objective: Recent guidelines for clinical trials of migraine drugs suggest that the global impact of migraine can be assessed using patient reported outcomes (PROs) such as disability or quality of life, in addition to clinical outcomes. This systematic literature review (SLR) aimed at summarizing PROs in randomized controlled trials (RCTs) examining prophylactic interventions for episodic (EM) or chronic migraine (CM).

Methods: A SLR was conducted using biomedical databases to identify RCTs published between January 1987 and September 2015. The following prophylactic interventions were included: anticonvulsants, beta-blockers, tricyclic antidepressants, serotonin and norepinephrine reuptake-inhibitors, calcitonin gene-related peptide-receptor antagonists, and botulinum toxin A. All psychometric PROs were outcomes of interest.

Results: Of the 74 RCTs identified, 51 were in EM patients and 19 in CM patients; migraine frequency was unclear for the remainder. Twenty-three studies (31%) collected data on at least one PRO instrument, of which thirteen were in EM and ten in CM patients. The most commonly used PRO instruments in the studies were the Headache Impact Test-6 (n = 10) and Migraine Disability Assessment (n = 10), followed closely by the Migraine-Specific Quality of Life (n = 9, and Visual Analogue Scale scales (n = 9). Twelve studies reported data on more than one PRO.

Conclusions: Despite profound impact of migraine on patient's lives, less than a third of the RCTs in our SLR reported PRO outcomes. There is need to collect more patient-centric outcomes in migraine RCTs. Consistent collection of PROs in RCTs will aid in providing better insights into the impact of migraine on a patient's life.

Conflict of interest
Disclosure statement:
This project was funded by Amgen.

EHMTC-0243
POSTER SESSION A

MIGRAINE PROPHYLAXIS TREATMENT PATTERNS IN JAPAN: ANALYSIS OF DATA FROM CLINICAL PRACTICE

J. Pike[1], A. Mutebi[2], N. Shah[2], J. Jackson[3], S. Cotton[4], P. Desai[2], S. Sapra[5]

[1]*Adelphi Real World, Statistics, Bolington- Macclesfield, United Kingdom*
[2]*Amgen- Inc., GHE, Thousand Oaks-, USA*
[3]*Adelphi Real World, Research, Bollington- Macclesfied, United Kingdom*
[4]*Adelphi Real World, Research, Bollington- Macclesfield, United Kingdom*
[5]*Amgen- Inc., GHE, Thousand Oaks, USA*

Objective: To explore the use and history of treatment failure of migraine prophylaxis in Japan.

Methods: Data were drawn from the 2014 Adelphi Migraine Disease Specific Program, a cross sectional survey of physicians and their consulting migraine patients. Analyses described and explored factors associated with prophylaxis use and the history of failure.

Results: Of 1019 patients surveyed, 76.4% female, with mean(SD) age of 43.9(14.9) years, 430 (42.1%) were prophylaxis users. Most common prophylaxis treatments used included lomerizine (34.9%), valproic acid (31.4%), and amitriptyline (17.4%). Of the 112(26.1%) current users with a history of treatment failures, 88(78.6%) had previously failed 1 prophylaxis, and 24(21.4%) had previously failed at least 2. Physicians reported lack of effectiveness (LOE) only (70.4%), poor tolerability (PT) only (14.8%), both LOE and PT (9.3%) as reasons for failure. Patients reported LOE only (37.5%), PT only (12.5%), both LOE and

PT (19.4%) as reasons for failure. Patients with 8–14 (vs. 0–3) headache-days-per-month (HD) and patients with depression (vs. no depression) were 3.3 times ($p = 0.002$) and 8.3 times ($p = 0.002$) more likely to use prophylaxis, respectively. Factors associated with the history of failure on prophylaxis treatment included: HD (ref: 0–3) 8–14 ($OR = 4.7$, $p = 0.012$), 15+ ($OR = 38.6$, $p = 0.034$), disease duration-years ($OR = 1.3$, $p = 0.005$), male (ref. female; $OR = 0.11$, $p = 0.006$), comorbidities ($OR = 2.74$, $p < 0.001$), and migraine disability assessment scale-MIDAS scores ($OR = 0.96$, $p < 0.001$).

Conclusion: Migraine prophylaxis use in Japan is low with slightly over a quarter of users having failed a prophylaxis in the past. LOE is commonly reported and comparable proportions of physicians and patients report PT only as reason for failure.

Conflict of interest
Disclosure statement:
The study was analysis was funded by Amgen Inc. AM, NS, PD, SS are employees and stockholders of Amgen Inc.

EHMTC-0244
POSTER SESSION A

MIGRAINE PROPHYLAXIS TREATMENT PATTERNS IN GERMANY: ANALYSIS OF DATA FROM CLINICAL PRACTICE

N. Shah[1], A. Mutebi[1], J. Pike[2], S. Cotton[2], P. Desai[3], S. Sapra[3]

[1]*Amgen- Inc., GHE, Thousand Oaks-, USA*
[2]*Adelphi Real World, Research, Bollington- Macclesfield, United Kingdom*
[3]*Amgen- Inc., GHE, Thousand Oaks, USA*

Objective: To explore the use and history of failure of migraine prophylaxis treatments in Germany.

Methods: Data were drawn from the 2014 Adelphi Migraine Disease Specific Program, a cross sectional survey of physicians and their migraine patients. Analyses described prophylaxis use, history of failure, and explored associations between current prophylaxis use, and patient demographics and clinical factors.

Results: Of 900 patients surveyed, 66.0% female, 96.5% white, with mean(SD) age of 39.2(13.7) years, only 22%(198) were prophylaxis users. Commonly used prophylaxis included metoprolol (32.8%), topiramate (17.7%), amitriptyline (14.7%), and propranolol (10.6%). Of the 83(41.9%) current users with a history of treatment failures, 71(85.5%) had previously failed 1 prophylaxis, and 12(14.5%) had previously failed at least 2. Physicians reported lack of effectiveness (LOE) only (49.48%), poor tolerability (PT) only (18.6%), both LOE and PT (28.9%) as reasons for failure. Patients reported LOE only (28.0%), PT only (28.0%), both LOE and PT (24.0%) as reasons for failure. Patients being treated by neurologists (vs. PCP) were 2.64 times ($p = 0.043$) more likely to be prescribed prophylaxis, and a unit increase in MIDAS scores was associated with 1.03 times ($p = 0.034$) increased likelihood of using a prophylaxis.

Conclusion: Use of migraine prophylaxis in Germany is low. Four out of ten users have failed a prophylaxis in the past. Physicians reported failures are largely due to LOE only, but an equal proportion of patients reported prophylaxis failures due to LOE alone vs. PT alone, demonstrating a need for more efficacious and tolerable prophylaxis treatments.

Conflict of interest
Disclosure statement:
The analysis was funded by Amgen Inc. NS, AM, PD, and SS are employees and stockholders of Amgen Inc.

EHMTC-0245
POSTER SESSION A

MIGRAINE PROPHYLAXIS TREATMENT PATTERNS IN FRANCE: ANALYSIS OF DATA FROM CLINICAL PRACTICE

A. Mutebi[1], J. Pike[2], N. Shah[3], S. Cotton[2], P. Desai[1], S. Sapra[1]

[1]*Amgen- Inc., GHE, Thousand Oaks, USA*
[2]*Adelphi Real World, Research, Bollington- Macclesfield, United Kingdom*
[3]*Amgen- Inc., GHE, Thousand Oaks-, USA*

Objective: To explore the current use, and history of failure of migraine prophylaxis treatments using clinical practice data in France.

Methods: Data were drawn from the 2014 Adelphi Migraine Disease Specific Program, a cross sectional survey of physicians and their consulting migraine patients. Analyses described prophylaxis use, history of failure, and explored associations between current prophylaxis use, patient demographics and clinical factors including headache days per month (HD).

Results: Of the 900 patients surveyed, 67.7% female, 86.2% white, with mean (SD) age of 37.3 (13.5), about half (420, 46.7%) were current prophylaxis users. Most common prophylaxis treatments used included propranolol (35.6%), topiramate (22.9%), and amitriptyline (14.1%). Of the 181 (43.1%) current users with a history of

treatment failures, 149 (82.3%) had previously failed 1 prophylaxis, and 32 (17.7%) had previously failed at least 2. Physician-reported reasons for prophylaxis treatment failure included: lack of effectiveness (LOE) only (51.8%), poor tolerability (PT) only (18.5%), both LOE and PT (26.2%). Patient-reported reasons for failure were LOE only (29.6%), PT only (25.4%), both LOE and PT (19.7%). HDs (4–7,OR = 5.0; 8–14,OR = 5.7; 15+,OR = 10.2; reference 0–3), and internist/neurologist vs. PCP (OR = 5.1) were significantly associated with current prophylaxis use ($p \leq 0.05$).

Conclusion: Over half of migraine patients surveyed in France were not using prophylaxis and nearly half of current users have failed a prophylaxis in the past. Failures are largely due to both lack of effectiveness and/or poor tolerability, as reported by both physicians and patients. This underscores substantial unmet need for efficacious and tolerable prophylaxis treatments in France.

Conflict of interest
Disclosure statement:
The analysis was funded by Amgen Inc. AM, NS, PD, and SS are employees and stockolders of Amgen Inc.

EHMTC-0376
POSTER SESSION A

DOES ANGIOTENSIN CONVERTING ENZYME PREVENT SLEEP DEPRIVATION-TRIGGERED MIGRAINE ATTACKS FOLLOWING AEROBIC EXERCISE TRAINING?

A.B. Oliveira[1], B. Visniauskas[2], J.R. Chagas[2], M.T. Mello[3], R.T. Ribeiro[4], S. Tufik[5], M.F.P. Peres[1]

[1]*UNIFESP, Neurologia e Neurocirurgia, São Paulo, Brazil*
[2]*UNIFESP, Biologia Molecular, São Paulo, Brazil*
[3]*UFMG, Esporte, Belo Horizonte, Brazil*
[4]*UNIFESP, Neurologia e Neurocirurgia, S, Brazil*
[5]*UNIFESP, Psicobiologia, São Paulo, Brazil*

Kallikrein (KKN) and angiotensin converting enzyme-1 (ACE) are proteases responsible for bradykinin (BK) formation and inactivation, respectively, which is operative in inflammation/nociception. Additionally, ACE mediates antinociception, via angiotensin-III formation, while increases pineal melatonin production via angiotensin-II, and is reduced after sleep deprivation in rodents.

We measured resting plasma KKN and ACE activities (Fluorescence Resonance Energy Transfer) in migraine (M) patients (ICHD-II) and controls (C) before and following intervention with aerobic exercise training (12-weeks, 3x/week), and tested correlations between changes in proteases and clinical outcomes.

Fifty-nine participants (M: n = 31; C: n = 28) gave signed consent form and concluded the study. At baseline, there were no differences between groups for both proteases. Exercise training significantly increased ACE (ANOVA $p < 0.05$) only in M trained group, and had no effect on KKN for any group. There was significant reduction in days with M only in M trained group (*t* test $p < 0.01$) after intervention period. There were no correlations between proteases and days with M neither at baseline nor for changes after intervention.

M trained group showed greater reduction in attacks attributed to sleep deprivation than M sedentary group (−21 *vs* −8, respectively; groups' sum). After categorization of groups, there was a significant association between ACE activity changes and whether patients reduced or not sleep deprivation-triggered attacks (χ^2 (1) = 7.950, $p = 0.005$). Based on the odds ratio, patients who increased ACE activity were 17 times more likely to reduce sleep deprivation-triggered attacks.

Higher ACE activity prevents migraine attacks triggered by sleep deprivation after aerobic exercise training.

EHMTC-0194
POSTER SESSION A

A PROPOSAL FOR ONABOTULINUMTOXINA INJECTION INTO TEMPORAL AREA FOR TREATMENT OF CHRONIC MIGRAINE

Y. Park[1], Y.K. Kim[1], J.H. Bae[2], S.J. Wang[3], J.J. Kim[1], S.T. Kim[1]

[1]*Yonsei University College of Dentistry, Orofacial pain & Oral Medicine, Seoul, Republic of Korea*
[2]*Yonsei University College of Dentistry, Oral Biology, Seoul, Republic of Korea*
[3]*Taipei Veterans' General Hospital, Neurology, Taipei, Taiwan*

Purpose: This study was to determine the topographical site of the auriculotemporal nerve (ATN) as it exits from the deep layer to the superficial layer in order to facilitate injections in chronic migraine(CM).

Methods: ATNs on 20 sides of 11 Korean cadavers were investigated. The infraorbital notch and tragus were set as landmarks. The vertical distance from H1 to the superficial appearance point of the nerve was measured.

Results: The ATN appeared superficially at a mean distance of 9.54 mm superior to H1, in front of the tragus. In that region, the nerve is positioned deeper than the superficial temporal artery and passes between the artery and the superficial temporal vein. After becoming superficial it splits into anterior and posterior divisions. The posterior division ascends in front of the ear and gives off several branches to the skin, while the anterior division ascends in a superior direction, perpendicular to H1. It usually has two or three branches, some of which travel superficially on the fascia.

Conclusions: BoNT-A injection into the temporal area can best be localized by palpating the tragus of the ear, measuring about 3 cm above the tragus in a vertical line for the first injection point, then following up along the same vertical line. A second injection is made at least 1.5 cm higher. A third injection is made between these first two injection points but about 1.5 cm anterior to them. The final injection in the temporalis is made in line with the second injection, approximately 1.5 cm in a posterior direction.

EHMTC-0214
POSTER SESSION A

REAL-LIFE USE OF ONABOTULINUMTOXINA FOR THE SYMPTOMATIC TREATMENT OF CHRONIC MIGRAINE: 12-MONTH REPOSE STUDY INTERIM ANALYSIS

J. Pascual[1], C. Gaul[2], B. Davies[3], S. Brown[4], F. Ahmed[5]

[1]*University Hospital Marqués de Valdecilla, Service of Neurology, Santander, Spain*
[2]*Migraine and Headache Clinic Koenigstein, Headache Diagnostic and Therapy, Koenigstein, Germany*
[3]*Royal Stoke University Hospital, Department of Neurology & Midlands Regional Headache Clinic, Staffordshire, United Kingdom*
[4]*Allergan plc, Specialty Care- International, Buckinghamshire, United Kingdom*
[5]*Spire Hesslewood Clinic- Hull York Medical School, Neurology, England, United Kingdom*

Background: Longer-term use of onabotulinumtoxinA for chronic migraine (CM) in clinical practice is not well-documented. The REPOSE Study describes 2-year, real-life use of onabotulinumtoxinA for CM in Europe.

Methods: This 12-month interim analysis assessed patient demographics, clinical characteristics, treatments, onabotulinumtoxinA injection practices, Migraine Specific Quality of Life Questionnaire [MSQ], EuroQol Group [EQ-5D], headache-day frequency, and adverse events (AEs).

Results: 405 patients (61 centres) were included (Table). Most patients received 4 treatments over 12 months, at approximately 3-month intervals. At all re-treatment visits, significant improvements from baseline in median MSQ and EQ-5D scores (all $P < 0.001$; Figure) and headache days (follow-up visits 1, 2, 3, and 4: –9, –10, –11, and –12 days/month, respectively; all $P < 0.001$) were observed. 15.3% of patients (62/405) reported 105 AEs; the most common were eyelid ptosis (n = 17, 4.2%), muscular weakness (n = 7, 1.7%), and neck pain (n = 7, 1.7%). No new safety signals were identified.

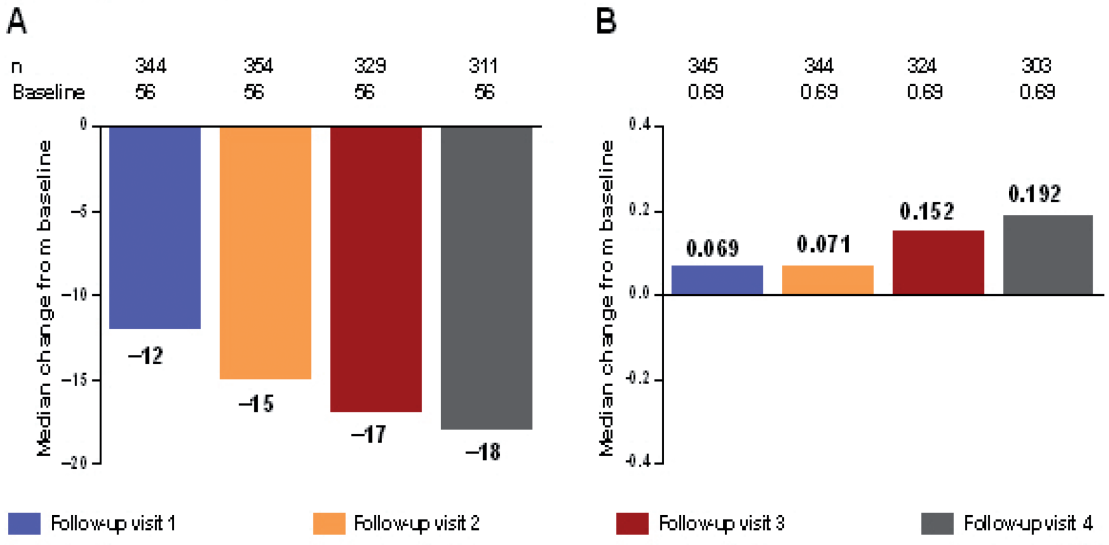
Conclusion: This 12-month interim analysis demonstrates that preventative treatment of CM with onabotulinumtoxinA in a real-world setting significantly improves quality-of-life while sustaining reductions in headache-day frequency and maintaining tolerability.

Funding: Allergan

Table. Patient Characteristics

Parameter	Interim Population (N=405)
Mean (SD) age of headache onset, years	18.0 (9.4)
Medication use in 26 weeks before baseline, %	
Acute treatment	85.4
Preventative treatment	64.7
Headache medication type, %	
Beta-blockers	71.4
Antidepressants	70.9
Antiepileptics	69.1

Figure. Median Change From Baseline in (A) MSQ and (B) EQ-5D Total Scores by Visit



P<0.001 vs baseline for all comparisons (Wilcoxon signed-rank test)

Conflict of interest
Disclosure statement:
Julio Pascual, MD, PhD, has served on advisory boards for Allergan, Amgen, Novartis, and Teva.

Charly Gaul, MD, PhD, has received honoraria from Allergan, Berlin-Chemie, MSD, electroCore, St. Jude Medical, Grünenthal, Desitin, Bayer, Boehringer Ingelheim, Autonomic Technologies, and Hormosan. Dr. Gaul has no ownership interests and does not own any pharmaceutical company stocks.

Brendan Davies, BSc, MB, BS, MD, FRCP, has received advisory board fees from Allergan, MSD, and Amgen. He has received consultancy fees from NICE and the UK MHRA. Dr. Davies has obtained unrestricted educational grants payable to the Univeristy of Keele Course on Headache Disorders, the Migraine Trust, and BASH from Allergan, eNeura, Cefaly, and MSD. Dr. Davies has no ownership interests and does not own any pharmaceutical company stocks.

Stephanie Brown, MBBS, MRCS, MFPM, is a full-time employee of Allergan and owns stock in the company.

Fayyaz Ahmed, MB, BS, MD, FRCP, MBA, MRCP, has served on the advisory board for Allergan and conducted workshops for which honoraria were received or paid to Migraine Trust or British Association for the Study of Headache.

EHMTC-0413
POSTER SESSION A

IV CHLORPROMAZINE AS A BRIDGE TREATMENT FOR CHRONIC MIGRAINE

N. Riggins[1], A. Ehrlich[1], L. Dapkus[1], M. Levin[1]

[1]*UCSF Headache Center, University of California, San Francisco, CA, USA*

Background: In the present work, we undertook a small pilot study to evaluate the effectiveness of an intravenous course of chlorpromazine as an intervention in refractory chronic migraine.

Methods: Seventeen patients with chronic migraine and resistant to oral medications were admitted for a 4-day course of IV chlorpromazine. Adult patients were started on either 10 mg or 12.5 mg of chlorpromazine. Additional IV doses of chlorpromazine were administered to maintain a moderate state of sedation over the 4 day admission period. Total doses of chlorpromazine given to the seventeen patients ranged from 85–200 mg. Premedication with 25 mg of diphenhydramine PO was done 60 minutes prior to each IV dose of chlorpromazine. Headache diaries were used to record headache days per month, headache intensity and days that acute medications were taken one month before and after their admission.

Results: A total of eleven out of seventeen (65%) patients had an improvement in their headache status post-admission and reported a reduction in headache frequency,

intensity or use of acute medications one month following their admission. Twelve out of seventeen (71%) patients reported an improvement during the admission period. The remaining patients reported no change in their headache status. The only side effect noted in the study was mild akathisia in one patient on day one of their inpatient admission, which resolved.

Conclusion: These results suggest that IV chlorpromazine is a safe, well tolerated, and useful medication for the treatment of resistant chronic migraine and warrant additional expanded studies.

EHMTC-0122
POSTER SESSION A

EFFECTS OF AMG 334 ON HUMAN ISOLATED CORONARY ARTERY

E. Rubio-Beltrán[1], A. Labastida[1], R. de Vries[1], A.H.J. Danser[1], G. Balasubramanian[2], C. Xu[2], H.M. Vargas[2], K.A. Haanes[1], A. MaassenVanDenBrink[1]

[1]*Erasmus University Medical Center, Div. of Pharmacology-Dept. of Internal Medicine, Rotterdam, Netherlands*
[2]*Amgen, Inc, Thousand Oaks- California, USA*

The efficacy and safety of the anti-CGRP receptor antibody AMG 334 is currently being evaluated in clinical trials of patients with episodic and chronic migraine. As a cardiovascular safety assessment of AMG 334, we studied the vasoconstrictor potential of AMG 334 in the human coronary artery and compared the results with those obtained with the 5-$HT_{1B/1D}$ receptor agonist sumatriptan as a reference.

Human proximal and distal coronary arteries were obtained from 6 heart valve donors, mean age 66 years [range 54 – 81]. Relaxant responses to CGRP (proximal coronary artery: E_{max} 36 ± 6% of contraction to 30 mM KCl, pEC_{50} <5.26, n = 4; distal coronary artery: E_{max} 81 ± 6%, pEC_{50} 9.01 ± 0.13, n = 6) were significantly shifted in the presence of 1 μM AMG 334 (proximal coronary artery: E_{max} 21 ± 2%, pEC_{50} < 4.69; distal coronary artery: E_{max} 84 ± 5% of contraction to 30 mM KCl, pEC_{50} 6.90 ± 0.13). Compared to sumatriptan, AMG 334 alone did not induce contraction of the coronary artery up to the highest concentration tested (1 μM), nor did it interact with sumatriptan-induced contractile responses in proximal (E_{max} 13 ± 2% of contraction to 100 mM KCl and pEC_{50} 6.21 ± 0.96 in the absence of AMG 334, E_{max} 26 ± 8% and pEC_{50} 5.70 ± 0.55, n = 6 in the presence of AMG 334) or distal coronary artery (E_{max} 37 ± 20% and pEC_{50} 6.05 ± 0.42, in the absence of AMG 334, E_{max} 38 ± 19% and pEC_{50} 6.16 ± 0.57, n = 6 in the presence of AMG 334).

In conclusion, AMG 334 does not induce a contraction of the human isolated coronary artery, nor does it interact with contractions induced by sumatriptan.

Conflict of interest
Disclosure statement:
Amgen Inc. supported the study.

EHMTC-0396
POSTER SESSION A

USING FLASH LIGHT STIMULATION TO TREAT MIGRAINE: A PROOF-OF-CONCEPT TRIAL USING A NOVEL STIMULATOR "STIMLUX"

S.L. Sava[1], A. Cosseddu[1], D. Magis[1], A. Maertens de Noordhout[1], J. Schoenen[1]

[1]*Headache Research Unit – Citadelle Hospital., University Deptartment of Neurology, Liege, Belgium*

Background: In a previous study we found that violet flash light stimulation delivered at 12 Hz-frequency and 1500 Lux-intensity with the novel *StimLux* is able to decrease trigeminal nociception in healthy subjects assessed with the nociceptive blink reflex. We performed in a pilot proof-of-concept trial as a preventive treatment in episodic (EM) and chronic migraine patients (CM).

Subjects and Methods: We enrolled 20 migraineurs: 11 EM and 9 CM. They were stimulated with the *StimLux* device daily for 20-minutes during 2 consecutive weeks and recorded headache frequency, intensity, duration and associated symptoms in a migraine diary.

Results: In EM patients, the 50% responder rate for migraine days was 36.4%; there was a significant decrease in the duration of headache attacks and NSAID intake.

CM patients had a significant decrease in total headache days/month, migraine days/month, mean duration of attacks and days per month with moderate headache. 77.7% of CM patients had a ≥50% reduction in monthly migraine days. The beneficial effect lasted for another 2 weeks after the last stimulation-session.

Conclusion: Flash light stimulation has not been studied heretofore in migraine as a prophylactic treatment, probably because most migraineurs are sensitive to light and treating them with a light stimulus may at first sight seem counterproductive. Our pilot study suggests, however, that a specific pattern of flash light stimulation can have a preventive therapeutic effect both in episodic and chronic migraine. A possible explanation for this effect could be

the a top-down inhibitory action of the visual cortex on the trigeminal nociceptive system.

EHMTC-0110
POSTER SESSION A

EFFICACY AND SAFETY OF LY2951742 IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY IN PATIENTS WITH MIGRAINE

V. Skljarevski[1], T. Oakes[1], M. Ferguson[2], Q. Zhang[3], J. Martinez[1], K. Johnson[4], A. Schacht[5], M. Due[6], P. Goadsby[7], D. Dodick[8]

[1]*Eli Lilly and Company, Pain Team- Medical, Indianapolis, USA*
[2]*Eli Lilly and Company, Clinical Operations, Ontario, Canada*
[3]*Eli Lilly and Company, Statistics-Neuroscience, Indianapolis, USA*
[4]*Eli Lilly and Company, Pain Migraine, Indianapolis, USA*
[5]*Eli Lilly and Company, Elanco, Indianapolis, USA*
[6]*Eli Lilly and Company, Global Scientific Communications, Indianapolis, USA*
[7]*King's College London, Department of Neurology, London, United Kingdom*
[8]*Mayo Clinic, Department of Neurology, Phoenix, USA*

Objective: The aim of Study CGAB was to evaluate the efficacy and safety of LY2951742, a monoclonal antibody to calcitonin gene-related peptide, in the prevention of migraine headache.

Methods: Patients with 4 to 14 migraine headache days (MHD) per month were randomized (2:1:1:1:1) to placebo or 1 of 4 LY2951742 dose groups (5, 50, 120, and 300 mg) given subcutaneously once monthly for 3 months. The primary objective was to assess whether at least one dose of LY2951742 was superior to placebo in the prevention of migraine headache, as measured by the mean change from baseline in the number of MHD in the last month of treatment phase. (ClinicalTrials.gov, NCT02163993).

Results: Compared with placebo, LY2951742 groups showed greater mean reduction in the number of MHD from baseline in the last month of the treatment phase, where the 120 mg dose of LY2951742 met the primary objective (-4.9 versus -3.6 days for the LY2951742 and placebo groups, respectively, $p = 0.004$). Common treatment-emergent adverse events (TEAEs) that occurred more frequently with LY2951742 than with placebo during the 3-month treatment phase included injection site pain, upper respiratory tract infections, nasopharyngitis, dysmenorrhea, and nausea. Additional TEAEs that were frequently ($\geq$1%) reported during the 3-month post-treatment phase were back pain, sinusitis, bronchitis, urinary tract infection, influenza, neck pain, and pain in extremity.

Conclusion: These results provide evidence that monthly subcutaneous injections of LY2951742 is safe, well tolerated, and efficacious in the prevention of migraine.

Conflict of interest
Disclosure statement:
Full-time employee and stockholder, Eli Lilly and Company

EHMTC-0111
POSTER SESSION A

EFFICACY OF LY2951742 IN SUBGROUPS OF PATIENTS WITH MIGRAINE OF DIFFERENT FREQUENCY

V. Skljarevski[1], J. Martinez[1], T. Oakes[1], M. Ferguson[2], Y. Tanaka[3], M. Due[4], A. Schacht[5]

[1]*Eli Lilly and Company, Pain Team- Medical, Indianapolis, USA*
[2]*Eli Lilly and Company, Clinical Operations, Ontario, Canada*
[3]*Eli Lilly and Company, RWA Capabilities and Datamart, Indianapolis, USA*
[4]*Eli Lilly and Company, Global Scientific Communications, Indianapolis, USA*
[5]*Eli Lilly and Company, Elanco, Indianapolis, USA*

Background: In a recently reported study, LY2951742 significantly reduced the number of migraine headache days (MHD). The baseline frequency of MHD was 4 to 14 MHD per month.

Objective: To examine mean change of MHD from baseline in subgroups of patients based on their baseline monthly frequency of MHD.

Methods: The post-hoc analyses were conducted using data from a double-blind, phase 2a study in adult patients randomly assigned to LY2951742 or placebo for 12 weeks (NCT01625988). The primary endpoint was the mean change in the number of MHD during the last 28-day period. Subgroups were examined based on the number of MHD during the baseline period from 5 (i.e., $\geq$5 vs. $<$5 MHD) to 10. 50% response rates were also examined for the same subgroups.

Findings: A total of 217 patients were randomized and received LY2951742 ($n = 107$) or placebo ($n = 110$). A difference from placebo was observed at Month 3 from 1.5 days reduction from baseline in MHD for the $\geq$5 MHD subgroup and continued to increase to 2.4 days reduction from baseline in MHD for the $\geq$8 MHD subgroup. The

increase in reduction of MHD failed to continue past the ≥8 MHD subgroup. Similarly, this trend was also observed when 50% response rates were examined for the same subgroups.

Conclusion: LY2951742 effect appeared maximized for the high-frequency subgroup (≥8 MHD).

Conflict of interest
Disclosure statement:
Full-time employee and stockholder, Eli Lilly and Company

EHMTC-0410
POSTER SESSION A

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF ALD403, AN ANTI-CGRP PEPTIDE ANTIBODY IN THE PREVENTION OF CHRONIC MIGRAINE

J. Smith[1], D. Dodick[2], P. Goadsby[3], S. Silberstein[4], R. Lipton[5], G. Chakava[6], T. O'Brien[7], R. Hill[8], R. Krause[9], J. Bonner[10], W. Koltun[11], J. Hirman[12]

[1]*Alder BioPharmaceuticals, Inc, Bothell, WA, USA*
[2]*Mayo Clinic, Phoenix, AZ, USA*
[3]*Department of Neurology, University of California, San Francisco, CA, USA*
[4]*Department of Neurology, Thomas Jefferson University, Jefferson Headache Center, Philadelphia, PA, USA*
[5]*Department of Neurology and the Montefiore Headache Center, Albert Einstein College of Medicine, Bronx, NY, USA*
[6]*Georgia Consilium Medulla, Tbilisi, Republic of Georgia*
[7]*The University of Melbourne, Melbourne, VIC, Australia*
[8]*Department of Neurology, Auckland Hospital, Auckland, New Zealand*
[9]*ClinSearch, LLC, Chattanooga, TN, USA*
[10]*Mercy Headache Center, Saint Louis, MO, USA*
[11]*Medical Center for Clinical Research, San Diego, CA, USA*
[12]*Pacific Northwest Stats, Bothell, WA, USA*

Background: CGRP is involved in the pathophysiology of migraine. We evaluated the efficacy and safety of ALD403, an anti-CGRP antibody, for the prevention of chronic migraine.

Methods: Patients with 15 to 28 headache days per month, of which at least 8 were migraine days were randomized to receive a single intravenous dose of ALD403 300 mg, 100 mg, 30 mg, 10 mg or placebo. The primary endpoint was the percentage of patients achieving a 75% reduction in migraine days per month from baseline to week 12. Statistical significance versus placebo for this phase II trial was pre-specified at the one sided p value <0.05.

Results: Of 662 patients randomized, 616 patients received treatment and 588 were included for efficacy. Baseline migraine days were between 16.2 and 16.5 days per month. Patients with a 75% reduction in migraine days for the entire 12 weeks (primary endpoint) was 33% ($p < 0.05$), 31% ($p < 0.05$), 28%, 27% and 21% for ALD403 300 mg, 100 mg, 30 mg, 10 mg and placebo. The percentage of severe migraines decreased relative to baseline by −21% ($p < 0.005$), −16% ($p < 0.05$), −18% ($p < 0.05$), −16% ($p < 0.05$), and −10% for ALD403 300 mg, 100 mg, 30 mg, 10 mg and placebo (post-hoc analysis). The infusion was well tolerated with no serious drug-related adverse events or infusion reactions identified.

Conclusions: ALD403 100 mg and 300 mg significantly reduced migraine days in patients with chronic migraine as measured by 75% responder rates. All doses of ALD403 significantly reduced the percentage of migraine attacks that the patients reported as severe. ALD403 was generally safe and well tolerated.

Conflict of interest
I am an employee, founder, and shareholder in Alder BioPharmaceuticals, Inc.

EHMTC-0411
POSTER SESSION A

PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF ERENUMAB (AMG 334) IN CHRONIC MIGRAINE PREVENTION

S. Tepper[1], K. Widnell[2], D. Dolezil[3], M. Ashina[4], U. Reuter[5], J. Lewis Brandes[6], S. Silberstein[7], P. Winner[8], D. Leonardi[9], D. Mikol[2]

[1]*Geisel School of Medicine at Dartmouth, Hanover, NH, USA*
[2]*Global Development, Amgen Inc., Thousand Oaks, CA, USA*
[3]*DADO MEDICAL s.r.o., Prague Headache Center, Czech Republic*
[4]*Dept of Neurology, Danish Headache Center, Glostrup Hospital, University of Copenhagen, Copenhagen, Denmark*
[5]*Dept of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany*
[6]*Nashville Neuroscience Group and Vanderbilt University School of Neurology, Nashville, TN, USA*
[7]*Jefferson Headache Center, Thomas Jefferson University, Philadelphia, PA, USA*
[8]*Premiere Research Institute*
Nova Southeastern University, West Palm Beach, FL, USA
[9]*Global Biostatistical Science, Amgen Inc., Thousand Oaks, CA, USA*

Introduction and Objectives: To evaluate safety and efficacy of erenumab (AMG 334), a fully human anti-CGRP receptor monoclonal antibody, in patients with chronic migraine (CM) (NCT02066415).

Methods: 667 adults with CM (≥15 headache days/month; ≥8 migraine days/month) were randomized (3:2:2) to monthly subcutaneous placebo or erenumab 70 mg or 140 mg. The primary endpoint (change from baseline in monthly migraine days [MMD]) and secondary endpoints (≥50% reduction in MMD and change from baseline in acute migraine-specific medication days and cumulative headache hours) were evaluated at the end of the double-blind period (weeks 9–12); safety/tolerability evaluated throughout.

Results: At baseline, patients reported 18.0 MMD. Patients experienced a mean 6.6-day reduction in MMD in each 70 mg and 140 mg dose groups versus a 4.2-day reduction for placebo ($p < 0.001$). 40% and 41% in the 70 mg and 140 mg dose groups, respectively, experienced ≥50% reduction in MMD versus 23% for placebo ($p < 0.001$) and a 3.5-day and 4.1-day reduction in acute migraine-specific medication use days versus a 1.6-day reduction for placebo ($p < 0.001$). Patients randomized to 70 mg and 140 mg erenumab, respectively, experienced a 66.2-hour ($p = 0.29$) and 75.7-hour ($p = 0.03$) reduction in monthly cumulative headache hours versus a 56.8-hour reduction for placebo. The safety profile of erenumab was similar to placebo for both erenumab-dose groups. Most common adverse events (AEs) for erenumab-dose groups were injection-site pain, upper respiratory tract infection, and nausea; no AE was reported in >5% of patients who received erenumab.

Conclusions: Erenumab 70 mg and 140 mg were efficacious in patients with CM and had a safety profile similar to placebo.

Conflict of interest
Dean Leonardi and Dan Mikol are employees of Amgen and own Amgen stock.

Katherine Widnell was an employee of Amgen during this study and owns Amgen stock.

Stewart Tepper was an employee of the Cleveland Clinic during this study. For 2015–2016, he received research Grants (no personal compensation): Allergan, Amgen, ATI, Avanir, ElectroCore, eNeura, Teva, Zosano Consultant: Acorda, Allergan, Amgen, ATI, Avanir, Depomed, ElectroCore, eNeura, Impax, KimberlyClark, Pfizer, Scion Neurostim,Teva, Zosano Speakers Bureau (2015 only): Allergan, Depomed, Impax, Pernix, Teva Advisors Board: Alder, Allergan, Amgen, ATI, Acorda, Dr. Reddy's, Kimberly Clark. Teva, Pfizer, Zosano Stock options: ATI Salary: American Headache Society Royalties: University of Mississippi Press, Springer.

David Dolezil received consulting fees, speaking and/or teaching fees from Allergan, Amgen, Biogen Idec, Novartis, Bayer, and Teva.

Messoud Ashina received consulting fees and/or scientific adviser/speaking fees from ATI, Allergan, Amgen, Alder and Eli Lilly.

Uwe Reuter received consulting fees, speaking/teaching fees, and/or research grants from Allergan, Amgen Inc., Autonomic Technologies, CoLucid, Electrocore, Novartis, Pharm Allergan.

Jan Brandes received consulting fees, speaking fees, and/or research grants from Allergan, Amgen, Avanir, Depomed, Clinvest, Daiichi-Sanko, Pernix, Merck, Supernus, Teva, Arteus/Eli Lilly.

Stephen Silberstein received consultant and/or advisory board fees from Alder Biopharmaceuticals, Allergan, Inc., Amgen, Avanir Pharmaceuticals, Inc., Curelator, Inc., Depomed, Dr. Reddy's Laboratories, eNeura Inc., electroCore Medical, LLC, Lilly USA, LLC, Supernus

Pharmaceuticals, Inc., Teva Pharmaceuticals, and Trigemina, Inc.

Paul Winner received research Grants from Allergan, Amgen, Biogen, Eli Lilly, Ipsen Ad Board and Speaker for Allergan, Eli Lily, Teva, and Avanir.

EHMTC-0423
POSTER SESSION A

Patient-Reported Outcomes in Chronic Migraine Patients Receiving Placebo or Erenumab (AMG 334) in a Phase 2, Randomized, Double-Blind Study

S. Tepper[1], R. Lipton[2], U. Reuter[3], S. Silberstein[4], W. Stewart[5], D. Leonardi[6], P. Desai[7], S. Cheng[8], D. Mikol[8], R. Lenz[8]

[1]*Geisel School of Medicine at Dartmouth, Hanover, NH, USA*
[2]*Dept of Neurology, Albert Einstein College of Medicine, Bronx, New York, USA*
[3]*Dept of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany*
[4]*Jefferson Headache Center, Thomas Jefferson University, Philadelphia, PA, USA*
[5]*Sutter Health, Walnut creek, CA, USA*
[6]*Global Biostatistical Science, Amgen Inc., Thousand Oaks, CA, USA*
[7]*Global Health Economics, Thousand Oaks, CA USA*
[8]*Global Development, Amgen Inc., Thousand Oaks, CA, USA*

Introduction and Objectives: To evaluate patient-reported outcomes in a phase 2 clinical trial of erenumab for chronic migraine (CM) (NCT02066415).

Methods: 667 adults with CM were randomized (3:2:2) to monthly subcutaneous placebo or erenumab 70 mg or 140 mg. Primary and secondary endpoints were assessed at week 12. Exploratory endpoints included: change from baseline in migraine-specific QoL measured by MSQ, headache impact measured by HIT-6, and migraine-related disability measured by MIDAS. No formal hypothesis was tested, p-values (placebo vs erenumab dose-groups) are descriptive.

Results: Baseline scores were similar between groups. Improvements were observed for all endpoints in both erenumab groups at week 12. The mean (95% CI) changes for placebo vs 70 mg and 140 mg groups, respectively, were 11.8 (9.4,14.1) vs 17.7 [(14.9,20.6), $p = 0.002$] and 19.1 [(16.3,22.0), $p < 0.001$] for MSQ role function-restrictive scores, 8.9 (6.8,11.0) vs 13.0 [(10.5,15.6), $p = 0.013$] and 13.8 [(11.3,16.4), $p = 0.003$] for MSQ role function-preventive scores, and 9.9 (7.3,12.5) vs 18.2 [(15.0,21.3), $p < 0.001$] and 18.8 [(15.6,21.9), $p < 0.001$] for MSQ emotional-function scores. Mean changes in HIT-6 scores were −3.1 (−3.9,−2.3) for placebo vs −5.6 [(−6.5,−4.6), $p < 0.001$] for both erenumab groups. Corresponding mean changes in the placebo, 70 mg, and 140 mg dose-groups were −7.5 days (−12.4,−2.7) vs −19.4 days [(−25.2, −13.6), $p = 0.002$] and −19.8 days [(−25.6, −14.0), $p = 0.001$] for MIDAS days of lost productivity, −5.2 days (−8.0,−2.4) vs −10.3 days [(−13.6,−6.9), $p = 0.023$] and −10.2 days [(−13.6, −6.8), $p = 0.024$] for MIDAS absenteeism, and −1.9 days (−4.7,0.8) vs −9.3 days [(−12.6,−6.1), $p < 0.001$] and −9.9 days [(−13.2,−6.7), $p < 0.001$] for MIDAS-presenteeism.

Conclusions: Erenumab-treated CM patients experienced consistent and clinically significant improvements in migraine-specific QoL and reductions in headache impact and disability.

Conflict of interest
Dean Leonardi, Pooja Desai, Sunfa Cheng, Dan Mikol, and Robert Lenz are employees of and own stock in Amgen Inc.

Stewart Tepper was an employee of the Cleveland Clinic during this study. For 2015–2016, he received research grants (no personal compensation) from Allergan, Amgen Inc., ATI, Avanir, ElectroCore, eNeura, Teva, and Zosano was a consultant for Acorda, Allergan, Amgen Inc., ATI, Avanir, Depomed, ElectroCore, eNeura, Impax, Kimberly-Clark, Pfizer, Scion NeuroStim, Teva, and Zosano was on Speakers' Bureau (2015 only) for Allergan, Depomed, Impax, Pernix, and Teva was on the advisory board of Alder, Allergan, Amgen Inc., ATI, Acorda, Dr. Reddy's Laboratories, Kimberly-Clark, Teva, Pfizer, and Zosano owned stock options in ATI has received salary from American Headache Society and has received royalties from University of Mississippi Press and Springer

Richard Lipton has received consultation fees, honoraria, and/or research grants from Allergan Inc., Amgen Inc., Avanir, Curelator, Dr. Reddy's Laboratories, eNeura, ElectroCore, Lilly, Teva, and Trigemina

Uwe Reuter received consulting fees, speaking/teaching fees, and/or research grants from Allergan, Amgen Inc., Autonomic Technologies, CoLucid, ElectroCore, Novartis, and Pharm-Allergan

Stephen Silberstein received consultant and/or advisory board fees from Alder Biopharmaceuticals, Allergan Inc., Amgen Inc., Avanir Pharmaceuticals, Inc., Curelator, Inc., Depomed, Dr. Reddy's Laboratories, eNeura Inc., ElectroCore Medical, LLC, Lilly USA, LLC, Supernus

Pharmaceuticals, Inc., Teva Pharmaceuticals, and Trigemina, Inc.

Walter Stewart received consultant fees from Amgen Inc. and Allergan.

EHMTC-0314
POSTER SESSION A

DOSE-RESPONSE ANALYSIS OF ONABOTULINUMTOXIN A IN CHRONIC MIGRAINE

M. Trimboli[1], A.P. Andreou[2], M. Murphy[1], A. Al-Kaisy[3], G. Lambru[2]

[1]*Guy's and St. Thomas' NHS Foundation Trust, Academic Headache Centre, London, United Kingdom*
[2]*Guy's and St. Thomas' NHS Foundation Trust & King's College London, Academic Headache Centre, London, United Kingdom*
[3]*Guy's and St. Thomas' NHS Foundation Trust, Pain Management & Neuromodulation Centre, London, United Kingdom*

Aim: To assess whether the Botulinum toxin type A (BoNT-A) follow-the-pain strategy improves clinical outcomes compared to the standard dose paradigm in chronic migraine (CM) patients treated with at least two cycles of BoNT-A.

Methods: This study is part of a broad, retrospective, real-life audit of CM patients with and without medication overuse treated with BoNT-A. Patients' diaries were used to establish the number of headache days, migraine days and headache-free days pre- and post BoNT-A treatment. Data regarding adverse events and the use of abortive medications were also collected, while disability was measured using HIT-6. Patients received a variable number of BoNT-A units, between 155 and 185U according to the PREEMPT paradigm.

Results: Out of 177 patients treated, we compared those in whom an average number of BoNT-A units between 155–160 U ($n = 46$) was administered to those in whom an average of 175–185 U ($n = 50$) of BoNT-A was administered. In both groups BoNT-A therapy significantly reduced the number of headache days, migraine days and HIT-6 compared to baseline ($P < 0.001$). The group of patients that received $\geq$175 U was not superior to the lower dose group for any of the above entries. Patients receiving higher number of BoNT-A units did not report additional side effects compared to those who received fewer units.

Conclusion: Our preliminary results showed that, in a real-life clinical setting, the follow-the-pain strategy may not offer additional benefits compared to the standard injection paradigm.

EHMTC-0316
POSTER SESSION A

INITIAL EXPERIENCE ON NON-INVASIVE VAGUS NERVE STIMULATION FOR PREVENTION OF REFRACTORY PRIMARY HEADACHES

M. Trimboli[1], A. Al-Kaisy[2], A.P. Andreou[3], M. Murphy[1], G. Lambru[3]

[1]*Guy's and St. Thomas' NHS Foundation Trust, Academic Headache Centre, London, United Kingdom*
[2]*Guy's and St. Thomas' NHS Foundation Trust, Pain Management & Neuromodulation Centre, London, United Kingdom*
[3]*Guy's and St. Thomas' NHS Foundation Trust & King's College London, Academic Headache Centre, London, United Kingdom*

Aims: To assess the efficacy of non-invasive vagus nerve stimulation (nVNS) (gammaCore®) in patients with medically refractory chronic primary headaches.

Methods: We audited our experience in 20 patients: twelve had chronic migraine (CM), seven had chronic cluster headache (CCH) and one had chronic SUNA syndrome. All patients were refractory to conventional medications. Patients were instructed to use the device daily. At three months, change in the headache days, migraine days, HIT-6, abortive medications intake and patient global impression of change (PGIC) from baseline was evaluated in the migraine group. Change in weekly attacks frequency, severity, medications intake and PGIC was evaluated in the TACs group.

Results: At three months follow-up, 3/12 CM patients (25%) reported respectively 20% (PGIC:50%), 40% (PGIC:15%) and 50% (PGIC:50%) reduction in headache days and migraine days, though the HIT-6 score improved only in one patient (from 67 at baseline to 60); 1 patient reported a 2-points reduction in average migraine severity on the VRS (PGIC:50%). Three patients continued the therapy for 1 year, though one needed further medical treatments. Two out of seven CCH (29%) reported respectively 65% and 40% average reduction in weekly CH attacks at 3 months; however only one patient continued the therapy. The SUNA patients did not benefit from nVNS.

Conclusion: Our experience suggests that nVNS may not constitute an effective preventive option in refractory chronic headache sufferers. It remains to be investigated

whether introducing the device at earlier stages of the management pathways of such patients may provide better outcomes.

EHMTC-0370
POSTER SESSION A

LONG-TERM EXPERIENCE OF ONABOTULINUMTOXINA IN A LARGE SERIES OF CHRONIC MIGRAINE PATIENTS

G. Lambru[1], M. Trimboli[2], A.P. Andreou[1], M. Murphy[2], A. Al-Kaisy[2]

[1]*Guy's and St. Thomas' NHS Foundation Trust and King's College London, Academic Headache Centre, London, United Kingdom*
[2]*Guy's and St. Thomas' NHS Foundation Trust, Academic Headache Centre, London, United Kingdom*

Aims: To describe the outcome of a large series of chronic migraine (CM) patients treated with OnabotulinumToxinA (BoNT-A) in a real-life setting since the publication of NICE guidelines.

Methods: We audited our CM patients treated with BoNT-A following the NICE criteria, between 2012 and 2016. All patients were treated according to the PREEMPT paradigm. Changes from baseline in headache days and migraine-related disability were measured using headache diaries and the Headache Impact Test (HIT-6) respectively. Patients with medication overuse (MO) were included.

Results: 178 patients (141 women, 37 men; mean age $\pm$ SD,46 $\pm$ 12 years) received at least two BoNT-A treatments. Of these, 93 patients received at least five cycles, 41 patients received at least nine cycles and ten patients at least 13 cycles. After the second treatment, 20/178 (11%) patients reported 30–49% reduction in headache days, 38/178 (21%) patients reported 50–74%, and 33/178 (19%) patients reported $\geq$75%. The proportion of patients with MO at baseline (51%) was reduced to 15% after the second treatment. At least 30% reduction in headache days was achieved by 73/93 (79%) patients at one year of treatment, by 35/41 (85%) patients after two years and by 7/10 (70 %) patients after three years. The average HIT-6 score was reduced from 69.1 at baseline to 62.8 at last visit in all patients. Sixteen percent of patients scored $\leq$55 on HIT-6 at their most recent visit.

Conclusions: Our real-life results show a sustained efficacy of BoNT-A in the majority of CM patients as well as in those with MO.

EHMTC-0239
POSTER SESSION A

BOTOX USE IN CHRONIC MIGRAINE IN SCOTLAND

A. Tyagi[1], C. Duncan[2]

[1]*Southern General Hospital, Neurology, GLASGOW, United Kingdom*
[2]*Aberdeen Royal infirmary, Neurology, Aberdeen, United Kingdom*

Background: Chronic migraine leads to a significant increase in healthcare utilization. Botox was licensed for use as a prophylactic treatment for chronic migraine in the UK in July 2010 and was recommended by NICE for use in England & Wales in June 2012. The Scottish Medicines Consortium reviewed botox treatment for chronic migraine in 2011 and 2013 and did not approve its use within nhs Scotland.

Methods: Botox treatment for chronic migraine was made available via the 'individual patient treatment request' process in Glasgow and by a specific agreement with pharmacy in Aberdeen. The threshold for the use of botox was significantly different from that advised by NICE with most patients having been tried on at least 7 oral preventive treatments.

Results: A total of 60 treatment cycles have been carried out in 29 patients over a period of 12 months since January 2015. In 13 treatment cycles the pain severity reduced by more than 50 %. In 15 treatment cycles there was no reduction in headache days or headache severity. In 42% (25/60) treatment cycles administered there was a more than 30% reduction in the number of headache days fulfilling the NICE criteria for response to treatment with botox.

Conclusions: This data is in keeping with the published literature and clinical experience in the UK with significant improvement in headache frequency and severity in patients with chronic migraine. This treatment should be made available routinely on the nhs to chronic migraineurs living in Scotland.

Conflict of interest
Disclosure statement:
I have attended advisory board meetings and conducted injector training workshops for Allergan. I have also received a research grant from Allergan.

EHMTC-0277
POSTER SESSION B

INHIBITION OF AMPA RECEPTOR REDUCED NEURONAL NITRIC OXIDE SYNTHASE EXPRESSION IN SPREADING DEPRESSION

A. Karimi Goudarzi[1], M. Ahmadi[2], B. Khodaie[2], A. Lotfinia[2]

[1]*Islamic Azad University, Physiology, Tehran, Iran*
[2]*Islamic Azad University, Neuroscience, Tehran, Iran*

Cortical spreading depression (CSD) has been implicated in migraine and as a headache trigger. Microglia and astrocytes are transformed into reactive glia (RG) by CSD and normal function. nitric oxide (NO), as intercellular mediators, may altered in CSD condition. Neuronal nitric oxide synthase (nNOS) expression is induced in neocortical astrocytes after CSD waves. Glutamate (specially AMAP receptors) had critical roles to introduced CSD. The aim of this present study is role of AMPA receptors in alternation of nNOS expression in hippocampus after CSD induction. SD induction was performed by KCl in rat brain. Following SD elicitation DNQX antagonist of (1,1.5, and 2 mg/kg) in different rat groups were administrated to investigate their possible role on glutamatergic receptors. In SD induced EEG continually was recorded from the cortex. nNOS of frontal cortex gene 25 rats were measured in parallel by competitive quantitative and TaqMan real-time RT-PCR. nNOS mRNA were determined by real-time PCR. Our results showed a linear relationship between competitive quantitative and real-time RT-PCR measurements of nNOS (P value = 0.87). This study results indicated dose dependent relationship between nNOS gene expression and AMPA antagonist.

EHMTC-0175
POSTER SESSION B

INTACT BLOOD-BRAIN BARRIER DURING ATTACKS OF MIGRAINE WITHOUT AURA: A 3T DCE-MRI STUDY

F.M. Amin[1], A. Hougaard[1], S.P. Cramer[2], C.E. Christensen[1], F. Wolfram[3], H.B.W. Larsson[2], M. Ashina[1]

[1]*Danish Headache Center, Department of Neurology, Glostrup, Denmark*
[2]*Functional Imaging Unit, Dept. of Clinical Physiology-Nuclear Medicine and PET, Glostrup, Denmark*
[3]*Department of Radiology, Department of Radiology, Glostrup, Denmark*

Objective: To investigate blood-brain barrier (BBB) permeability during spontaneous attacks of migraine without aura.

Methods: We recruited 74 patients suffering from migraine without aura to participate in this cross-sectional dynamic contrast-enhance magnetic resonance imaging (DCE-MRI) study. The patients were instructed to report at the hospital for DCE-MRI scan during and outside of a spontaneous migraine attack. Primary endpoint was a difference in the BBB permeability (mL/100 g/min) between the attack and the headache-free days. The permeability was assessed in five different regions of interest (ROI) located in the anterior (ACA), middle (MCA) and posterior (PCA) cerebral region, brain stem (BS), and brain hemisphere (BH). We used the paired samples t-test to compare K_i (permeability) values between the attack and attack-free days.

Results: Nineteen patients completed the study. We found no change in the mean BBB permeability between the attack (ACA: 0.095; MCA: 0.077; PCA: 0.108; BS: 0.096; BH: 0.138 mL/100g/min) and the attack-free (ACA: 0.072; MCA: 0.076; PCA: 0.096; BS: 0.087; BH: 0.122 mL/100g/min) days (ACA: $p = 0.052$; MCA: $p = 0.915$; PCA: $p = 0.278$; BS: $p = 0.353$; BH: $p = 0.213$). We found no relationship between the pain side and BBB permeability in 15 patients with unilateral pain during the examined attack.

Interpretation: We demonstrated that the BBB permeability during spontaneous migraine attacks without aura is intact. Our findings suggest that most of current and future anti-migraine drugs are likely to exert their effects outside of the BBB.

EHMTC-0297
POSTER SESSION B

MRI IMAGING POST-PROCESSING REVEALS CORTICAL MORPHOMETRIC DIFFERENCES BETWEEN PATIENTS WITH MIGRAINE AND HEALTHY CONTROLS

R. belvis[1], G. Garcia-Marti[2], N. Mas[1], A. Aceituno[1], I. Ormazabal[3], R. Sanz[2], R. Ramos[3]

[1]*DEXEUS UNIVERSITY HOSPITAL, NEUROLOGY, Barcelona, Spain*
[2]*Quiron Hospital. Valencia, R&D Biomedical Engineering, Valencia, Spain*
[3]*DEXEUS UNIVERSITY HOSPITAL, RADIOLOGY, Barcelona, Spain*

Studies with small sample sizes have compared migraine patients with healthy controls-HC with different MRI post-processing techniques, showing heterogeneous results in the analysis of the cortex. In this work, we apply two complementary post-processing techniques to determine

whether subtle cortical tissue differences between groups exist.

We included patients with episodic migraine with aura-MA, without aura-M0A, and chronic-CM; and HC without any painful pathology. All patients presented a normal brain MRI without migraine pain in the previous 72 hours. All subjects were explored with a 1.5T magnet (Signa,General Electric) with a high-resolution T13D gradient-echo sequence. We analyse the cortical thickness distribution with the Freesurfer tool and grey matter density differences with a Voxel-Based Morphometry (VBM) approach, using the SPM package.

We have included 80 patients (24-MA, 49-M0A, 7-CM) and 16 HC. The groups were homogeneous with respect to age and years of migraine evolution. A reduction in cortical thickness in migraine patients facing the HC only was found in the precentral gyrus ($p < 0.005$). The VBM technique detected a significant reduction in neuronal density in grey matter in the group migraine front of HC in the same circumvolution ($p < 0.005$). Additionally, the precentral region showed a negative correlation with years of migraine evolution in the group of patients (to more years of evolution, less cortical thickness) ($p < 0.005$).

The precentral area appears as a differential region between patients with migraine and controls, simultaneously showing less cortical thickness and fewer neuronal density in grey matter in patients. These changes are negatively correlated with years of evolution.

EHMTC-0014
POSTER SESSION B

PROSTAGLANDINS AND NOT SUBSTANCE P INVOLVED IN TRPA1 INDUCED VASODILATATION IN HEALTHY VOLUNTEERS

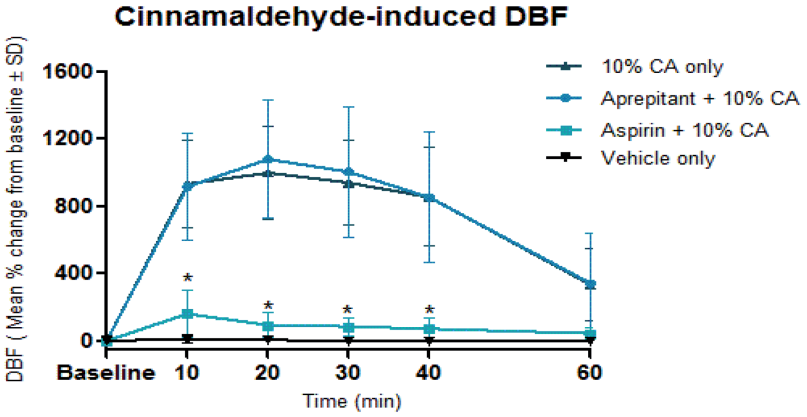
L. Buntinx[1], J. Vandendriessche[1], L. Chang[1], B. Morlion[2]

[1]*Catholic University of Leuven, Center for Clinical Pharmacology, Leuven, Belgium*
[2]*Catholic University of Leuven, Leuven Center for Algology, Leuven, Belgium*

Background: TRPA1 is an emerging target for anti-migraine drugs. TRPA1 activation by cinnamaldehyde (CA) is thought to result in vasodilatation via the release of pro-inflammatory neuropeptides, prostaglandins (PGs) and substance P (SP). This study investigates the role of PGs and SP in CA-induced dermal blood flow (DBF) in healthy volunteers.

Methods: This study is a randomized, cross-over study in 13 healthy males. Volunteers were not allowed to take medication, caffeine and alcohol. CA (10%) and its vehicle are applied topically on the volar surface of the forearm at screening visit and the 2 following study visits. During the study visits, aspirin (1 g, non-selective, irreversible COX-inhibitor) or aprepitant (375 mg, NK1-antagonist) were administered orally with a wash-out period of 14 days. CA-induced DBF was assessed using laser Doppler imaging (LDI) at baseline and after 10, 20, 30, 40 and 60 minutes.

Results & Discussion: 10% CA induced a >100% increase in DBF in all volunteers at screening. Aprepitant



The CA-induced DBF at screening (10% CA only) and after aprepitant intake was significantly different compared with the CA-induced DBF after aspirin intake and the vehicle-induced DBF (0% CA) at 10, 20, 30 and 40 min, expressed as % change from baseline. The CA-induced DBF response after aspirin intake was not different from the vehicle-induced DBF (0% CA), idem for the DBF to 10% CA only and after aprepitant intake.
*Kruskal-Wallis with post-hoc Bonferroni: $p<0.05$ between aprepitant + 10% CA and aspirin + 10% CA, between aprepitant + 10% CA and vehicle only, between 10% CA only and aspirin + 10% CA and between 10% CA only and vehicle only. Data are presented as mean± standard deviation (SD).

(EHMTC-0014)

was not able to block the CA-induced DBF in contrast to aspirin, which almost completely blocked the DBF response (see figure). Therefore, in healthy volunteers, PGs play an important role in CA-induced DBF. Interestingly, in mice, indomethacin (non-selective, reversible COX-inhibitor) was not able to block CA-induced DBF[1]. This makes us hypothesize whether CA-induced DBF is species-specific (mice versus human) or drug-specific (aspirin versus indomethacin)?

Reference

1. Aubdool AA and Brain SD. Neurovascular aspects of skin neurogenic inflammation. *J Investig Dermatol Symp Proc* Dec 2011; 15(1): 33–39.

EHMTC-0385
POSTER SESSION B

DEVELOPMENT OF A TARGET ENGAGEMENT BIOMARKER FOR THE PAC1-RECEPTOR IN HUMANS

L. Buntinx[1], M. Depré[1], E. Ampe[1], A. Van Hecken[1], G. Vargas[2], K. Gabriel[2], S. Sands[2], J. de Hoon[1]

[1]*Catholic University of Leuven, Center for Clinical Pharmacology, Leuven, Belgium*
[2]*Amgen, Inc., Thousand Oaks, USA*

Background: Maxadilan, isolated from the sand fly *Lutzomyia longipalpis*, is a potent vasodilator peptide which activates the mammalian PAC_1 receptor. Therefore, maxadilan has been proposed as a target-engagement tool to study PAC_1 antagonists.

Objectives: (1) To determine, as a first in man study, the dose response, safety and time course of the dermal blood flow (DBF) after intradermal (ID) injections of maxadilan in the human forearm and (2) to assess the inter-arm and inter-period reproducibility of this response, as measured with Laser Doppler Imaging (LDI).

Results: Maxadilan was found to be safe based on AE reporting, ECG, vital signs, physical examination and safety laboratory assessments. ID maxadilan (0.9, 3 and 10 ng) produced a robust increase in DBF compared to baseline and placebo. Forearm DBF response to 0.9 ng ID injections of maxadilan in healthy male volunteers was reproducible between periods (Concordance correlation coefficient (CCC) > 0.7) and between arms (CCC > 0.7) when data were calculated as $AUC_{0-180min}$ (perfusion units*min). An increase in DBF was observed from 5 minutes until 72 hours after maxadilan injection compared to baseline and placebo. Sixty minutes after ID maxadilan, DBF response was stable and reached a plateau-phase. Sample size calculations based on maxadilan-induced DBF responses show that samples of approximately 10 subjects are sufficient to detect a 50% difference between 2 independent groups with 80% power.

Conclusion: As intradermal injections of maxadilan induce reproducible changes in dermal blood flow, it is an attractive target-engagement biomarker for the study of PAC1 receptor antagonists in early clinical development studies.

Conflict of interest
Disclosure statement:
This project was supported by a grant from Amgen Inc.

EHMTC-0172
POSTER SESSION B

STRUCTURAL ALTERATIONS OF THE BRAINSTEM IN MIGRAINE

C. Chong[1], J. Plasencia[2], D. Frakes[3], T. Schwedt[1]

[1]*Mayo Clinic, Neurology, Phoenix, USA*
[2]*Arizona State University, School of Biological and Health Systems Engineering, Phoenix, USA*
[3]*Arizona State University, School of Electrical- Computer and Energy Engineering, Phoenix, USA*

Introduction: Atypical brainstem modulation of pain might play an integral role in the altered sensory processing typical of migraine. The objective of this study was to investigate whether migraine is associated with brainstem structural alterations that correlate with this altered pain processing.

Methods: MRI T1-weighted images of 55 interictal migraine patients and 58 healthy controls were used to: 1) create deformable mesh models of the brainstem that allow for shape analyses; 2) calculate volumes of the midbrain, pons, medulla and the superior cerebellar peduncles.

Results: Migraineurs had smaller midbrain volumes (migraineurs $= 58.80 mm^3$, SD $= 6.64$ healthy controls $61.28\,mm^3$, SD $= 5.98$; $p = 0.038$) and significant inward deformation in the ventral midbrain and pons and outward deformations in the lateral medulla relative to healthy controls *(Figure 1)*. For migraineurs, there was a significant negative correlation between allodynia symptom scores during headache with midbrain volume ($r = -0.32$; $p = 0.019$) and a significant *positive* correlation between cutaneous heat pain thresholds with medulla ($r = 0.337$; $p = 0.012$) and cerebellar peduncle volumes ($r = 0.435$; $p = 0.001$).

Discussion: Migraineurs with greater symptoms of allodynia have smaller midbrain volumes and migraineurs with

lower heat pain thresholds have less volume in the medulla and the cerebellar peduncles. Results suggest that brainstem structure might reflect severity of allodynia and hypersensitivity to pain in migraine and support the notion that the brainstem plays an important role in altered sensory processing in migraine.

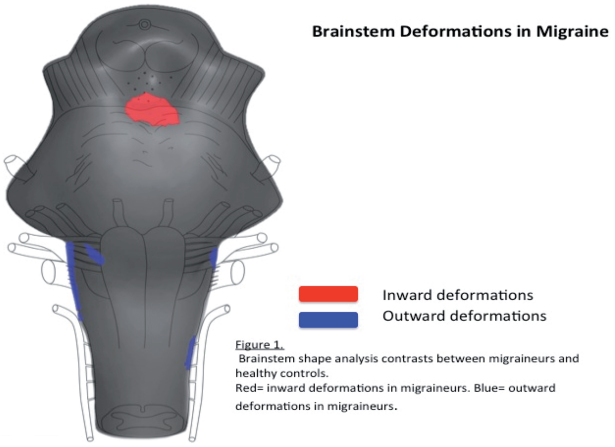


Figure 1.
Brainstem shape analysis contrasts between migraineurs and healthy controls.
Red= inward deformations in migraineurs. Blue= outward deformations in migraineurs.

EHMTC-0405
POSTER SESSION B

LOW 5-HT1B RECEPTOR BINDING IN THE MIGRAINE BRAIN: A PET STUDY

M. Deen[1,2,3], H.D. Hansen[3], A. Hougaard[1], S. da Cunha Bang[2,3], M. Nørgaard[3], C. Svarer[3], S.H. Keller[4], C. Thomsen[5], M. Ashina[1,2], G.M. Knudsen[2,3]

[1]*Danish Headache Center, Department of Neurology-Rigshospitalet, Glostrup, Denmark*
[2]*Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*
[3]*Neurobiology Research Unit and Center for Experimental Medicine Neuropharmacology, Department of Neurology-Rigshospitalet, Copenhagen, Denmark*
[4]*PET and Cyclotron Unit, Rigshospitalet, Copenhagen, Denmark*
[5]*Department of Radiology, Rigshospitalet, Copenhagen, Denmark*

Background: Serotonin 1B (5-HT_{1B}) receptors contribute to the anti-migraine effect of triptans. To date, no study has investigated *in vivo* cerebral 5-HT_{1B} receptor binding in migraine patients.

Aim: To examine the cerebral 5-HT_{1B} receptor binding in migraine patients without aura and compare it to controls.

Methods: 16 controls and 18 migraine patients outside of migraine attacks were examined with positron emission tomography (PET) and [^{11}C]AZ10419369 for quantification of cerebral 5-HT_{1B} receptor binding. Patients who reported migraine attacks <48 hours after the scan were excluded, leaving 14 migraine patients for the final analysis. The 5-HT_{1B} receptor binding was assessed in predefined regions of interest involved in pain modulation.

Results: Patients had lower 5-HT_{1B} receptor binding in the regions of interest compared to controls ($p = 0.04$). In a whole-brain voxel-based analysis, we found that duration since last migraine attack correlated positively with 5-HT_{1B} receptor binding in the dorsal raphe and in the midbrain.

Conclusion: Outside attacks, migraine patients have low cerebral 5-HT_{1B} receptor binding in regions involved in emotional and cognitive aspects of pain. Further investigations are needed to determine whether these changes are migraine-specific or related to repeated activation of pain modulating areas.

EHMTC-0183
POSTER SESSION B

ROLE OF ADIPOCYTOKINES IN MIGRAINE CHRONIFICATION. A CROSS-SECTIONAL STUDY

C. Dominguez Vivero[1], A. Vieites-Prado[1], M. Pérez-Mato[1], T. Sobrino[1], X. Rodríguez-Osorio[1], A. López[1], F. Campos[1], F. Martínez[1], J. Castillo[1], R. Leira[1]

[1]*Health Research Institute of Santiago IDIS/SERGAS, Department of Neurology. Clinical Neurosciences Research Laboratory., Santiago de Compostela, Spain*

Background: Several studies have shown that obesity constitutes a risk factor for migraine chronification. However mechanisms that underlie this association remain unclear. Fat tissue releases different proinflammatory and inflammatory mediators, including adipocytokines, involved in migraine pathophysiology.

Aim: The aim of this study is to analyse the association between serum adipocytokine levels and biochemical parameters related with inflammation and migraine chronification.

Methods: We selected a group of episodic and chronic migraine patients (IHS 2013) and healthy controls. We calculated body mass index (BMI). Levels of adipocytokines (leptin and adiponectin), interleukin 6 (IL-6), interleukin 10 (IL-10), tumor necrosis factor α (TNF-α), high-sensitivity C-reactive protein (hs-CRP), pentraxin 3 (PTX3) and soluble TNF-like weak inducer of apoptosis (sTWEAK) were measured in peripheral blood.

Results: One hundred and eleven patients (mean age 39.7 years, 93.7% female) and twenty-four healthy controls (mean age 35.9 years, 90% female) were included. Leptin and adiponectin serum levels were higher in migraine patients compared to controls ($15.2 + 10.5$ *vs.* $3.1 + 0.9$ ng/mL; $p < 0.0001$ and $72.3 + 38.5$ *vs.* $37.7 + 16.4$ μg/mL; $p < 0.0001$), and in chronic compared to episodic migraine patients ($15.5 + 9.7$ *vs.* $10.8 + 6.0$ ng/mL; $p < 0.0001$ and $65.8 + 42.9$ *vs.* $33.2 + 31.0$ μg/mL; $p < 0.0001$). Leptin and adiponectin serum levels were correlated with BMI ($r = 0.445$; $p < 0.0001$ and $r = -0.281$; $p < 0.0001$). Leptin levels were correlated with levels of IL6 ($r = 0.498$; $p < 0.0001$), TNF-α ($r = 0.389$; $p < 0.001$) and hs-CRP ($r = 0.422$; $p < 0.0001$).

Conclusions: Our findings suggest that adipocytokines could play a role in migraine chronification. This relation may be mediated by persistent systemic and neurogenic inflammation.

Conflict of interest
Disclosure statement:
This project has been partially supported by grants from the Spanish Ministry of Economy and Competitiveness-Instituto de Salud Carlos III (PI12/00532 PI13/00292 PI14/01879 PI15/01578).

EHMTC-0355
POSTER SESSION B

BRAINSTEM ACTIVATION, BUT NO BLOOD-BRAIN BARRIER DISRUPTION, DURING ATTACKS OF MIGRAINE WITH AURA: A DYNAMIC CONTRAST-ENHANCED MRI STUDY

A. Hougaard[1], F.M. Amin[1], C.E. Christensen[1], S. Younis[1], F. Wolfram[2], S.P. Cramer[3], H.B. Larsson[3], M. Ashina[1]

[1]*Rigshospitalet Glostrup- University of Copenhagen, Danish Headache Center & Department of Neurology, Copenhagen, Denmark*
[2]*Rigshospitalet Glostrup, Department of Radiology, Copenhagen, Denmark*
[3]*Rigshospitalet Glostrup- University of Copenhagen, Functional Imaging Unit- Department of Clinical Physiology-Nuclear Medicine and PET, Copenhagen, Denmark*

Background: The relation between the intense cortical disturbances of the migraine aura and the subsequent disabling migraine headache is not understood. Animal studies suggest that migraine aura triggers pain through disruption of the blood-brain barrier causing activation of trigeminal nociceptors and brainstem nuclei. We aimed to test this hypothesis in patients by measuring blood-brain barrier permeability and brain perfusion in the course of spontaneous attacks of migraine with aura.

Methods: We used a sensitive and validated technique of dynamic contrast-enhanced high-field MRI to simultaneously investigate blood-brain barrier permeability and brain perfusion in the pons, visual cortex, and areas of the anterior, middle and posterior cerebral circulation. Patients reported to our institution to undergo MRI after presenting with typical visual aura and subsequent headache.

Findings: Nineteen patients were scanned during attacks and on an attack-free day. The mean time from attack onset to scanning was 7·6 hours. We found no increase in blood-brain barrier permeability in any of the investigated regions. Brainstem perfusion increased bilaterally during attacks (mean increase from 18·1 to 21·2 ml/100g/min, $P = 0{\cdot}04$). Perfusion also increased in the visual cortex and posterior white matter of the affected hemispheres.

Interpretation: The blood-brain barrier remains intact during attacks of migraine with aura, indicating no facilitation of anti-migraine drug access to the CNS during attacks. Intrinsic brain activity during migraine aura may trigger central pain pathways as suggested by preclinical data.

EHMTC-0196
POSTER SESSION B

MORPHOLOGICAL EVALUATION IN PATIENTS WITH CHRONIC MIGRAINE USING VOXEL-BASED MORPHOMETRY

N. Imai[1]

[1]*Japanese Red Cross Shizuoka Hospital, Shizuoka, Japan*

Background: Voxel-based morphometry (VBM) is a powerful analytical tool that enables semi-quantitative, unbiased evaluation of morphological data from MR images. Recently, many VBM studies suggested that migraine might be associated with subtle brain lesions. We evaluated the differences of global or focal gray or white matter alterations between episodic and chronic migraine patients using VBM.

Methods: Twenty-three episodic migraine right-handed patients and 7 chronic migraine patients were selected for the study. All patients fulfilled the International Headache Society criteria for episodic migraine or chronic migraine. MRI scans were analyzed with MATLAB R2015b and SPM12 software, using VBM method.

Results: In comparison with episodic migraineurs, chronic migraineurs showed significant gray matter decrease in the left Inferior parietal lobule (probability for area 2), left inferior frontal gyrus (area45), right angular gyurus and left temporal pole as well as significant gray matter increase in the right fusiform gyrus, left superior frontal, left inferior parietal lobule (area hIP1) and right angular gyrus.

Conclusions: These morphometric gray matter changes between episodic and chronic migraine suggest that abnormal structural changes may be an important mechanism of migraine chronification. Complicated changes of left inferior parietal lobule and right angular gyrus may reflect complicated mechanism of migraine chronification.

EHMTC-0139
POSTER SESSION B

THE DEVELOPMENT AND VALIDATION OF HIGH SENSITIVITY CGRP ASSAYS USING MESO SCALE DISCOVERY AND QUANTERIX PLATFORMS

K. Johnson[1], X. Chai[2], J. Xu[2], T. Pottanat[3], R. Osborne[3], K. Cox[4], R. Benschop[4], J. Dage[2], K. Merchant[5], L. Adams[6], J. Talbot[6], B. Miller[6]

[1]*Eli Lilly and Company, Pain Migraine, Indianapolis, USA*
[2]*Eli Lilly and Company, TTx Neuroscience, Indianapolis-Indiana, USA*
[3]*Eli Lilly and Company, LEM-Tailored Therapeutics, Indianapolis- Indiana, USA*
[4]*Eli Lilly and Company, TTx Autoimmune, Indianapolis-Indiana, USA*
[5]*Trans Thera Consulting Company, Trans Thera, Indianapolis, USA*
[6]*Eli Lilly and Company, Neuroscience Tailoring, Indianapolis-Indiana, USA*

Calcitonin gene-related peptide (CGRP) is widely expressed in the CNS and PNS and is implicated in the pathophysiology of migraine. A CGRP monoclonal antibody is being developed for migraine prevention. As a biomarker for neurogenic inflammation, detecting changes in circulating levels of CGRP could facilitate monitoring disease progression and development of efficacious preventive drugs. Here we developed a high sensitivity CGRP assay in both Meso Scale Discovery (MSD) and Quanterix to quantitatively measure plasma CGRP. The CGRP MSD assay was developed using a biotin-labeled anti-CGRP A1 capture antibody and a Sulfo-Tag labeled anti-CGRP A2 detection antibody in a Streptavidin MSD small plot plate. The assay was validated through dilutional linearity, spike recovery and immunodepletion. The CGRP Quanterix assay was developed using the 3-step protocol from the SiMoA Homebrew kit. An anti-CGRP A3 antibody conjugated to activated paramagnetic beads was used at the capture antibody. A detection antibody anti-CGRP A2 was biotinylated. The CGRP MSD assay demonstrated a high sensitivity with a low limit of quantification (LLOQ) of 0.8 pg/ml in P100 plasma. It also showed good dilutional linearity and good spike and recovery. The assay demonstrated high specificity in the immunodepletion assay. The P100 plasma CGRP levels in healthy subjects ranged from 0.53–0.87 pg/ml utilizing the MSD assay. The Quanterix assay demonstrated a sensitivity of 0.02 pg/ml with good dilutional linearity in plasma. The plasma CGRP levels measured by Quanterix assay are highly correlated with those measured by MSD CGRP assay.

Conflict of interest
Disclosure statement:
Full-time employee and stockholder, Eli Lilly and Company

EHMTC-0044
POSTER SESSION B

THE PHENOTYPE OF PREMONITORY SYMPTOMS AND MIGRAINE HEADACHE TRIGGERED WITH NITROGLYCERIN

N. Karsan[1], P. Bose[1], P.J. Goadsby[1]

[1]*King's College London, Headache Group- Basic and Clinical Neuroscience- Institute of Psychology- Psychiatry and Neuroscience and NIHR-Wellcome Trust King's Clinical Research Facility, London, United Kingdom*

The migraine attack starts hours to days before pain onset. Given capturing this early stage during spontaneous attacks is challenging, triggered attacks offer insights into this phase of migraine.

Subjects ($n = 30$) with migraine and without aura who reported premonitory symptomatology during spontaneous attacks were screened and recruited following informed consent. Each subject was exposed to a 0.5 mcg/kg/min nitroglycerin infusion over 20 minutes. Symptoms and timelines to development of premonitory and headache phases were recorded.

Thirty (100 %) of subjects developed NTG-related headache 1–10 minutes into the infusion. Twenty-nine (97%) subjects developed premonitory symptoms 4–136 minutes after the infusion start (mean 35 minutes). Twenty-five (83 %) subjects developed a migraine headache within 4.5 hours of infusion (range 21–278 minutes after the infusion start, mean 104 minutes). All twenty-five responded within 2 hours of 1 g intravenous aspirin or 6 mg subcutaneous sumatriptan. Typical aura was triggered in four (13 %) subjects, and 'Alice in Wonderland' syndrome in two (7 %).

The commonest premonitory symptoms were tiredness in twenty-two (73 %), photophobia in twenty-one (70 %) and concentration difficulty in eighteen (60 %). Three subjects reported one premonitory symptom (10 %) and twenty--seven subjects reported three or more symptoms (90 %). Common migraine symptoms were photophobia, phonophobia and neck discomfort. At least one cranial autonomic symptom was triggered in 47 %; the most common were a sensation of throat swelling and aural fullness.

We demonstrate that NTG effectively triggers migraine premonitory symptoms even without headache, and can trigger cranial autonomic symptoms.

EHMTC-0065
POSTER SESSION B

THE TRIGGERING OF VERTIGO AND CRANIAL ALLODYNIA IN MIGRAINEURS WITH NITROGLYCERIN

N. Karsan[1], P. Bose[1], P.J. Goadsby[1]

[1]*King's College London, Headache Group- Basic and Clinical Neuroscience- Institute of Psychiatry- Psychology and Neuroscience and NIHR-Wellcome Trust Kings Clinical Research Facility- Kings College London, London, United Kingdom*

It is well known that nitroglycerin can effectively trigger migraine attacks in migraineurs. The associated non-pain features of an attack can also be triggered, such as premonitory symptomatology. However, it is not clear as to whether associated symptoms such as vertigo and allodynia can be triggered by nitroglycerin in humans.

Subjects ($n = 30$) with migraine and without aura were screened and recruited following informed consent. Each subject was exposed to a 0.5 mcg/kg/min nitroglycerin infusion over 20 minutes. Symptom development from baseline through the infusion and to 4.5 hours post infusion was recorded.

Twenty-nine (97%) subjects developed premonitory symptoms 4–136 minutes after the infusion start (mean 35 minutes). Twenty-five (83 %) subjects developed a migraine headache within 4.5 hours of infusion (range 21–278 minutes after the infusion start, mean 104 minutes). Twelve subjects reported a history of cranial allodynia (40%) and this was triggered in seven (58%), and another three subjects (27%) who did not usually report allodynia during spontaneous attacks reported it after nitroglycerin triggering. Eleven subjects (37%) reported vertigo during spontaneous attacks and four of these (36%) reported similar symptoms after triggering. Vertigo was not triggered in any other subjects.

We demonstrate that NTG can trigger associated migraine symptoms, such as vertigo and allodynia. Allodynia seems to be able to be triggered in those who report it and those who do not during spontaneous attacks, whereas the vertigo was only reported in those with a history of it.

EHMTC-0091
POSTER SESSION B

REVERSIBLE CEREBRAL VASOCONSTRICTION (RCV) IN FAMILIAR HEMIPLEGIC MIGRAINE HEADACHES (FHMH) IN CHILDREN AND ADULT PATIENTS

N. Khizanishvili[1,2], M. Beridze[2], M. Alpaidze[3], T. Kherkheulidze[4], N. Kvirkvelia[2]

[1]*Archangel St Michael multiprofile clinical hospital, Department of Neurology, Tbilisi, Georgia*
[2]*Tbilisi State Medical University, Neurology, Tbilisi, Georgia*
[3]*Tbilisi State Medical University, Neurology, Neurology, Georgia*
[4]*Tbilisi State Medical University, Neurosurgery, Tbilisi, Georgia*

Purpose: Detection and Evaluation of sonographic and MRI characteristics of Familiar Hemiplegic Migraine Headaches (FHMH) in children and adult patients.

Patients and Methods: Totally 64 migraine patients (34 children: 20 male, 14 female; 30 adults: 18 female, 12 male) aged 11 to 60 years, with 1–3 attacks per month had been investigated. Control consisted with 16 healthy individuals. Patients investigated neurologically, brain contrast MRI (1.5 Tesla) was made in ictal period, the ultrasound investigations were made during 1 year: patients were researched 2 times per month during FHMH attack and interictal period. Controls researched 1 time after year. Sonography examinations performed using Transcranial Dopplerography (TCD) and Transcranial Color-Coded Duplex Sonography (TCCD) methods. Data were calculated by nonparametric Binomial test.

Results: Brain MRI showed lacunar ischaemic foci in parietal or occipital lobes in 37.5% of FHMH patients. Vasospasm was revealed during and after headache attacks in 54.69% of patients. The mean flow velocity (MFV) in carotid siphons' (CS) was 73.7 ± 11.6 cm/sec, MFV in middle cerebral arteries' (MCA) amounted 114.8 ± 23.5 cm/sec, MFV in anterior cerebral arteries' (ACA) 100.2 ± 13.6, MVF in Basilar Artery(BA) 73.8 ± 15.4, averaged Lindegaard Index (LI) was 2.8 ± 0.7 and revealed

vasospasm as compared to controls: MFV (MCA) amounted 61.9 ± 8.7 cm/sec, LI (2.3 ± 0.2), $p < 0.001$; The MCA was involved in 15.63%, the ACA-in 14.06%, the PCA-in 31.25% and the BAS-in 43.75% of FHMH patients. Positive correlation was found between the site and side of pain, pain intensity and hemiplegia ($r = +0.27$' $p < 0.05$).

Conclusion: The RCV in FHMH is more determined to posterior circulation.

EHMTC-0345
POSTER SESSION B

MIGRAINE AND COMORBID NECK PAIN

A. Zenkevich[1], E. Filatova[1], N. Latysheva[1]

[1]*I.M. Sechenov First Moscow State Medical University, Neurology, Moscow, Russia*

Objective: Neck pain and migraine are among the most common disorders of the nervous system. Relatively little is known about mechanisms of their comorbidity. We analyzed the prevalence and clinical structure of neck pain in migraine to study possible mechanisms of their comorbidity.

Methods: We recruited 103 migraine patients, defined by ICHD – 3rd edition (beta version): 63 with chronic migraine (CM) and 40 – with episodic migraine (EM). The presence of chronic neck pain was assessed with a questionnaire. Neck muscle tenderness was examined by manual palpation and assessed with the Jensen tenderness score.

Results: Prevalence of chronic neck pain was 33.5 % in the whole migraine population. In the rare EM group (<4 headache (HA) days/month) it was 9.1% vs. 45.34% in the frequent EM (5–14 HA days/month) plus CM group ($p = 0.001$). The total tenderness score was also higher in patients with frequent EM + CM group comparing to rare EM: 9.07 ± 4.6 vs. 2.5 ± 2.4 ($p = 0.00$). The HIT-6 disability index was 61 ± 6 vs. 56 ± 8 in the frequent EM + CM and rare EM patients, correspondingly ($p = 0.0004$). In patients with unilateral HA no correlation was observed between the side of migraine and neck pain.

Conclusion: Neck pain is highly prevalent in CM patients, with its prevalence exceeding that in the general population. The high tenderness score in CM may reflect a cause of peripheral and/or a consequence of central sensitization and antinociceptive dysfunction in trigeminal nociceptive pathways.

EHMTC-0302
POSTER SESSION B

HABITUATION IN SUB-COMPONENTS OF VISUAL EVOKED POTENTIALS: A SHORT-TIME FOURIER TRANSFORM ANALYSIS IN HEALTHY AND MIGRAINE SUBJECTS.

M. Lisicki[1], K. D'Ostilio[1], R. Nonis[1], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit, University Department of Neurology- CHR Citadelle, Liege, Belgium*

Background: Deficient habituation of visual evoked potentials (VEP) is a reproducible neurophysiological finding in migraine patients between attacks. Knowing which VEP sub-components have this abnormality might help identifying pathophysiological mechanisms and their localization within the visual pathways.

Objective: Our purpose was to isolate the VEP sub-components using short time Fourier transform (STFT), and to analyze their change in power during prolonged stimulation.

Subjects and Methods: We analyzed 6 sequential blocks of 100 pattern-reversal VEPs during uninterrupted stimulation in 30 migraineurs (MO) and 30 healthy volunteers (HV). We selected the subjects such that half of them in each group had deficient N1-P1 habituation between the last and the first block. Using STFT we identified four main sub-components in accordance with published data: C1, early P1, late P1 and N150; their power was compared with VEP amplitudes.

Results: Power of log-transformed C1, early P1 and late P1 together predicted N1-P1 amplitude (multiple linear regression $p < 0.001$). N1-P1 first block amplitude was significantly smaller in subjects with deficient habituation ($p = 0.009$), which could be accounted for by power of the late P1 subcomponent ($p = 0.041$). Subjects with normal habituation showed a significant reduction in the power of late P1 between the 1st and the 6th block ($p = 0.026$), whereas in MO the power of C1 increased across blocks compared to HV ($p = 0.036$).

Conclusion: STFT allows to distinguish 4 VEP sub-components. The habituation process seems to involve C1 and late P1 components. In MO, uncompensated power augmentation of the C1 component could be responsible of the habituation deficit.

EHMTC-0126
POSTER SESSION B

A MACHINE-LEARNING CLASSIFIER FOR EPISODIC MIGRAINE BASED ON VISUAL EVOKED GAMMA BAND ACTIVITY

K. D'Ostilio[1], M. Lisicki[1], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit, University Department of Neurology CHR, Liege, Belgium*

Introduction: Objective and reliable biomarkers of migraine may be of interest for diagnosis and research purposes. Neuroimaging-based machine-learning classifiers are promising but hampered by availability and cost issues. Conversely, evoked potential are of easy access and affordable. They have provided increasing evidence that sensory information processing is impaired in migraine. We have used gamma band oscillations (GBOs) of visual evoked potentials (VEPs) to compute a machine-learning neural network classifier in episodic migraine.

Materials and methods: We analyzed GBOs from VEPs (6x100 responses). Recordings were performed in two matched samples: a training sample composed of 43 migraine patients (EM) and 20 healthy volunteers (HV) and a validating sample of 18 EM and 10 HV. A logistic regression model of the training sample was performed to evaluate the relevance of the predictor variables. Ten neural networks were automatically generated based on late component frequency, n3-p4 and p4-n4 slopes, 1st block n1-p2 amplitude and age.

Results: The logistic regression model of the training sample reached a significant classification rate of 79% (EM: 88%; HV: 60%, $p = 0.002$). The best neural network was able to classify the groups with an accuracy of 73% in the training phase and 89% in the subsequent validation (success rate HV: 90%; EM: 88%). The mean global accuracy within the training and validating samples were 69% (63–78%) and 84% (82–89%).

Conclusions: This machine-learning neural network classifier based on visual GBOs provides an accurate and cost-efficient tool for objective migraine diagnosis. Further training and validation studies with new cohorts are warranted.

EHMTC-0136
POSTER SESSION B

NON-INVASIVE CERVICAL VAGUS NERVE STIMULATION: IS THERE ELECTROPHYSIOLOGICAL EVIDENCE FOR GENUINE VAGAL AFFERENTS ACTIVATION?

R. Nonis[1], K. D'Ostilio[1], M. Lisicki[1], S. Sava[1], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit, University Department of Neurology- CHR Citadelle, Liege, Belgium*

Background: Animal experiments suggest that non-invasive cervical vagus nerve stimulation (nVNS) acts via activation of vagal sensory afferents, but proof in humans is lacking.

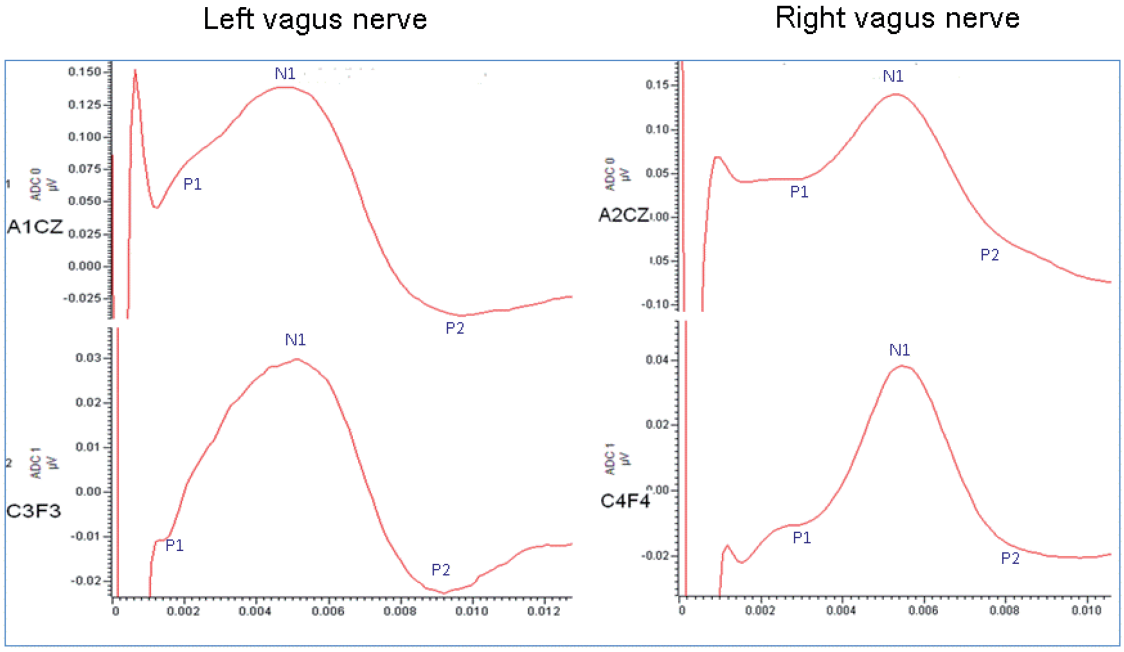
Objective: To search for reliable vagus nerve somatosensory evoked potentials (vSEP) during nVNS (GammaCore®) in controls and migraineurs.

Methods: In 12 controls (HV), early vSEP were obtained at A1/A2 (ref Cz) and C3/C4 (ref F3/F4) during 2-minute right/left cervical nVNS (figure 1, below) and compared to monopolar stimulation of vagus nerve afferents in the outer ear. Additional recordings were performed in 13 episodic migraineurs (MO).

Results: We identified 3 reproducible peaks in all 25 subjects (HV: mean latencies P1: 2.05 ms, N1: 5.20 ms, P2: 9.13 ms; MO: P1: 1.97 ms, N1: 4.26 ms, P2: 7.94 ms, $p > 0.05$), when stimulating over the cervical vagus nerve, but not over the sternocleidomastoid muscle. P1-N1 amplitude increased significantly ($p < 0.01$) with nVNS voltage. Inner tragus stimulation gave similar vSEP with shorter latencies. A Fourier's analysis by continuous wavelet transform showed that cervical nVNS evoked a response that included a myogenic potential ($\sim$150 Hz) and a vSEP ($\sim$75 Hz).

Conclusion: Cervical nVNS elicits vSEP similar to those described before with invasive VNS and stimulation of the vagal afferents in the ear. Therapeutic effects reported with nVNS in primary headaches are thus likely mediated by genuine activation of vagus nerve afferents.

Figure 1. Cervical nVNS-evoked vSEP



Conflict of interest
Disclosure statement:
This work was supported by Electrocore (research grant to RN)

EHMTC-0162
POSTER SESSION B

DOES REGIONAL SOLAR RADIATION INFLUENCE HABITUATION OF VISUAL EVOKED POTENTIALS IN MIGRAINE? A TENTATIVE HYPOTHESIS BASED ON RETROSPECTIVE LITERATURE ANALYSIS

M. Lisicki[1], K. D'Ostilio[1], R. Nonis[1], M. Erpicum[2], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit., University Department of Neurology- CHR Citadelle, Liege, Belgium*
[2]*Meteorology Department, University of Liege, Liege, Belgium*

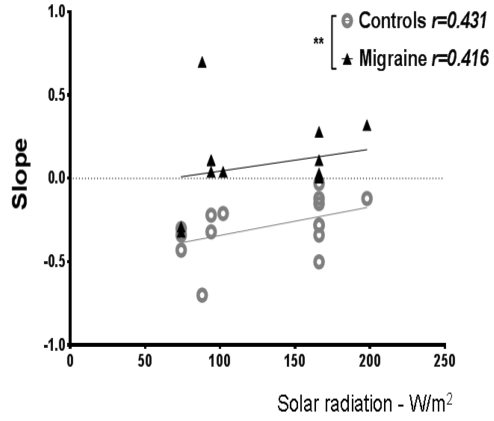
Background: Deficient habituation of visual evoked potentials (VEP) is a redundant neurophysiological finding in interictal episodic migraine sufferers. However, not all studies were able to retrieve this neurophysiological "hallmark". The discrepancies can probably not be explained on the sole basis of methodology. Migraine is a multifaceted disease that arises from the interaction of a genetic predisposition with an enabling environment.

Aim and methods: We hypothesized that environmental factors such as regional solar radiation could modulate the activity of visual pathways in migraine patients and account for some discrepancies between VEP studies. We performed a retrospective analysis of studies that evaluated VEP habituation in episodic migraine and correlated the available data with in-situ mean solar radiation.

Results: Twenty-six studies were included. Mean solar radiation was significantly higher in locations of studies reporting deficient habituation (133.3+/−41.05 vs. 99.43+/−42.81 W/m^2, $p = 0.022$). Interestingly, the VEP habituation slope positively correlated with solar radiation in both migraineurs ($n = 351$, $p < 0.001$) and healthy controls ($n = 348$, $p < 0.001$, figure 1). Moreover, there was a significant difference between VEP slopes reported in controls from northern compared to southern countries (−0.34 vs.−0.28 μV/block, $p < 0.01$).

Conclusions: Higher solar radiation could favor low VEP habituation in migraine patients. As this is also the case in healthy subjects, different genetic backgrounds may in addition play a role in migraine. A prospective study addressing these aspects would be of major interest.

Figure 1. Amplitude slope of visual evoked potentials (µV/block) according to mean yearly solar radiation (W/m²)



Conflict of interest
Disclosure statement:
This work was supported by Euroheadpain (FP7- grant n°602633)

EHMTC-0163
POSTER SESSION B

DOES NON-INVASIVE VAGUS NERVE STIMULATION NORMALIZE HABITUATION OF EVOKED POTENTIALS IN PATIENTS WITH EPISODIC MIGRAINE?

R. Nonis[1], K. D'Ostilio[1], M. Lisicki[1], S. Sava[1], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit., University Department of Neurology- CHR Citadelle, Liege, Belgium*

Background: Deficient habituation of visual evoked cortical responses (VEP) is a frequent interictal finding in episodic migraine and is likely secondary to thalamocortical dysrhythmia. In epilepsy, VNS is able to modulate thalamic and cortical activities.

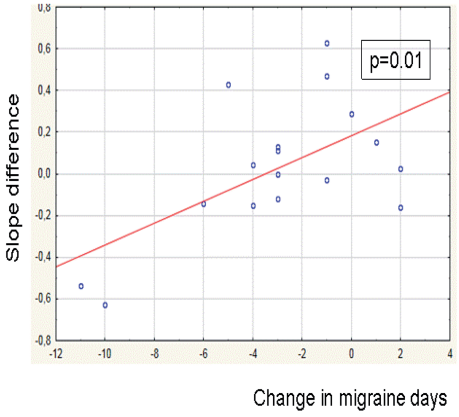
Aim: To determine short- and long-term effects of cervical non-invasive VNS (nVNS) on VEP habituation in episodic migraineurs and to search for correlations with therapeutic effects.

Methods: In 21 episodic migraineurs, VEP were recorded before (t0), after one session (t1) and after 3 months of daily sessions (t2) with nVNS (gammaCore®). VEP amplitude changes were assessed over 6 blocks of 100 averaged responses, clinical outcome with headache diaries.

Results: Seventeen patients ended the study; 9 had a VEP habituation deficit (i.e. positive slope) at t0 that normalized at t1 ($p = 0.07$). At t2, average number of migraine days decreased significantly ($p < 0.01$), as well as mean attack intensity ($p = 0.016$) and acute medication intake ($p < 0.01$). Habituation deficit, when present at t0, decreased significantly at t2 ($p = 0.03$). Slope reduction correlated positively with the change in migraine days between t2 and t0 ($p = 0.012$, *figure 1*)

Conclusions: nVNS with the gammaCore® is able to increase habituation of VEP after one session and after 3 months of daily sessions, which could be due to its effect on thalamo-cortical circuits. These electrophysiological modifications correlates positively with the clinical improvement induced by nVNS.

Figure 1. Individual correlation between VEP slope difference and difference in migraine days, between t2 and t0



Conflict of interest
Disclosure statement:
This work was supported by Electrocore LLC (research grant to RN)

EHMTC-0165
POSTER SESSION B

FAMILIAL HISTORY OF MIGRAINE INFLUENCES HABITUATION OF VISUAL EVOKED POTENTIALS

M. Lisicki[1], E. Ruiz-Romagnoli[2], K. D'Ostilio[1], R. Piedrabuena[2], R. Giobellina[2], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit, University Department of Neurology. CHR Citadelle, Liege, Belgium*
[2]*Clinica Universitaria Reina Fabiola, Servicio Universitario de Neurologia – Universidad Catolica de Cordoba, Cordoba, Argentina*

Background: Lack of habituation of visual evoked potentials (VEP) is a common finding in migraine patients between attacks. Previous studies have suggested an

electrophysiological familial aggregation pattern associated with migraine. The aim of this study was to evaluate the influence of a positive family history of migraine on VEP amplitude and habituation.

Methods: We recorded 6 blocks of 100 VEP during continuous pattern-reversal stimulation in 30 patients with migraine between attacks (MO) and in 30 healthy volunteers of whom 15 had a 1st degree relative suffering from migraine (HVm) and 15 had not (HV).

Results: Both MO and HVm had a significant deficit of VEP habituation and similarly reduced N1-P1 1st block amplitudes, compared to HV (habituation slope: MO = 0.033, HVm = 0.02133, HV = −0.02533, HV vs. MO $p < 0.01$, HV vs. HVm $p = 0.036$; mean N1-P1 amplitude in the first block: MO = 9.078 μV, HVm = 9.29 μV, HV = 12.19 μV. HV vs. MO $p = 0.041$, HV vs. HVm $p > 0.05$). The first block N1-P1 VEP amplitude was negatively correlated to the habituation slope in MO ($r = -0.5688$ $p < 0.001$) and in HVm ($r = -0.6123$ $p = 0.015$) but not in HV.

Conclusions: Lack of habituation of visual evoked potentials is likely a genetically determined endophenotypic trait associated with migraine and migraine susceptibility.

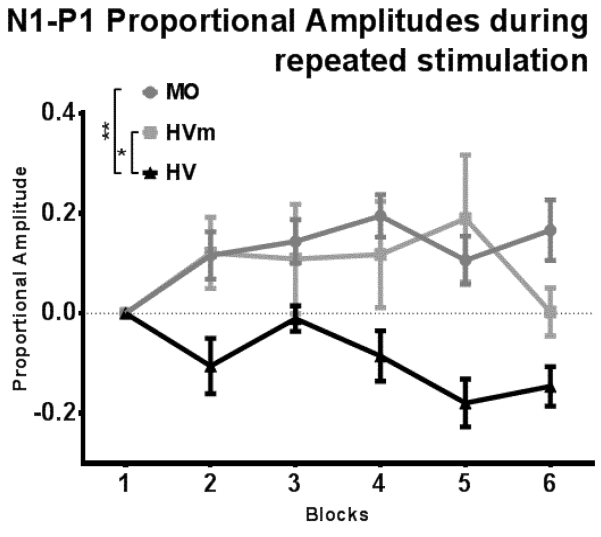


Figure1. N1-P1 Mean proportional amplitudes of successive blocks in relation to the first block. The error bars correspond to the standard error of the mean (SEM). *p<0.05; **p <0.01.

EHMTC-0211
POSTER SESSION B

METABOLIC CHANGES IN THE MIGRAINE BRAIN IN RELATION TO AGEING AND DISEASE LOAD

K. D'Ostilio[1], M. Lisicki[1], R. Nonis[1], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit, University Department of Neurology- CHR Citadelle, Liege, Belgium*

Introduction: Migraine prevalence tends to decrease with advancing age. Morphological and functional brain changes occuring in migraine could be secondary to repeated attacks and/or to abnormal sensory processing. In normal ageing, brain modifications could traduce a progressive refinement to cope with the environment, associated with a reduction in the complexity of brain connections. We hypothesized that metabolism in various brain regions might be differentially modified by age in migraine patients.

Materials and methods: Forty-one subjects underwent a FDG-PET scan: 21 patients with interictal episodic migraine without aura (MO, age range: 20–63 years, 5 M) and 20 healthy controls (HV, 21–59 years, 5 M).

Results: In MO vs. HV, the overall FDG uptake was reduced in the left visual cortex, left medial frontal gyrus and bilaterally in the insula, somatosensory and motor cortices. Metabolisms of the posterior thalamus, brainstem including the periaqueductal gray (PAG), visual cortex, and (para)hippocampus, strongly increased with age in MO patients but not in HV. Disease duration positively correlated with PAG, (para)hippocampus and rostral anterior cingulate cortex (rACC) metabolisms in MO.

Conclusion: Migraine patients, compared to HV, have a decreased resting metabolism in several areas belonging to the "pain/salience matrix", which is in line with previous neuroimaging studies. Metabolism of the rACC is specifically related to disease load whereas metabolism of other sensory processing regions is more affected by age. Whether these functional changes are due to repeated stereotyped attack-related stimulations and to a learning process with complexity reduction of neuronal connections and/or compensatory age-related hyperactivity, remains to be demonstrated.

Conflict of interest
Disclosure statement:
This work was supported by Euroheadpain (FP7-602633)

EHMTC-0263
POSTER SESSION B

METABOLIC CORRELATES OF VISUAL EVOKED POTENTIALS HABITUATION IN MIGRAINEURS AND CONTROLS

K. D'Ostilio[1], M. Lisicki[1], J. Schoenen[1], D. Magis[1]

[1]*Headache Research Unit, University Department of Neurology- CHR Citadelle, Liege, Belgium*

Background: On average, migraineurs recorded interictally have a habituation deficit of pattern-reversal visual evoked potentials (VEP) compared to control subjects. Studies on cortical generators of visual evoked potential (VEP) have revealed at least four principal subcomponents with different origins, that are obtained using short time Fourier transform (STFT). Hypothesizing that habituation requires coupled metabolic functioning we correlated the VEP subcomponents' power to resting state FDG-PET metabolism.

Materials and Methods: FDG-PET and pattern reversal VEP were recorded in 41 subjects: 21 interictal migraineurs without aura (MO), and 20 controls (HV). VEP subcomponents were extracted using a STFT. Habituations of C1, Early P1, Late P1, and N150 subcomponents' power (expressed as proportion $6^{th}/1^{st}$ block) were correlated with resting FDG uptake.

Results: Significant metabolic correlates of habituation for each VEP subcomponent are shown in table 1.

Conclusion: Habituation of VEP subcomponents is correlated to resting state metabolism in different areas of the visual network. These metabolic correlates of VEP subcomponents are similar to those already described using fMRI and EEG (Di Russo Hum Brain Mapp 2002), but differ between HV and MO. Hence, habituation of early P1 seems to be associated with thalamic metabolic variations in HV but not in MO. These results provide new insight about the central substrates of VEP habituation and visual information processing in migraineurs.

Conflict of interest
Disclosure statement:
This work was supported by Euroheadpain (FP7- grant n°602633)

All subjects	Positive	Negative
C1	V2/V3	V1
Early P1	Precuneus/cuneus, Temporo-occipital	-
Late P1	V1, V2, Fusiform Gyrus	-
N150	Precuneus	-

By group	Migraineurs Positive	Migraineurs Negative	Healthy Volunteers Positive	Healthy volunteers Negative
C1	-	V1	V2, V3	-
Early P1	Mid temporal	Cuneus	V3, Thalamus	Thalamus
Late P1	V2, fusiform gyrus, mid temporal	-	V2, V3	-
N150	Precuneus	Cuneus, precuneus	V2, V3	V1

EHMTC-0115
POSTER SESSION B

MODIFICATIONS OF GRAY MATTER VOLUME IN MIGRAINE PATIENTS OVER FOUR YEARS: A TENSOR-BASED MORPHOMETRY STUDY

R. Messina[1], M.A. Rocca[1], B. Colombo[2], E. Pagani[1], G. Comi[2], A. Falini[3], M. Filippi[4]

[1]*IRCCS Ospedale San Raffaele, Neuroimaging research Institute, Milano, Italy*
[2]*IRCCS Ospedale San Raffaele, Department of neurology, Milano, Italy*
[3]*IRCCS Ospedale San Raffaele, Department of Neuroradiology, Milano, Italy*
[4]*IRCCS Ospedale San Raffaele, Neuroimaging research Institute-, Milano, Italy*

Background: Previous studies have shown diffuse gray matter (GM) abnormalities in regions involved in pain and visual processing in migraine patients. A one-year longitudinal study found GM atrophy of sensory-discriminative brain regions in these patients.

Objectives: To explore longitudinal GM changes over a four-year follow up period in migraine patients and their association with patients clinical characteristics and disease activity.

Methods: Using a 3.0 Tesla scanner, brain dual-echo and 3D T1-weighted scans were acquired from 24 migraine patients and 25 healthy controls at baseline and after 4 years. Tensor-Based Morphometry and SPM12 were used to assess longitudinal changes of GM volumes according to the disease duration and attack frequency.

Results: Eight patients reported an increased number of migraine attacks at follow up. At baseline, compared to controls, migraine patients showed cerebellar GM atrophy and increased volume of regions located in the fronto-temporal lobes. At follow up, compared to controls, migraine patients with a longer disease duration and a higher baseline attack frequency experienced a GM volume increase of fronto-parietal regions that are part of the modulatory pain circuitry. Patients with clinical worsening also showed increased and decreased volumes of cortical regions subserving pain perception. Compared to controls, migraine patients with a baseline low disease activity and a worse clinical evolution developed over the follow up period GM atrophy of extrastriate cortical areas.

Conclusions: The migraine brain changes dynamically over time. Various *pathophysiological* mechanisms might affect different brain regions in migraineurs over 4 years.

EHMTC-0207
POSTER SESSION B

EVENT RELATED DYNAMICS OF PRIMARY SENSORIMOTOR CORTEX DURING BRIEF HAND MOVEMENTS WITH AND WITHOUT DISCRIMINATIVE SENSORY STIMULATION IN MIGRAINE

M.S. Mykland[1], M.H. Bjørk[2,3], M. Stjern[1,4], T. Sand[1,4]

[1]*Norwegian University of Science and Technology, Department of Neuroscience, Trondheim, Norway*
[2]*University of Bergen, Department of Clinical Medicine, Bergen, Norway*
[3]*Haukeland University Hospital, Department of Neurology, Bergen, Norway*
[4]*St. Olavs Hospital, Department of Neurology and Clinical Neurophysiology, Trondheim, Norway*

Cortical excitability is probably altered in migraine between attacks and in the preictal phase. Most studies have used sensory evoked potentials to study phase-locked post-synaptic mass-potentials. However, EEG-oscillations can also be induced in a non-phase-locked way, for instance as event-related synchronization (ERS).

Thirty-three interictal migraine patients (27 without aura) and 31 healthy controls were studied. Preictal (within 36 hours before attack) – interictal paired differences were available in 12 migraine patients. EEG was recorded blindly from 21 channels with average reference. The C3 and C4 electrodes overlying the primary sensorimotor cortex was analysed. A motor and a sensorimotor task (flexion-extension without/with object touching and surface discrimination) of the right wrist was repeated 15 times. FFT spectral curves was calculated for beta bands, and averaged from four- second segments for pre-movement baseline and for the post-movement period.

Strong beta-ERS during post-activation, was seen in both groups for the motor (C3 $p < 0.0001$; C4 $p < 0.0001$) and sensorimotor (C3 $p < 0.00003$; C4 $p < 0.00004$) task. However we found no group differences between migraine patients and headache-free controls. Sensorimotor beta-ERS was significantly stronger at C4 (3.0 vs 2.0 uV; $p = 0.02$) in the preictal than the interictal phase ($p = 0.02$).

Primary sensorimotor cortex reactivity to brief movements seems to be normal interictally in migraine. This result is in line with a majority of TMS-studies that show normal motor thresholds. However, when sensory discrimination was added to the motor task we observed that ipsilateral beta-ERS was increased in the preictal phase, possibly suggesting altered cortical inhibition prior to the attack.

EHMTC-0170
POSTER SESSION B

NO CHANGE IN INTERICTAL PACAP LEVELS IN PERIPHERAL BLOOD IN WOMEN WITH CHRONIC MIGRAINE

J. Pascual[1], E. Cernuda-Morollón[2], N. Riesco[2], P. Martinez-Camblor[3], E. Serrano-Pertierra[2], C. García-Cabo[2]

[1]*University Hospital Marqués de Valdecilla, Service of Neurology, Santander, Spain*
[2]*University Hospital Central de Asturias, Neurology, Oviedo, Spain*
[3]*Oficina de Investigación Biosanitaria, Statistics, Oviedo, Spain*

Objective: To determine pituitary adenylate cyclase activating polypeptide (PACAP) in peripheral blood as a potential marker of the activation of the parasympathetic arm of the trigemino-vascular system (TVS) in chronic migraine (CM).

Methods: Women older than 17 and diagnosed as CM were recruited. Matched healthy women with no headache history and women with episodic migraine (EM) served as control groups. PACAP and VIP levels were determined in blood samples obtained from the right antecubital vein by ELISA outside a migraine attack and having taken no symptomatic medication the day before.

Results: We assessed serum samples from 86 women with CM, 32 healthy women and 35 matched women with EM. There were no differences in PACAP levels in CM patients (109.8 ± 43.8, 97.4 [32.5–253.1] pg/ml), controls (108.7 ± 43.0, 98.7 [50.7–197.3] pg/ml) or EM patients (98.8 ± 34.3, 94.2 [52.0–190.7] pg/ml). VIP levels were significantly increased in CM as compared to control healthy women and EM patients. Variables such as age, CM duration, the presence of aura, analgesic overuse, depression, fibromyalgia, vascular risk factors, history of triptan consumption or kind of preventative treatment did not significantly influence PACAP or VIP levels.

Conclusion: In contrast to VIP, interictal PACAP level measured in peripheral blood does not seem to be a biomarker reflecting parasympathetic activation in CM.

This study was supported by the PI14/00020 FISSS grant (Fondos Feder, ISCIII, Ministry of Economy, Spain)

EHMTC-0177
POSTER SESSION B

RELATIONSHIP BETWEEN SERUM LEVELS OF VIP, BUT NOT OF CGRP AND CRANIAL AUTONOMIC PARASYMPATHETIC SYMPTOMS IN CHRONIC MIGRAINE PATIENTS

J. Pascual[1], N. Riesco[2], E. Cernuda-Morollón[2], E. Serrano-Pertierra[2], P. Martínez-Camblor[3], A. I. Pérez-Alvarez[2], C. Garcia-Cabo[2], L. Verano[2]

[1]*University Hospital Marqués de Valdecilla, Service of Neurology, Santander, Spain*
[2]*University Hospital Central de Asturias, Neurology, Oviedo, Spain*
[3]*Oficina Investigación Biosanitaria, Statistics, Oviedo, Spain*

Background: Cranial autonomic parasympathetic symptoms (CAPS) appear in at least half of migraine patients theoretically as a result of release of peptides by the trigemino-vascular system (TVS). Cranial pain pathways become sensitised by repeated episodes of TVS activation, leading to migraine chronification.

Objective: To correlate the presence of CAPS with serum levels of vasoactive intestinal peptides (VIP) and calcitonin gene-related peptide (CGRP).

Patients and Methods: Chronic migraine (CM) patients were asked on the presence -during migraine attacks- of 5 CAPS, which were scored from 0 to 10 by using a quantitative scale. Interictal serum VIP and CGRP levels were determined by ELISA.

Results: We interviewed 87 CM patients (82 females; mean age 44.7 ± 10.6 years). Seventeen had no CAPS, while 70 reported at least one CAPS. VIP levels ranged from 20.8 to 668.2 pg/ml (mean 154.5 ± 123.2). There was a significant positive correlation between CAPS scale scores and VIP levels (Spearman coefficient $= 0.227$; $p = 0.035$). VIP levels were higher in CM patients with at least 1 point in the scale *vs* those with 0 points ($p = 0.002$). Analysing symptoms individually, VIP levels were numerically higher in those patients with symptoms, though significantly higher only in those patients with lacrimation *vs* those without it ($p = 0.013$). There was no significant correlation between CGRP levels and the score in the CAPS scale.

Conclusions: Serum VIP, but not CGRP, levels seem to reflect the rate of activation of the parasympathetic arm of the TVS in migraine.

Supported by PI14/0020 FISSS grant (Plan Nacional I + D + I, Fondos Feder, ISCIII, Ministry of Economy, Spain)

EHMTC-0225
POSTER SESSION B

HIGH EXPRESSION OF NSE AND S100B IN MIGRAINE PATIENTS: MORE EVIDENCE FOR BRAIN DAMAGE IN CHRONIC MIGRAINE?

X. Rodriguez-Osorio[1], T. Sobrino[1], C. Domínguez[1], A. López[1], F. Campos[1], F. Martínez[1], J. Castillo[1], R. Leira[1]

[1]*Health Research Institute of Santiago de Compostela IDIS, Department of Neurology- Clinical Neurosciences Research Laboratory, Santiago de Compostela, Spain*

Background: Migraine constitutes a common but disabling disease usually considered of benign course. However complications such as ischemic stroke have been described and neuroimaging studies have revealed the presence of extended microstructural changes which appear to be more prominent in chronic migraine. Molecular markers of brain damage could participate in pathophysiological mechanisms for migraine chronification.

Aim: To investigate the presence of glial (S100B protein) and neuronal (neuron-specific enolase, NSE) damage markers in patients with episodic and chronic migraine in order to elucidate their relation with migraine chronicity.

Methods: Prospective study of episodic (EM) and chronic migraine (CM) patients (2013 IHS criteria) and healthy control subjects. Epidemiological and clinical data was collected. NSE and S100B expression on peripheral venous blood was determined in free-pain periods.

Results: N = 112 migraine patients and N = 25 healthy subjects were included. N = 105 (93.7%) migraines and N = 23 (92%) controls were females. Mean age was 35.1 ± 11.7 years old for EM, 44.4 ± 11.1 for CM and 36.1 ± 7.9 for controls. S100B and NSE levels were higher in chronic (S100 B: 0.17 ± 0.08 ng/ml; NSE: 21.7 ± 3.2 ng/ml) than episodic migraines (S100B: 0.07 ± 0.02 ng/ml; NSE: 13.1 ± 2.8 ng/ml) (both $p < 0.0001$). ANOVA test among the three groups (EM, CM, controls) was also significant ($p < 0.0001$).

Conclusions: Chronic migraine patients show higher expression of brain damage markers. These findings suggest that glial and neural damage is present in chronic migraine patients thus migraine may not be a such benign disease.

Conflict of interest
Disclosure statement:
This project has been partially supported by grants from the Spanish Ministry of Economy and Competitiveness-Instituto de Salud Carlos III (PI12/00532 PI13/00292 PI14/01879 PI15/01578).

EHMTC-0215
POSTER SESSION B

PRESSURE PAIN SENSITIVITY OVER THE HEAD AFTER ONABOTULINUMTOXIN A THERAPY IN CHRONIC MIGRAINE: RESULTS IN A SERIES OF 24 PATIENTS

M. Ruiz Piñero[1], J. Barón[2], E. Martínez[1], A. Juanatey[1], L. Blanco[1], Á.L. Guerrero-Peral[1], M. Palacios-Ceña[3], P. Madeleine[3], C. Fernández-de-las-Peñas[3]

[1]*Hospital Clínico Universitario de Valladolid, Neurology, Valladolid, Spain*
[2]*Hospital Clínico Universitario de Valladolid, Neurophysiology, Valladolid, Spain*
[3]*Universidad Rey Juan Carlos, Physioterapy, Madrid, Spain*

Introduction: In experimental pain models of migraine, the application of botulinum neurotoxin type A reverses mechanical hypersensitivity or prevents its development when applied to meningeal nociceptors.

Aim: To investigate changes in pressure pain sensitivity in people with Chronic Migraine after application of OnabotulinumtoxinA (OnabotA).

Methods: We included patients treated with OnabotA according to the PREEMPT paradigm. Pressure pain thresholds (PPTs) over 21 points distributed over the scalp were assessed 2 weeks before and 1 month after two OnabotA injections. The nomenclature and location of points were based on standard positions of 10/20 and 10/10 systems for electroencephalogram recordings: 8 points on the right side (Fp2, F4, F8, C4, T4, P4, T6, O2), 8 points on the left (Fp1, F3, F7, C3, T3, P3, T5, O1) and 5 points along the mid-sagittal line (Fpz, Fz, Cz, Pz, Oz). Topographical pressure pain sensitivity maps were constructed. Subjects did not present migrainous pain the day of assessment. Patients exhibiting a reduction of at least 50% in the number of migraine days after OnabotA procedure were considered as responders.

Results: Twenty four patients (age: 43.4 ± 8.9 years) were included. Mean PPT values increased in 18 out of 21 points after OnabotA therapy. When we considered OnabotA responders, the increases in mean PPT values were observed in all the points.

Conclusions: Our results suggest that treatment with OnabotA modifies pressure pain sensitivity maps in the head in chronic migraine, particularly in those considered as clinically responders to therapy.

Conflict of interest
Disclosure statement:
Financial Support: This study has been partially funded by Allergan.

EHMTC-0216
POSTER SESSION B

TOPOGRAPHICAL PRESSURE PAIN SENSITIVITY MAPS OVER THE HEAD: COMPARING CHRONIC AND EPISODIC MIGRAINE PATIENTS WITH HEALTH CONTROLS

M. Ruiz Piñero[1], M. Palacios-Ceña[1], J. Barón[2], A. Juanatey[1], Á.L. Guerrero-Peral[1], P. Madeleine[3], C. Fernández-de-las-Peñas[3]

[1]*Hospital Clínico Universitario de Valladolid, Neurology, Valladolid, Spain*
[2]*Hospital Clínico Universitario de Valladolid, Neurophisiology, Valladolid, Spain*
[3]*Universidad Rey Juan Carlos, Phisioterapy, Madrid, Spain*

Introduction: Pressure pain hyperalgesia, defined as decreased pressure pain thresholds (PPT), is considered a manifestation of sensitization mechanisms. The fronto-temporal scalp seems to be the most sensitive part of the head in both people with and without headache. Previous investigations on pressure pain hypersensitivity in migraine showed inconclusive results.

Aim: To determine differences in PPTs over the scalp between subjects with migraine and healthy controls and to compare results obtained in episodic and chronic migraineurs.

Methods: Eighty-four patients with episodic migraine (EM), 77 with chronic migraine (CM), and 41 matched healthy controls included. PPTs were measured over 21 points distributed over the scalp. Location and nomenclature of assessed points were based on standard positions of 10/20 and 10/10 systems for electroencephalogram recordings: 8 points on the right side (Fp2, F4, F8, C4, T4, P4, T6, O2), 8 on the left (Fp1, F3, F7, C3, T3, P3, T5, O1) and 5 along the mid-sagittal line (Fpz, Fz, Cz, Pz, Oz). Topographical pressure pain sensitivity maps were constructed. All subjects were headache-free the day of evaluation.

Results: PPTs were lower in frontal and temporal scalp both in patients and healthy controls. PPTs were decreased ($P < 0.05$) in both migraine groups compared to controls in all points ($P < 0.05$). Patients with CM had lower PPTs in the frontal and temporal areas ($P < 0.05$ in Fp2 and F7) than those with EM.

Conclusions: We observed pressure pain hyperalgesia in the head in people with migraine, which could be higher in those with CM rather than EM.

Conflict of interest
Disclosure statement:
Financial Support: This study has been partially funded by Allergan.

EHMTC-0395
POSTER SESSION B

EFFECTS OF FREQUENCY-COLOUR-INTENSITY OF LIGHT STIMULATION ON THE NOCICEPTIVE BLINK REFLEX IN HEALTHY SUBJECTS USING A NEW PROTOTYPE "STIMLUX"

S.L. Sava[1], V. de Pasqua[1], R. Baschi[1], D. Magis[1], A. Maertens de Noordhout[1], J. Schoenen[1]

[1]*Headache Research Unit – Citadelle Hospital., University Department of Neurology, Liege, Belgium*

Background: In a previous study we demonstrated that white flash light stimulation decreases amplitude of the trigeminal nociceptive blink reflex (nBR) and forehead pain sensitivity in healthy subjects (HS) (Sava et al., 2014). To identify the most effective stimulation parameters, we developed a prototype flash light stimulator (*StimLux*) that allows varying frequency, colour and intensity of the stimulus.

Subjects and Methods: We studied 11 HS in three different 7-min flash light stimulation sessions: 1) variation of frequency: 8, 10, 12, 15 and 20 Hz; 2) variation of colour: violet, blue, green, yellow, orange and red; 3) variation of intensity: 500, 1000, 1500, 2000, 3000 and 4000 Lux. The nBR and pain threshold were elicited and measured as previously reported. We assessed also visual discomfort on a visual analogue scale.

Results: In overall 160 measurements, the pain threshold (PT) increased whichever stimulation frequency, wavelength or intensity were used. The most efficient in increasing the PT and decreasing the ipsi- and contralateral 1st nBR block amplitude were the 12 Hz frequency and the 1500Lux. The only colour that was associated with an inverse correlation between the VAS visual discomfort score and nBR habituation was violet.

Discussion: The *StimLux* device allowed identifying in each healthy subject the physical parameters of flashing light that have the greatest inhibitory effect on trigeminal nociception and induce the least visual discomfort. This paved the way for a proof-of-concept trial using

flash light stimulation as preventive therapy in migraine patients.

EHMTC-0201
POSTER SESSION B

THE HYPOTHALAMUS AS THE TRUE MOTOR OF MIGRAINE ATTACKS: CONTINUOUS SCANNING OF THE MIGRAINE CYCLE OVER A WHOLE MONTH

L. Schulte[1], A. May[1]

[1]*University Medical Center Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*

Functional neuroimaging revealed a particular brainstem area to be specifically activated in migraine during, but not outside of the attack and has been coined the migraine generator. However, the pathophysiological concept behind this keyword is not undisputed. Typical migraine premonitory symptoms such as fatigue and yawning and the typical association of attacks with circadian and menstrual cycles all make the hypothalamus a possible regulating region of migraine attacks. Neuroimaging-studies investigating native human migraine attacks however are scarce and there are currently no studies investigating the last 24 hours before headache onset. Here we aim at identifying the specific motors of the different phases of spontaneous human migraine attacks and their specific functional connectivity by daily fMRI over a period of 30 days.

We report a migraine patient who underwent MRI scanning every day for 31 days, always in the morning, to cover, using functional imaging of standardized trigeminal nociceptive stimulation, a whole month and 3 complete, untreated migraine attacks.

We found that hypothalamic activity is altered during the last 24 hours prior to pain onset, i.e. increases towards the next migraine attack. More importantly, the hypothalamus shows altered functional coupling with the spinal trigeminal nuclei and the region of the "migraine generator" i.e. the dorsal rostral pons during the premonitory day and the pain phase of native human migraine attacks.

These data suggest that although the brainstem is highly linked to the migraine biology, the real motor of attacks are the functional changes in hypothalamic activity and hypothalamo-brainstem connectivity.

EHMTC-0327
POSTER SESSION B

PREMONITORY AND NON-HEADACHE SYMPTOMS INDUCED BY CGRP AND PACAP38 IN MIGRAINE PATIENTS

G. Song[1], A.L.H. Vollesen[2], J. Olesen[2], M. Ashina[2]

[1]*Danish Headache Center, Department of Neurology, Glostrup, Denmark*
[2]*Danish Headache Center, Department of Neurology, Glostrup- Copenhagen, Denmark*

Background: Migraine attacks are often preceded by premonitory symptoms (PS) that may be triggered. We investigated the incidence of PS after administration of calcitonin gene-related peptide (CGRP) or pituitary adenylate cyclase-activating peptide-38 (PACAP38) in migraine patients without aura (MO) who reported and not reported migraine-like attacks induced by these pharmacological triggers. In addition, we investigated the association between PS and familial predisposition for migraine.

Methods: MO-patients received continuous intravenous infusion of α-CGRP ($n = 40$) and PACAP38 ($n = 32$) for 20 min. PS and non-headache symptoms were recorded by a self-administered questionnaire. Information of familial predisposition was obtained by telephone interview of first-degree relatives using a validated semi-structured questionnaire.

Results: 25 out of 40 (63%) developed a migraine-like attack after CGRP infusion and 23 out of 32 (72%) patients developed an attack after PACAP38. Only 2 patients (9%) with a CGRP-induced attack reported PS, whereas 11 patients (48%) reported PS after PACAP38. Patients who developed a migraine-like attack did not report more PS than patients with no attack after CGRP ($P = 0.519$) or PACAP38 ($P = 0.103$). We found no difference in PS between patients with familial predisposition of migraine (75%) and patients with no predisposition (56%) ($P = 0.101$).

Conclusion: CGRP did not induce PS, whereas PACAP38 induced PS in 48% of patients. However, CGRP and PACAP38 did not induce more PS in patients who developed an attack compared to those who did *not* develop an attack.

EHMTC-0079
POSTER SESSION B

SUSTAINED DISRUPTION OF SENSORY PROCESSING IN CHRONIC MIGRAINE

D. Vuralli[1,2], H.E. Boran[1,2], B. Cengiz[3], O. Coskun[1], H. Bolay[1,2]

[1]*Gazi University Faculty of Medicine, Department of Neurology and Algology, Ankara, Turkey*
[2]*Gazi University, Neuropsychiatry Center, Ankara, Turkey*
[3]*Gazi University Faculty of Medicine, Department of Neurology- Motor Control Laboratory, Ankara, Turkey*

Background and Objective: Somatosensory temporal discrimination (STD) test is used for the assessment of temporal threshold to discriminate two discrete stimuli. The processing of somesthetic stimuli is altered and somatosensory temporal discrimination is prolonged during a migraine attack. The aim of this study is to measure somatosensory temporal discrimation thresholds (STDTs) in order to evaluate sensory perception in chronic migraine (CM) patients.

Methods: 10 healthy volunteers without headache and 12 CM patients (without medication overuse and prophylactic treatment) were included in the study. CM patients were evaluated twice during a headache and headache-free period (at least three consecutive headache-free days, with at least one headache-free day before and after the test day). STDT values were evaluated in both hands.

Results: In healthy volunteers, STDTs were 33.9 ± 5.3 for the right hand and 35.4 ± 5.0 for the left hand. In CM group, both ictal (134.1 ± 17.8 for the right hand and 140.9 ± 18.2 for the left hand) and inter-ictal STDTs (123.4 ± 13.7 for the right hand and 122.6 ± 12.3 for the left hand) were significantly higher than STDTs of healthy volunteers ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$ and $p < 0.0001$ respectively). Visual analogue scale scores of CM patients were positively correlated with the contralateral STDT values when the pain was unilateral ($r = 0{,}781$ $p = 0.022$).

Conclusion: For the first time it is shown that somatosensory temporal discrimation thresholds are elevated not only during the attack but also during the pain-free period in CM. By providing evidence for continuous disturbance of sensory perception, STD test could be used as a electrophysiological biomarker for CM.

EHMTC-0364
POSTER SESSION B

DO PATIENTS WITH CHRONIC MIGRAINE PERCEIVE SWAY DIFFERENTLY TO NORMAL CONTROLS?

S. Williams[1], S. Zaidi[2], M. Lewis[1]

[1]*Leeds Teaching Hospitals NHS Trust, Neurology Department, Leeds, United Kingdom*
[2]*Hull and East Yorkshire Hospitals NHS Trust, Neurology Department, Hull, United Kingdom*

Background: Migraine is a common cause of balance disorders, possibly through the mechanism of deranged sensory perception. Many patients with vestibular migraine complain of a swaying sense of imbalance. The aims of this study were to develop a questionnaire to quantify this sensation and to establish if it was a perceptual problem or a genuine increase in objective sway.

Method: Consecutive patients attending a regional headache clinic with an established diagnosis of chronic migraine, but no overt balance disorder were invited to participate. All subjects and controls were asked to score their feeling of sway using a seven point semantic differential scale during a series of tasks. Objective sway was recorded using the *SwayStar* system.

Results: Twelve patients and 12 controls were recruited. The median sway score in the patients was 15 and in the controls was 9.5 ($p < 0.005$). There was no abnormality in objective measures of sway.

Conclusion: Patients with chronic migraine perceive a greater degree of sway on a series of standard tasks than normal controls. The objective degree of sway did not differ between the two groups. The sense of swaying described by migraineurs is a perceptual problem rather than an increased level of actual sway.

EHMTC-0029
POSTER SESSION B

THE EFFECT OF FOETAL GROWTH RESTRICTION ON THE DEVELOPMENT OF MIGRAINE IN YOUNG ADULTS. THE NORD-TRØNDELAG HEALTH STUDY

S. Boerte[1,2], B.S. Winsvold[1,2,3], S.O. Stensland[1], J.A. Zwart[1,2]

[1]*Oslo University Hospital, FORMI, Oslo, Norway*
[2]*University of Oslo, Institute of clinical medicine, Oslo, Norway*
[3]*Oslo University Hospital, Department of Neurology, Oslo, Norway*

Objectives: To examine whether growth-restriction in utero is associated with development of migraine and tension-type headache in young adults.

Background: Little is known about factors early in life and the development of migraine.

Methods: We linked the Nord-Trøndelag Health Study (HUNT-3) with data from the Norwegian Medical Birth Registry including 4557 females and 2798 males 19–41 years of age. Participants were assessed for the presence of migraine and frequent tension-type headache, and for being born growth-restricted, based on weight by gestational age at birth. Participants were categorized as appropriate for gestational age (AGA, 10^{th}-90^{th} percentile), small for gestational age (SGA, 3^{rd}-10^{th} percentile) or very small for gestational age (VSGA, $<3^{rd}$ percentile). Logistic regression was used to assess the effect of growth restriction on the prevalence of migraine and frequent tension-type headache.

Results: The effect of growth restriction on migraine was modified by sex, with a significant association in males ($p < 0.001$), but not in females ($p = 0.23$). In particular males born VSGA where at high risk of developing migraine (OR 2.73, 95% CI 1.62–4.61 $p < 0.001$), with an intermediate risk among those born SGA (OR 1.51, 95% CI 0.96–2.37, $p = 0.07$). There was no significant association between growth-restriction and tension-type headache ($p = 0.051$).

Conclusions: Growth restriction was associated with an increased risk of migraine in young adulthood among males, but not among females. This suggests that migraine might in part be caused by influences in early life, and that males seem to be particularly vulnerable.

EHMTC-0023
POSTER SESSION B

AN AUDIT OF THE MIGRAINE POSTDROME-HOW COMMON ARE THE SYMPTOMS IN A CLINIC COHORT?

P. Bose[1], S. Kader[1], P. Goadsby[1]

[1]*Kings College London, Headache group, London, United Kingdom*

Background: Migraine is the most common cause of neurological disability worldwide. While its pathophysiology is beginning to be unraveled, the least well studied component remains the postdrome.

Aim: To explore, using a clinical audit, the migraine postdrome as it presents and to categorize the disabling symptoms patients report.

Method: Clinic records of patients under our care (Headache Group- PJG) at a UK Neurology tertiary care centre (King's College Hospital, London) were examined to obtain data against an audit collection tool. A pre-determined set of data was extracted from a preliminary cohort of 50 patients. Data were tabulated for summary statistics.

Results: Patients ($n = 50$; 41 female) aged from 18 to 76 years, with an average headache duration of 57 hours with ICHD-3beta migraine were included. A postdrome was reported in 88% with an average duration of 44 hours in documented cases. The most prevalent symptoms in the postdrome include tiredness (84%) neuropsychiatric (32%) and gastrointestinal (12%). A breakdown of the neuropsychiatric symptoms highlights concentration difficulties (24%) as the most common, followed by mood changes (16%). The majority (85%) had side locked headache.

Conclusion: Our audit demonstrates the postdrome is common and impactful to patients. The disability related to migraine is not limited to the headache phase such that studying and understanding the postdrome offers a further avenue to reduce the disability of this very common disorder.

EHMTC-0058
POSTER SESSION B

PREVALENCE AND CLINICAL CHARACTERISTICS OF PRIMARY HEADACHE AMONG THE OFFICE WORKERS

S. Enkhtuya[1], O. Luvsannorov[2]

[1]*Ulaanbaatar, Mongolia*
[2]*Mongolian National University of Medical Sciences, Neurology, Ulaanbaatar, Mongolia*

Headache is the most common disorder among the population, which is considered as a global public health problem. The purpose of this study was to investigate prevalence of the primary headaches and assess clinical characteristics among the office workers. This is descriptive cross-sectional, questionnaire-based survey. The questionnaire included diagnostic questions based on International Classification of Headache Disorders-III (ICHD-III). We surveyed totally 369 participants; the prevalence of all types of headaches was 64.0%. The prevalence rates of migraine, tension type headache (TTH), both migraine and TTH, and chronic TTH were 10.6% (n = 39), 36.3% (n = 134), 1.9% (n = 7) and 3.3% (n = 12), respectively. Sociodemographic factors found associated with statistically significant difference prevalence of migraine: genders (p = 0.029), marital status (p = 0.007), working hours (p = 0.049), working stress (p = 0.010) and body mass index (BMI) (p = 0.019). However the risk factors of TTH were working stress (p = 0.014) and BMI (p = 0.031). The clinical features of migraine were predominating unilateral and pulsating and TTH were often bilateral and pressing or tightening. The primary headaches are triggered by changes in sleeping habit, stress and flu, relieved by relaxation, medications use and massages. In conclusion, the prevalence of primary headache was high among the office working population.

Conflict of interest

EHMTC-0103
POSTER SESSION B

HEADACHE OCCURRENCE IN RETRIED PROFESSIONAL SOCCER PLAYERS OF THE ITALIAN FIRST DIVISION

F. Mainardi[1], E. Alicicco[2], G. Zanchin[3], F. Maggioni[3]

[1]*Headache Centre, SS Giovanni e Paolo Hospital, Venice, Italy*
[2]*Tor Vergata Univeristy, Sport Medicine, Rome, Italy*
[3]*Padua University, Headache Centre- Deprtment of Neurosciences, Padua, Italy*

Introduction: To assess the occurrence and the clinical features of primary headaches in a sample of retired players of the Italian Soccer League first division.

Material and methods: 31 retired professional soccer players were randomly contacted and asked to fill in an anonymous questionnaire, which allowed to reproduce the diagnosis of primary headaches according to the ICHD 3beta criteria. Furthermore, the questionnaire investigated the: actual employment; years of activity; familiarity for headache; previous relevant head injuries.

Results: Among the 31 subjects (average age: 58.5 ± 4.8, mean years of activity: 14.7 ± 1.3), 20 (64.5%) referred the onset of recurrent headache attacks during (n = 8) or after (n = 12) their professional career. The headache intensity was reported as mild (n = 14) or moderate (n = 6); the pain was pressing in 18 cases, pulsating in 2. The attacks lasted less than 4 hours in 18 subjects; accompanying symptoms were present in 5 cases (isolated phonophobia, n = 4; isolated photophobia, n = 1). Physical efforts did not provoke or aggravate the attacks in any of the patients. The reported average frequency of attacks in the last 6 months was 2.7.

Conclusion: Headache fulfilling ICHD3beta criteria for tension-type headache appears to be quite frequent among the retired professional soccer players. Despite the results of our previous prospective survey (1), the onset of a non disabling headache during the agonistic career does not seem to be a rare event. Instead, these results confirm the absence of more disabling headache such migraine.

References

1. Mainardi F, et al. *Neurol Sci* 2009; 30: 33–36.

EHMTC-0386
POSTER SESSION B

CLASSIFICATION OF CASES WITH DIAGNOSIS OF ACUTE HEADACHE IN EMERGENCY DEPARTMENT OF REGIONAL HOSPITAL DURRES, ALBANIA

E. Harizi[1], F. Domi[2]

[1]*Regional Hospital Durres -Albania, Neurology, Durres, Albania*
[2]*Regional Hospital Durres -Albania, Emergency Department, Durres, Albania*

The symptom of headache is a frequent cause of emergency Department to continue valuation with some examinations as CT.MRI or EEG of these patients, but on the other side, this symptom is often considered to be a little clinical problem in front of some big emergencies, and is treated symptomaticlly. To see how frequently can a simple headache mask a severe pathology we have done a study with patients of two years 2014–2015 in our Emergency Department with diagnosis of acute headache.We had 438 patients in total with acute headache, 263(62%) were essential and 175 (38%) were symptomatic: from which 39(22%) cases had clinical manifestation of severe cerebral pathology(11 intracerebral hemorrhage, 4 subarachnoid hemorrhage,3 subdural hemorrhage-done with CT, 9 cases with ischemias -done with MRI, 5 cases neuroinfection-done with MRI and rachicentesis and EEG, 6 tumors - done with MRI.)

In cases with essential headache we had 193(73%) with migraine of which 152(79%) with migraine without aura and 41 (21%) with migraine with aura. Other 60 patients (27%) with essential headache were 51 with tension type headache and 9 with cluster headache. Our data show the importance of careful evaluation of symptom of headache in Emergency Department and the need to send any doubtful case to do all necessary examinations to have a right diagnosis,and don't see this symptom as a little problem in comparison with other cases in Emergency.

EHMTC-0089
POSTER SESSION B

CLINICAL PROFILE OF MIGRAINE (BASED ON ICHD-3 BETA CLASSIFICATION): AN URBAN PRIVATE HOSPITAL BASED OBSERVATIONAL STUDY IN SOUTH INDIA

S. Jaiswal[1], Y.M. Reddy[1]

[1]*CARE INSTITUTE OF MEDICAL SCIENCES, DEPT. OF NEUROLOGY, HYDERABAD, India*

Objective: To highlight the clinical profiles of Migraine patients in an urban private Hospital in South India

Background: Data collection from private hospital with recent trends will help in defining clinical profiles and classification of Migraine in Asian population.

Methods: From 1st May,2014 to 31st March,2016, during 23 months of duration, total 2737 neurology patients consulted to me in my General Neurology OPD. The detailed history, the pattern of headache and associated features with demographic profiles were taken. The international classification of headache disorder(ICHD) version 3 beta was adapted for classification.

Results: Total 373 patients of Migraine consulted to me. 302 (81%) patients were female and 71(19%) were male. Details of all these patients are shown in Table 1:

Type of Headache	Total no. of Patients
Migraine without aura	220 (59%)
Migraine with Visual aura	60 (16%)
Migraine with Sensory aura	72 (19.3%)
Vertiginous Migraine	20 (5.4%)
Migraine with Brain stem aura	01 (0.3%)

22 patients (5.9%) were with nuchal pain, among 17 were without aura and 5 with aura.14 patients(3.75%) were with multiple auras, 12 with visual and sensory auras both and 2 with visual and vertiginous auras. 5 patients(1.34%) without aura had TTH too.2 patients had Catamanial migraine, 1 patient had orgasmic headache, 1 patient presented with Status Migrainous.

Conclusions: In my observational studies, this is the first kind, where organization has done on the basis of ICHD-3 beta, considering all auras, even sensory and multiple auras.In this study, nuchal pain has been considered an important symptomlogy in Migraine, which is not included in ICHD.

EHMTC-0399
POSTER SESSION B

POST PROCEDURE HEADACHE IN PATIENTS TREATED FOR CEREBRAL ARTERIOVENOUS MALFORMATIONS AND ANEURYSMS USING ENDOVASCULAR THERAPY

S. Khan[1], F. Amin[1], J. Hauerberg[2], M. Holtmannspoetter[3], J. Falkenberg Petersen[1], Z. Fakhril-Din[1], D. Gaist[4], M. Ashina[1]

[1]*Danish Headache Center- Rigshospitalet, Department of Neurology, Glostrup, Denmark*
[2]*Rigshospitalet, Department of Neurosurgery, Copenhagen, Denmark*
[3]*Rigshospitalet, Department of Radiology, Copenhagen, Denmark*
[4]*Odense University Hospital, Department of Neurology, Odense, Denmark*

Background: Though endovascular therapy (EVT) is increasingly used in treatment of intracranial vascular lesions, little is known about the effect of EVT on post-procedure headache.

Aim: To investigate the prevalence of headache in patients who have undergone EVT for cerebral arteriovenous malformations (AVMs) and aneurysms.

Methods: 324 patients underwent EVT treatment for aneurysms and AVMs at the Danish National Hospital from January 2012 to December 2014. We applied strict exclusion criteria to minimize the effect of other factors on headache occurrence, e.g., craniotomy. Eligible subjects were phone-interviewed using a purpose-developed semi-structured questionnaire. Headaches were classified according to ICHD-III beta criteria.

Results: The 59 patients underwent treatment of aneurysms ($n = 43$), cranial dural fistulas ($n = 11$), and AVMs ($n = 5$). There was a significant increase in overall headache ($p = 0.017$) and tension-type headache (TTH) ($p = 0.01$) within the first 3 months after EVT compared to 1 month before EVT. However, at interview time (mean 2.5 years post-EVT), the increase in overall headache, migraine, and tension-type headache was not statistically significant. A minority of patients experienced headaches for the first time within 3 months of their EVT (migraine: $n = 4$; TTH: $n = 10$). At interview time, 50% of these new headaches still persisted.

Conclusion: Our results suggest a temporary increase in headache in the first 3 months after EVT, which normalizes over time. Clinicians may use this knowledge to better inform their patients of functional outcomes after the EVT procedure.

EHMTC-0389
POSTER SESSION B

MIGRAINE, METABOLIC SYNDROME AND OBESITY: A CROSS SECTIONAL STUDY

S. Krongsut[1], S. Tanprawate[1]

[1]*Northern Neuroscience center, Neurology, Chiang Mai, Thailand*

Background: Migraine headache is a common cause of disability in general population. Migraine co-morbidities have been identified including metabolic syndrome and obesity. Identifying these is useful for therapeutic propose, and modifying disease course. Prior studies reported a link between migraine,metabolic syndrome and obesity.

Objection: To study an association between migraine, metabolic syndrome, obesity and explore its risk factor.

Methods: A cross-sectional study of adult with migraine was enrolled from CMU headache clinic during January 1st 2015 to December 31st,2015.Demographic data, headache characters, frequency, severity, migraine medication and headache impact were interviewed. The metabolic syndrome, blood test for triglyceride,HDL and sugar, and psychiatric co-morbidity were record.

Result: 162 patients were included in our study, 21 were male (12.8 %) and 141 were female (87.2%). The migraine subtypes comprised of migraine without aura (64.6%) and migraine with aura (35.4%). Mean frequency of migraine attacks per month was 7.13 ± 6.8 (range 1–14 days). Most common severity was mild (41.5%) following by very severe (26.2%), moderate (19.5%), and severe (12.8%) consequently. Our result showed that metabolic syndrome was present in 18.5% patients and 4.3% were obese. Male and high score of migraine headache severity had significant association with metabolic syndrome ($P = 0.014$ and 0.012 respectively). Headache frequency, type of medication used, psychiatric co-morbidities (depression and anxiety) were not associated with metabolic syndrome and obesity in migraineurs.

Conclusion: Our results demonstrate that male and very severe headache in migraineurs had significant association to metabolic syndrome.

EHMTC-0118
POSTER SESSION B

MIGRAINE ASSOCIATED WITH ALTITUDE: RESULTS FROM A POPULATION-BASED STUDY IN NEPAL

M. Linde[1], L. Edvinsson[2], K. Manandhar[3], A. Risal[3], T. Steiner[4]

[1]*Norwegian University of Science and Technology, Department of Neuroscience, Trondheim, Norway*
[2]*Lund University, Institute of Clinical Sciences, Lund, Sweden*
[3]*Kathmandu University Hospital, Dhulikhel Hospital, Dhulikhel, Nepal*
[4]*Imperial College London, Division of Brain Sciences, London, United Kingdom*

Background: Studies of twins indicate that there are environmental aetiological factors underlying migraine, but epidemiologists have not so far been able to corroborate their existence.

Methods: In a nationwide cross-sectional population-based study, 2,100 adults representative of the Nepali-speaking population aged 18–65 years and living in Nepal were randomly recruited using stratified multistage cluster-sampling. Over half (1,100; 52.4%) were resident above 1,000 m and almost one quarter (470; 22.4%) at or above 2,000 m. They were visited unannounced at home by trained interviewers who used a culturally-adapted Nepali translation of the structured Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire. Altitude of dwelling was measured by portable altimeter.

Results: Migraine prevalence increased with altitude in an almost linear relationship between 0 and 2,000 m. Multivariate logistic regression using the lowest altitude category (0–500 m) as reference, and adjusting for age and gender, showed that migraine prevalence was highly associated with altitude already at 1,000–1,499 m (AOR = 1.5 [95% CI: 1.2–1.9]; $p = 0.001$). Average migraine attack frequency increased by 43% ($p < 0.001$) and average migraine attack duration increased by 80% ($p < 0.001$) from the lowest altitude up to 2,000–2,499 m. Migraine pain intensity also increased significantly at higher altitudes ($p < 0.001$), the proportion with severe pain being greatest at 2,000–2,499 m (56.9%).

Conclusion: Chronic continuous exposure to high altitude increased not only the prevalence of migraine, but also the frequency, duration and intensity of attacks. In practice, this means that the adverse influence of altitude is real for 100 million people with migraine.

EHMTC-0030
POSTER SESSION B

2ND CYCLE AUDIT OF HEADACHE REFERRALS FROM PRIMARY CARE TO A REGIONAL HEADACHE SERVICE

A. Tyagi[1], S. Lip[2]

[1]*Queen Elizabeth University Hospital, Department of Neurological Sciences, Glasgow, United Kingdom*
[2]*Queen Elizabeth University Hospital, Core Medical Trainee 1, Glasgow, United Kingdom*

Headache is the most common neurological symptom with which patients attend their GPs and is the commonest reason for referral to neurology outpatient clinics. We have previously conducted an audit from 1st June 2012–30th June 2012 to review the referrals to the regional specialist headache service in Glasgow. We presented our findings to QOF meetings for GPs in Aug-Sept 2012. The aim of this second cycle was to look at headache referrals following our intervention and to see if there was any change in referral pattern. From the 2nd December 2013–13th Jan 2014, data was collected from GP referral letters to obtain the number of referrals for headache, reason for referral, gender, duration of headache and acute treatments given for headache. Data collected was compared to current local QOF guidelines and referral pathways. A total number of 224 patient referral letters were received from primary care during the 6 week period. Most were routine referrals (79%,177) and 67%(150) were females. 42%(95) had a referral diagnosis of migraine. 114(50.9%) patients had complained of headaches for more than 2 years. At the time of vetting 53 (23.7%) were deemed to have likely medication overuse headache of which 10 (4.5%) had an attempt at treatment prior to referral. Overall, 176(78.6%) patients met the referral criteria whereas previously, in the audit cycle conducted in 2012,the majority of referrals did not meet the criteria. Enhanced vetting of headache referrals neurology services can be very useful and consideration should be given to extending it to general neurology referrals as well.

EHMTC-0042
POSTER SESSION B

WILLINGNESS TO PAY FOR EFFECTIVE TREATMENT OF HEADACHE DISORDERS IN NEPAL: ESTIMATES FROM A POPULATION-BASED SURVEY

K. Manandhar[1], A. Risal[2], M. Linde[3], T.J. Steiner[4]

[1]*BANEPA, Nepal*
[2]*Norwegian University of Science and Technology-, Neuroscience, – Trondheim, Norway*
[3]*Norwegian University of Science and Technology-, Department of Neuroscience, Trondheim, Norway*
[4]*Norwegian University of Science and Technology, Department of Neuroscience-, Trondheim, Norway*

Background: Headache disorders, particularly migraine and tension-type headache (TTH), are highly prevalent and burdensome public-health problems, demanding effective health care. We have shown this to be as true in Nepal as it is globally. Information on willingness to pay (WTP) can inform pricing and economic forecasts before new health-care services are introduced. These are the first national data on WTP for headache care within South-East Asia Region.

Methods: In a nationwide population-based cross-sectional study, a representative sample of Nepali-speaking adults (18–65 years) were selected by stratified multistage cluster-sampling. Trained interviewers visited households unannounced and enquired into headache and its attributable burden using a culturally-adapted Nepali translation of the Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire. They enquired into WTP using a bidding game method.

Results: Among 2,100 participants, 1,794 (85.4%; mean age 36.1 ± 12.6 years) reported headache during the preceding year. Participants with headache were willing to pay on average NPR $1{,}134 \pm 2{,}760$ (median 250 [IQR: 100–1,000]) per month for effective headache care (USD $1.00 \approx$ NPR 106). WTP differed significantly ($p = 0.013$) between headache types, being highest among those with probable medication-overuse headache. WTP was positively associated with both frequency and intensity of headache ($p < 0.001$), and therefore least in TTH.

Conclusion: NPR 250 is a day's earnings for an average Nepalese citizen. As a measure of burden, this suggests heavy burden. As a measure of what people with headache would invest in headache services, it signals need but probably not sufficient willingness (or ability) to pay.

EHMTC-0120
POSTER SESSION B

CHRONIC PAIN PATIENT NEUROLOGIST ATTENDANCE IN THE PAIN MANAGEMENT DEPARTMENT

L. Medvedeva[1], O. Zagorulko[1], V. Osipova[2], G. Shevtsova[3]

[1]*Petrovsky National Research Center of Surgery RAMS, Pain Medicine, Moscow, Russia*
[2]*I.M. Sechenov First Moscow State Medical University, Neurology and clinic neurophysiology, Moscow, Russia*
[3]*I.M. Sechenov First Moscow State Medical University, Neurology, Moscow, Russia*

Background and Goal of Study: A cross-sectional study of headaches (HA) prevalence at visits with neurologists in the pain management department in January, 2012 – April, 2014. We analyzed HA distribution, gender-age structure, marital status, education level, pain severity and duration.

Materials and methods: At the first visit to the clinic 556 patients individually filled in a questionnaire, developed in the pain management department and included all the analyzed parameters. The obtained data was processed with IBM SPSS Statistics and MS Excel. The study was approved by local Institution Review Board.

Results and discussion: HA was found in 556 (66.7%) out of 833 patients visited a neurologist, mostly in women (71%) aged 41–50 years. The most common primary HA were tension-type HA (43.2%) and migraine (10.8%). Cluster HA accounted for 0.9%. The secondary HA structure included HA attributed to cerebrovascular disorders (13.3%), cervicogenic HA (10%), myofascial facial pain (8.1%), temporomandibular joint disorder (7%), cranial neuralgia (6.7%). The majority of patients got a higher education (60.9%) and was married (54.3%). The disease history more than three months was in 89.7%, daily pain occurred in 78.2%, moreover 17% estimated the pain severity over 5 points by visual analogue scale. Most patients sought medical help (98.6%), 32% visited five specialists and more. 5.9% sought emergency medical care in the last year. 100% used analgesics to relieve pain, one in three patients did it on the daily basis.

Conclusions: HA is common in pain management department and is marked by high intensity and duration descriptors.

EHMTC-0028
POSTER SESSION B

ROLE OF EEG (ELECTROENCEPHALOGRAPHY) IN PRIMARY HEADACHE

M. Moorthy[1], B. Kesavamurthy[2], S. A. V.[2]

[1]*ERODE, India*
[2]*Madras Medical College, Neurology, Chennai, India*

Introduction: Primary headache is a major cause of work loss in adult males and females, and also major reason for school abstinence in school children.

Aim: To study about the EEG changes in primary headache in children and adults.

Inclusion Criteria: All patients presented with primary headache were included.

Exclusion Criteria: Patients presented with secondary headache of non neurological causes were excluded.

Methods: EEG was done to all patients presented with primary headache, secondary headache of intracranial etiology.

Results: This study is done in 300 patients with neurogenic headache. Males were (45.65 % (137)), Females were (54.35% (163)), Mean age in male adults (43.82) years, male children (9.66) years, Mean age in adult females (38.12) years, female children (11) years, Migraine headache (60%), Tension headache (13%), Autonomic Cephalalgia (12%), Secondary headache due to CNS problem (15%). Primary headache patients showed normal EEG pattern (alpha rhythm) in adults, mixed alpha and theta pattern in children, Comparing secondary headache patients, primary headache patients showed statistically significant normal EEG pattern in tension headache ($P < 0.00001$), Migraine headache ($P < 0.00001$), Autonomic Cephalalgia ($P < 0.00001$). EEG abnormalities noted are occasional slow wave pattern during hyperventilation in primary headache patients; secondary headache patients had slow wave, sharp wave, spike and wave pattern according to the etiology. Secondary headache patients with traumatic head injury showed predominant slow wave pattern in EEG.

Conclusion: EEG is predominantly normal in primary headache. Secondary cause of headache has to be excluded in headache patients with EEG changes.

Keywords: Electroencephalography, Primary headache, Secondary headache.

EHMTC-0409
POSTER SESSION B

PREDICTORS OF INADEQUATE 24-HOUR SUSTAINED RESPONSE TO MEDICATION IN EPISODIC MIGRAINE (EM): RESULTS FROM AMERICAN MIGRAINE PREVALENCE AND PREVENTION STUDY (AMPP)

Sagar Munjal[1], Michael L. Reed[2], Dawn C. Buse[3,4], Alexandre Bennett[1], Kristina M. Fanning[2], Richard B. Lipton[3,4]

[1]*Promius Pharma, Princeton, NJ*
[2]*Vedanta Research, Chapel Hill, NC*
[3]*Montefiore Medical Center, Bronx, NY*
[4]*Department of Neurology, Albert Einstein College of Medicine, Bronx, NY*

Objective: In a sample of persons with migraine we identified the 1) proportion who are usually pain free 2 hours after acute treatment (2hPF), 2) proportion of these with sustained 24 h pain response (2hPF/24hSPR), and 3) factors associated with an inadequate sustained response to treatment.

Background: Rapid pain relief with no recurrence is rated as very important by migraine patients. Population-level predictors of 2 h pain freedom with 24 h sustained response (2hPF/24hSPR) can inform clinical decision-making.

Methods: The AMPP obtained longitudinal postal survey data from a representative US sample of persons with migraine. The 2006 survey included 8333 migraineurs aged 18+ reporting on their initial response to treatment (2hPF, Half the time or more) and on whether a sustained response was achieved (24PR, Does one dose of your migraine medication usually relieve your headache and keep it away for at least 24 hours?). Persons who reported both 2hPF and also responded, Half the time or more, to the sustained response question, were considered to have adequate 24hSPR and those answering, Never, Rarely or Less than half the time, had an inadequate sustained response. Variables not associated with the outcome were trimmed from the final model.

Results: Among those with 2hPF (44%, 3667/8333, 82% female, mean age 47) we found 74.3% (2689/3621) had adequate 24hSPR response while 25.7% (932/3621) had inadequate 24hSPR. The significant ($p < .01$) predictors of inadequate sustained response were higher monthly headache frequency (OR 1.06, 95% CI 1.04–1.07 for each increase in headache), presence of allodynia (OR 1.55, 95% CI 1.30–1.84), clinical depression (OR 1.48, 95% CI 1.19–1.84) and medication overuse (OR 1.29, 95% CI 1.06–1.59).

Conclusions: Among migraineurs who achieve 2hPF (44%) we found that adequate 24hSPR was common (73.4%). However, 25.7% reported return of headache. Persons with frequent headache, allodynia, depression, and medication overuse may be susceptible to headache return despite a robust 2hPF response.

Financial Support: This study was funded and sponsored by Promius Pharma, Princeton, NJ 08540, USA.

Document not received

EHMTC-0067
POSTER SESSION B

PRESENCE OF THE "VISUAL SNOW" PHENOMENON AND ADDITIONAL VISUAL DISTURBANCES IN MIGRAINEURS

I. Petrusic[1], B. Gojsina[1], A. Podgorac[2], J. Zidverc-Trajkovic[3]

[1]*Faculty of Medicine- University of Belgrade- Serbia, Neurology, Belgrade, Serbia*
[2]*Institute of Mental Health- Belgrade- Serbia, Psychiatry, Belgrade, Serbia*
[3]*Neurology Clinic- Clinical Center of Serbia, Center for headaches, Belgrade, Serbia*

Introduction: "Visual Snow" phenomenon presents persistent small flickering dots in the entire visual field and could be accompanied with other visual disturbances. Visual disturbances are often associated with migraine aura, but not every patient with a "Visual snow" phenomenon has migraine. Our goal was to assess the prevalence of the "Visual Snow" phenomenon in patients with migraine without aura (MwoA), migraine with aura (MwA) and healthy controls (HC).

Methods: This study included 150 subjects (MwoA/MwA/HC = 50), aged 18 to 60 years. Each subject had an interview about characteristics for "Visual snow" phenomenon and additional visual disturbances (e.g. flickering dots in the dark, palinopsia). These groups were compared with each other by age, gender and the presence of "Visual Snow" phenomenon and additional visual disturbances.

Results: MwoA and MwA did not differ significantly from HC in relation to age and gender (38,2 ± 11,6 vs. 39,4 ± 10,9 vs. 37,2 ± 11,6; 84% vs. 76% vs. 76% females), respectively. The frequency of "Visual Snow" phenomenon did not differ significantly in compared groups (8% vs. 6% vs. 6%), respectively. There was a statistically significant difference between the groups in relation to the interictal presence of additional visual disturbances (68% vs. 54% vs. 22%), respectively.

Conclusion: Based on these data, it was observed that the frequency of "Visual Snow" phenomenon does not differ between groups, but concomitant visual symptoms are more common in patients with migraine (with and without aura) compared to healthy controls.

EHMTC-0039
POSTER SESSION B

COMORBIDITIES OF PSYCHIATRIC AND HEADACHE DISORDERS IN NEPAL: IMPLICATIONS FROM A NATIONWIDE POPULATION-BASED STUDY

A. RISAL[1], K. Manandhar[2], A. Holen[2], T.J. Steiner[2], M. Linde[2]

[1]*LALITPUR, Nepal*
[2]*NTNU, Neuroscience, Trondheim, Norway*

Background: Headache disorders, anxiety and depression, the major disorders of the brain, are highly comorbid in western countries. Whether this is so in South Asia has not been investigated.

Methods: In a nationwide, cross-sectional survey of the adult Nepalese population (N = 2,100), trained interviewers applied: 1) a culturally-adapted version of the HARDSHIP(*Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation*) questionnaire to diagnose headache disorders; 2) a validated Nepali version of HADS (*Hospital Anxiety Depression Scale*) to detect anxiety (HADS-A), depression (HADS-D) and comorbid anxiety and depression (HADS-cAD); 3) a validated Nepali version of EPQRS-N (*Eysenck Personality Questionnaire Revised Short Form-Neuroticism*); and 4) WHOQOL-8 (*WHO Quality-of-Life [QoL] 8-question scale*). Associations with headache types (migraine, tension-type headache [TTH] and headache on ≥15 days/month[H ≥ 15 d/m]) were analysed using logistic regression for psychiatric casenessand linear regression for neuroticism.

Results: HADS-A was associated with any headache ($p = 0.024$), most strongly with H ≥ 15 d/m(AOR = 3.2) followed by migraine (AOR = 1.7). HADS-cAD was also associated with any headache ($p = 0.050$, females > males [$p = 0.047$]), most strongly with H ≥ 15 d/m(AOR = 2.7), then migraine (AOR = 2.3). Likewise, neuroticism was associated with any headache ($p < 0.001$), most strongly with H ≥ 15 d/m (B = 1.6), followed by migraine (B = 1.3). Psychiatric caseness of any sort, when comorbid with migraine or TTH, aggravated the negative impact on QoL ($p < 0.001$).

Conclusion: Headache disorders are highly comorbid with anxiety and associated with neuroticism in Nepal,

with negative consequences for QoL. These findings call for reciprocal awareness among physicians and others treating headache or psychiatric disorders, and a holistic coordinated approach to management.

EHMTC-0070
POSTER SESSION B

THE PREVALENCE OF MIGRAINE IN IRAN: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Togha[1], M. Behzadifar[2], M. Behzadifar[3]

[1]*Tehran University of Medical Sciences, 6. Headache Department- Iranian Neurological research Center-Neuroscience Institute, Tehran, Iran*
[2]*Iran University of Medical Sciences, Health management and economics research center, Tehran, Iran*
[3]*Lorestan University of Medical Sciences, Department of Public Health, Khorramabad, Iran*

Objective: Headaches and especially migraine are among the most common diseases all over the world. The objective of this study was to determine the prevalence of migraine in Iran.

Methods: We conducted a systematic search in Pub Med, Web of Science (ISI), Embase, Scopus, Ovid, Google Scholar as well as Iranian databases including: MagIran, IranMedex and Scientific Information Databank (SID) from 1980 to November 2015.The Der-Simonian/Laird's random-effects model with a 95% confidence interval employed to estimate the overall pooled prevalence. Heterogeneity was investigated using subgroup analysis based on sample size and time of study.

Results: Thirty studies including 33873 participants met inclusion criteria for analysis. The overall prevalence of migraine in Iran was 14% (95% CI 12%–17%). The results of subgroup analysis by diagnostic criteria showed that pooled prevalence of migraine regarding ICHD-1, ICHD-2, and ID-Migraine was 8 %,17% and 18 % respectively. The pooled prevalence with geographical approach was as follows: Center 11%, North 14%, South 19%, West 21 % and East 8%. Also the pooled prevalence by target groups was as follows: students 13%, general populations 18%, and teachers 10%. Meta-regression model showed that the prevalence of migraine increased by year of publication and decreased by sample size.

Conclusions: This study indicates that the prevalence of Migraine in Iran is high compared with other developing countries. As the emotional and economic impacts of migraine on the society could be significant, social awareness and planning for effective migraine management is necessary.

EHMTC-0024
POSTER SESSION B

QUALITY OF LIFE AND ANXIETY-DEPRESSION SYMPTOMS IN PATIENTS WITH MULTIPLE SCLEROSIS AND COMORBID HEADACHE VERSUS PATIENTS WITH HEADACHE

A. velázquez[1], S. Santos[2], C. iñiguez[3], E. Bellosta[3], C. Pérez[3]

[1]*zaragoza, Spain*
[2]*Lozano Blesa Hospital, Neurology, Zaraggoza, Spain*
[3]*Lozano Blesa Hospital, Neurology, Zaragoza, Spain*

Introduction: Multiple sclerosis (MS) is a demyelinating disease and the main cause of disability in young adults.

Headaches are one of the most common neurological diseases.

Objective: To examine differences in quality of life and anxiety-depression symptoms in patients with MS and headache versus patients with headache.

Material-Methods: The study was performed in the Lozano Blesa Hospital of Zaragoza (Spain) from May 2014-May 2015. We included patients with MS or clinical isolated syndrome (CIS) and headache (migraine, tension type headache, trigeminal neuralgia) and patients only suffering from headache (migraine, tension type headache, trigeminal neuralgia). The following tests were used: HIT6, MIDAS, HADS, SF36. The statistical program SPPS 19.0 was used and p value <0.05 was determined as significant.

Results: We included 83 patients with MS or CIS and headache and 47 patients with headache. There were no differences in mean age and sex.

When comparing quality of life and anxiety and depression symptoms in both groups we found that subject without MS had poorer results in SF36 and higher levels of anxiety with significant differences.

We compared patients with migraine and found that those without MS had higher values in the HADS test and poorer results in SF36. MIDAS results were also higher in these patients.

Conclussions: Although MS is a severe disease with a known impact in patients, with these results we emphasize that headaches can also be disabling. Maybe psychological aspects such as deficient coping strategies, personality traits and pain management can be different in both groups, but this need to be confirmed.

EHMTC-0116
POSTER SESSION B

CAN MIGRAINE BE SPREAD THROUGH SOCIAL NETWORKS IN YOUNG ADOLESCENTS?

S.J. Wang[1,2], S.P. Chen[1,2], Y.R. Pan[1,3], F. Jong-Ling[1,2]

[1]*National Yang-Ming University, Faculty of Medicine, Taipei, Taiwan*
[2]*Taipei Veterans General Hospital, Neurological Institute, Taipei, Taiwan*
[3]*Far Eastern Memorial Hospital, Department of Psychiatry, New Taipei City, Taiwan*

Purpose of the study: The influence of peers' behavior on the youths' own behavior through clustering or contagion effects has been suggested to peak during adolescence. The current study aimed to explore whether the odds of having migraine would be influenced by a youth's friendship with a migraineur.

Methods: A school-based cohort of 620 ninth graders were included in the current analysis among whom 7.6% had migraine. We used a model based on generalized estimating equations to explore the effect of a friend's migraine status on the youth's presence of migraine while simultaneously taking into consideration other related factors including depressive symptoms, socio-economic status and body mass index. Both cross-sectional and longitudinal associations were explored including the type of friendship in order to distinguish between confounding and induction effects.

Results: In cross-section, if a friend had migraine, the risk for the adolescent to have migraine increased by 109% (RR = 2.09, 95% CI: 1.35, 3.22). Longitudinally, when the friendship choices were mutual rather than unilateral, the risk for the adolescent to become a migraineur was 3.59 (RR = 3.59, 95% CI: 1.30, 9.93) if his or her friend became a migraineur during the two-year observational period. No such effects were found in non-mutual friendships.

Conclusion: The study may suggest, that in young adolescents, the presence of induction effects on the development of migraine by one's friendship with a migraineur. Such peer effects are observed only when the friendship choices are mutual. Future efforts to unravel the underlying mechanisms are warranted.

EHMTC-0034
POSTER SESSION B

THE DAILY DYNAMICS OF HEART RATE VARIABILITY IN YOUNG PERSONS WITH TENSION TYPE HEADACHE

K. Grigoreva[1], I. Grigoryeva[1], A. Bahchina[2], S. Polevaia[2]

[1]*Nizhniy Novgorod State Medical Academy, Department of Neurology- Neurosurgery and Medical genetics, Nizhniy Novgorod, Russia*
[2]*Lobachevsky State University of Nizhniy Novgorod, Department of psychophysiology, Nizhniy Novgorod, Russia*

The aim of this study was to investigate the dynamics of heart rate variability (HRV) in patients with tension headache (TTH) during daily activity in order to identify the indicators of autonomic dysfunction.

Materials and methods: We studied 22 patients with a chronic and episodic TTH (age: 23.1 ± 3.1) and 19 healthy persons (age: 23.2 ± 2.3). The investigation included neurological examination, Hospital Anxiety and Depression Scale, assessment of subjective level of emotional disadaptation and telemetric recording of cardiorhythmography under daily life conditions. HRV was recorded 4 times a day. Autonomic regulation of heart rate was assessed by means of both time and frequency domain analyses of HRV with measuring of standard deviation of inter-beat interval (SDNN), total power (TP), power in low frequency and power in high frequency (HF).

Results: The TTH patients had higher levels of anxiety and depression, as well as reduced average daily SDNN, TP and HF in compare with the healthy controls. The difference also concerned the dynamics of HVR during the day. SDNN and TP increased in the second half of the day in compare with the first half of the day in the healthy persons but not in the patients ($p < 0{,}01$). The monotony of daily HRV profile in the patients was associated with high level of emotional stress.

These findings can be used to identify the objective indicators of autonomic dysregulation in TTH as well to control the effectiveness of patients treatment.

EHMTC-0166
POSTER SESSION B

THE COMPARISON OF STRENGTHING EXERCISE EFFICACY BETWEEN TENSION HEADACHE PLUS NECK PAIN AND CERVICOGENIC HEADACHE

F. martami[1], M. abolhasani[2], S. Razeghi Jahromi[1], S. Maryam[1], M. Togha[3]

[1]*National Nutrition and Food Technology Research Institute, faculty of nutrition and food technology, Tehran, Iran*
[2]*Neuroscience Institute, Sport Medicine Research Center, Tehran, Iran*
[3]*Neuroscience Institute, Headache department- Iranian Center of Neurological Research, Tehran, Iran*

Objective: Tension type headache (TTH(is the most prevalent form of adult benign headache. TTH contribute to a large burden of disability.Cervicogenic headache (CH) is a recently validated type of headache.The aim of thisstudy is the comparison of Strengthing Exercise efficacy between tension headache and cervicogenic headache.

Methods: In this study we enrolled 70 untrained patients in two groups. One group($n = 35$) had tension headache plus cervicogenic headache and other group had only cervicogenic headache. Both groups received a training program consist of isometric Strengthing exercise of neck muscles, strengthing of deep flexors of neck and shoulder girdle muscles, 3 times per week during 8 weeks.The intensity of headache was measured at the baseline and after intervention with VAS (Visual Analog Scale).

Results: Both groups had reduction of pain intensity at the end of study but As a result, exercise program reduced significantly The intensity of pain in tension headache plus cervicogenic headache group (2.5 ± 1.3)as comparison with cervicogenic headache significantly. (0.86 ± 1.3). ($p = 0.00$).

Conclusion: Exercise may be an option for the treatment of tension and cervicogenic headache. According to these study isometric strengthing exercises of neck muscles, strengthening of deep flexors and shoulder girdle muscles exercise can reduce intensity of pain in tension headache plus cervicogenic headache superior than cervicogenic headache alone. Further high quality research is required to determine the effectiveness of different types of exercise in different types of headache.

EHMTC-0077
POSTER SESSION B

PECULIARITIES OF MYOFASCIAL COMPONENT OF PAIN IN PATIENTS WITH TENSION-TYPE HEADACHE

Y. Romanenko[1], V. Romanenko[2], I. Romanenko[3]

[1]*Kiev Regional Clinical Hospital, Department of Neurology, Kiev, Ukraine*
[2]*Bohomolets National Medical University, Department of Neurology, Kiev, Ukraine*
[3]*Lugansk State Medical University, Department of Neurology, Rubizhne, Ukraine*

Aim of Investigation: The aim of this study was to determine the role of myofascial component of pain in patients with episodic (ETTH) and chronic tension-type headache (CTTH), as well as its relation to anxiety and depression.

Methods: Twenty seven patients (11 men and 16 women) aged 20 to 60 years were examined. Data of the classical neurological and manual examination, Spielberger State and Trait Anxiety Inventory, Beck's Depression Inventory and Visual Analogue Scale (VAS) were analyzed. To assess the level of pain during palpation 4 point qualitative scale was used, where 0 is no pain, 1 – weak pain, 2 – moderate pain, 3 – severe pain.

Results: 62.96% of patients had ETTH and 37.04% – CTTH. Mean intensity of pain was 7.29 and 8.20 points on VAS in ETTH and CTTH groups accordingly. Levels of anxiety and depression were higher in CTTH group comparing to ETTH group. Mean levels of pain during palpation of pericranial and cervical muscles was higher in patients with ETTH comparing to patients with CTTH (1,18 and 1,3 accordingly). Comorbid anxiety and depression resulted in higher levels of pain during muscle palpation in both groups and was higher in CTTH group (2,1 points) comparing to ETTH group (1,9 points).

Conclusions: Patients with CTTH have higher levels of pain, anxiety and depression comparing to patients with ETTH. Presence of anxiety, depression or both to clinical picture facilitates higher levels of pain.

EHMTC-0080
POSTER SESSION B

SOMATOSENSORY TEMPORAL DISCRIMATION TEST DIFFERENTIATES MIGRAINE HEADACHE FROM TENSION TYPE HEADACHE

D. Vuralli[1,2], H.E. Boran[1,2], B. Cengiz[3], O. Coskun[1], H. Bolay[1,2]

[1]*Gazi University Faculty of Medicine, Department of Neurology and Algology, Ankara, Turkey*
[2]*Gazi University, Neuropsychiatry Center, Ankara, Turkey*
[3]*Gazi University Faculty of Medicine, Department of Neurology- Motor Control Laboratory, Ankara, Turkey*

Background and Objective: Somatosensory temporal discrimination (STD) evaluates temporal threshold to discriminate two separate stimuli. STD was recently demonstrated to be transiently prolonged during a migraine attack, though our knowledge about sensory processing in tension type headache (TTH) is still lacking. We aim to compare STD thresholds during TTH and migraine attack period.

Methods: STDTs were recorded during the headache attacks for TTH and migraine patients. Clinical features of the patients during the headache attack were also recorded.The study included 9 TTH, 9 migraine patients and 9 healthy volunteers without headache. None of the patients were under preventive treatment for TTH or migraine. STDTs were measured at the dorsum of the hands bilaterally (dermatome of C7) by a blind neurologist.

Results: In migraine group, ictal STDTs (137.4 ± 38.0 for the right hand and 119.2 ± 36.3 for the left hand) were significantly higher than ictal STDTs of TTH patients ($p < 0.0001$) and STDTs of healthy volunteers ($p < 0.0001$). There was no statistically significant difference between healthy volunteers and TTH group according to STDTs of the right (38.6 ± 5.3 vs 39.0 ± 5.5, $p = 0.863$) and left (38.3 ± 7.2 vs 40.6 ± 4.6, $p = 0.489$) hand. Ictal STDTs of the contralateral hand (158.1 ± 22.1) were significantly higher ($p = 0.008$) than the ipsilateral hand (98.5 ± 21.6) in migraine patients. The visual analogue scale scores of the migraine patients were positively correlated with the contralateral STDT values ($r = 0.962$, $p < 0.001$).

Conclusion: Sensory perception remains normal during the headache attack in TTH patients. Somatosensory temporal discrimation thresholds may help discriminate TTH attack from migraine attack.

EHMTC-0371
POSTER SESSION C

DOPAMINE BETA HYDROXYLASE (DBH) 19BP INSERTION/DEL POLYMORPHISM INFLUENCES MEDICATION OVERUSE HEADACHE

P. Barbanti[1], R. Palmirotta[2], M.L. De Marchis[2], C. Ialongo[3], G. Egeo[1], C. Aurilia[1], L. Fofi[1], F. Fratangeli[2], D. Della-Morte[4], F. Guadagni[2]

[1]*IRCCS SAN RAFFAELE PISANA, Headache and Pain Unit, Roma, Italy*
[2]*IRCCS SAN RAFFAELE PISANA, Research Center, Roma, Italy*
[3]*University of Rome Tor Vergata, Department of Internal Medicine, Rome, Italy*
[4]*University of Rome Tor Vergata, Department of Systems Medicine, Rome, Italy*

Background: Dopamine is involved in migraine pathophysiology. Dopamine Beta Hydroxylase (DBH) is an enzyme which determines dopamine level, catalyzing its conversion to norepinephrine. The functional DBH 19 bp insertion/deletion (Ins/Del) polymorphism (rs72393728) controls DBH function: deletion correlates to low and insertion to high DBH activity. DBH and dopamine activities show and inverse correlation.

Objective: To assess DBH 19 bp Ins/Del polymorphism in episodic and chronic migraine (CM).

Methods: We studied 400 consecutive patients affected by migraine without aura ($n = 199$), with aura ($n = 71$), CM ($n = 130$) and 204 healthy controls. Sociodemographic factors and the full set of migraine clinical parameters were screened by face-to face interviews using a semi-structured questionnaire. The DBH gene 19 bp Ins/Del polymorphism was determined by a standard PCR amplification PGR and direct sequencing analysis.

Results: Genotypes and the allele frequencies of DBH 19 bp Ins/Del polymorphism in patients with episodic migraine did not significantly differ from those predicted by the Hardy-Weinberg equilibrium while the CM group showed a slight significant deviation from the expected frequencies ($p = 0.04$). Using a dominant inheritance model, the DBH 19 bp Ins/Ins genotype was found to be significantly associated ($p = 0.006$) with patients without medication overuse headache having an OR of 6.79 (95% CI: 1.95–29.70).

Conclusions: Our results indicate that DBH 19 bp ins/del polymorphism does not influence episodic migraine susceptibility or endophenotype but the presence of the insertion allele, associated with high DBH activity, plays a

protective role against medication overuse in the CM patients.

EHMTC-0249
POSTER SESSION C

TRPM8 GENETIC VARIANT IS ASSOCIATED WITH ASTHMA, THERMAL SENSITIVITY, AND ALLODYNIA IN MIGRAINEURS

S.P. Chen[1], J.L. Fuh[1], C. Ming-Yi[2], C.C. Yu[1], S.J. Wang[1]

[1]*Taipei Veterans General Hospital, Department of Neurology, Taipei, Taiwan*
[2]*Taipei Veterans General Hospital, Department of Medical Research, Taipei, Taiwan*

Introduction: TRPM8 is a ligand-gated cation channel responsible for cold pain. Genetic variants of *TRPM8* are associated with migraine susceptibility, and TRPM8 has been hypothesized to be important for cold-induced exacerbation of asthma. We aimed to investigate the role of *TRPM8* variant on asthma, thermal sensitivity and allodynia in migraineurs.

Methods: We prospectively recruited 1,256 clinic-based Taiwanese migraineurs at Department of Neurology, Taipei Veterans General Hospital. All participants received questionnaire-based interview. The diagnosis of migraine was based on the criteria proposed in the International Classification of Headache Disorders, 2nd edition (ICHD-2). rs10166942 in *TRPM8* was genotyped using the Sequenom MassARRAY iPLEX platform, and the genotypes were correlated with clinical variables.

Results: The mean age of the participants was 39.2 ± 12.1 year-old; 80% of them were female. In comparison with T homozygotes ($n = 188$), patients carrying the C allele of rs10166942 (CC and TC genotypes, $n = 1088$) have higher rate of asthma (1.1% vs. 5.2%, $p = 0.008$). In a subset of patients who were specifically inquired for allodynia ($n = 103$), the rs10166942 genotypes were associated with allodynia evoked by wearing earrings ($p = 0.03$), wearing necklaces ($p = 0.03$), wearing anything over arm or wrist ($p = 0.03$), and pouring water over the face ($p = 0.03$). Patients carrying the T allele were especially sensitive to water-induced facial cutaneous allodynia than C homozygotes (21.2% vs. 5.9%, $p = 0.04$).

Conclusion: *TRPM8* rs10166942 is associated with risk of asthma and tactile- and thermal-associated allodynia in migraineurs, with differential allelic effects. Further studies are required to dissect the mechanism.

EHMTC-0256
POSTER SESSION C

GENETIC SCREENING OF CLOCK IN A SWEDISH CLUSTER HEADACHE CASE-CONTROL MATERIAL

C. Fourier[1], M. Zinnegger[1], A. Steinberg[2], C. Sjöstrand[2], E. Waldenlind[2], C. Ran[1], A. Carmine Belin[1]

[1]*Karolinska Institutet, Department of Neuroscience, Stockholm, Sweden*
[2]*Karolinska University Hospital, Department of Clinical Neuroscience, Stockholm, Sweden*

Background: The pathophysiology of cluster headache is largely unknown but one of the main features is a striking rhythmicity in attacks. The CLOCK gene is a transcription factor which serves as a basic driving force for circadian rhythm in humans. A causative role has been suggested for genetic variations in the CLOCK gene and cluster headache.

Aim: To screen three CLOCK single nucleotide polymorphisms (SNPs) in our Swedish case-control material and test for association with the disease. CLOCK gene expression was compared in a subset of patients and controls.

Method: 390 cluster headache patients and 578 healthy controls were genotyped for three CLOCK SNPs using TaqMan® quantitative real-time PCR (qPCR). Additionally, CLOCK mRNA expression was measured in fibroblasts from five patients and five controls with quantitative real-time reverse transcription PCR using SYBR® Green chemistry.

Results: Our genotype data show significant association between one of the SNPs, rs12649507, and cluster headache ($p < 0.0051$), and variable CLOCK gene expression can be observed in a subset of our cluster headache case-control material. Preliminary data suggests that patients have lower CLOCK mRNA expression compared to controls.

Conclusion: A significant association has been found between rs12649507 and cluster headache in Sweden. Furthermore, variable CLOCK mRNA expression has been observed in patients and controls. We will validate these findings in a larger sample set and study the functional consequences of rs12649507 in order to draw conclusions on CLOCK involvement in cluster headache.

EHMTC-0368
POSTER SESSION C

CALCA GENE POLYMORPHISM INFLUENCES THERAPEUTIC RESPONSE TO ONABOTULINUMTOXIN A IN FEMALE CHRONIC MIGRAINE PATIENTS

R. Moreno[1], M. Ruiz[2], E. Cernuda-Morollón[3], A. Gago[4], I. Vidriales[1], M. Gallego de la Sacristana[4], J. Pascual[3], J.J. Tellería[5], A.L. Guerrero[6]

[1]*Hospital Clínico Universitario de Valladolid, Clinical Analysis, Valladolid, Spain*
[2]*Hospital Clínico Universitario de Valladolid, Neurology, Valladolid, Spain*
[3]*Hospital Universitario Central de Asturias, Neurosciences, Oviedo, Spain*
[4]*Hospital Universitario La Princesa, Neurology, Madrid, Spain*
[5]*University of Valladolid, IBGM, Valladolid, Spain*
[6]*Hospital Clínico Universitario de Valladolid, Neurologist, Valladolid, Spain*

Introduction: Onabotulinumtoxin A (OnabotA) is effective in Chronic Migraine (CM) patients, but some migraineurs do not respond adequately. Interictal levels of Calcitonin gene-related peptide (CGRP) are increased in women with CM and may be of help in predicting response to OnabotA. Calcitonin related polypeptide alpha (CALCA) gene encodes calcitonin, katacalcin and CGRP and its polymorphisms have been proposed to be associated with migraine.

Aim: To analyze the influence of CALCA gene promoter polymorphism rs3781719 c.−767 T > C in the response to OnabotA in women with CM.

Methods: We included 150 CM female patients treated with OnabotA according to the PREEMPT paradigm in three headache units. OnabotA was offered to patients that had not responded to topiramate and at least one other preventive. Age at inclusion 43.7 ± 11.8 years (16–74). Patients with a reduction of at least 50% in the number of migraine days after two OnabotA procedures were considered as responders. Genotyping was performed using KASP probes and data were obtained in a LyghtCycler-480 (Roche-Diagnostics). Allelic, genotypic frequencies and dominance hypothesis of each allele between responders and non-responders were compared by X^2-test.

Results: Response to OnabotA was achieved in 117 patients (78%). All the comparisons showed significant differences between groups. C allele represents 40.9% in nonresponders, while it represents 26.9% in responders ($p = 0.029$). There were also significant differences in C dominance hypothesis ($p = 0.007$).

Conclusion: Polymorphic variations of CALCA gene might play a role as a prognostic marker of efficacy of OnabotA in women with CM in our population.

EHMTC-0301
POSTER SESSION C

ANALYSIS OF HYPOCRETIN RECEPTOR 1 GENE (HCRTR1) AND SEROTONIN TRANSPORTER GENE (SLC6A4) POLYMORPHISMS IN POLISH PATIENTS WITH MIGRAINE

M. Kowalska[1], M. Kapelusiak-Pielok[2], W. Kozubski[2], J. Dorszewska[1]

[1]*University of Medical Sciences, Department of Neurology-Laboratory of Neurobiology, Poznan, Poland*
[2]*University of Medical Sciences, Chair and Department of Neurology, Poznan, Poland*

Migraine (MA, migraine with aura; MO, migraine without aura) is a common neurological disorder that affects 11% of population worldwide. It is believed that both hypocretinergic and serotonergic systems play a role in migraine pathomechanism. Hypocretin is involved in the autonomic processes and modulation of pain. The serotonergic system is responsible for both physiological and pathological conditions. Moreover, serotonin (5-HT) inhibits activity of hypocretin neurons.

The aim of the study was to analyze *HCRTR1* G1222A and 5-HTTLPR polymorphisms and hypocretin-1, and 5-HT plasma level in migraine patients.

The study included 48 migraine patients (MA:22, MO:26; mean age 40 ± 15) and 75 controls (mean age 39 ± 14). The PCR, HRMA, sequencing were used to determine genetic polymorphisms of analyzed genes. 5-HT concentration was determined by HPLC/EC technique, while hypocretin-1 level by ELISA method.

The genotype AA (G1222A) *HCRTR1* was more frequent in migraine than in controls. The hypocretin-1 level was lower in migraine as compared to controls ($p < 0.05$). Short (S) allele of 5-HTTLPR polymorphism occurred more frequent in migraine than in controls and was associated with increased 5-HT plasma concentration tendency in migraine. The 5-HTTLPR SL was associated with lower concentration of hypocretin-1 and higher 5-HT level in migraine as compared to controls ($p < 0.05$). The 5-HT concentration was reduced in both MA and MO patients with migraine attack longer than 48 hours.

The *HCRTR1* G1222A seems to be a risk factor for migraine in Polish population. The level of 5-HT is decreased only in patients with longer time of migraine attack.

EHMTC-0248
POSTER SESSION C

EPIGENETIC DNA METHYLATION CHANGES ASSOCATED WITH HEADACHE CHRONIFICATION: A RETROSPECTIVE CASE-CONTROL STUDY

B.S. Winsvold[1], P. Palta[2], E. Eising[3], C.M. Page[4], A.M.J.M. van den Maagdenberg[5], A. Palotie[2], J.A. Zwart[1]

[1]*FORMI and Department of Neurology, Oslo University Hospital and University of Oslo, Oslo, Norway*
[2]*Institute for Molecular Medicine Finland FIMM, University of Helsinki, Helsinki, Finland*
[3]*Department of Human Genetics, Leiden University Medical Centre, Leiden, Netherlands*
[4]*Division of epidemiology, Norwegian Institute of Public Health, Oslo, Norway*
[5]*Department of Human Genetics and Department of Neurology, Leiden University Medical Centre, Leiden, Netherlands*

Background: The biological mechanisms of headache chronifiction are not well understood. We aimed to identify changes in DNA methylation associated with the transformation from episodic to chronic headache.

Methods: Participants were recruited from the population-based HUNT-Study, Norway. Cases (36 women) who transformed from episodic to chronic headache between examinations at baseline and follow-up 11 years later were matched against 35 controls not developing chronic headache. We quantified DNA methylation at both time points at >450,000 sites. Change in DNA methylation level for each site was compared between cases and controls by linear regression. Data were analyzed in two stages and in a combined meta-analysis.

Results: The 20 CpG sites identified in stage 1 did not replicate in stage 2 after correction for multiple testing. In the combined meta-analysis the strongest association was found for marker cg01010870 (P-value $= 6.17 \times 10^{-6}$) related to SH2D5, a gene highly expressed in the brain with a presumed role in regulating synaptic plasticity. Functional enrichment analysis pointed to specific processes including calcium ion binding and estrogen receptor pathways.

Conclusion: In this first epigenome-wide study of DNA methylation in headache chronification we identify genetic loci potentially implicated in the transformation to chronic headache. The study exemplifies the use of prospectively collected population data to search for epigenetic mechanisms of disease.

EHMTC-0372
POSTER SESSION C

CHRONIC POSTTRAUMATIC HEADACHE IN CHILDREN AND ADOLESCENTS: SYSTEMATIC REVIEW AND VALIDITY OF ICHD-3 BETA

I. Abu-Arafeh[1], L. Shaw[2]

[1]*Royal Hospital for Children, Fraser of Allander Neurosciences Unit, Glasgow, United Kingdom*
[2]*Forth Valley Royal Hospital, Paediatrics, Larbert, United Kingdom*

Objectives: To ascertain the incidence of chronic headache in children after head injury and to assess the validity of ICHD- 3 beta for the diagnosis, based on clinical features and onset of symptoms.

Methods: Electronic search of all published studies on headache in children and adolescents after head injury. Search included Pubmed, embase, google scholar and scopus. Only papers with original data were included and review papers were screened for possible missing studies. Conference abstracts were also screened for original data. Descriptive analysis and simple statistics were used.

Results: Four Studies were eligible for inclusion with a total number of 3308 patients under the age of 18 years (Mean age 12 years). Boys were slightly more likely to be affected than girls. Most cases followed mild traumatic head injuries. The incidence of chronic headache at follow up between 3 and 12 month was 13.2%. Headache types were consistent with primary headache disorders including migraine, tension-type headache and chronic daily headache. Available data show good validity of the diagnostic criteria of ICHD- 3beta. Most patients had their headache started within one week of injury and persisted beyond 3 months. Other concussion symptoms were also present.

Conclusions: Chronic posttraumatic headache is a common disorder affecting an average of 13% of children after head injury and ICHD-3 beta is a valid tool for diagnosis.

EHMTC-0097
POSTER SESSION C

MENSTRUATION- RELATED HEADACHES IN A SAMPLE OF NIGERIAN TEENAGE GIRLS

P. Adebayo[1], F. Otubogun[2], R. Akinyemi[3]

[1]*Ladoke Akintola University and Teaching Hospital, Internal Medicine/Neurology, Ogbomoso, Nigeria*
[2]*Federal Medcial Centre, Internal Medicine, Abeokuta-Ogun State, Nigeria*
[3]*Institute forAdvanced Medical Research and Training., College of Medicine- University of Ibadan, Ibadan, Nigeria*

Introduction: Migraine attacks associated with menstruation are generally perceived as more severe than attacks outside this period. There is paucity of data-driven scientific reports from sub-Saharan African on the burden of menstrually-related migraine(MRM) especially among adolescents.

Aim and Objective: The study aimed at determining the frequency of mestrually-related headaches among a cohort of high school girls in Abeokuta,south-western, Nigeria. We also aimed to document headache burden among these school girls.

Methodology: A cross-sectional study using a validated adolescent headache survey questionnaire. Self-administration of the instrument was done in three(3) high schools. Headaches were classified using the ICHD-II criteria.

Results: Of the 183 students that were interviewed, 123(67.2%) had recurrent headaches. Mean age $\pm$ SD, 16.18 $\pm$ 1.55 (range 12–19). Migraine headache was present in 21/183(11.5%%), 11/183 (6.0%) had possible migraine, 71(38.8%) had tension type headaches while other headaches types were 5/183(2.7%). Twenty-six subjects (21.1%) had mestrually-related headaches (MRH). The mean age of subjects with MRH and those without MRH is 16.52 $\pm$ 1.80 and 16.09 $\pm$ 1.48 (p value = 0.386). Median pain severity score is higher among MRH group ($p = 0.043$).The median number of days of reduced productivity was significantly higher in the MRH group ($p = 0.001$);so also is the median number of days of missed social activities ($p = 0.03$). Only 43(35%) respondents have visited a doctor for their headaches.

Conclusion: Menstrually-related headache is prevalent among this cohort of adolescent girls and it has an adverse effect on their productivity and social lives. Headache education should be intensified among Nigerian adolescent and their parents/caregivers. Headache care should equally be optimized.

EHMTC-0298
POSTER SESSION C

BRAIN AND ANGIO-MRI IN CHILDREN WITH HEADACHE

E. Antonaci[1], S. Spairani[1], M.M. Mensi[1], E. Maffioletti[1], M.A. Chiappedi[1], A. Pichiecchio[1], U. Balottin[1]

[1]*C. Mondino National Neurological Institute, Child Neuropsychiatry Unit, Pavia, Italy*

Introduction: Very few studies investigated findings of brain and angio-MRI in children and adolescents.

Aim: To evaluate whether brain and angio-MRI can help investigating the aetiology of headache in children.

Methods: Twenty-four patients (mean age = 11 y-old) seen for headache in a third-level Italian Centre were diagnosed using ICDH-IIIβ criteria. All patients were physically examined for associated neurological and psychiatric problems and a detailed history was taken to assess headache frequency and, when organic underlying pathology was suspected, instrumental brain and angio-MRI were obtained.

Results: The patients' clinical diagnosis were: tension headache 46%, migraine with aura 17% and without aura 21%, headache with mixed characteristics 12%, cluster headache 4%. Comorbidities were present in 37.5% of patients: psychiatric 44%, both psychiatric and neurological 34%, general medicine comorbidities 22%. Brain MRI showed normal findings in 65% of patients, anatomical variants in 4%, findings of uncertain pathological significance in 9% and pathological alterations in 17%. No pathological angio-MRI findings could be detected; only 2 cases showed anatomical variants (that is hypoplasia of vertebral artery and anterior cerebral artery trifurcation). No correlation between headache and angio-MRI anatomical variants was found.

Conclusions: Brain MRI was normal in the majority of our patients, while angio-MRI findings were normal in all patients. These results highlight the difficulty for physicians to decide when, in addition to brain MRI, to require further angiographic neuroimaging for an underlying potential vascular brain pathology. Considering the small cohort investigated, further studies are necessary to confirm our data.

EHMTC-0198
POSTER SESSION C

QUALITY OF LIFE, MOOD AND ACCESS TO PSYCHOLOGICAL SERVICES IN CHILDREN AND YOUNG PEOPLE SEEN IN A SPECIALIST HEADACHE CLINIC

H. Bullock[1], P. Prabhakar[2]

[1]*Great Ormond Street Hospital, Psychological Services, London, United Kingdom*
[2]*Great Ormond Street Hospital, Neurology, London, United Kingdom*

Objectives: All children and young people (CYP) attending their first appointment in the Children's Headache Clinic were asked to complete a number of questionnaires to inform assessment and treatment. Data collected in relation to quality of life (QOL), anxiety and depression and access to psychological services was collated and analysed.

Methods: The Paediatric Quality of Life Inventory (PedsQL) was completed by parents and CYP. The Revised Children's Anxiety and Depression Scale (RCADS) was completed by CYP only. Parents reported on input received from other services.

Results: PedsQL: Completed by 112 CYP and 110 parents. Mean scores indicated impaired QOL relative to the UK population, with school functioning the area in which the greatest percentage scored at least one standard deviation below the mean (71% self report, 61% parent report).

Rcads: Completed by 109 CYP. 48/109 (44%) scored at the borderline clinical threshold or above on at least one scale.

Only 26 CYP were reported to have access to psychological services.

Discussion: Overall, CYP presenting to a specialist headache clinic report reduced QOL. A large number also report symptoms of anxiety or depression. While a questionnaire can help to identify these CYP, there is an overlap between symptoms of migraine and those used to assess mood (e.g. reduced energy) and further assessment by a clinician is required. Despite the impact on QOL and mood concerns, only a minority of CYP referred to a specialist headache clinic have accessed psychological services.

Conflict of interest
Disclosure statement:
Dr Prab Prabhakar:
Paid Research undertaken for
MSD (Rizatriptan)
NIHR (Propanalol, Pizotifen)
BMS
Almirall
Advisory role for OUCH, Migraine Trust, BASH
Member Paediatric Sub Committee IHS

EHMTC-0066
POSTER SESSION C

SITE LOCKED HEADACHES IN CHILDREN AND ADOLESCENTS

S. Grossman[1], M. Ahmed[2]

[1]*Great Ormond Street Hospital for Sick Children- WC1N 3JH- UK, Deptartment of Cardiology, London, United Kingdom*
[2]*Queen's University Hospital- Rom Valley Way- RM7 0AG- UK, Paediatric department, Essex, United Kingdom*

Objective: Main aim of this study was to examine the aetiology and the yield of brain imaging among children with SLH.

Methods: Patients must have SLH, be at least 5 years of age, have had at least 5 headache attacks and have normal neurological examination. Those with bilateral or alternating unilateral headaches were excluded. Data collected prospectively. Headache diagnosis was based on to the ICHD.

Results: In total 292 eligible patients with SLH were identified (60% females; 39% of ethnic origin; age range = 5.1 to 17 years). SLH were unilateral (177/292), occipital (104/292) and vertex (11/292). Topographically, anterior headache was the most frequent (133/292). Headache diagnoses included migraine (192/292), tension type headaches (30/292), medication-overuse headaches (22/292), and others (5/292). Headache remained not yet specified in 43/292. MRI brain of scanned (283/292) patients was either normal (96%) or showed a non-specific non-significant abnormality (4%).

Conclusion: In the absence of abnormal neurological findings, SLH is unlikely to be caused by an underlying sinister aetiology, and brain imaging should not be arranged routinely. Our findings showed that SLH is more likely to be caused by primary headaches and in particular migraine. Further studies to examine the precise mechanism underlying the topography of primary headaches are required.

EHMTC-0045
POSTER SESSION C

CHARACTERISATION OF THE PREMONITORY STAGE OF MIGRAINE IN PAEDIATRIC MIGRAINEURS

N. Karsan[1], P. Goadsby[1], P. Prabhakar[2]

[1]*King's College London, Headache Group- Basic and Clinical Neuroscience- Institute of Psychiatry- Psychology and Neuroscience and NIHR-Wellcome Trust King's Clinical Research Facility, London, United Kingdom*
[2]*Great Ormond Street Hospital for Children NHS Foundation Trust, Department of Neurology, London, United Kingdom*

The premonitory phase of migraine is an increasingly recognised area of interest within headache research. This phase has not been studied in paediatric patients.

Data was collected from clinic letters of paediatric patients who had premonitory symptomatology recorded. These patients were seen between 2010 and 2015 at Great Ormond Street Hospital by an experienced headache neurologist. The age range of patients was 1 to 15 years. The phenotype of recorded premonitory symptoms, headache diagnosis, migraine markers, mode of delivery and developmental milestones were noted.

Of the 87 patients, 59 (68 %) were female. The most common diagnosis was chronic migraine ($n = 47$, 54 %), followed by episodic migraine, New Daily Persistent Headache with migrainous features and sporadic hemiplegic migraine. 93% were born between 38 and 42 weeks gestation, with 74 % born by spontaneous vaginal delivery. Infantile colic was recorded in 29 (33 %), and was the most common migraine marker. One premonitory symptom was reported in 11 (13 %) while at least two premonitory symptoms were reported in 76 (87 %). The most common premonitory symptoms reported were mood change, followed by fatigue, yawning and neck stiffness.

Although the population prevalence of premonitory symptoms in paediatric migraineurs is unknown, it is clear the premonitory stage of migraine exists in children as young as a year old. The clinical phenotype is comparable to adults. Better documentation of this stage will aid parents and clinicians to understand the phenotype of attacks, better recognise migraine and initiate appropriate management.

EHMTC-0294
POSTER SESSION C

BRAIN MRI IN A POPULATION OF PEDIATRIC PATIENTS WITH HEADACHE

M.M. Mensi[1], S. Spairani[1], E. Antonaci[1], E. Maffioletti[1], A. Pichiecchio[2], M.A. Chiappedi[1], U. Balottin[1]

[1]*C. Mondino National Neurological Institute, Children and Adolescent Neuropsychiatry, Pavia, Italy*
[2]*C. Mondino National Neurological Institute, Neuroradiology, Pavia, Italy*

Introduction: In children, there are not many studies that correlate headache and brain MRI results.

Aims: investigate the radiological brain MRI findings in children diagnosed with headache.

Methods: Eighty-four patients (mean age = 11 y-old) seen for headache in a third-level Italian Centre were diagnosed using ICDH-IIIβ criteria. All patients were physically examined for associated neurological and psychiatric problems and a detailed history was taken to assess headache frequency and, in suspicious case of organic pathology, they performed different instrumental exams on the clinical basis and all of them underwent brain-MRI to clarify their diagnosis.

Results: The patients' clinical diagnosis were: tension headache 46%, migraine with aura 17% and without aura 21%, headache with mixed characteristics 12%, cluster headache 4%. Comorbidities were present in 37.5% of patients: psychiatric 44%, both psychiatric and neurological 34%, general medicine comorbidities 22%. Brain MRI showed normal findings in 62% of patients, anatomical variants in 8%, findings of uncertain pathological significance in 19%) and pathological alterations in 11% (1 case of pseudotumor and 1 of cerebellar astrocytoma correlated with headache). ENT (Ear, Nose, Throat) disorders were documented in 24% of patients: 5% nasopharynx hypertrophy, 19% paranasal sinus disease, 5% mastoid involvement.

Conclusions: The majority of our patients had normal MRI findings, while 27% presented nonspecific findings. We encourage others studies with the aim to clarify the role of this nonspecific findings. Moreover, it is important to highlight that 24% had ENT disorders with the advice to exclude during assessment ENT disorders that could be easy treatable.

EHMTC-0295
POSTER SESSION C

INTELLECTUAL ABILITIES IN ADOLESCENTS WITH HEADACHE USING THE WISC-IV: A CONTROLLED STUDY

M.M. Mensi[1], E. Zavani[1], E. Antonaci[1], E. Maffioletti[1], M.A. Chiappedi[1], U. Balottin[1]

[1]*C. Mondino National Neurological Institute, Child Neuropsychiatry Unit, Pavia, Italy*

Introduction: In literature studies regarding cognitive aspects of headache in children and adolescents are not consistent.

Aims: To address this issue, we conducted a controlled study to investigate the intellectual abilities of adolescents affected by idiopathic headache compared to a control group of healthy peers.

Methods: Thirty patients aged 11.0–14.0 (male:female ratio: 1:2), seen for headache in a third-level centre in Italy, and 30 healthy subjects matched for age and gender, attending a state school in the same geographic area, were enrolled in this study. The diagnosis of headache in the case group was established according to the ICHD-III criteria. The general cognitive functioning of cases and controls was evaluated by the WISC-IV test.

Results: The patient group included 14 subjects with Tension-Type Headache and 16 with Migraine. All adolescents had a normal cognitive performance, but those with headache had a statistically significant lower score in the WISC-IV subtests Digital Span ($p < 0{,}001$) and Similarities ($p < 0{,}001$) and in the Working Memory Index ($p = 0{,}012$).

Conclusions: Our results suggest that, even in the normal range, cognitive functions of adolescents with headache related to memory and verbal skills are lower when compared to healthy peers.

EHMTC-0310
POSTER SESSION C

TENSION-TYPE HEADACHES AND CO-MORBID CONDITIONS IN CHILDREN AND ADOLESCENTS

Y. Nesterovskiy[1], N. Zavadenko[2], E. Shipilova[2]

[1]*Moscow, Russia*
[2]*Pirogov Russian National Research Medical University, Department of neurology- neurosurgery and medical genetics Pediatric faculty, Moscow, Russia*

Objective: to study the influence of TTH on daily activities and incidence of co-morbid conditions in pediatric patients including emotional disorders, fatigue syndrome.

Method: 50 patients aged 7–17 years with TTH were examined. The assessment of headache influence on daily life was carried out by HIT-6 [Kosinsky M. et al., 2003]. Parents and children were interviewed using R.A. Barkley [1997] neurobehavioral assessment. For the assessment of fatigue manifestations the Multidimensional Fatigue Inventory (MFI-20) [Smets E.M. et al., 1995] was used.

Results: according to the results of the HIT-6 index, the influence of TTH on the quality of life was estimated as moderate in 54% and marked in 26 % of patients.

Anxiety disorders were diagnosed in totally 80% of patients, among them specific phobias in 58%, sociophobia in 48%, generalized anxiety disorder in 34%. Dysthymic disorder was confirmed in 12% of patients, depressive disorder in 10%. Manifestations of chronic fatigue syndrome were revealed in 72%. The average total score for MFI-20 in our group of patients with TTH was $58{,}2 \pm 1{,}9$. The scores for MFI-20 subscales had attained $13{,}2 \pm 0{,}6$ for "the general fatigue", $12{,}3 \pm 0{,}5$ for "the lowered activity" $11{,}2 \pm 0{,}6$ for "the physical fatigue".

Conclusions: anxiety disorders, fatigue syndrome are prevalent in child and adolescent patients with TTH. The clinical features of TTH and their course are dependent on the co-morbid disorders and their expression. Thus, not only characteristics of TTH, but also manifestations of the co-morbid disorders must be considered for the management of TTH in children and adolescents and optimal choice of pharmacotherapy.

EHMTC-0234
POSTER SESSION C

HOW DO WE MANAGE CHILDREN WITH PRIMARY HEADACHES IN A TERTIARY CENTRE?

A. Psychogiou[1], M. Ray[2]

[1]*Manchester, United Kingdom*
[2]*Leeds Teaching Hospital, Paediatric Neurology, Manchester, United Kingdom*

Background and aims: Headaches are common in childhood and adolescence and are associated with lower quality of life and poor academic performance. We audited whether headaches were being managed in accordance with National Institute for Health and Clinical Excellence guidelines.

Methods: We reviewed the case notes of 30 patients, who were referred to the paediatric neurology outpatient clinic at Leeds Teaching Hospital for recurrent headaches, in the period of September 2014- February 2015. Children were diagnosed using the International Classification of headache disorders –II criteria.

Results: The majority of patients (80%) came from general practice. Neuroimaging was performed in 60% and incidental abnormalities were detected in 13.3%. Headache diaries were suggested in only half of the children. 67% were migraineurs and 20% had chronic daily headaches. 7 children with migraines were offered preventive medications but the choice of drugs used varied amongst clinicians. Records of advice provided regarding non-pharmacological management was suboptimal. The documentation of explanation of risk of medication overuse headache was available only in 53.3%. Formal quality of life assessment in follow-up was unavailable.

Conclusions: Migraines are common and treatment practices vary widely as evidence based guidance for pharmacological therapy is only available in those >12y. Making patients aware of medication overuse headaches and documentation of advice for non-pharmacological treatment warrants attention. The use of headache diary as well as provision of written information about headaches disorders and support organizations is inadequate and needs encouragement. The development of headache service is desirable.

EHMTC-0274
POSTER SESSION C

WHEN MOM ISN'T AROUND- THE INNOVATIVE USE OF A MIGRAINE ACTION PLAN TO DECREASE HEADACHE RELATED DISABILITY IN SCHOOL

E. Rende[1]

[1]*Duke University Medical Center, Pediatric Neurology- DUMC 3922, Durham- North Carolina, USA*

Childhood migraine headache (CMH) is a disabling headache disorder that affects 2.7–11% of school- aged children five through 12 years of age. For children with CMH, the degree of disability is directly associated with headache severity, duration, and frequency; 8% of children with CMH miss at least six school days per year. To decrease school absences and headache related disability, children must have ready access to their prescribed treatment. Administration of medication within the recommended 15–30 minutes means the difference between resolution of the headache and staying in school, or having the headache worsen, requiring the child to go home.

A Migraine Action Plan (MAP), used by the child and modeled after the Asthma Action Plan, facilitates communication between the child/parent, provider, school nurse, teacher and school staff, and helps the child get their prescribed headache medication in a timely manner. The MAP helps determine whether the child has a CMH or less severe headache, the correct medication and dose, and lists individualized comfort measures such as a dark room or caffeinated drink.

This presentation will discuss features of CMH, differences between CMH and ordinary headache, and current medications used to treat CMH. Barriers to prompt treatment of CMH will be identified. Examples of individualized MAPs will be discussed and blank forms will be available.

Collaboration between the school nurse, child/parent, provider and teacher is essential to prevent school absences from CMH. The use of the MAP fosters self-management skills, promotes health and builds confidence in the growing child.

EHMTC-0276
POSTER SESSION C

A PEDIATRIC HEADACHE CLINIC EXEMPLAR-THE ROLE OF THE ADVANCED PRACTICE NURSE IN THE ASSESSMENT AND MANAGEMENT OF CHILDHOOD HEADACHES

E. Rende[1]

[1]*Duke University Medical Center, Pediatric Neurology-DUMC 3922, Durham- North Carolina, USA*

Childhood headaches affect greater than 50% of children from early childhood through 18 years of age. Though childhood headaches are often managed by the primary care provider, a significant number of children are referred to pediatric neurologists for further evaluation. Both headache-related disability and parental anxiety necessitates the prompt evaluation and establishment of a headache management plan. Access to the appropriate specialty care is limited by the lack of sufficient pediatric headache specialists and prolonged wait times.

The advanced practice nurse (APN) role is developing and being implemented across European and non-European countries. This exemplar demonstrates how the use of the APN with expertise in pediatric headache can augment this specialty care. The APN has been proven to be a cost effective provider. Other benefits of the use of the APN include, but are not limited to, improved access to specialty care and enhanced coordination of care with primary care providers and school staff. The APN's impact on patient care indicates that patient satisfaction is at least equal, if not higher, than their physician counterparts.

The education and role description of the APN will be defined. Barriers to the implementation of the advanced practice nursing role in an out-patient setting will be examined. Additional dialogue focuses on the rules and regulations that define the APN's scope of practice and the implementation of health workforce planning.

This presentation highlights the feasibility and importance of the APN's role as an integral part of the pediatric headache health care team.

EHMTC-0262
POSTER SESSION C

CLINICAL PROFILE AND TREATMENT OUTCOME OF MIGRAINE IN CHILDREN: A 2 YEARS FOLLOW UP OBSERVATIONAL STUDY FROM NORTH INDIA

A. Srivastava[1], D. chowdhury[1], G.A. Khwaja[1]

[1]*GB Pant Hospital, Neurology, NEW DELHI, India*

Background: Migraine in children has a distinct clinical profile and differs from adults in terms of certain unusual associated symptoms, attack duration and treatment.

Objective: To elaborate the clinical profile and treatment outcome of migraine in children ($\leq$12 years).

Methods: Pediatric migraine patients (diagnosed by ICHD3β) were followed up for 2 years. The clinical profile, treatment and outcomes were studied.

Results: 75 children diagnosed with migraine had headache onset at 4 ± 1.9 years. Migraine was commoner in boys (64%vs36%). Mean attack duration was 8.2 ± 7.8 hours but 21% had duration only upto 2 hours (probable migraine). Nausea (70.7%), vomiting (40%), phonophobia (86.7%), photobhobia (82%) and inhibition of activity (89.3%) was seen. 53% had holocranial, 37% hemicranial and 20% hemi-holocranial headaches. Headaches were severe ($70\% \geq 6$ on VAS). Attack frequency was 9.25 ± 10.2d/month. 17% had chronic migraine at presentation. Migraine with aura was present in 4%. Commonest trigger was sunlight exposure followed by stress, missing meals and sleep deprivation. 8% had episodic syndromes (abdominal migraine, cyclical vomiting). 30% had bilateral cranial autonomic symptoms, 28% vertigo, 15% syncope and 8% allodynia during attacks. 65% had family history of headaches. 96% were treated with preventives. 61% received monotherapy and 39% polytherapy. 80% had significantly reduced headache frequency ($\leq$50%) by 6 months. However, only 40% of responders could be withdrawn from preventives after 6 months.

Conclusions: One fifth of pediatric migraine patients did not fulfill ICHD3β 'duration' criteria. Family history of migraine was seen in two third. More than half of the children needed to continue preventives despite good response.

EHMTC-0145
POSTER SESSION C

BIOFEEDBACK AS PROPHYLAXIS FOR PEDIATRIC MIGRAINE: A SYSTEMATIC REVIW WITH META-ANALYSIS

A. Stubberud[1], E. Varkey[2], D.C. McCrory[3,4], S.A. Pedersen[5], M. Linde[1,6]

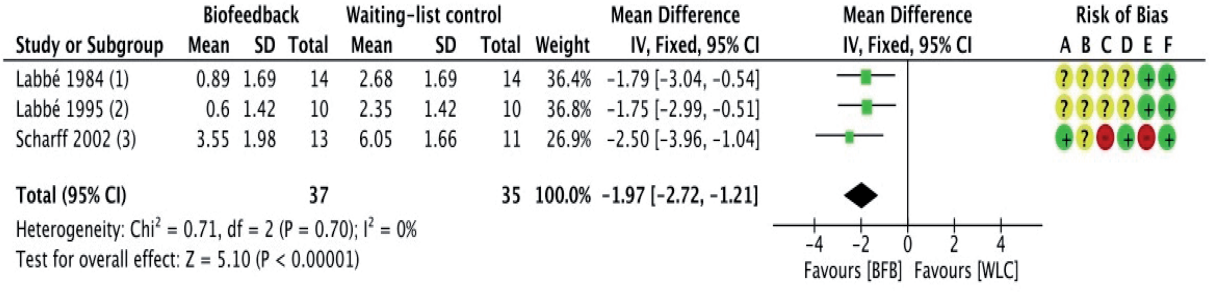
[1]*Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway*
[2]*Department of Health and Rehabilitation/Physiotherapy- The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*
[3]*Duke Evidence Synthesis Group- Duke Clinical Research Institute- Department of Medicine, Duke University School of Medicine, Durham, USA*
[4]*Center for Health Services Research in Primary Care, Durham Veterans Affairs Medical Center, Durham, USA*
[5]*Section for Medicine- NTNU University Library, Norwegian University of Science and Technology, Trondheim, Norway*
[6]*Norwegian Advisory Unit on Headaches, St. Olavs Hospital, Trondheim, Norway*

Aims: To investigate the pooled evidence for the effectiveness of using biofeedback to reduce migraine in children and adolescents.

Methods: A systematic database search was conducted across the databases MEDLINE, EMBASE, CENTRAL, CINAHL, and PsychINFO to locate prospective randomized controlled trials of biofeedback for pediatric migraine. The primary outcome analyzed was reduction of mean attack frequency, but a series of secondary outcomes, including adverse events, were also extracted. Forest plots were created using a fixed-effects model, and mean difference (MD) was reported. Risk of bias was also assessed.

Results: Five studies with a total of 137 participants met the inclusion criteria. Biofeedback reduced migraine frequency (MD: −1.97; 95% CI −2.72 to −1.21; $p < 0.00001$), attack duration (MD: −3.94; 95% CI −5.57 to −2.31; $p < 0.00001$), and headache intensity (MD: −1.77; 95% CI −2.42 to −1.11; $p < 0.00001$). Biofeedback did not demonstrate an adjuvant effect when combined with other behavioral treatment; neither did it have significant advantages over other active treatment. Only 40% of bias judgments were deemed as 'low' risk.

Discussion: Biofeedback seemed to be an effective intervention for pediatric migraine, though methodological issues hampered the meta-analyses. It was possible to include only a few studies, and they suffered from incomplete reporting of data and risk of bias. Therefore, further investigation is needed to confirm the effectiveness of biofeedback in pediatric migraine cases.



Footnotes
(1) SD estimated form ANOVA F-values
(2) SD estimated from ANOVA F-values
(3) SEM derived by hand from graph

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of outcome assessment (detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

EHMTC-0408
POSTER SESSION C

RANDOMIZED CONTROLLED TRIAL OF IG-G-BASED FOOD ELIMINATION FOR TREATMENT OF PRIMARY HEADACHE IN CHILDREN – INTERIM ANALYSIS

S. Taheri[1], C. Campbell[2], E. Mazza[3], M. Devries[2]

[1]*London, Canada*
[2]*London Health Sciences Centre, Paediatric Neurology, London, Canada*
[3]*Lawson Health Research Institute, Paediatric Neurology, London, Canada*

Objective: Evidence is emerging that HAs may be secondary to immunological mechanism mediated by IgG against certain foods, and that exclusion of foods based on IgG positivity leads to significant reduction of symptoms. This study aims to evaluate effect of food elimination on HA frequency in a cohort of children with primary HA.

Methods: Randomized, controlled, single-center trial in outpatient HA clinic. 50 patients aged 7–16 years are being recruited. Serum IgG against 90 foods is taken on first visit. Those in intervention group with high IgG levels are advised to eliminate the food with the strongest positivity for 6 weeks; those in standard group receive conventional treatment. Both groups are reassessed using diaries and QOL questionnaires, and non-responders in each group are crossed over to other arm of the trial and assessed at 6-weekly intervals over 4 visits.

Results: Of 25 patients recruited to study so far, 15 randomized to standard arm and 10 to intervention arm. 2 drop-outs. 12 from standard group were crossed over to intervention arm for non-response, and food elimination was instituted. 2 non-responders from elimination arm were crossed over to standard arm. 19 reported significant improvement in HA scores following food elimination. For 8 patients reaching end of study, repeat serum IgG levels fell by 20–70% compared to initial levels, correlating with clinical improvement.

Conclusions: IgG-based food elimination leads to significant reduction in HAs, and correlates with reduction in IgG levels. These results support immunological basis for link between food and HA in children.

EHMTC-0093
POSTER SESSION C

TEENS: HEADACHE AND LIFESTYLE IN ADOLESCENTS

M. Torres-ferrus[1], C. Vila-sala[1], S. Ajanovic[2], M. Quintana[1], J. Alvarez-sabin[1], P. Pozo-rosich[1]

[1]*VALL D'HEBRÓN HOSPITAL, NEUROLOGY, Barcelona, Spain*
[2]*VALL D'HEBRÓN HOSPITAL, PEDIATRICS, Barcelona, Spain*

Objective: To evaluate the prevalence and characteristics of headache and its relationship with lifestyle in a teenage population.

Methods: This is a cross-sectional study. Data was collected from students aged 12–18 years from six different schools in Catalonia. They completed an anonymous questionnaire with demographic, lifestyle, medical data, the presence of recurrent headaches and their characteristics. We defined probable migraine if headache presented ≥ 3 ICHD-IIIbeta criteria for migraine. An analysis was done to evaluate headache characteristics and compare lifestyles between headache and probable migraine sufferers and those who didn't have headache.

Results: 1619 students completed the survey. From these, 30.5% (493) suffered from recurrent headache and 11.3% (184) had migraine features. Amongst headache sufferers 32.9% had weekly attacks, 48.1% were significantly disabled (PedMIDAS moderate-severe) and 60.7% had never consulted a physician.

Headache was significantly more frequent in girls (35.1% *vs* 25.5% $p < 0.001$), teenagers with poor sleeping habits (36.6% *vs* 27.6% $p < 0.001$), lower physical activity ($p = 0.002$) who did not have breakfast (37.3 *vs* 28.4% $p = 0.001$), smokers, alcohol or caffeine overusers ($p < 0.001$). Teenagers with headache were more likely to be overweight. Adolescents with probable migraine were more disabled (meanPedMIDAS 23.2 *vs* 12.2, $p < 0.001$), had a higher prevalence of family headache history (43.3% *vs* *26.0%* $p = 0.002$) and consulted more (48.4% *vs* 30.8% $p < 0.001$)

Conclusions: Headache is a frequent and disabling health problem among adolescents.

Headache is significantly related with "unhealthy lifestyles".

It is essential to educate teenagers' healthier lifestyles and raise awareness of headache and migraine impact during adolescence.

EHMTC-0094
POSTER SESSION C

TEENS: HEADACHE, STRENGTHS AND DIFFICULTIES IN AN ADOLESCENT POPULATION

C. Vila-sala[1], M. Torres-ferrus[1], S. Ajanovic[2], M. Quintana[1], J. Alvarez-sabin[1], P. Pozo-rosich[1]

[1]*VALL D'HEBRÓN HOSPITAL, NEUROLOGY, Barcelona, Spain*
[2]*VALL D'HEBRÓN HOSPITAL, PEDIATRICS, Barcelona, Spain*

Objectives: To describe and evaluate the presence ofmedical and psychiatric disorders in teenagers and their relationship withsuffering from recurrent headaches.

Methods: This is a cross-sectional study. Data wascollected from students aged 12–18 years from six different schools in Catalonia.They completed an anonymous questionnaire assessing presence of headaches, medical, psychiatric disorders and the "Strengths and Difficulties Questionnaire", whichevaluates 25-behavioral items divided into 5 areas: emotional, conduct, peer relationship problems,hyperactivity/inattention and prosocial behavior. We defined probable migraine if headache presented ≥ 3 ICHD-IIIbeta criteria for migraine. An analysis was done to evaluate thepresence of comorbid medical and psychiatric disorders and headache or probablemigraine.

Results: 1619 students completed the survey. From these,30.5% (493) suffered from recurrent headache and 11.3% (184) had migrainefeatures.

Comorbidities significantly associated toheadache but not specifically to migraine were: allergy (38.8% vs 29.3% $p = 0.007$), other chronic pain disorders(44.7% vs 27.6% $p < 0.001$) and mentalhealth problems (53.2% vs 29.0% $p < 0.001$).Adolescents with headache believed that health problems affected their qualityof life (49.0% vs 27.7% $p < 0.001$).

Adolescents with headache presented worsescores in total SDQ ($p < 0.001$), specifically in: emotional symptoms,conduct, hyperactivity ($p < 0.001$) and peer relationship ($p = 0.004$). Higher scores in emotional andhyperactivity areas were positively correlated with disability (PedMIDAS) ($p < 0.001$). No significant differenceswere found in probable migraineurs.

Conclusions: Adolescents with headache also suffer from other medicals conditions that reduce their quality of life.

• Headaches associated with emotional, conduct, hyperactivity and peer-relationship symptoms in teenagers.

EHMTC-0174
POSTER SESSION C

DOES MIGRAINE FOLLOW BENIGN PAROXYSMAL TORTICOLLIS AND CYCLICAL VOMITING?

M.C. Bernucci[1], R. Frusciante[1], S. Tarantino[1], L. Papetti[1], A. Capuano[1], F. Vigevano[1], M. Valeriani[1]

[1]*Pediatric Hospital Bambino Gesu', Neuroscience, Roma, Italy*

Migraine equivalents are clinical conditions often involving children who do not suffer from headache. The relationship between migraine equivalents and subsequent headache has been rarely demonstrated in the same sample of children. The aim of our study is to investigate whether children referred for cyclical vomiting (CV) or benign paroxysmal torticollis (BPT) developed migraine at distance from the first observation. The study is based on an online survey addressed to 30 families with children affected by CV and 34 families with children affected by BPT, between January 2000 and December 2013. Migraine was diagnosed in 61% and 41% of the children previously affected by CV and BPT, respectively. Headache appeared at the age of 7 years in 35% and 14% of children with previous diagnosis of CV and BPT, respectively. As for CV children, 48.5% complained abdominal migraine, 42% limb pain, 32% motion sickness, 12% paroxysmal vertigo, 9.7% BPT. As for BPT children, 73% had abdominal migraine, 55% paroxysmal vertigo, 45% limb pain, 27% motion sickness, 27% CV. No further migraine equivalent was referred by 6% and 45% of the patients with CV and BPT, respectively. Our data suggest that CV and BPT can be considered as symptoms of the migraine disease, which can precede the appearance of the headache.

EHMTC-0176
POSTER SESSION C

MIGRAINE IN CHILDREN AND ADOLESCENT, BODY WEIGHT AND PSYCHOLOGICAL FACTORS: A POSSIBLE RELATIONSHIP?

S. Tarantino[1], C. De Ranieri[1], M. D'Ambrosio[1], A. Rocco[1], R. Frusciante[1], L. Papetti[1], A. Capuano[1], F. Vigevano[1], S. Gentile[1], M. Valeriani[1]

[1]*Pediatric Hospital Bambino Gesu', Neuroscience, Roma, Italy*

The link between body weight, headache and the psychological profile has hardly been examined in children. Aims of the present study were 1) to study the prevalence overweight in migraine children/adolescents; 2) to analyze the possible relationship between frequency and severity of

migraine and overweight; 3) to explore the role of anxiety and somatization on body mass index (BMI) in migraine patients. We studied 107 migraineurs (mean age 11.6 ± 2.4 years; 47 M and 60 F). Patients were divided into two groups according to the attack frequency (low and high). Pain intensity was rated on a 3-levels graduate scale (mild, moderate and severe pain). Given the low frequencies, the "moderate" and the "mild" intensity were collapsed in the same category. The psychological screening was assessed by SAFA Anxiety and Somatization scales. Most patients (60.8%) were classified as "normal weight", 39.2% of the children were "overweight". The weight did not correlate with frequency and intensity of the migraine attacks (respectively: $\chi(2) = 1.43$, $p = 0.23$; $\chi(2) = 0.03$; $p = 0.86$). Compared to normal weight children, overweight patients showed a significant higher score in "Separation anxiety" subscale. In the "overweight" patients, the BMI showed a positive correlation with Anxiety (SAFA-A Total, $p = 0.03$). Our results suggest that in children/adolescents there is an association between migraine, weight and psychological symptoms.

EHMTC-0236
POSTER SESSION C

FEATURES OF MIGRAINE WITH AURA IN PEDIATRIC AGE

M. Balestri[1], D. Maiorani[2], A. Capuano[1], S. Tarantino[1], R. Frusciante[1], L. Papetti[1], F. Vigevano[1], M. Valeriani[1]

[1]*Pediatric Hospital Bambino Gesu', Neuroscience, Roma, Italy*
[2]*Belcolle Hospital, Pediatrics, Viterbo, Italy*

Though common in pediatric age, migraine with aura (MA) has been scarcely studied in children. Our aims were to investigate: 1) the clinical characteristics of the aura in a cohort of MA children, and 2) the features of the headache associated with the aura. The present study was based on data retrospectively collected from 164 MA children referred to our 3rd level Headache Centre. In our patients, the visual symptoms were far more frequent (93%) than the somatosensory, motor, and speech disturbances. The aura anticipated the headache onset in most cases (69.1%) and its duration ranged from 5 to 60 minutes. When we divided our patients in 4 different age groups (less than 7 years, between 7 and 10 years, between 11 and 14 years, more than 14 years), no difference in the aura characteristics was found between the groups. On the other hand, when the headache type was classified according to the ICHD-IIIb criteria, migraine was diagnosed only in 40.2% of patients and the diagnosis remained undetermined in 4.3% of MA children. However, if headache duration was not considered, the migraineurs raised to 67% of patients and in no child the diagnosis was undetermined. In conclusion, our pediatric population showed aura features that did not depend on the age and were similar to those of adult patients. However, the headache could be difficult to be classified if headache duration was considered.

EHMTC-0323
POSTER SESSION C

VISUAL SNOW IN A PAEDIATRIC POPULATION: A CASE SERIES OF 8 PATIENTS

F. Sutton[1], L. Mewasingh[1], S. Beri[2], M. Weatherall[2]

[1] *St Mary's Hospital, Department of Paediatric Neurology, London, United Kingdom*
[2]*Charing Cross Hospital, Department of Neurology, London, United Kingdom*

Visual snow is a condition in which patients experience a whole field positive visual disturbance resembling static or snow, as well as a number of other characteristic phenomena including floaters, blue field entopic phenomena, visual persistence, and nyctalopia. Standard neuroimaging and ophthalmological investigation is normal. We present a case series of eight paediatric patients with visual snow, all female, with age of onset ranging from 2–13 years. Five of the patients also suffer from migraine with aura, one developing attacks after the onset of visual snow; one other patient also experiences non-migrainous headaches. One patient describes tinnitus. Three patients (both with concomitant migraine with aura) are significantly functionally impaired by their symptoms. Paediatric neurologists should be aware that visual snow can present in childhood, but continue to investigate appropriately to ensure that there is no other organic pathology to account for the persistent visual disturbance.

EHMTC-0383
POSTER SESSION C

GABAPENTIN AND PREGABALIN TOLERABILITY IN FACIAL PAIN PATIENTS

E. Besi[1], M. Kyrtsos[2], D. Boniface[3], J.M. Zakrzewska[4]

[1]*Edinburgh Dental Institute, Oral Surgery, Edinburgh, United Kingdom*
[2]*Eastman Dental Institute – UCL, Oral Surgery, London, United Kingdom*
[3]*Eastman Dental Institute – UCL, Health Behaviour Research Centre, London, United Kingdom*
[4]*Eastman Dental Institute – UCL, London, United Kingdom*

Objectives: UK guidelines suggest gabapentin and pregabalin, among others, as drugs of choice for facial pain. Little work has been done around the side effects of these drugs

in this population. This study examines the adverse events of gabapentin and pregabalin in facial pain patients.

Methods: 73 participants from 2012–2015 on gabapentin or pregabalin only. Patients completed the adverse events profile questionnaire (Baker et al., 1994) in relation to the current drugs being taken for pain control, as well as the Hospital Anxiety and Depression Scale (HADS). The first questionnaire contains 19 brief items that assess the frequency of different adverse effects using a Likert scale of 1 to 4, with 4 indicating more frequent occurrences. Score range from 19 to 76 and scores >45 suggest significant toxicity.

Patients on polytherapy, abusing alcohol, were excluded.

Results: Using the logistic models for probability of >45, it was found that there was no relationship between the prescribed dose and the adverse events for both gabapentin and pregabalin. Most common side effects using gabapentin are tiredness, memory problems, disturbed sleep, difficulty in concentration and sleepiness, whereas for pregabalin are tiredness, sleepiness, disturbed sleep, weight gain and difficulty in concentrating. Comparing the scores of depression in the adverse events profile questionnaire and HAD Scale, it showed a clear correlation.

Conclusion: There is no correlation between dose and side effects. Tiredness is the most common side effect for both gabapentin and pregabalin. Pregabalin shows better results in controlling anxiety.

EHMTC-0344
POSTER SESSION C

DEVELOPING A DIAGNOSTIC TOOL FOR THE EARLY DIAGNOSIS OF CLUSTER HEADACHE

A. BUTURE[1], L. DIKOMITIS[2], F. AHMED[1]

[1]*HULL YORK MEDICAL SCHOOL, DEPARTMENT OF NEUROSCIENCES, HULL, United Kingdom*
[2]*HULL YORK MEDICAL SCHOOL, DEPARTMENT OFSOCIAL SCIENCES, HULL, United Kingdom*

Background: Cluster headache (CH), the most common of the trigeminal autonomic cephalalgias (TAC) is a rare, severe condition. CH is characterized by unilateral V1 trigeminal distribution pain, ipsilateral cranial autonomic features and tendency to circadian and circannual periodicity. Although CH has very distinct features the patients face delays in diagnosis, misdiagnosis and mismanagement.

Objective: The project aims to pilot a new diagnostic tool to help primary care doctors and physicians in emergency departments to correctly diagnose CH.

Diagnostic tool: The new diagnostic tool will include: visual and verbal component that will facilitate differentiation of CH and other primary headache disorders; in addition few key questions that differentiate CH from migraine will be included in the diagnostic tool.

Method: Patients will be recruited from the Hull Headache Clinic. A cohort of CH patients will be invited to participate and patients with migraine will be used as control group. The diagnosis will be based on the International Headache Society Criteria. We aim to apply the new diagnostic tool on at least 100 participants in each group for validation and the sensitivity and specificity for each component will be evaluated.

Results: We aim to produce an A4 sheet for the new diagnostic tool to be available at the GP practices and emergency departments to assist in diagnosing CH.

Conclusions: The new tools of diagnosis have the potential to improve the delays in diagnosis, misdiagnosis and mismanagement.

Conflict of interest
Disclosure statement:
Fayyaz Ahmed has received honorarium paid to the British Association for the Study of Headache and the Migraine Trust from Allergan, eneura and electrocore as advisory board member and running training workshops.

EHMTC-0209
POSTER SESSION C

CLINICAL, BEDSIDE AND ELECTROPHYSIOLOGICAL AUTONOMIC ABNORMALITIES IN TRIGEMINAL AUTONOMIC CEPHALALGIAS: A COMPARATIVE STUDY BETWEEN THE SUBTYPES

R. Chopra[1], D. Chowdhury[2], G. Khwaja[3]

[1]*Delhi, India*
[2]*GB Pant institute of post graduate medical education and research, neurology, New Delhi, India*
[3]*GB Pant institute of post graduate medical education and research, neurology, New Delhi, India*

Background: Patterns & extent of cranial autonomic symptoms/signs (CAS) have not been previously compared between subtypes of Trigeminal Autonomic Cephalalgias (TACs).

Objective: To compare CAS, bedside & electrophysiological tests for dysautonomia in TACs patients.

Methods: TACs patients (diagnosed by ICHD3β) were prospectively evaluated for CAS, blood pressure (BP) response to standing up & sustained handgrip, RR variation, sympathetic skin response (SSR) & 24 hour Holter using structured performa.

Results: 37 Cluster headache (CH), 26 paroxysmal hemicrania (PH), 22 SUNCT/SUNA & 10 hemicrania continua (HC) patients were studied. All CH & HC patients had CAS. 96%PH & 95%SUNCT/SUNA patients had CAS. Lacrimation in CH, facial sweating in PH and eyelid edema in HC/SUNCT/SUNA were the most common CAS (Table1). CH patients had maximum CAS (≥4). Aural fullness, a new ICHD3β feature was most common in HC (60%). Impaired BP response on sustained handgrip (89%CH, 88%PH, 86%SUNCT/SUNA & 60%HC) was more common than standing up. R-R variation was increased in all. SSR was unrecordable in 10%PH, 12%CH and 20%SUNCT/SUNA patients. Holter was abnormal in 1 CH & 1 PH patient (multiple pauses, runs of sinus bradycardia).

Conclusions: TACs subtypes differ in terms of pattern and distribution of CAS. Aural fullness was commonly reported when enquired. Impaired BP (sustained handgrip) and RR variations were the commonest abnormalities found on testing.

Table1-: Distribution of CAS (%)

CAS	CH	PH	SUNCT/SUNA	HC
Lacrimation	**86**	52	71	60
Conjunctival Injection	65	32	62	40
Facial sweating/flushing	61	**60**	40	40
Eyelid edema	38	32	**43**	**70**
Aural fullness	38	48	40	60
Ptosis/Miosis	43	16	14	40
Nasal congestion	24	12	9	0
Rhinorrhea	16	16	9	0

EHMTC-0336
POSTER SESSION C

NON-INVASIVE VAGUS NERVE STIMULATION FOR HEMICRANIA CONTINUA: A CASE SERIES OF 3 PATIENTS

B. Davies[1], K. Chatterton[1]

[1]*Royal Stoke University Hospital, Neurology, Stoke-on-Trent, United Kingdom*

Introduction: Hemicrania Continua (HC) is an uncommon primary headache disorder, characterized by continuous unilateral pain, where pain exacerbations are associated with cranial autonomic features. This condition is responsive to indomethacin but unfortunately some patients cannot tolerate this drug. There are limited options in non-pharmacological treatments for this condition.

Aim: Non-Invasive external Vagus Nerve Stimulation i.e. gammaCore® has shown clinical benefit in cluster headache. There are limited reports on its use in HC. We present three patient case studies showing a beneficial treatment response with gammaCore®.

Methods: Three patients with HC had a positive treatment response to indomethacin but side effects limited long term use of this drug. They were treated with gammaCore® therapy both acutely and preventatively for HC and were asked to keep diaries whilst using the device.

Results: The three patients all found benefit from using the gammaCore® device. Patients continuous pain severity was significantly reduced by more than 50% in all. Exacerbations of pain occurred significantly less frequently. Indometacin was rarely needed in one patient when on device treatment. The other two patients reported a beneficial treatment response with Non-Invasive Vagus Nerve Stimulation similar to to indomethacin but without side effects.

Conclusions: Non-Invasive external Vagus Nerve Stimulation (using the gammaCore® device) may be a useful treatment option for HC where indomethacin is not tolerated.

Conflict of interest
Disclosure statement:
Dr B Davies – Received advisory board consultancy fees from NICE, AMGEN, Allergan. The gammaCore device was provided free to patients via the NHS in the UK.
K Chatterton – No conflicts of interest

EHMTC-0299
POSTER SESSION C

LONG-TERM THERAPEUTIC EFFECTIVENESS OF SPHENOPALATINE GANGLION (SPG) STIMULATION FOR CHRONIC CLUSTER HEADACHE (CCH) – PATHWAY CH-1 STUDY 24 MONTH RESULTS

T. Jürgens[1], M. Barloese[2], A. May[3], J.M. Láinez[4], J. Schoenen[5], C. Gaul[6], A. Goodman[7], A. Caparso[7], R. Jensen[2]

[1]*University Medical Center Rostock, Department of Neurology, Rostock, Germany*
[2]*Rigshospitalet-Glostrup- University of Copenhagen, Danish Headache Centre- Department of Neurology, Glostrup, Denmark*
[3]*Universitäts-Klinikum Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*
[4]*Hospital Clinico Universitario- Universidad Católica de Valencia, Department of Neurology, Valencia, Spain*
[5]*CHR Citadelle- Liège University, Headache Research Unit. Department of Neurology, Liège, Belgium*
[6]*Migraine- and Headache Clinic Königstein, Migraine- and Headache Clinic Königstein, Königstein, Germany*
[7]*Autonomic Technologies- Inc., Clinical, Redwood City, USA*

Background: In the Pathway CH-1 randomized, double-blind, multi-center study of an inserted sphenopalatine ganglion (SPG) microstimulator, 68% of medically refractory patients experienced clinically significant improvements with SPG stimulation within the 24 month study period. We evaluated long-term response to SPG stimulation for chronic cluster headache (CCH).

Method: 43 medically refractory CCH patients (minimum 4 attacks/week) enrolled in the Pathway CH-1 study; 33 continued into a long-term follow-up study and completed at least 24 months of follow-up. Each attack was evaluated for effective therapy (relief/freedom from $\geq$moderate pain, or freedom from mild pain) within 15 minutes or at end of stimulation. Acute responders were defined as effective therapy in $\geq$50% of evaluable treatments; frequency responders as $\geq$50% reduction in attack frequency versus baseline. Therapeutic response is acute and/or prophylactic response. Patients were similarly evaluated for $\geq$75 and $\geq$30% therapeutic response.

Results: 5956 attacks were evaluated (180.5 ± 344.8, range 2–1581 per patient). At 24 months, 61% (20/33) of patients were therapeutic responders per the protocol at a 50% therapeutic response level, with 5 experiencing both acute and frequency responses, 10 acute responders, and 5 frequency responders. 39% (13/33) experienced an effective response in $\geq$75% of attacks and 82% (27/33) in $\geq$30% of attacks. Therapeutic response to SPG stimulation was maintained from 12 to 18 to 24 months at 67%, 64%, and 61%, respectively. No predictors of response were identified.

Conclusion: The previously demonstrated effects of SPG stimulation with the Pulsante Microstimulator System are sustained in a majority of medically refractory CCH patients two years following microstimulator insertion.

Conflict of interest
Disclosure statement:
AG and AC are employees of Autonomic Technologies, Inc., the sponsor of the study.

EHMTC-0306
POSTER SESSION C

PATHWAY REGISTRY 12 MONTH INTERIM RESULTS – LONG-TERM THERAPEUTIC EFFECTIVENESS OF SPHENOPALATINE GANGLION (SPG) STIMULATION FOR CLUSTER HEADACHE (CH)

M. Barloese[1], H. Kaube[2], U. Reuter[3], P. Stude[4], A. Böger[5], T. Jürgens[6], C. Gaul[7], K. Solbach[8], P. Storch[9], C. Wöber[10], A. Straube[11], O. Summ[12], A. Goodman[13], A. Caparso[13], R. Jensen[1], A. May[14]

[1]*Rigshospitalet-Glostrup- University of Copenhagen, Danish Headache Centre- Department of Neurology, Glostrup, Denmark*
[2]*Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Munich, Germany*
[3]*Charite – Mitte Campus, Neurologische Klinik und Poliklinik, Berlin, Germany*
[4]*Schmerztherapie- Geriatrie und Palliativmedizin, Schmerztherapie- Geriatrie und Palliativmedizin, Bochum, Germany*
[5]*Rotes Kreuz Krakenhaus Kassel, Rotes Kreuz Krakenhaus Kassel, Kassel, Germany*
[6]*University Medical Center Rostock, Department of Neurology, Rostock, Germany*
[7]*Migraine- and Headache Clinic Königstein, Migraine- and Headache Clinic Königstein, Königstein, Germany*
[8]*Universitätsklinikum Essen, Klinik und Poliklinik für Neurologie, Essen, Germany*
[9]*Universitätsklinikum Jena, Klinik f.Neurologie, Jena, Germany*
[10]*Medizinische Universität Wien, Klinik für Neurologie, Vienna, Austria*
[11]*Klinikum der Universität München, Neurologische Klinik und Poliklinik, Munich, Germany*
[12]*Universitätsklinikum Münster, Klinik für Neurologie, Münster, Germany*

[13]*Autonomic Technologies- Inc., Clinical, Redwood City, USA*
[14]*Universitäts-Klinikum Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*

Background: The Pathway Registry evaluated sphenopalatine ganglion (SPG) stimulation for cluster headache (CH). Previously, in a randomized, double-blind, multicenter study (Pathway CH-1), 68% of patients experienced clinically significant improvements. We evaluated long-term therapeutic effectiveness of SPG stimulation.

Method: Acute pain response following SPG stimulation and attack frequency reduction were analyzed at 12 months following SPG microstimulator insertion. Acute effectiveness is relief/freedom from ≥moderate pain, or freedom from mild pain. Therapeutic responders achieved acute effectiveness in ≥50% of attacks by end of stimulation, or ≥50% attack frequency reduction versus baseline. Patients were similarly evaluated for ≥75 and ≥30% therapeutic response.

Results: Through March 2016, 119 patients were enrolled. 80 patients (74 chronic CH, 6 episodic CH) had a microstimulator inserted and progressed through the 12 month study visit (374 ± 31 days post-insertion, range 322–475).

In these 80 patients (59 male, 21 female, age 46 ± 12 years), baseline attack frequency was 24.9 ± 20.8 attacks/week with severely CH impact (HIT-6: 64.0 ± 6.9). 66% (53/80) were therapeutic responders with a response of ≥50%. Frequency responders (43/80) reduced attack frequency by 86% (26.5 ± 23.2 to 3.6 ± 6.6 attacks/week, $p < 0.001$). Acute responders (25/80) achieved effective therapy in 87% of attacks (4212/4863) by end of stimulation.

46% (37/80) of patients experienced a very strong therapeutic response of at least 75%; 75% (61/80) experienced at therapeutic response of at least 30%.

Conclusion: Therapeutic effectiveness of SPG stimulation in chronic medically refractory cluster patients (Pathway CH-1 trial) is confirmed in an open label registry of a large series of cluster patients through 12 months.

Conflict of interest
Disclosure statement:
AG and AC are employees of Autonomic Technologies, Inc.

EHMTC-0308
POSTER SESSION C

ATTACK FREQUENCY REDUCTION WITH SPHENOPALATINE GANGLION (SPG) STIMULATION FOR CLUSTER HEADACHE–PATHWAY REGISTRY 12 MONTH INTERIM RESULTS

H. Kaube[1], U. Reuter[2], P. Stude[3], A. Böger[4], A. May[5], C. Gaul[6], K. Solbach[7], P. Storch[8], C. Wöber[9], A. Straube[10], O. Summ[11], A. Goodman[12], A. Caparso[12], R. Jensen[13]

[1]*Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Munich, Germany*
[2]*Charite – Mitte Campus, Neurologische Klinik und Poliklinik, Berlin, Germany*
[3]*Schmerztherapie- Geriatrie und Palliativmedizin, Schmerztherapie- Geriatrie und Palliativmedizin, Bochum, Germany*
[4]*Rotes Kreuz Krakenhaus Kassel, Rotes Kreuz Krakenhaus Kassel, Kassel, Germany*
[5]*Universitäts-Klinikum Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*
[6]*Migraine- and Headache Clinic Königstein, Migraine- and Headache Clinic Königstein, Königstein, Germany*
[7]*Universitätsklinikum Essen, Klinik und Poliklinik für Neurologie, Essen, Germany*
[8]*Universitätsklinikum Jena, Klinik f.Neurologie, Jena, Germany*
[9]*Medizinische Universität Wien, Klinik für Neurologie, Vienna, Austria*
[10]*Klinikum der Universität München, Neurologische Klinik und Poliklinik, Munich, Germany*
[11]*Universitätsklinikum Münster, Klinik für Neurologie, Münster, Germany*
[12]*Autonomic Technologies- Inc., Clinical, Redwood City, USA*
[13]*Rigshospitalet-Glostrup- University of Copenhagen, Danish Headache Centre- Department of Neurology, Glostrup, Denmark*

Background: The Pathway Registry is an open label evaluation of sphenopalatine ganglion (SPG) stimulation for cluster headache (CH). In a randomized, double-blind, multi-center study (Pathway CH-1), 68% of medically refractory patients experienced clinically significant improvements. We aimed to evaluate long-term attack frequency response with SPG stimulation.

Method: In patients implanted with an SPG microstimulator, attack frequency response was evaluated over 4 weeks at baseline (prior to microstimualtor insertion) and at 12 months. Frequency responders experienced reductions in attack frequency of at least 50% compared to baseline.

Results: Through March 2016, 80 patients (74 chronic CH, 6 episodic CH) progressed through the 12 month study visit; 79 provided complete attack frequency data and in total, 13,477 attacks were evaluated. Average attack frequency was reduced by 39% (from 24.9 ± 20.8 to 15.2 ± 18.1 attacks/week, $n = 79$, $p < 0.001$). Frequency responders (43/80) reduced attack frequency by 86% (26.5 ± 23.2 to 3.6 ± 6.6 attacks/week, $n = 43$, $p < 0.001$). Further, 25% (20/80) reported no attacks in the preceding 4 weeks at 12 months, with 12 of these 20 reporting no attacks at consecutive clinic visits at least 3 months apart. Of these 20 patients reporting no attacks, 18 had been chronic at baseline, and their average baseline attack frequency was 21.6 ± 18.8 attacks/week.

Conclusion: SPG stimulation is associated with clinically meaningful reductions in attack frequency at 12 months in 54% of patients, and remission from cluster attacks in 25% of patients.

Conflict of interest
Disclosure statement:
AG and AC are employees of Autonomic Technologies, Inc.

EHMTC-0312
POSTER SESSION C

REDUCED ACUTE AND PREVENTIVE MEDICATION USE WITH SPHENOPALATINE GANGLION (SPG) STIMULATION FOR CLUSTER HEADACHE– PATHWAY REGISTRY 12 MONTH INTERIM RESULTS

H. Israel[1], H. Kaube[2], U. Reuter[1], P. Stude[3], A. Böger[4], A. May[5], C. Gaul[6], K. Solbach[7], P. Storch[8], C. Wöber[9], A. Straube[10], O. Summ[11], A. Goodman[12], A. Caparso[12], R. Jensen[13]

[1]*Charite – Mitte Campus, Neurologische Klinik und Poliklinik, Berlin, Germany*
[2]*Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Munich, Germany*
[3]*Schmerztherapie- Geriatrie und Palliativmedizin, Schmerztherapie- Geriatrie und Palliativmedizin, Bochum, Germany*
[4]*Rotes Kreuz Krakenhaus Kassel, Rotes Kreuz Krakenhaus Kassel, Kassel, Germany*
[5]*Universitäts-Klinikum Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*
[6]*Migraine- and Headache Clinic Königstein, Migraine- and Headache Clinic Königstein, Königstein, Germany*
[7]*Universitätsklinikum Essen, Klinik und Poliklinik für Neurologie, Essen, Germany*
[8]*Universitätsklinikum Jena, Klinik f.Neurologie, Jena, Germany*
[9]*Medizinische Universität Wien, Klinik für Neurologie, Vienna, Austria*
[10]*Klinikum der Universität München, Neurologische Klinik und Poliklinik, Munich, Germany*
[11]*Universitätsklinikum Münster, Klinik für Neurologie, Münster, Germany*
[12]*Autonomic Technologies- Inc., Clinical, Redwood City, USA*
[13]*Rigshospitalet-Glostrup- University of Copenhagen, Danish Headache Centre- Department of Neurology, Glostrup, Denmark*

Background: The Pathway Registry is an open label evaluation of sphenopalatine ganglion (SPG) stimulation for cluster headache (CH). In a randomized, double-blind, multi-center study (Pathway CH-1), 68% of medically refractory patients experienced clinically significant improvements. We evaluated changes in medication use at 12 months.

Method: In patients using SPG stimulation, acute medication use (average uses/week over prior 4-weeks) was compared between baseline (prior to microstimulator insertion) and the 12-month study visit. Preventive medications during the same periods were compared.

Results: Through March 2016, 80 patients (74 chronic CH, 6 episodic CH) progressed through the 12 month visit; 74 and 78 provided complete data at both time points, respectively. At baseline, 70% (56/80) used preventive medications, with 50% (40/80) using verapamil. 91% (73/80) used acute medications, with 10 using only oxygen.

At 12 months 66% (53/80) were therapeutic responders to SPG stimulation (response of $\geq$50% of attacks by end of stimulation). Acute medication consumption was reduced by 45% between baseline and 12 months (21.6 ± 21.0 and 11.8 ± 18.5 uses/week, respectively, $p = 0.002$); triptans were reduced by 50% (10.8 ± 12.8 and 5.4 ± 10.4 uses/week, respectively, $p < 0.001$). Therapeutic responders further reduced acute medications by 78% (21.7 ± 22.2 and 4.7 ± 9.4 uses/week, $p < 0.001$) and triptans by 68% (9.8 ± 11.6 and 3.1 ± 7.6 uses/week, respectively, $p < 0.001$).

71% (55/78) stopped all (18/78), stopped some and/or reduced dose of others (19/78), or remained off (18/78) all preventive medications.

Conclusion: SPG stimulation is associated with dramatic and statistically significant decreases in acute medication use. Clinically relevant improvements in preventive medication use are also observed after 12 months.

Conflict of interest

Disclosure statement:
AG and AC are employees of Autonomic Technologies, Inc.

EHMTC-0313
POSTER SESSION C

PATIENT SATISFACTION AND HEADACHE DISABILITY IMPROVEMENTS WITH SPHENOPALATINE GANGLION (SPG) STIMULATION FOR CLUSTER HEADACHE–PATHWAY REGISTRY 12 MONTH INTERIM RESULTS

A. Petersen[1], H. Kaube[2], U. Reuter[3], P. Stude[4], A. Böger[5], A. May[6], C. Gaul[7], K. Solbach[8], P. Storch[9], C. Wöber[10], A. Straube[11], O. Summ[12], A. Goodman[13], A. Caparso[13], R. Jensen[1]

[1]*Rigshospitalet-Glostrup- University of Copenhagen, Danish Headache Centre- Department of Neurology, Glostrup, Denmark*
[2]*Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Neurologie und Kopfschmerzzentrum Muenchner Freiheit, Munich, Germany*
[3]*Charite – Mitte Campus, Neurologische Klinik und Poliklinik, Berlin, Germany*
[4]*Schmerztherapie- Geriatrie und Palliativmedizin, Schmerztherapie- Geriatrie und Palliativmedizin, Bochum, Germany*
[5]*Rotes Kreuz Krakenhaus Kassel, Rotes Kreuz Krakenhaus Kassel, Kassel, Germany*
[6]*Universitäts-Klinikum Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*
[7]*Migraine- and Headache Clinic Königstein, Migraine- and Headache Clinic Königstein, Königstein, Germany*
[8]*Universitätsklinikum Essen, Klinik und Poliklinik für Neurologie, Essen, Germany*
[9]*Universitätsklinikum Jena, Klinik f.Neurologie, Jena, Germany*
[10]*Medizinische Universität Wien, Klinik für Neurologie, Vienna, Austria*
[11]*Klinikum der Universität München, Neurologische Klinik und Poliklinik, Munich, Germany*
[12]*Universitätsklinikum Münster, Klinik für Neurologie, Münster, Germany*
[13]*Autonomic Technologies- Inc., Clinical, Redwood City, USA*

Background: The Pathway Registry is an open label evaluation of sphenopalatine ganglion (SPG) stimulation for cluster headache (CH). In a randomized, double-blind, multi-center study (Pathway CH-1), 68% of medically refractory patients experienced clinically significant improvements. We evaluated headache disability changes and patient satisfaction at 12 months.

Method: In patients using SPG stimulation, HIT-6 headache disability was compared from baseline prior to microstimulator insertion to the 12 month study visit; responders experienced clinically meaningful decreases in headache disability score of −2.3. Patient satisfaction at 12 months was characterized.

Results: Through March 2016, 80 patients (74 chronic CH, 6 episodic CH) progressed through the 12 month study visit; 69 and 74 provided complete HIT-6 and survey data, respectively.

Headache disability improved from severe to significant impact (64.0 ± 6.9 and 57.5 ± 10.1 at baseline and 12 months, respectively, $p < 0.001$). 54% (37/69) had clinically meaningful reductions in HIT-6 headache disability.

A majority of patients responded positively to a patient survey administered at 12 months. 70% (52/74) rated the Pulsante Microstimulator System as 'good' or 'very good', 75% (56/74) found SPG stimulation useful for treating their headaches, and 79% (59/74) found side effects from the insertion procedure tolerable. 81% (60/74) found the inserted microstimulator comfortable or did not feel it, found the stimulation sensation tolerable, and would make the same decision again. 88% (64/74) would recommend the system to someone else.

Conclusion: SPG stimulation is associated with statistically significant and clinically meaningful long-term improvements in headache disability and patient satisfaction is high at 12 months follow up.

Conflict of interest
Disclosure statement:
AG and AC are employees of Autonomic Technologies, Inc.

EHMTC-0356
POSTER SESSION C

LONG TERM OUTCOME OF OCCIPITAL NERVE STIMULATION IN DRUG REFRACTORY CHRONIC CLUSTER HEADACHE

A. Proietti Cecchini[1], G. Messina[2], A. Franzini[2], M. Leone[1]

[1]*Neurological Institute "C. Besta", Pain Neuromodulation Unit- Headache and Pain Department, Milano, Italy*
[2]*Neurological Institute "C. Besta", Functional Neurosurgery Unit, Milano, Italy*

Introduction: Medical treatments may fail to achieve a satisfactory response in a minority of CCH. The invasive

neurostimulation technics have been helpful to support these disabled cases. We focus on the efficacy and safety of occipital nerve stimulation (ONS) in a cohort of drug refractory Chronic Cluster Headache (drCCH).

Method: patients resistant to any prophylaxis and to sphenopalatine ganglion blocks with daily attacks in the last year received bilateral ONS in the period from march 2004 to February 2014 and were followed up in a prospective open-label study.

Results: 35 drCCH (30 male, mean age 42 years, mean illness duration 6,7 years) were implanted. The first 5 failed to respond in the short term (<6 months) and were hastily shifted to Deep Brain Stimulation. After a median follow up of 6years, 20/30 (66%) were responders (≥50% reduction in mean headache number per day): 12 showed a stable improved condition with sporadic attacks; five had 70% reduction in mean daily attacks whereas in the remaining three the chronic pattern reverted to episodic. Ten patients still remained unresponsive: 50% of them performed well for a temporary period ranging from 2 to 48 months, then relapsed. Natural course of disease and tolerance to treatment may play a part. Battery depletion (21 patients 70%) and electrode migration (6 patients- 20%) were the most frequent cause of additional surgery.

Discussion and conclusions: long-term follow-up confirms ONS efficacy in drug resistant chronic CH. ONS is safe and should be offered before other more invasive procedures.

EHMTC-0084
POSTER SESSION C

EPISODIC CLUSTER HEADACHE TRANSFORMS INTO CHRONIC, AFTER OPERATION FOR LARYNGEAL CARCINOMA AND A FOLLOWING RADIOTHERAPY

V. Grozeva[1], I. Milanov[2]

[1]*Multiprofile hospital for active treatment in neurology and psychiatry St. Naum, Sofia, Bulgaria*
[2]*Multiprofile hospital for active treatment in neurology and psychiatry St. Naum, Headache, Sofia, Bulgaria*

Introduction: Seasons, strong smelling substances and alcohol are the most common triggers for cluster headache attacks. Less is known about other possible triggers and why the episodic cluster headache can transform to chronic.

Case presentation: We report a 57 years old man whose attacks were triggered by an extensive surgical operation due to a squamous cell carcinoma of the larynx, followed by radiotherapy. Multiple cranial nerves on the side of the headache, together with the sympathetic branches on the same side of the neck were impaired. During the recovering period the patient's cluster headache attacks appeared again, after 10 years of remission. First symptoms had started at the age of 25. The patient had a classical presentation of episodic cluster headache. He had noticed the attacks are worsened after an intake of alcohol. The cluster periods lasted between 2 and 3 months and were always appearing in the beginning of spring. After the surgical operation and the multiple cranial nerve impairment on the same side, the patient's episodic cluster headache transformed to chronic.

Conclusion: The classical episodic from of cluster headache in the past can transform into a chronic one, following an extensive surgical intervention in the neck area, and/or radiotherapy (known to impair the cranial nerves around the selected area). The case can serve as an example where a possible impairment of the peripheral pain mechanisms can influence the central pain mechanisms through the trigemino-cervical neurons.

EHMTC-0186
POSTER SESSION C

SLEEP DISORDERS IN CLUSTER HEADACHE: AN INVESTIGATION OF 223 JAPANESE CASE SERIES

S. Kikui[1], J. I. Miyahara[1], S. Hanako[1], K. Yamakawa[1], K. Ishizaki[2], D. Danno[3], Y. Kashiwaya[1], T. Takeshima[1]

[1]*Tominaga Hospital, Headache Center, Osaka, Japan*
[2]*Kaikokai Rehabilitation Hospital, Neurology, Yatomi, Japan*
[3]*Hyogo College of Medicine hospital, Neurology, Nishinomiya, Japan*

Background and aim: Cluster headache (CH) is a sleep-related disorder, and its attacks have both circadian and circannual rhythmicity. To assess the prevalence of sleep disorders in CH population.

Subjects and methods: We studied 223 consecutive CH patients (179 males and 44 females; average age, 38.0 ± 10.0 years; age of onset 27.6 ± 10.9 years) who presented at a tertiary Headache center (Tominaga hospital) since 2012. Patients completed comprehensive questionnaires covering demographic data, clinical characteristics, sleep, and periodicity of attacks. CH subjects were categorized by their characteristics and we explored possible relationship.

Results: Insomnia was present in 44.8%. Headache attacks during sleep occurred in 53.8%, and those at the time of

rising did in 33.2%. 5.4% of CH subjects had restless leg syndrome(RLS), and 41.7% subjects with RLS had both CH and migraine. Epworth sleepiness scale (ESS) was 8.4 ± 4.5. When excessive daytime sleepiness (EDS) is defined as more than 11 points of ESS. EDS was present in 28.3%. The age of disease onset was significantly earlier in the group of headache attacks during sleep and/or at the time of rising than in the others ($P = 0.03$), by the Welch's t-test. There was no significant correlation between age of onset and insomnia ($P = 0.07$).

Conclusion: CH patients have sleep disorders and EDS. We found positive correlation between age of onset and headache attacks both during sleep and at the time of rising. Prevalence of coexisting RLS was low in CH subjects. Further studies are necessary concerning underling pathophysiology of sleep disorders and possible central nervous system disorders in patients with CH.

EHMTC-0226
POSTER SESSION C

BOTULINUM TOXIN A IN THE TREATMENT OF REFRACTORY CHRONIC CLUSTER HEADACHE – A PILOT STUDY

C. Lampl[1], R. Mirjam[1]

[1]*Hospital Sisters of Charity Linz, Headache Medical Center Seilerstaette, Linz, Austria*

Introduction: For the treatment of refractory Chronic Cluster Headache (rCCH) only limited treatment options are available. The objective of this open single-centre study was to evaluate the efficacy and tolerability of Botulinum Toxin Type-A (BTX-A) as add-on therapy in the prophylactic treatment of rCCH.

Methods: rCCH is described as a situation that fulfills the criteria of ICHD-3 beta for CCH[(1)] with at least three severe attacks per week despite at least three consecutive trials of adequate preventive treatments[(2)]. Between March 2014 und December 2015 rCCH patients, 18–65 years of age, were identified. Exclusion criteria were the standard ones for BTX therapy. According to the PREEMPT I und II study protocol[(3,4)] 150 Allergan IU were administered. Treatment period was 48 weeks. We compared the sum of headache minutes per headache day at baseline (last 4 weeks before BTX treatment) vs week 12, 24, 48.

Results: We identified 5 patients, age 37 ± 9 (mean $\pm$ SD) years, mean duration of the disease was 7,2 years. 2 patients experienced total cessation of attacks within the first 3 treatment periods; in 3 patients the primarily chronic form changed into an episodic one with improvement in attacks frequency and intensity.

Discussion: Our data suggest that the injection of BTX - A could be beneficial as add-on in some patients with otherwise drug rCCH. Usefulness of BTX-A as a new alternative therapeutic tool in the treatment of rCCH has to be confirmed in double-blind, randomized, controlled studies.

EHMTC-0369
POSTER SESSION C

NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) FOR TREATMENT OF CLUSTER HEADACHE: EARLY UK CLINICAL EXPERIENCE

J. Marin[1], E. Consiglio[2], C. McClure[3], E. Liebler[4]

[1]*King's College London, Clinical Research Facility- Wellcome Foundation Building, London, United Kingdom*
[2]*Interface Clinical Services, Clinical Pharmacy, Leeds, United Kingdom*
[3]*North American Science Associates, Biostatistics, Minneapolis, USA*
[4]*electroCore- LLC, Scientific- Medical and Governmental Affairs, Basking Ridge, USA*

Background: Audits of clinical experience in the United Kingdom have supplemented clinical trial data on the safety, tolerability, and efficacy of non-invasive vagus nerve stimulation (nVNS; gammaCore®) for the acute and prophylactic treatment of cluster headache. Early UK post-marketing experience suggests that nVNS may offer an attractive, novel therapeutic option for patients with cluster headache.

Aim: To explore early UK clinical experience with nVNS for the acute or prophylactic treatment of cluster headache.

Methods: A retrospective analysis of National Health Service (NHS) individual funding requests (IFRs) was completed for 30 patients previously diagnosed with refractory cluster headache (29 chronic and 1 episodic) that responded to adjunctive treatment with nVNS over an evaluation period typically lasting between 3 and 6 months. Data on all IFRs were collected from patient interviews, treatment diaries, and physician notes. Outcomes are presented as mean $\pm$ SD. Paired *t* tests were used to examine statistical significance.

Results: The mean number of cluster headache attacks decreased from 27.3 ± 16.7 per week prior to initiation of therapy to 9.8 ± 11.0 ($p < 0.001$); mean duration of attacks

decreased from 53.2 ± 36.1 minutes to 24.5 ± 28.2 minutes ($p < 0.001$); and the reported severity of attacks on a 10-point scale decreased from 7.8 ± 2.2 to 5.4 ± 3.0 ($p = 0.003$). Use of acute abortive medications was also reduced. No serious device-related adverse events were reported.

Conclusions: nVNS provided real-world clinical benefits that were considered meaningful to both patients and physicians. These benefits led to the approval of physicians' IFRs for reimbursement of long-term nVNS treatment for cluster headache by the NHS.

Conflict of interest
Disclosure statement:
Juana Marin has received consultancy and advisory fees from electroCore, LLC. Elizabeth Consiglio is an employee of Interface Clinical Services, which receives fees for services from electroCore, LLC. Candace McClure is an employee of North American Science Associates Inc., which receives fees for services from electroCore, LLC. Eric Liebler is an employee of electroCore, LLC, and receives stock ownership.

EHMTC-0141
POSTER SESSION C

GENDER DIFFERENCES IN THE LIFESTYLE OF CLUSTER HEADACHE PATIENTS: RESULTS FROM THE DANISH CLUSTER HEADACHE SURVEY

N.L.T. Lund[1], M. Barloese[2], A.S. Petersen[2], A.H. Snoer[2], R.H. Jensen[2]

[1]*København, Denmark*
[2]*Danish Headache Center, Dept. of Neurology- Rigshospitalet- University of Copenhagen, Copenhagen, Denmark*

Introduction: Cluster headache (CH) is often associated with poor lifestyle habits. We aimed to characterize possible gender differences in terms of lifestyle factors in a clinical CH patient population, compared to controls.

Methods: Male and female CH patients from the Danish CH-survey aged 18–65, diagnosed according to ICHD-II, were compared to gender- and age matched controls. Participants completed questionnaires and structured interviews. Alcohol consumption higher than 14 units/week for females and 21 units/week for males was considered damaging.

Results: 275 CH patients and 145 controls were included (male:female ratio of 2.3:1). More CH patients had a damaging intake of alcohol compared to controls (9.1% vs. 1.4%, $p < 0.05$), and more patients were current smokers (53.8% vs. 11.7%, $p < 0.0001$) or had a history of smoking (82.2% vs. 42.8%, $p < 0.0001$). Mean BMI was higher among patients compared to controls (25.5 *(CI 25.0–26-0)* vs. 24.5 (*CI 23.9–25.1*), $p < 0.05$).

More CH males had negative lifestyle factors than females, in relation to damaging alcohol consumption (11.5% vs. 3.6%, $P < 0.0001$), current smoking (59.7% vs. 40.5%, $P < 0.0001$), a history of smoking (88.5% vs. 67.9%, $P < 0.0001$) and BMI (25.9 vs. 24.8, $P < 0.05$).

Conclusion: Negative lifestyle factors were much more prevalent among CH patients than among controls. Especially male patients had a very poor lifestyle. Our findings emphasize the need for increased awareness of lifestyle factors in order to prevent development of comorbid diseases. The presence of certain comorbid diseases would exclude already limited treatment possibilities, such as triptans and verapamil, thereby augmenting disease burden.

EHMTC-0142
POSTER SESSION C

MARKED DIAGNOSTIC DELAY IN CLUSTER HEADACHE – AN ANALYSIS OF THE CLINICAL FEATURES: RESULTS FROM THE DANISH CLUSTER HEADACHE SURVEY

N. Lund[1], M. Barloese[2], A.S. Petersen[2], A.H. Snoer[2], R.H. Jensen[2]

[1]*Danish Headache Center, Dept. of Neurology- Rigshospitalet- University of Copenhagen, København, Denmark*
[2]*Danish Headache Center, Dept. of Neurology- Rigshospitalet- University of Copenhagen, Copenhagen, Denmark*

Introduction: Data on clinical features in Cluster Headache (CH) and whether it presents differently in women are limited. Therefore, we aimed to characterize clinical features, diagnostic delay, and gender differences in a large CH population.

Methods: CH patients from the Danish CH-survey aged 18–65, diagnosed according to ICHD-II, completed a questionnaire and structured interview.

Results: 275 CH patients were included (male:female ratio of 2.3:1). On average, patients reported 3.8 attacks/day, a pain intensity of 3.6 on a scale from 0–4, attack duration of 100.5 minutes, cluster duration of 8.4 weeks, and 1.7 clusters/year. The diagnostic delay was 6.2 years in average and 50.6% were misdiagnosed.

No significant differences between males and females were found: 3.7 vs. 4.1 attacks/day, attack duration 102.1 vs. 96.7 minutes, pain intensity 3.5 vs. 3.6, cluster duration 8.9 vs. 7.3 weeks, and 1.7 vs. 1.9 clusters/year. Associated symptoms are described in Table 1. Male patients had the longest diagnostic delay (6.5 vs. 5.6 years, NS), but more females were misdiagnosed (58.3% vs. 47.1 %, NS), and not diagnosed until reaching a tertiary headache center (35.8 % vs. 23.4 %, $P < 0.05$).

Conclusion: There is no difference in the clinical presentation of male and female CH patients. For both genders, misdiagnosis was common and the diagnostic delay long, emphasizing the need for increased education and awareness.

Table 1: Associated Symptoms During Cluster Headache (CH) Attacks in Male and Female CH Patients

	% All patients	% Males	% Females
Ptosis	52,4	45,0**	69,1**
Conjunctival injection	62,2	67,5*	50*
Lacrimation	82,6	82,7	82,1
Eyelid oedema	25,5	21,5	34,5
Nasal congestion	53,5	49,2	63,1
Miosis	18,2	16,2	22,6
Need to move	60.4	55*	72,6*
Irritability	59,6	58,1	63,1
Restlessness	52,4	48,7	60,7

CH: Cluster Headache. * (P<0.05), ** (P<0.001).

EHMTC-0016
POSTER SESSION C

OXYGEN THERAPY FOR CLUSTER HEADACHE. A MASK COMPARISON TRIAL. A SINGLE-BLINDED, SEMI-RANDOMIZED, PLACEBO-CONTROLLED CROSSOVER STUDY

A.S. Petersen[1], M. Barloese[1], N. Lund[1], R. Jensen[1]

[1]*Rigshospitalet, Danish Headache Center- Department of Neurology, Glostrup, Denmark*

Introduction: We investigated possible differences in effect between three types of masks in the acute treatment of cluster headache (CH).

Methods: Fifty-seven CH-patients, diagnosed according to ICHD-II-criteria, participated in a single-blinded, semi-randomized, placebo-controlled crossover study during admission and 102 CH-attacks were evaluated. 100 % oxygen delivered by Demand Valve Oxygen (DVO), Optimask or simple mask (15 liters/min) or placebo delivered by DVO for fifteen minutes at the beginning of an attack. Primary and secondary endpoints: Two-point decrease of pain on a five-point rating scale within 15 min and patients preference.

Results: Only 10 patients had at least four attacks and received placebo. After 15 min 48% had a two-point decrease using the DVO compared to 45% with placebo ($p = 0.867$). After 30 min 68% were pain free or had a two point decrease using DVO and 45% using placebo ($p = 0.061$). In the first attack the DVO, was significantly better at achieving pain-relief at 15 min ($p = 0.018$). The DVO was preferred by 62% compared to simple mask by 5% ($p < 0.0001$) and to Optimask by 33% ($p = 0.06$). Treatment with DVO, or Optimask reduced the need for rescue medication compared to simple mask (23%, 19%, 50%, resp). No treatment-related adverse-events were observed.

Conclusion: The analysis of the first attack significantly favors treatment with DVO compared to simple mask and Optimask. Optimask and DVO treatment resulted in a decreased need of rescue medication compared to simple mask and placebo. We recommend that CH-patients are offered DVO or Optimask before oxygen therapy is abandoned.

Conflict of interest
Disclosure statement:
Declaration of conflicting interests:
Anja Sofie Petersen and Nunu Lund declared no potential conflicts of interest with respect to the research, authorship or publication of this article. The remaining authors declared the following potential conflicts of interest: Mads Barløse has received honorarium from ATI Inc and an unrestricted research grant from Linde Healthcare, AGA A/S. Rigmor Jensen is a member of the advisory boards of Autonomic Technologies, Medotech and ElectroCore.

EHMTC-0303
POSTER SESSION C

COST IMPACT OF OCCIPITAL NERVE STIMULATION VS STANDARD OF CARE THERAPY FOR THE TREATMENT OF MEDICALLY-INTRACTABLE CHRONIC CLUSTER HEADACHE

S. Thavaneswaran[1]

[1]*Medtronic International, Reimbursement and Health Economics, Tolochenaz, Switzerland*

Objectives: Chronic cluster headache (CCH) inflicts extreme pain and significant disability. Standard of care (SoC) employs a variety of acute and prophylactic

medications. In some patients with medically-intractable CCH (miCCH), occipital nerve stimulation (ONS) has demonstrated effectiveness in reducing attack frequency and pain intensity. Here, we evaluate the cost-impact of ONS to treat miCCH vs. SoC in the UK over a 1-year period.

Methods: Baseline SoC costs were established by referencing resource use from consultations, hospital stays and medication from a 2011 German cost study. British formulary prices and national tariff lists (2015–16) were then applied to afford total annual healthcare costs.

Clinical effectiveness for ONS ((reduction in mean attack frequency (MAF) by at least 30% or 50%)), reductions in acute medication, and the proportion of non-responders to ONS were accounted for in the model and sourced from literature review, allowing for 1-year costs associated with ONS to be modelled.

Results: The main cost drivers of miCCH appear to be hospitalisations and acute medication. Assuming that for ONS therapy a reduction in MAF is proportional to a reduction in medication use alone, the introduction of ONS therapy at 30% improvement affords 1-year cost savings of approximately 1,200 GBP, and with a 50% improvement reduces costs by approximately 1,400 GBP.

Conclusions: Results suggest that ONS can demonstrate cost savings in the treatment of miCCH vs SoC within 1 year, based on medication costs alone. Further analysis should investigate the impact of ONS device costs to assess at what time-point ONS becomes cost-neutral vs SoC.

Conflict of interest
Disclosure statement:
I am an employee and share-holder of Medtronic.

EHMTC-0346
POSTER SESSION C

TRIGEMINAL AUTONOMIC CEPHALALGIAS IN TERTIARY MULTIDISCIPLINARY OROFACIAL PAIN CLINIC

D.Y. Wei[1], T.F. Renton[2], P.J. Goadsby[1,3]

[1]*King's College London, Headache Group- Department of Basic and Clinical Neuroscience, London, United Kingdom*
[2]*King's College London, Lead Oral Surgery- Institute of Dentistry, London, United Kingdom*
[3]*King's College Hospital, NIHR Wellcome Trust Clinical Research Facility, London, United Kingdom*

Introduction: Patients with headache often present to different specialities and in particular Trigeminal Autonomic Cephalalgia (TACs) patients are often seen by dentists. Of patients with cluster headaches 45% have consulted a dentist prior diagnosis and many have had procedures performed for the pain (1).

Aim: To evaluate the final diagnosis made from patients seen at a tertiary Multidisciplinary Orofacial Pain clinic.

Methods: A retrospective review of clinic letters of patients who have attended the Multidisciplinary Orofacial Pain clinic over a six month period, from September 2015 till March 2016, looking specifically at the final diagnoses.

Results: Of patients ($n = 81$) seen in clinic, 14 were follow up assessments and excluded. New patients ($n = 67$) had an average age of 52 years, and most were female ($n = 45$, 67%). More than half (57%) of the patients seen had an associated dental issue and 42% of these patients had a dental procedure performed for the pain. The most common diagnosis made in the Clinic was a TAC (40 %), followed by migraine (36 %) and post-traumatic trigeminal neuropathy (10%).

Conclusion: TACs are the most common diagnosis made in our Multidisciplinary Orofacial Pain clinic. The data stress the importance of a multidisciplinary team approach to seeing these complex patients.

Reference

1. Bahra A and Goadsby PJ. Diagnostic delays and mismanagement in cluster headache. *Acta Neurologica Scandinavica* 2004; 109(3): 175–9.

EHMTC-0341
POSTER SESSION D

LASMIDITAN ACTS SPECIFICALLY ON THE 5-HT1F RECEPTOR IN THE CENTRAL NERVOUS SYSTEM

J. Kovalchin[1], A. Ghiglieri[2], E. Zanelli[3], R. Ings[4], T. Mathers[1]

[1]*CoLucid Pharmaceuticals Inc., Research, Cambridge, USA*
[2]*Accelera Srl, Drug Disposition, Milano, Italy*
[3]*Independent Consultant, Research, Sudbury, USA*
[4]*RMI-Pharmacokinetics LLC, Pharmacokinetics, Carlsbad, USA*

Lasmiditan, a highly selective 5-HT_{1F} agonist, is clinically effective in reducing headache pain along with associated symptoms of migraine, and is currently in Phase 3 clinical development. In animal models, lasmiditan inhibits neurogenic inflammation in the dura mater and decreases trigeminal stimulation-induced c-fos expression in the nucleus caudalis. Achieving pharmacologically relevant concentrations in the central nervous system of lasmiditan is therefore critical.

Using the human carcinoma epithelial cell line Caco-2, lasmiditan has significant permeability ($>10^{-6}$ cm/s) in the apical to basolateral direction, without being a substrate for the multidrug resistance protein 1 (P-gp). Albino mice having received a single IV dose of lasmiditan at 1 mg/kg have lasmiditan concentrations reaching, 2 hours after administration, 94.1 ng/mL (249 nM) and 60.9 ng/mL (161 nM) in the brain and plasma, respectively, with a brain/plasma ratio of 1.57 and an unbound fraction (f_u) of 50.5% in the brain.

In human subjects dosed with 100 mg of lasmiditan, plasma C_{max} of ~250 nM has been observed. Consequently, the unbound compound concentration is estimated to be ~200 nM in the brain of these subjects. In comparison and based on literature, this value is 15-fold higher than the estimated concentration achieved in the brain of subjects dosed with 100 mg of sumatriptan. Lasmiditan K_i value for 5-HT_{1F} is 2.2 nM versus >1000 nM for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1D}, implying that lasmiditan specifically targets the 5-HT_{1F} receptor in the brain.

Our results demonstrate lasmiditan's ability to cross the blood-brain barrier and alleviate migraine attack through a novel, central mechanism.

Conflict of interest
Disclosure statement:
I am a full-time employee of CoLucid Pharmaceuticals, Inc.

EHMTC-0105
POSTER SESSION D

ISOMETHEPTENE ENANTIOMERS IN HUMAN BLOOD VESSELS AND RAT MIDDLE MENINGEAL ARTERY

A. Labastida[1], K.A. Haanes[1], R. de Vries[1], B. Daugherty[2], S. Lederman[2], A.H.J. Danser[1], C.M. Villalón[3], A. MaassenVanDenBrink[1]

[1]*Division of Vascular Medicine and Pharmacology Department of Internal Medicine, Erasmus University Medical Center, 3000 CA Rotterdam, Netherlands*
[2]*Tonix Pharmaceuticals Inc., 509 Madison Avenue Suite 306, 10022 New York NY, USA*
[3]*Departamento de Farmacobiología, Cinvestav-Coapa Czda. Tenorios 235 Col. Granjas-Coapa, Deleg. Tlalpan 14330 México D.F, Mexico*

Background/Aims: Isometheptene (IMH) is a racemic drug with sympathomimetic actions used in the acute treatment of migraine; it produces a direct vasoconstriction on cranial and cerebral arterioles; and has been separated into its individual enantiomers, (*R*)-IMH and (*S*)-IMH, with one believed to provide its therapeutic effect, while the other may only contribute to side-effects (i.e. vasospasm).

The present study investigated the vasoconstrictor properties of the isometheptene enantiomers in human isolated blood vessels (middle meningeal artery, coronary arteries, and saphenous vein) and rat middle meningeal artery (intravital microscopy model).

Methods: Blood vessels were mounted in organ baths and concentration-response curves for sumatriptan, noradrenaline, isometheptene racemate, *(R)*-IMH and *(S)*-IMH were constructed. In Male Sprague-Dawley rats parietal bone was thinned to visualize the meningeal artery. Then, vasodilator responses to endogenous (released by i.v. capsaicin and electrical stimulation) and exogenous (i.v.) CGRP were elicited in the absence or presence of the enantiomers.

Results/conclusions: Neither isometheptene racemate, nor its enantiomers, did induce any contraction on blood vessels at concentrations up to 10 μM. Only at the supratherapeutic concentration of 100 μM, isometheptene and its enantiomers induced a modest contraction (*ca*. 20–40% of contraction to 100 mM KCl) in middle meningeal artery. Moreover, these compounds did not modify the vasodilator responses to endogenous or exogenous CGRP *in vivo*. Therefore, isometheptene is probably effective in alleviating migraine through a non-vascular mechanism. The exact mechanisms need to be elucidated.

* (R)-isometheptene is being investigated in the US for tension-type headache under a US IND and is not approved for any indication.

Conflict of interest
Disclosure statement:
This study was supported by Tonix Pharmaceuticals

EHMTC-0155
POSTER SESSION D

NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) FOR THE ACUTE TREATMENT OF MIGRAINE WITHOUT AURA IN ADOLESCENTS: PRELIMINARY CLINICAL EXPERIENCE

L. Grazzi[1], G. Egeo[2], E. Liebler[3], P. Barbanti[2]

[1]*Carlo Besta Neurological Institute and Foundation, Headache Center, Milan, Italy*
[2]*Istituto di Ricovero e Cura a Carattere Scientifico- San Raffaele Pisana, Headache and Pain Unit- Department of Neurological Motor and Sensorial Science, Rome, Italy*
[3]*electroCore- LLC, Scientific- Medical and Governmental Affairs, Basking Ridge, USA*

Background: Recent study results and clinical experience have demonstrated the safety, tolerability, and efficacy of non-invasive vagus nerve stimulation (nVNS; gammaCore®) for the acute and prophylactic treatment of migraine. nVNS has a favorable adverse event profile, making it an attractive option for sensitive patient populations.

Aim: To explore the safety, tolerability, and efficacy of nVNS as an acute treatment of migraine without aura in adolescents.

Methods: Eight 13- to 18-year-old patients with migraine without aura according to *International Classification of Headache Disorders, 3rd edition (beta version)* criteria (4 to 8 migraine days per month) were recruited. In a one-hour training workshop, the patients and their parents were instructed to treat attacks acutely with nVNS for one month. Each attack was treated with one 2-minute stimulation on the right side of the neck; a second stimulation was allowed within one hour of the first treatment. Patients recorded the pain intensity of the treated attack at several prespecified time points between 30 minutes and 24 hours after treatment. Rescue medication was allowed after 2 hours from device use.

Results: Of the 44 treated migraine attacks, 17 (38.6%) were pain free at one hour. Pain intensity for an additional 4/44 (9.1%) attacks decreased to mild at 2 hours. These attacks (21/44; 47.8%) did not require rescue medication. No device-related adverse events were recorded.

Conclusions: In this preliminary evaluation, nVNS had favorable safety and tolerability and was practical and effective in acutely treating migraine without aura in adolescents.

Conflict of interest
Disclosure statement:
Licia Grazzi, MD, has received consultancy and advisory fees from Allergan, Inc., and electroCore, LLC. Gabriella Egeo, MD, PhD, has nothing to disclose. Eric Liebler is an employee of electroCore, LLC, and receives stock ownership. Piero Barbanti, MD, PhD, has received consultancy fees from Allergan, Inc., electroCore, LLC, Janssen Pharmaceuticals, Inc., and Lusofarmaco and advisory fees from Abbott Laboratories and Merck & Co., Inc.

EHMTC-0329
POSTER SESSION D

LASMIDITAN AND SUMATRIPTAN: COMPARISON OF IN VIVO VASCULAR CONSTRICTION IN THE DOG AND IN VITRO CONTRACTION OF HUMAN ARTERIES

E. Rubio Beltran[1], H. Kristian[1], A. Labastida[1], R. de Vries[1], J. Danser[1], G. Michael[2], S. Peter[2], J. Kovalchin[3], C. Villalón[4], A. MaassenVanDenBrink[1]

[1]*Erasmus MC, Div. of Pharmacology- Dept. of Internal Medicine, Rotterdam, Netherlands*
[2]*CorDynamics, Chicago, USA*
[3]*CoLucid Pharmaceuticals, Cambridge, USA*
[4]*Cinvestav-Coapa, Dept. de Farmacobiología, Mexico City, Mexico*

Antimigraine triptans are vasoconstrictive 5-$HT_{1B/1D}$ receptor agonists that are contraindicated in patients with coronary artery disease. In contrast to sumatriptan, lasmiditan is a selective 5-HT_{1F} receptor agonist that lacked in vitro vasoconstrictive effects in rabbit saphenous vein. To further assess the cardiovascular effects of lasmiditan, we studied the vascular effect of lasmiditan in dogs and in human isolated arteries and compared it to sumatriptan.

Anesthetized female beagle dogs (5.4–7.9 kg) were implanted with carotid and coronary artery crystals for measurement of vascular diameter. Lasmiditan, sumatriptan and vehicle were administered by intravenous infusion over 20 minutes in escalating cumulative doses ranging from 0.03 to 11.13 mg/kg (n = 6/group). Statistically significant decreases in both coronary and carotid artery

diameters occurred in the sumatriptan-treated group at clinically relevant doses compared to the vehicle control ($p < 0.025$). Conversely, lasmiditan was devoid of any vasoconstrictive activity at all doses tested.

In human isolated blood vessels, sumatriptan induced contractions in the proximal (E_{max} 44% of contraction to 100 mM KCl, pEC_{50} 6.29, $n = 2$) and distal (E_{max} 139%, pEC_{50} 6.45, $n = 2$) coronary artery. In internal mammary artery, sumatriptan also induced contractions (E_{max} $30 \pm 16\%$, pEC_{50} 5.86 ± 0.56, $n = 5$). and contractions were augmented (E_{max} $79 \pm 19\%$, pEC_{50} 6.42 ± 0.66, $n = 5$) after precontraction with threshold concentrations of U46619. Vehicle and lasmiditan did not contract any of the arteries studied, either from baseline or after precontraction with U46619.

Thus, in canine and most importantly, in human blood vessels, the lack of vasoconstrictive properties of lasmiditan may be a cardiovascular safety advantage compared to the triptans.

Conflict of interest
Disclosure statement:
This study was supported by CoLucid Pharmaceuticals

EHMTC-0010
POSTER SESSION D

PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF DFN-02, AN INTRANASAL SUMATRIPTAN SPRAY CONTAINING A PERMEATION ENHANCER, COMPARED WITH SUBCUTANEOUS (SC) SUMATRIPTAN IN HEALTHY ADULTS

Sagar Munjal[1], Anirudh Gautam[2], Elliot Offman[3], Elimor Brand Schieber[1], Kent Allenby[1], Dennis M. Fisher[4]

[1]*Promius Pharma/Dr. Reddy's Laboratories, Princeton, NJ*
[2]*Dr. Reddy's Laboratories, Hyderabad, India*
[3]*Celerion, Neptune, NJ*
[4]*P Less Than, San Francisco, CA.*

Objective: To compare the pharmacokinetic characteristics of two commercial sumatriptan products, 4 mg and 6 mg SC sumatriptan with DFN-02, an intranasal formulation comprised of sumatriptan 10 mg plus 0.20% permeation enhancer 1 O n Dodecyl-β-D-Maltopyranoside (DDM, Intravail® A3) in healthy adults.

Background: Intranasal sumatriptan (Imitrex®) may be an alternative for patients who refuse injections and cannot tolerate oral agents, but low bioavailability and slow absorption limit the clinical utility of the currently marketed formulation, highlighting an unmet need for an effective non-oral migraine medication with a rapid onset of action.

Methods: We conducted an open-label, randomized, single-dose, three-way crossover bioavailability study comparing DFN-02 with 4 mg and 6 mg SC sumatriptan in 78 healthy, fasted adults. Subjects received a single dose of each treatment with at least three days between treatments. Blood was sampled for pharmacokinetic evaluation of sumatriptan and DDM through 24 hours post-dose.

Results: Median tmax was 10 minutes for DFN-02 compared to 15 minutes for 4 mg and 6 mg SC sumatriptan ($P < .0001$). Mean sumatriptan exposure metrics were similar for DFN 02 and 4 mg sumatriptan: AUC0–2 values were 35.12 and 44.82 ng*hr/ml, respectively; AUC0-∞ values were 60.70 and 69.21 ng*hr/mL, respectively; Cmax values were 51.79 and 49.07 ng/mL, respectively. DDM exposure was low (mean Cmax = 1.63 ng/ml), tmax was 30 minutes, and DDM was undetectable by 4 hours. There were no serious adverse events, discontinuations due to adverse events, or any clinically remarkable findings.

Conclusions: Plasma sumatriptan concentrations of DFN-02 peaked five minutes earlier than 4 mg and 6 mg SC sumatriptan. The rapid absorption of DFN-02 suggests that its efficacy will be comparable to that of 4 mg SC sumatriptan.

Financial Support: This study was funded and sponsored by Promius Pharma, Princeton, NJ 08540, USA.

Document not received

EHMTC-0069
POSTER SESSION D

VITAMIN B COMPOUND COULD BE EFFECTIVE IN MENSTRUAL RELATED MIGRAINE

S. Razeghi Jahromi[1,2], M. Togha[2]

[1]*Shahid-Beheshti University of Medical Sciences, School of Nutrition and Food Technology, Tehran, Iran*
[2]*Tehran University of Medical Sciences, Headache department- Iranian Center of Neurological Research-Neuroscience Institute, Tehran, Iran*

Background: Migraine headaches are disabling problem for women with many of them experience more severe attacks before menstruation. Homocysteinemia results in overproduction of homocysteic acid which in turn stimulates the trigeminovascular system and provokes

inflammation in cerebral vessels that could lead to migraine. Vitamin B6 and B12 are required for catalyzation of homocysteine. Studies also suggested that thiamine could reduce migraine index. We conducted this study to assess the effect of vitamin B compound (B1, B6 and B12) on menstrual related migraine (MRM).

Methods: In current open label before-after trial thirty women (age: 34 ± 9.05 years) with MRM, diagnosed according to the International Headache Society criteria (IHCD III β), were recruited. The patients were asked to record the duration and intensity (using visual analog scale) of migraine attacks during the 2 days prior to menstruation for 3 months. First three month: baseline characteristic (T1). Second three month: receiving B compound (vitamin B1-100 mg, B6-100 mg, Bl2-1000 mcg, in 3 ml of aqueous solution), 4 days prior to menstruation (T2). Third three months: withdrawal period (T3).

Results: The mean duration of MRM attacks (hours) was 21.6 ± 4.5, 8.8 ± 6.4, and 20.9 ± 4.6 during T1, T2, and T3 respectively. The mean intensity of MRM attacks was 7.7 ± 0.9, 3 ± 1.6, and 7.4 ± 1.02 during T1, T2, and T3 respectively. B compound reduced the mean duration of MRM by $61 \pm 24\%$ ($P < 0.005$) and the mean intensity by $61 \pm 22\%$ ($P < 0.005$). The mean intensity and duration of MRM reached the baseline level after cessation of injections.

Conclusion: Vitamin B compound could be effective in menstrual related migraine.

EHMTC-0217
POSTER SESSION D

DISCONTINUATION OF OPIOIDS AND DECREASED HEADACHE FREQUENCY IN CHRONIC MIGRAINE

B. Torphy[1], J. Babione[2], K. Naylon[2]

[1]*Diamond Headache Clinic, Headache, Chicago, USA*
[2]*Adler University, Psychology, Chicago, USA*

Excessive opioid use has been associated with Medication Overuse Headache (MOH) and increased risk of opioid dependence. A retrospective chart review assessed headache frequency in a group of 55 patients with Chronic Migraine (CM) who took opioids 10 or more days per month at four different time points, over an 8 month period (i.e. Baseline, 1–2 months, 3–4 months, and 6–8 months). Patients who discontinued opioids as well as those who continued opioids were included. The measured outcomes at each visit were total number of headache days within the past month and the total number of those headache days that were considered to be severe. Statistical analysis revealed that patients who discontinued opioid use reported significantly fewer total and severe headache days at follow-up, as compared to baseline. Patients who continued opioids showed no change in their headache frequency. These results indicate that when patients with CM, who are taking opioids on 10 or more days per month, refrain from opioid use they may experience decreased headache frequency and severity that persists over time.

EHMTC-0128
POSTER SESSION D

THERAPEUTIC EFFECT OF DIFFERENT TABLES IN HEADACHE WITH TYPE2 DECOMPRESSION SICKNESS

J.Y. Ahn[1], H.T. Kim[2]

[1]*Seoul Medical Center, Neurology, Seoul, Republic of Korea*
[2]*Hanyang University hospital, Neurology, Seoul, Republic of Korea*

Backgrounds: There are different causes associated with headaches and diving. Most of headaches are benign and spontaneously disappear. However headaches can also be a sign of severe type DCS(type2 decompression sickness). Recompression therapy is well established in the treatment of DCS including type2 DCS. However it was not confirm whether each United State Navy(USN) treatment tables had different therapeutic effect in headache of type2 DCS. We want to know which table is more effective for headache.

Methods: We applied different USN treatment tables(6, 6a and 6a1) to headache with type2 DCS for 10 years. 68 patients with type2 DCS were treated with recompression therapy, 16 patients by table 6, 31 by 6a and 21 by 6a1. We reviewed the outcome of headache before and after each treatment. And we investigated age, diving experience, depth of dive. bottom time of dive, and onset to treatment before the treatment in each treatment group.

Results: There were no significant differences between each treatment group in age, diving experience, depth of dive. bottom time of dive and onset to treatment. Marked improvements of headache were noticed in 85.3%(table 6; 50%, 6a; 93.5%, and 6a1; 95.2%). There were significant differences of improvement between groups 6 and 6a($p = 0.0077$) and 6 and 6a1($p = 0.0073$).

Conclusions: We think that table 6a1 or 6a should be used in headache of type2 DCS. And table 6 is less useful in headache of type2 DCS.

EHMTC-0179
POSTER SESSION D

IS THE USE OF EPIDURAL BLOOD PATCHES FOR REFRACTORY, SPONTANEOUS, LOW-PRESSURE HEADACHES EFFECTIVE?

S. Ansel[1], A. Tyagi[1], A. Rae[1]

[1]*Queen Elizabeth University Hospital, Institute for Neurological Sciences, Glasgow, United Kingdom*

Background: Intracranial hypotension often results from a spontaneous cerebrospinal fluid (CSF) leak at a spinal level and patients typically present with an orthostatic headache. Although imaging may be helpful, it remains largely a clinical diagnosis. Following analgesia and intravenous caffeine, an epidural blood patch (EBP) may be attempted. We aimed to evaluate the efficacy of EBP in refractory, spontaneous, low-pressure headaches.

Methods: We retrospectively analysed 17 patients who had an EBP performed for a refractory, spontaneous, low-pressure headache. All EBPs were performed at the Institute of Neurological Sciences, Glasgow between December 2013 and October 2015. We used information available on an electronic patient record system to record patient demographics, radiological findings, and subjective improvement reported at clinic follow-up. Questionnaires enquiring about outcome were also sent to patients.

Results: 12/17 (71%) patients were female and the cohort's mean age was 43 years. Fifteen patients had a spinal MRI prior to EBP: two had identifiable CSF leaks, one at the cervico-thoracic junction and the other at L5. All patients had a lumbar EBP performed. Fourteen patients attended clinic follow-up, half reported some degree of relief from headaches. Eight patients responded to questionnaires, five reported permanent reduction in pain whilst 3 reported no relief.

Discussion: Pathophysiology of intracranial hypotension due to a spontaneous CSF leak is poorly understood. The site of a CSF leak is infrequently found thus, treatment protocols are difficult to establish. Additionally, pain is a subjective, temporal outcome measure with psychosocial confounders and response to treatment is difficult to assess.

EHMTC-0098
POSTER SESSION D

HEADACHE WITH TOTAL LOSS OF VISION, NON-HYPERTENSIVE POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME(PRES) CASE REPORT

A. Bakir[1]

[1]*Izmir Asker Hastanesi, Neurology Department, Izmir, Turkey*

Introduction: Posterior reversibl encephalopathy syndrome (PRES) presents with rapid onset of symptoms including headache, seizures, altered consciousness and visual disturbance. It is often –but by no means always-associated with acut hypertension more than %70 of patients with PRES are hypertensive, though a sigificiant proportion have normal or only mildly raised blood pressure.

Case: We report a case of non-hypertensive PRES due to corticosteroid treatment in 60-year-old man, with ITP (idiopathic thrombocytopenic purpura) disease. He was treated wtih 1 mg/kg a day prednisone for 21 days. After five days, when the symptoms first appeared, characterised by severe headache, dizziness, blurred vision, he went to a local hospital. He underwent an encephalon CT, which was normal. After two weeks he was totally blind. Cerebral magnetic resonance imaging (MRI) was carried out showing "T2 hyperintensity in the bilateral occipital-parietal region"

Conclusion: The cause of PRES is certainly multifactorial. The key to diagnosis is certainly the image, but clinicians must raise suspicion when there is a case with these characteristics. MRI is considered the gold standard for confirmation of diagnosis and typically demonstrates hyperintense T2 weighted and FLAIR lesions due to high water mobility, which appear normal on diffusion-weighted imaging predominantly occuring at the occipital regions.

EHMTC-0283
POSTER SESSION D

MICROSURGERY REVEALS SPINAL MICRO-SPURS AS THE PREDOMINANT CAUSE OF CSF-LEAKS AND CURES PATIENTS WITH INTRACTABLE SPONTANEOUS INTRACRANIAL HYPOTENSION

J. Beck[1], C. Ulrich[2], C. Fung[2], J. Fichtner[2], K. Seidel[2], W. Z'Graggen[2], J. Gralla[3], A. Raabe[2]

[1]*Inselspital- University Hospital Bern-, Dept. of Neurosurgery, Bern, Switzerland*
[2]*Inselspital- University Hospital, Dept. of Neurosurgery, Bern, Switzerland*
[3]*Inselspital- University Hospital, Inst. of Diagnostic and Interventional Neuroradiology, Bern, Switzerland*

Background: What is the exact nature of spinal CSF leaks in spontaneous intracranial hypotension? To visualize CSF leaks we performed a systematic workup in all patients with intractable symptoms, including spinal microsurgical exploration.

Methods: Patients from Feb 2013 to June 2015 were included. The diagnostic work-up included: spinal MRI without and with intrathecal contrast, dynamic myelography, post-myelography CT, and microsurgical exploration.

Results: Out of 114 consecutive patients, 15 had intractable symptoms despite conservative treatment and blood patching. 14 underwent microsurgical exploration, one patient refused surgery. Microsurgery identified and visualized all CSF-leaks as a longitudinal dural slit (6.1 ± 1.7 mm), on ventral (10), lateral (3), and dorsal (1) aspect of the dura (cervical $n = 2$, cervico-thoracic $n = 1$, thoracic $n = 11$). In 10 patients (71%) a ventral, calcified micro-spur, slitting the dura like a knife, caused the CSF-leak. In 3 patients (22%) a lateral dural tear in the axilla of the nerve root with an associated spinal meningeal diverticulum, and in one patient (7%) a dorsal osteophyte caused the CSF leak. The micro-spurs were removed and the dural slits sutured or sealed with immediate cessation of CSF leaking.

Conclusions: Neurosurgical visualization of the CSF-leak revealed a ventral, lateral, or dorsal longitudinal dural slit in all cases and identified ventral spinal calcified micro-spurs, slitting the dura, as the predominant and underestimated etiology. The current notion that CSF leaks in SIH are spontaneous or that a weak dura is a predisposition is challenged. Microsurgery is the treatment of choice in cases with intractable SIH.

EHMTC-0350
POSTER SESSION D

COMPLICATIONS FROM MANAGEMENT OF IDIOPATHIC INTRACRANIAL HYPERTENSION: A CASE OF CSF OVERDRAINAGE FROM A LUMBOPERITONEAL SHUNT

L. Beeravolu[1], I. Ahmed[2]

[1]*Research Medical Center, Neurology, SAINT LOUIS, USA*
[2]*Research Medical Center, Neurology, Kansas city, USA*

Lumbo-peritoneal shunts are placed to treat patients with refractory idiopathic intracranial hypertension. They can be associated with complications due to overdrainage which include secondary tonsillar herniation, subdural hematomas and spinal syrinx. We present a case of progressive cerebellar tonsillar descent as a complication of overdrainage from lumboperitoneal shunt resulting in clinical and radiological evidence of brainstem herniation which remarkably improved upon shunt ligation.

A patient with history of idiopathic intracranial hypertension with a non-programmable lumboperitoenal shunt presented with acute respiratory failure which led to emergent intubation. Neurological exam revealed her to be minimally responsive to sternal rub with intact pupillary reflexes and no spontaneous movement of extremities. CT and MRI brain revealed Chiari I malformation with cerebellar tonsils descending 19 mm below the level of foramen magnum. Acute ischemic infarcts were seen in tonsils, right lateral medulla, left cingulate gyrus and right frontal lobe all consistent with mechanical compression of blood vessels from brainstem herniation. Comparison with past studies revealed the cerebellar tonsils to be in normal position in 2011 and slight descent of tonsils but within upper limits of normal in 2013. Due to concern for progressive tonsillar herniation, the shunt was ligated. Following the ligation, patient remarkably improved with respect to mentation, respiratory status and motor function although she had dysphagia. A repeat MRI brain 12 days after ligation of the shunt showed resolution of the herniation, tonsillar descent with persistence of the infarcts. Patient was eventually discharged to acute rehabilitation with a gastrostomy tube and finally went home.

EHMTC-0192
POSTER SESSION D

USE OF INTRAVENOUS LACOSAMIDE FOR REFRACTORY TRIGEMINAL NEURALGIA

J. Camiña Muñiz[1], H. Vico Bondía[1], A. Moreno Rojas[1], M. Crespí Monjó[2], F.J. Molina Martínez[1]

[1]*Hospital Universitari Son Espases, Neurology, Palma de Mallorca, Spain*
[2]*Hospital Universitari Son Espases, Clinical Pharmacology, Palma de Mallorca, Spain*

Background: Trigeminal neuralgia is characterized by episodes of short-lasting severe paroxysmal facial pain. Medical treatment includes antiepileptic and non-antiepileptic drugs. Sometimes, an empirical combination of both therapies is needed. In case of a severe outbreak of symptoms intravenous administration of drugs is a common practice. In this context we have tried the use of lacosamide.

Methods: We have retrospectively searched our hospital's pharmacy database all the endovenous prescriptions of lacosamide in 2014 and 2015. Later, we checked the medical histories in the clinical system and we included the patients with confirmed diagnosis of trigeminal neuralgia.

Results: A total of 8 patients were found. Prior to the lacosamide administration, polypharmacy was needed for pain management in all of them. 6 of them were lacosamide-naive patients, and the remaining 2 had already started lacosamide prior to 2014. In 5 of them, the treatment started in the Emergency Department, and in the remaining 3, as inpatients. In the follow-up, only one of the patients discontinued lacosamide because of side effects (dizziness).

Conclusions: These findings provide preliminary evidence suggesting that lacosamide may be able to control neuropathic pain in refractory trigeminal neuralgia and is well tolerated. Its intravenous administration should be considered in case of an exacerbation.

EHMTC-0390
POSTER SESSION D

"PURE" DETOXIFICATION IS THE MOST EFFECTIVE TREATMENT FOR MEDICATION-OVERUSE HEADACHE: A CONTROLLED RANDOMIZED TRIAL WITH 6 MONTHS FOLLOW-UP

N.L. Find[1], S.B. Munksgaard[1], R.H. Jensen[1], L. Bendtsen[1]

[1]*Danish Headache Center, Neurology Department, Glostrup, Denmark*

Background: Detoxification is the guideline recommended treatment for medication-overuse headache (MOH). However, there is no scientific evidence on how to compose a detoxification program.

Aim: To compare the effect of a restricted intake of acute medication versus no acute medication during the detoxification period, at 6-months follow-up.

Methods: Patients with MOH were included in a prospective, open-label study and randomized to 2 months detoxification with either A) no acute medication or B) acute medication restricted to 2 days/week. Both protocols were out-patient programs.

Results: We included 71 patients. Sixty-two (87.3%) succeeded in detoxification, and 43 (60.6%) were followed-up at 6 months. Patients in protocol A had a significantly lower headache frequency (reduction from 30 to 11) than patients in program B (reduction from 30 to 17) at 6 months follow-up ($p = 0.03$). There were no significant differences between the two groups in reduction of medication days/month (13 vs. 15.6; $p = 0.38$), percentage with remission to episodic headache (63.6 vs. 50.0; $p = 0.37$) or percentage of cured MOH (72.7 vs. 75; $p = 0.87$) at 6 months.

Conclusion: Detoxification without any acute medication was more effective than detoxification with restricted intake of acute medications in decreasing headache frequency.

EHMTC-0362
POSTER SESSION D

AN UNCOMMON PRESENTATION OF AN UNCOMMON CAUSE OF A COMMON SYMPTOM

N. Praveen Chander[1], D. Halprashanth[2], P. P Vanamoorthy[3]

[1]*Global Hospital Chennai, Neurology Department, Chennai, India*
[2]*Global Hospitals, Neurology, Chennai, India*
[3]*Global Hospitals Chennai, Neuro Critical Care, Chennai, India*

Case Report: A 31 years female with no co-morbid illness came to Emergency room(ER) with complaints of severe headache. The headache was pulsatile and unilateral. She had nauseating sensation with photophobia and phonophobia without any aura. Patient had H/O similar episodes in the past. A CT imaging was done which was normal. Based on International Headcahe Society Classification, diagnosis of Migraine without aura was made and treatment started.

Three days later she developed worsening of headache, more on assuming upright posture.

Patient's blood investigations were normal. Her MRI imaging showed diffuse thickened pacchymeninges with contrast enhancement. Her spinal imaging showed fluid in epidural compartment in cervico dorsal region leading to suspicion of dural tear.

Harmonizing with the imaging, CSF pressure was only 2 cms of water, suggestive of intracranial hypotension

A final diagnosis of Spontaneous intracranial hypotension was made. Patient did not improve with conservative treatment(bed rest and caffeine) and hence was treated with epidural blood patching. Patient improved clinically and is being followed up for past 3 months on outpatient basis.

Discussion: Intracranial hypotension may have inconsistent clinical presentations. Diminution of CSF volume leads to downward pulling force in the brain and the pain sensitive structures in accordance with Monro-Kellie hypothesis.

The rarity of this case-vignette is the unusual presentation of an uncommon cause(INTRACRANIAL HYPOTENSION) of a very common symptom(headache). The typical Neuroimaging findings with postural nature of the headache are always a clue in diagnosing this condition. The instantaneous response by epidural patching is also noteworthy.

EHMTC-0086
POSTER SESSION D

CLINICAL EFFICACY OF PULSED RADIOFREQUENCY NEUROMODULATION FOR THE TREATMENT OF OCCIPITAL NEURALGIA

H.J. Choi[1]

[1]*Hallym Unversity, Neurosurgery, Chuncheon-Si- Gangwon-Do, Republic of Korea*

Objective: Occipital neuralgia is characterized by paroxysmal jabbing pain in the dermatomes of the greater or lesser occipital nerves caused by irritation of these nerves. Although several therapies have been reported, they have only temporary therapeutic effects. We report the results of pulsed radiofrequency treatment of the occipital nerve, which was used to treat occipital neuralgia.

Methods: Patients were diagnosed with occipital neuralgia according to the International Classification of Headache Disorders classification criteria. We performed pulsed radiofrequency neuromodulation when patients presented with clinical findings suggestive occipital neuralgia with positive diagnostic block of the occipital nerves with local anesthetics. Patients were analyzed according to age, duration of symptoms, surgical results, complications and recurrence. Pain was measured every month after the procedure using the visual analog and total pain indexes.

Results: From 2010, ten patients were included in the study. The mean age was 52 years (34–70 years). The mean follow-up period was 7.5 months (6–10 months). Mean Visual Analog Scale and mean total pain index scores declined by 6.1 units and 192.1 units, respectively, during the follow-up period. No complications were reported.

Conclusion: Pulsed radiofrequency neuromodulation of the occipital nerve is an effective treatment for occipital neuralgia. Further controlled prospective studies are necessary to evaluate the exact effects and long-term outcomes of this treatment method.

EHMTC-0347
POSTER SESSION D

HOW DO CLINICIANS THINK ABOUT CLUSTER HEADACHE

L. Dikomitis[1], K. Paemeleire[2], P.J. Goadsby[3], F. Ahmed[4]

[1]*Keele University, School of Medicine, Keele, United Kingdom*
[2]*Ghent University, Department of Neurology, Ghent, Belgium*
[3]*NIHR-Wellcome Trust Clinical Research Facility, King's College London, London, United Kingdom*
[4]*Hull Royal Infirmary, Department of Neurology, Hull, United Kingdom*

Background: We have little in-depth understanding of how clinicians perceive cluster headache and of their experiences with cluster headache patients.

Aim: In this interdisciplinary study we aim to bridge neurology and sociology of health by gaining insight into the perceptions, experiences and understandings of cluster headache. We focus here on data collected in the north of England.

Method: Qualitative study using semi-structured interviews with general practitioners (n = 8) and neurologists (n = 8). This included 10 male and 6 female clinicians with an average age of 49. All clinicians were interviewed by a health sociologist between March and December 2015. A systematic qualitative analysis was applied to the transcribed interviews.

Result: The following overarching themes emerged after analysis: (1) perceptions of primary headache disorders; (2) challenges with diagnosis; (3) communication between primary and secondary care and (4) effective treatment and management of cluster headaches. We identified specific barriers to early diagnosis of cluster headache and effective treatment pathways for cluster headache patients. For instance, some GPs found it challenging to take an effective history and could often not distinguish key differences between migraine and cluster headache. Neurologists regularly experienced that their suggested treatments, often around sumatriptan injections, were not followed through when patients were referred back to primary care.

Conclusion: This research contributes to our understanding of professional responses to cluster headache. This could form the starting point for the development of interventions to increase early diagnosis in primary care, optimize referrals to specialist care and improve communication between primary and secondary care.

EHMTC-0074
POSTER SESSION D

EMOTIONAL TRIGGERS IN REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

J. Nivelle[1], C. Burcin[2], J. Mawet[2], A. Ducros[1]

[1]*Montpellier University Hospital, Neurology, Montpellier, France*
[2]*Lariboisière Hospital- APHP, Emergency Headache Centre, Paris, France*

Aims: To analyze the role of emotional stress in reversible cerebral vasoconstriction syndrome (RCVS).

Background: RCVS is typically characterized by thunderclap headache (TCH) and segmental constriction of cerebral arteries that resolves within three months. Various precipitants are found in at least half the cases, the commonest being exposure to adrenergic or serotoninergic drugs.

Methods: From January 2004 to January 2011, we prospectively recruited 173 consecutive patients with RCVS of whom 46 (30 females, 16 males, mean age: 44.6 years) described emotional distress before the first TCH.

Results: Forty patients reported a threatening experience during the 6 months before RCVS and 10 stated an acute emotion triggered their first TCH. Most patients (29/46) had a history of anxiety or depression, and 10 had a history of migraine. Other precipitants of RCVS were present in 27 patients (vasoactive drugs in 26), while emotional stress was the only precipitant in 19 patients. Clinical manifestations of RCVS included TCH in all patients (recurrent in 43), focal neurological deficit in 7, and blood pressure surge in 13. Brain lesions were found in 12 patients, including convexity subarachnoid hemorrhage (11), intracerebral hemorrhage (3), cerebral infarction (1) or posterior reversible encephalopathy (3). An associated cervical artery dissection was present in 3 cases. Two patients had a persistent neurological deficit at 3 months of follow-up.

Conclusion: Emotional stress may precipitate RCVS and trigger TCH in RCVS. Adrenergic overactivity together with a neural discharge might induce acute cerebral microvascular dysfunction with TCH, and sometimes stroke.

Conflict of interest
Disclosure statement:
Advisory boards for Amgen and Lilly

EHMTC-0296
POSTER SESSION D

AN UNUSUAL CASE OF POST PARTUM VASOSPASM

C. Duncan[1]

[1]*Aberdeen Royal Infirmary, Neurology, Aberdeen, United Kingdom*

This 35 year old lady developed gradually progressive headache 2 days after an uncomplicated caesarean section under spinal anaesthesia. She had mild hypertension throughout pregnancy and delivery. The obstetric anaesthetists initially thought her headache was due to iatrogenic intracranial hypotension and administered an epidural blood patch. When this was not successful she underwent cranial imaging which demonstrated cortical subarachnoid haemorrhage and extensive vasospasm. There was no evidence of pre-eclampsia or eclampsia and an underlying aneurysm was excluded. She required aggressive management for severe vasospasm causing significant cortical ischaemia, but went on to make an excellent recovery. Although there are a number of unusual features, a final diagnosis of Reversible Cerebral Vasoconstriction Syndrome (post partum angiopathy) was made.

Reversible Cerebral Vasoconstriction Syndrome is recognised as an important cause of post partum headache. It is a self limiting condition that usually presents with recurrent triggered or spontaneous thunderclap headaches and is associated with a typical strings and beds appearance on angiography. Comparison is made with a typical case and other causes of post partum headache are reviewed.

Conflict of interest
Disclosure statement:
I have no potential conflict of interest to disclose

EHMTC-0204
POSTER SESSION D

THE EFFECTIVENESS OF CERVICAL FACETS INFILTRATION OF C2-3 IN THE TREATMENT OF TRANSFORMED MIGRAINE (TM) PLUS CERVICOGENIC COMPONENT

Z. Elchami[1], M.B. Issa[1], A. Mirambel[1], E. Umlas[1], R. Massoud[1], S. delos Santos[1], A. Villamar[1]

[1]*International Medical Center, Pain & Headache Management Center, Jeddah, Kingdom of Saudi Arabia*

Background and Aims: Transformed migraine (TM) is a chronic, daily headache, with vascular quality. Patients usually use large doses of analgesics and experience withdrawal headaches. Cervicogenic migraine, on the other hand, is a secondary headache due to an underlying structural problem in the head or neck. The objective of this study is to evaluate the effectiveness of cervical facets infiltration of C2-3 in the treatment of transformed migraine (TM) plus cervicogenic component.

Methods: 30 patients were evaluated at the Pain & Headache Center, IMC, KSA according to IHS classification. Patients were allocated to receive either cervical infiltration of C2-3 facets on the same side of migraine (13); or oral bridge therapy (Eletriptan and Etoricoxib) which was administered daily for 15 days, and which was followed by Topiramate 100 mg daily for 6 month as a preventive therapy in both groups. Inclusive criteria: 10 males, 20 females; ages 30–50 years, with a mean of 40. Exclusive criteria: pediatrics; patients older than 50, with uncontrolled diabetes, blood pressure, other neurological deficits; or pregnancy.

Results: Average symptomatic improvement of 78%, according to numeric pain scale, was recognized in patients receiving cervical facets infiltration therapy and appreciated within 10–20 days of therapy. However, an average improvement of 58% was recognized by patients receiving oral bridge therapy and appreciated within one month of therapy.

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

EHMTC-0374
POSTER SESSION D

TRIGEMINAL NEVRALGIA AS A FIRST SYMPTOM OF NASOPHAYRNX TUMOR; A CASE REPORT

S.U. Ersoy[1]

[1]*Nicosia, Cyprus*

Trigeminal nevralgia is a kind of neuropathic pain. It affects the areas where trigeminal nerve branches are found. Paitens suffers from sudden and severe, thunderclap pain.The pain lasts for a few seconds.Trigeminal nevralgia can be primary or secondary headache. Red flag signs for headache are; onset of headaches after fifty years old, worsening syptoms, first and the worst headache,

A fifty two years old man admitted to our neurolgy clinic. For the last two months he was having electric shock like headaches spreading to the half part of his face. The pain was sudden and severe. It was repeating all day and was

lasting for a few seconds. His dentist putted him on carbamazepine therapy and diagnosed him as primary trigeminal nevralgia. But his pain was getting worser. He never had a pain like this before. His neurologic examination and blood tests were normal. His Cranial Magnetic Resonance Imaging showed that there was a tumor on the nasopharynx region. So he referred to an Ear-Nose-Throat specialist. After further investigations he was diagnosed as early stage nasopharynx cancer. After treatment of the tumor his headaches disappeared.

Clinicians should examine patients with trigeminal nevralgia very carefully. Especially the ones who have red flag signs. Even if the cranial scan shows no lesion; neurologist should insist and scan nasophayrnx.

Conflict of interest
Disclosure statement:
Paid positions on advisory boards

EHMTC-0015
POSTER SESSION D

OLFACTORY HALLUCINATIONS DURING A MIGRAINE ATTACK (OHM): A NEW MANIFESTATION OF AURA?

F. Mainardi[1], A. Rapoport[2], G. Zanchin[3], F. Maggioni[3]

[1]*Headache Centre, Department of Neurology- SS Giovanni e Paolo Hospital, Venice, Italy*
[2]*UCLA, The David Geffen School of Medicine, Los Angeles, USA*
[3]*University of Padua, Headache Centre- Department of Neurosciences, Padua, Italy*

Introduction: Olfactory hallucination during a migraine attack (OHM) is a rare phenomenon. At present, it is not considered a manifestation of migraine aura

Material and methods: The clinical features of OHM were collected in 11 patients.

Results: Of the 11 patients, 10 had migraine without aura and 1 migraine with aura (MA) associated with OHM. Mean age at onset of headache and at appearance of OHM were respectively 17.8 and 32.3 years. Migraine average frequency was of 3.9 attacks/month, 19% of them being associated with OHM. The temporal pattern of OHM maintained the same characteristics in the different attacks. OHM onset was described as sudden (n = 5), gradual (n = 3), initially sudden and then gradual (n = 2), or developing in a few seconds (n = 1). In most of the cases (n = 8), OHM lasted from 3 to 10 min; it persisted during the pain phase (2–24 h) in only 3 patients. The type of the perceived smell was invariably constant in 9 patients.

Conclusion: OHM features fulfilled the ICHD-III beta criteria for typical aura.

EHMTC-0321
POSTER SESSION D

PERSISTENT HEADACHE ATTRIBUTED TO MODERATE OR SEVERE TRAUMATIC INJURY OF THE HEAD: A DRAMATIC EVOLUTION IN A FAMOUS 19TH-CENTURY SOPRANO

F. Mainardi[1], G. Zanchin[2], F. Paladin[1], F. Maggioni[2]

[1]*Headache Centre, Neurological Division- SS Giovanni e Paolo Hospital, Venice, Italy*
[2]*Headache Centre, Department of Neurosciences- Padua University, Padua, Italy*

The career of Maria Garcia Malibran (1808–1836), one of the most famous opera singers of the 19th century, started at age of 17 in London, singing the role of *Rosina* in the *Barbiere di Siviglia* by Rossini. She belonged to a famous musical family, thanks to which the Italian opera was introduced for the first time in America in 1825. Her European debut (Paris, January 1828) crowned her as a star and since that moment she was requested by the most famous European theatres. During a visit in London (July 1836), she took part at an equestrian excursion in Regent Park; unfortunately, "*her horse broke into a non controlled gallop which led her to be dragged along the ground, her head dashing against the stone of the road, and resulting in a state of insensibility*" (1). From that moment, she complained of "*continual headache and nervous attacks*" (1). Nevertheless, she continued to work. Two months later during a tour in Manchester (September 1836), episodes of headache, fainting and "*nervous attacks*" rapidly worsened until she was attacked by violent convulsions at the end of a representation. She spent the following nine days in a "*kind of stupor*" (1). Afterward, she died at the age of 28. Rebleedings of a pre-existent chronic subdural heamatoma due to the frequent Valsalva-like maneuver efforts while singing should be taken into account as a possible cause of her untimely death.

Reference

1. Merlin M. Memoirs and letters of Madame Malibran vol I. Carey and Hart, Philadelphia, 1840.

EHMTC-0291
POSTER SESSION D

REVERSIBLE SPONTANEOUS INTRACRANIAL HYPOTENSION CAUSING REM BEHAVIOUR DISORDER

G. Ferrigno[1], M.R. Mazza[1], M. Salsone[2], D. Salvino[1], L. Mumoli[1], C. Bombardieri[3], A. Quattrone[1], F. Bono[1]

[1]*Institute of Neurology, Headache Group. Department of Medical and Surgical Sciences, Catanzaro, Italy*
[2]*Institute of Bioimaging and Molecular Physiology- National Research Council, Neuroimaging Research Unit, Catanzaroi, Italy*
[3]*Institute of Neuroradiology, Department of Medical and Surgical Sciences, Catanzaro, Italy*

A 65-year-old woman presented with chronic lingering headache and rapid eye movement sleep behavior disorder. MRI at presentation showed spontaneous intracranial hypotension with severe brain sagging at the level of the tentorial incisura with a swollen aspect of the upper brainstem and diencephalon, and flattening of the pons against the clivus. Cerebrospinal fluid opening pressure was 13 mm H_2O. She was treated with lumbar epidural blood patch. Within 3 months, she became entirely asymptomatic with improvement of deep brain swelling. Follow-up MRI after three months demonstrates amelioration of brainstem configuration. The brainstem, however, has not returned to a completely normal shape. Since spontaneous intracranial hypotension with deep brain swelling is related to brain sagging with deformity of brainstem,[1] and since focal brainstem lesions may cause rapid eye movement sleep behavior disorder,[2] the distortion and the dysfunction of brainstem REM sleep circuits may be caused by deep brain swelling in this patient with spontaneous intracranial hypotension[3]. Rapid eye movement sleep behavior disorder expands the clinical spectrum of spontaneous intracranial hypotension.

References

1. Savoiardo M, Minati L, Farina L, et al. Spontaneous intracranial hypotension with deep brain swelling. *Brain*. 2007; 130: 1884–1893.
2. Iranzo A and Aparicio J. A lesson from anatomy: focal brain lesions causing REM sleep behavior disorder. *Sleep Med*. 2009; 10(1): 9–12.
3. Salsone M, Salvino D, Mazza MR, et al. Reversible deep brain swelling causing REM behavior disorder. *Neurology*. 2016; 86(14): 1360.

EHMTC-0168
POSTER SESSION D

CLUSTER HEADACHE TREATMENT PATTERNS AND ANALGESIC USE IN THE CLINICAL PRACTICE RESEARCH DATALINK (CPRD)

E.M. Flahavan[1], M.E. Jones[2], L. Mitchell[1], J.L. Swain[2], J.M. Martinez[3], A.H. Ahn[3]

[1]*Eli Lilly & Co., Global Patient Safety Pharmacopidemiology, Windlesham, United Kingdom*
[2]*Eli Lilly & Co., Global Patient Safety Pharmacopidemiology, Indianapolis, USA*
[3]*Eli Lilly & Co., Medical, Indianapolis, USA*

Background: Cluster Headache (CH) is an uncommon but severe and disabling primary headache disorder. Literature suggests that unfamiliarity with CH and its treatment contribute to delays in its diagnosis and effective treatment. We present real-world data describing medication prescribed to patients with a diagnosis of CH and examine how these compare with the standard of care.

Methods: We examined the primary care records from the UK Clinical Practice Research Datalink (CPRD) (1999 to 2013). Cohort 1 consists of those in whom a CH diagnosis was recorded on at least 1 visit and Cohort 2 consists of those with $\geq$2 visits with a CH diagnosis. In these groups, we examined the population characteristics, prescribed CH treatments and analgesics subsequent to their first CH record.

Results: There were >3.5 million individuals in the CPRD in 2013 (49.7% male). The demographics and medications prescribed to patients with a CH diagnosis are presented below:

	Cohort 1	Cohort 2
Patients with CH diagnosis	12.258	2.745
Proportion male	47.7%	62.7%
Sumatriptan injection	6.8%	20.9%
Oxygen	2.6%	9.1%
Verapamil	10.8%	31.3%
Corticosteroids	18.3%	30.8%
Pizotifen	12.2%	18.6%
NSAIDs	56.6%	60.4%
Oral opioids and opioid combinations	38.0%	42.0%

The proportion of males in both cohorts was lower than expected for this disorder. Additionally, the prescription of recognized treatments for CH was low, although 2/3 of patietns in both cohorts had been prescribed analgesics, including many opioids.

Conclusions: These real-world clinical data raise significant concerns about the awareness of the diagnosis and treatment of CH in the CPRD population.

Conflict of interest
Disclosure statement:
All authors are full time employees of Eli Lilly and Company and hold stock or stock options.

EHMTC-0285
POSTER SESSION D

RESISTANCE TO CEREBROSPINAL FLUID OUTFLOW: A DIAGNOSTIC MARKER OF SPONTANEOUS INTRACRANIAL HYPOTENSION

C. Fung[1], C. Ulrich[1], J. Fichtner[1], P. Mordasini[2], W. Z'Graggen[1], J. Gralla[2], A. Raabe[1], J. Beck[1]

[1]*Inselspital- Bern University Hospital- University of Bern, Neurosurgery, Bern, Switzerland*
[2]*Inselspital- Bern University Hospital- University of Bern, Interventional and Diagnostic Neuroradiology, Bern, Switzerland*

Introduction: Spontaneous intracranial hypotension (SIH) is caused by spinal cerebrospinal fluid (CSF) leaks. We evaluated CSF dynamics by computerized lumbar infusion test in suspected SIH patients.

Methods: Patients suspected of SIH were included between January 2012 and February 2015. Spinal CSF leaks were proven by myelography, post-myelography-CT, or MRI after intrathecal contrast application. 14 patients with leaks were compared to 17 patients without a leak. A computerized lumbar infusion test was performed in all patients to analyze CSF outflow resistance, baseline and plateau pressure and pulse amplitude, craniospinal elastance and pressure volume index (PVI).

Results: Rcsf in patients with a proven leak was 1.97 compared to 11.78 mmHg/ml/min ($p < 0.001$). Sensitivity, specificity, and positive and negative predictive values for RCSF (cutoff of ≤ 5 mmHg/ml/min) were 0.86, 1.0, 1.0, and 0.89 (AUC of 0.96) respectively. Patients with a proven leak had a lower opening pressure (5.26 vs 11.77 mmHg, $p < 0.001$), plateau pressure (16.11 vs 32.06 mmHg, $p < 0.001$), baseline (0.18 vs. 0.38 mmHg, $p = 0.017$) and plateau (1.03 vs. 2.80 mmHg, $p < 0.001$) pulse amplitudes, and a higher median PVI (26.43 vs. 20.93 ml, $p = 0.003$)

Conclusion: Patients with spinal CSF leak show a distinct CSF dynamic in computerized lumbar infusion tests. Rcsf has the highest diagnostic accuracy and might be a useful diagnostic marker in SIH.

EHMTC-0096
POSTER SESSION D

OCCIPITAL NEURALGIAS: A CASE SERIES IN AN IRANIAN POPULATION AND LITERATURE REVIEW

A. Ghabeli Juibary[1], P. Sasannejad[1], F. Rezaeitalab[1]

[1]*Ghaem Educational Hospital -Mashhad University of Medical Sciences MUMS, Department of Neurology, Mashhad, Iran*

Introduction: Occipital neuralgias are unilateral or bilateral paroxysmal, shooting or stabbing pain in the posterior part of the scalp, in the distribution of the greater, lesser or third occipital nerves sometimes accompanied by diminished sensation or dysaesthesia in the affected area and commonly associated with tenderness over the involved nerve(s).

Methods: A prospective case series was done in a university neurology department of Ghaem educational hospital (Injection unit) at Mashhad University of Medical Sciences during a 1.5-year period from January 2014 to June 2015. Patients rated pain relief on a 10-point scale. Eleven patients met the criteria for occipital neuralgia and were included in the study.

Results: Age at onset of the clinical signs and symptoms was 46.5 ± 24.1 years (range: 23–79 years). Intracranial or cervical pathology was ruled out by brain and cervical MRI in all patients. Baseline pain was generally an intensity of 6.5 ± 1.2 on the verbal analogue scale. All patients reported at least 70% decrease of pain after lidocaine injection, and 54.4% had complete pain relief. Clinical features, other than headache, that were common in patients included scalp paresthesia, 36.3%; tinnitus in 18.1%; nausea, 45.4%; dizziness, 54.5%; visual disturbances, 27.2% and mood changes in 36.3%.

Conclusion: In this series from a specialized unit, occipital neuralgia is an infrequent condition. Local anesthetic injections create significant relief of the headaches and can assist in the diagnosis of this type of headaches.

EHMTC-0064
POSTER SESSION D

ENHANCING THERAPY FOR CHRONIC DAILY HEADACHE ASSOCIATED WITH MEDICATION OVERUSE HEADACHE IN RUSSIA: OUTCOMES OF MULTIDISCIPLINARY INTEGRATED TREATMENT PROGRAM

V. Golovacheva[1], V. Parfenov[1], G. Tabeeva[1], D. Pushkarev[2], A. Andruschenko[2], V. Osipova[1]

[1]*I.M.Sechenov The First Moscow State Medical University, Neurology, Moscow, Russia*
[2]*I.M.Sechenov The First Moscow State Medical University, Psychiatry and psychosomatics, Moscow, Russia*

Introduction: Chronic daily headache (CDH) associated with medication overuse headache (MOH) is common, disabling condition that is poorly managed in clinical practice in Russia. Effective treatment approaches are needed.

Methods: This study investigated outcomes of in- and outpatient multidisciplinary integrated treatment program (MITP) and predictors of treatment response. N = 73 patients with CDH and concomitant MOH were enrolled and evaluated in terms of socio-demographic characteristics, headache features, psychometric parameters (levels of depression, anxiety, Leeds Dependence Questionare (LDQ) scores, pain's catastrophizing, sleep and life quality), psychiatric disorders. All patients were treated by MITP that included education, withdrawal therapy, optimization of pharmacotherapy, cognitive-behavioural therapy and relaxation training. Prospective analysis of clinical-psychological characteristics was performed at baseline, 3-, 6- and 12-month follow-ups.

Results: CDH + MOH group was composed of chronic migraine (41,1%), chronic TTH (24,7%), chronic TTH+ episodic migraine (34,2%). Participants overused non-prescribed combined analgesics (53,4%), prescribed combined analgesics (9,6%), triptans (4,1%), NSAIDs (13,7%), combination of pain-killers (19,2%), none overused ergots. After 12 months of MITP 75,3% of patients (responders) experienced >50% reduction in headache frequency and no longer overused acute medications. Only 6,2% had relapse of MOH within 1 year. Significant positive correlations were revealed between non-responders and lower educational level, unemployment, higher LDQ subscore for items 3 and 9, personality disorders of all clusters ($p < 0,05$).

Conclusion: CDH associated with MOH can be successfully treated with multidisciplinary integrated treatment program. Predictors of not effective treatment are lower educational level, unemployment, higher LDQ subscore for items 3 and 9, personality disorders of all clusters.

EHMTC-0061
POSTER SESSION D

THE ANDRO-METABOLIC SIGNATURE OF IDIOPATHIC INTRACRANIAL HYPERTENSION COMPARED WITH POLYCYSTIC OVARY SYNDROME AND SIMPLE OBESITY

C. Hornby[1], M. O'Reilly[2], H. Botfield[1], P. Kempegowda[2], K. Markey[1], A. Taylor[2], B. Hughes[2], J. Tomlinson[3], W. Arlt[2], A. Sinclair[1]

[1]*University of Birmingham, Neurometabolism- Institute of Metabolism and Systems Research, Birmingham, United Kingdom*
[2]*University of Birmingham, Centre of Endocrinology-Diabetes and Metabolism- Institute of Metabolism and Systems Research, Birmingham, United Kingdom*
[3]*University of Oxford, Oxford Centre for Diabetes-Endocrinology and Metabolism, Oxford, United Kingdom*

Idiopathic intracranial hypertension (IIH) is a disorder of raised intracranial pressure (ICP) of unknown cause. This condition is primarily seen in obese females of childbearing age, a phenotype similar to that in polycystic ovary syndrome (PCOS). We aimed to characterise the androgen metabolic signature in IIH compared to PCOS and simple obese controls.

Age, gender and BMI matched groups of IIH (n = 25), PCOS (n = 31) and obese controls (n = 15) were studied. The IIH group also underwent a weight loss intervention. Serum androgens were measured by liquid chromatography/tandem mass spectrometry (LCMS) and urinary steroids using gas chromatography/mass spectrometry (GCMS). Subcutaneous adipose tissue from IIH patients and age matched controls were analysed for gene expression differences using quantitative PCR.

Serum testosterone was significantly higher in IIH and PCOS than in controls ($p = 0.01$). Serum androstenedione was significantly increased in PCOS compared to IIH and controls ($p = 0.008$). Gene expression of 5a-reductase is significantly lower in the subcutaneous adipose tissue of IIH patients compared to controls. Following weight loss, there were significant reductions in serum testosterone, 5a-reductase activity (metabolises conversion of testosterone to dihydrotestosterone) and disease activity (intracranial pressure and papilloedema).

These results demonstrate a unique androgen metabolic signature in IIH (distinct from PCOS and simple obesity),

characterised by increased testosterone but normal androstenedione, potentially driven by increased AKR1C3 activity (which converts androstenedione to its active metabolite testosterone), or decreased 5a-reductase. Further evaluation of AKR1C3 and 5a-reductase in IIH would be of interest.

EHMTC-0062
POSTER SESSION D

CHARACTERISING FAT DISTRIBUTION AND RESPONSE TO WEIGHT LOSS IN IDIOPATHIC INTRACRANIAL HYPERTENSION

C. Hornby[1], F. Ali[1], H. Botfield[1], M. O'Reilly[2], K. Markey[1], W. Scotton[1], J. Tomlinson[3], W. Arlt[2], A. Sinclair[1]

[1]*University of Birmingham, Neurometabolism- Institute of Metabolism and Systems Research, Birmingham, United Kingdom*
[2]*University of Birmingham, Institute of Metabolism and Systems Research- Centre of Endocrinology- Diabetes and Metabolism, Birmingham, United Kingdom*
[3]*University of Oxford, Oxford Centre for Diabetes-Endocrinology and Metabolism, Oxford, United Kingdom*

Idiopathic intracranial hypertension (IIH) is a condition characterised by raised intracranial pressure of unknown pathogenesis. Over 94% of sufferers are young, obese women, but little is known about their metabolic phenotype. Previous studies measuring waist-hip ratios in IIH have suggested predominant lower body adiposity. We aimed to characterise the pattern of fat distribution using dual energy X-ray absorptiometry (DEXA) and metabolic phenotype (fasting lipids, glucose and insulin), and evaluate changes following weight loss.

At baseline, IIH ($n = 29$) had a similar centripetal fat distribution and lipid profile to BMI and gender matched obese controls ($n = 47$). The glucose:insulin ratio (G:I) and HOMA-IR were elevated at baseline indicating insulin resistance in IIH, although akin to what was seen in simple obesity (G:I 0.4 ± 0.2 vs 0.8 ± 0.9 and HOMA-IR 2.1 ± 2.1 vs 1.6 ± 1.1).

Weight loss resulted in a significant reduction in disease activity (decrease in intracranial pressure and papilloedema) alongside a significant reduction in fat mass ($-4.1 \pm 2.7\%$, $p < 0.001$), predominantly from the truncal region ($-4.7 \pm 3.7\%$) compared to the limbs ($1.1 \pm 2.1\%$, $p < 0.001$).

These results indicate that fat distribution in IIH is centripetal, similar to simple obesity. Clinical resolution of IIH is associated with preferential loss of truncal fat. The role of truncal adiposity in the pathogenesis of IIH warrants further investigation.

EHMTC-0158
POSTER SESSION D

RECURRENT EPISODES OF HEADACHE AND CONFUSION 33 YEARS POST RADIATION: A CASE OF STROKE-LIKE MIGRAINE ATTACKS AFTER RADIATION THERAPY SYNDROME

S. Kalaitzaki[1], M. Petrou[1], M. Gryllia[2], S. Tsiara[2], S. Lachanis[3]

[1]*General Hospital of Athens "Georgios Gennimatas", Neurology Department, Athens, Greece*
[2]*General Hospital of Athens "Georgios Gennimatas", Neurology Department, Athens, Greece*
[3]*401 General Military Hospital of Athens, Magnetic Resonance Department, Athens, Greece*

We present a case of a 53-year-old male with recent onset of headache, confusion, disorientation and ataxia, who had no markers indicating infection. The patient reported a history of cystic astrocytoma of right posterior fossa operated and radiated 33 years ago. Initially, the Computer Tomography (CT) scan revealed only a small hypodense region in the right frontal lobe, while the cerebrospinal fluid (CSF) analysis showed only moderate elevation in protein. We proceeded to a Magnetic Resonance Imaging (MRI) of brain parenchyma, which pointed increased signal in T2 and diffusion weighted imagining (DWI) in the right temporal, parietal and occipital cortical regions, with diffuse leptomeningeal enhancement after gadolinium, while MR Angiography was normal. He improved clinically and radiologically without specific treatment in 2 weeks. Reassessing the MRIs of the patient when he was hospitalized in 2014 with the same symptoms and was treatedempirically for meningoencephalitis, we noted that identical findingsappeared then and also resolved within a month. Therefore, we concluded that our patient had two episodes of stroke-like migraine attacks after radiation therapy (SMART) syndrome.

SMART syndrome is a disorder that should be considered in patients with former radiation therapy for brain tumor and new neurological deficits that resolve spontaneously. The MRI findings are fundamental for the diagnosis and it is important to exclude other diagnostic possibilities with appropriate extensive diagnostic workup.

EHMTC-0235
POSTER SESSION D

MEDICATION OVERUSE HEADACHE: EPIDEMIOLOGIC FEATURES AND CLINICAL EXPERIENCE FROM OUR DEPARTMENT IN A YEAR FOLLOW UP

S. Kalaitzaki[1], E. Papantonakis[1], G. Panagopoulos[1], S. Tsiara[1]

[1]*General Hospital of Athens "Georgios Gennimatas", Neurology, Athens, Greece*

Medication overuse headache (MOH) is a frequent secondary headache that occurs almost nearly daily, due to excess overusing of analgesics, on a former ground of a chronic primary headache. Major factors of MOH are the absence or the insufficient treatment of the primary chronic headaches and the uncontrolled self administration of painkillers.

In 2015 the Headache Outpatient Department in our hospital examined 219 new patients with headache. We diagnosed 21 cases of MOH, 16 women and 5 men, who overused more than one medication in 29%, while 52% admitted daily use of painkillers for more than 1 year. Most of the patients were receiving paracetamol (62%) and codein (38%). Surprisingly, 24% reported excessive usage (almost daily) of tryptans. After full clinical evaluation and detailed description of the current and past headache attacks, we concluded that 43% had chronic migraine and 57% chronic tension-type headache. We treated all 21 patients in an outpatient basis with abrupt withdraw of the drug responsible for the MOH, close follow up for at least 6–12 months, counseling and preventive medication. The majority (57%) started prophylactive treatment with amitryptiline, 24% topiramate, 10% flunarizine and 9% valproate. In an almost one year follow up, only 2 patients relapsed, but with more frequent visits, counseling and prophylactic treatment modification, they are also free of frequent headache attacks as well.

The increasing incidence of MOH should draw neurologists' attention, to identify and properly educate, counsel and treat these patients.

EHMTC-0332
POSTER SESSION D

ONABOTULINUMTOXINA IN CHRONIC MIGRAINE; PREDICTING RESPONSE TO TREATMENT BASED ON HEADACHE DAYS AT BASELINE

M. Khalil[1], A. Buture[2], R. Nimeri[2], F. Ahmed[2]

[1]*Hull York Medical School, Neurology Deparment, Kingston-Upon-Hull, United Kingdom*
[2]*Hull York Medical School, Neurology Department, Kingston-Upon-Hull, United Kingdom*

Background: Chronic migraine (CM) is a very disabling condition with substantial impact on quality of life; in the UK, the use of OnabotulinumtoxinA on the National Health Service (NHS) for CM is approved provided that patient failed three preventive treatments.

Predicting response to treatment, although unknown, may help decide which patients are suitable for treatment where issues of cost-efficiency contribute towards decision in recommending treatment.

Objective: To establish whether the number of headache days at the baseline predict response to treatment with Botox in patients with CM.

Methods: Adult CM patients received OnabotulinumtoxinA as per the PREEMPT study protocol at the Hull Migraine Clinic were followed up prospectively.

Data were extracted for headache, migraine, and headache-free days, 1 month before and after treatment at cycle 1 between July 2010 and March 2016.

Statistical Methods: Patients were categorised into three groups based on the number of headache days pre-treatment. Classifications were made into low frequency (15–20 days), moderate frequency (21–25 days) and high frequency (26–30 days); Chi-Square test was used to compare the three groups' responses.

Results: Full data were available on 536 patients, 17.7% had low frequency headaches; 20.3% had moderate frequency headaches and 61.7% had high frequency headaches.

Results suggest that low or moderate frequency headache patients tend to have more chances of response than those with high frequency headaches, the improvement in migraine days was similar in the three groups, the achievement of headache-free days are more likely in the high headache frequency.

Conflict of interest
Disclosure statement:
Modar Khalil has received honararium from Allergan for delivering a talk in the advanced chronic migraine masterclass.

Fayyaz Ahmed runs BOTOX a headache workshop for which honorarium is paid to the British Association for the Study of Headache. Dr Ahmed has received honorarium for attending advisory board meetings organised by Allergan

EHMTC-0109
POSTER SESSION D

PREDICTORS OF SUCCESSFUL WITHDRAWAL IN PRIMARY CARE PATIENTS WITH MEDICATION-OVERUSE HEADACHE– THE BIMOH STUDY (A PRAGMATIC CLUSTER-RANDOMISED CONTROLLED CROSS-OVER TRIAL)

E.S. Kristoffersen[1], J. Straand[1], J. Saltyte-Benth[2], M.B. Russell[3], C. Lundqvist[4]

[1]*University of Oslo, Department of General Practice, Oslo, Norway*
[2]*University of Oslo, Institute of Clinical Medicine- Campus Akershus University Hospital, Nordbyhagen, Norway*
[3]*Akershus University Hospital, Head and Neck Research Group, Lørenskog, Norway*
[4]*Akershus University Hospital, Research Centre, Lørenskog, Norway*

Background and purpose: Medication-overuse headache (MOH) is a common, but preventable and treatable chronic headache.

Methods: This was a pragmatic cluster-randomized controlled trial with single cross-over carried out among 50 general practitioners in Norway. A brief intervention (BI) (early or after cross-over) was compared to business as usual (BAU) for the treatment of MOH. Patients were followed-up after three months. Primary efficacy outcomes were headache and medication days/month after three months. Predictors of successful withdrawal were assessed.

Results: Sixty MOH patients where included. In total, 46 patients received the BI and 14 BAU. Headache and medication days were reduced by 7.6 and 7.9 (95% CI 2.0–13.2 and 1.4–14.4) days/month for the BI compared to the BAU. No significant predictors for successful withdrawal were identified in the pre-specified analyses, though days/month with headache and medication use at baseline were significant predictors in post hoc analyses.

Conclusions: Withdrawal therapy in MOH in primary care is effective. Since detoxification through BI is simple and no other individual predictors for treatment success were identified, we conclude that a withdrawal attempt should be conducted in primary care before referral of the more treatment-resistant cases to secondary care.

EHMTC-0279
POSTER SESSION D

THE ROLE OF NATRIURETIC PEPTIDES IN HEMODIALYSIS HEADACHE – A PILOT STUDY

L. Larsson[1], C. Rydahl[2], H. Post Hansen[2], C. Kistorp[3], J.P. Goetze[4], C. Rostrup Kruuse[1]

[1]*Herlev Hospital, Department of Neurology- Neurovascular Research Unit, Copenhagen, Denmark*
[2]*Herlev Hospital, Department of Nephrology, Copenhagen, Denmark*
[3]*Herlev Hospital, Department of Endocrinology, Copenhagen, Denmark*
[4]*Rigshospitalet University Hospital, Department of Clinical Biochemistry, Copenhagen, Denmark*

Aim: Hemodialysis headache (HDH) is a secondary headache occurring during hemodialysis (HD). The plasma concentrations of natriuretic peptides are increased in HD patients. Such may activate cyclic guanosine monophosphate (cGMP) production. Augmented cGMP levels induce headache with migraine-like attacks in migraine patients. We aimed to assess fluctuations of natriuretic peptides concentrations during hemodialysis and correlate the findings to HDH. We further aimed to describe the clinical characteristics of such headache.

Methods and materials: 18 patients reporting dialysis headache and 20 controls participated in the study. At the day of study, blood samples were collected hourly during HD. The occurrence of headache and associated symptoms were recorded every fifteen minutes. Pericranial muscle tenderness was evaluated regularly as a total tenderness score (TTS).

Results: HDH patients were younger; mean 51versus 68 years ($p = 0.003$), and with higher diastolic blood pressure; 83 versus 72 mmHg ($p = 0.013$). Nine (50 %) HDH patients developed a mainly mild, frontal headache, appearing two hours after initiation of HD without accompanying symptoms. TTS was increased in headache patients ($p = 0.024$). During HD, proCNP and proANP concentrations in circulation decreased in both groups ($p < 0.0001$). In the last period of the study, proCNP concentrations were lower in the headache group (last value 72 pmol/L vs. 60 pmol/L, $p = 0.029$). There was no significant

difference at any time point in proANP concentrations between groups.

Conclusion: ProCNP concentrations in circulation decreased during HDH and were associated with headache induction.

EHMTC-0167
POSTER SESSION D

LEPTOMENINGEAL ENHANCEMENT IN REVERSIBLE CEREVRAL VASOCONSTRICTION SYNDROME: IMPLICATIONS FOR PATHOPHYSIOLOGY AND DIAGNOSIS

M.J. Lee[1], J. Cha[2], H.A. Choi[1], C. Lee[1], C.S. Chung[1]

[1]*Samsung Medical Center, Department of Neurology-Neuroscience Center, Seoul, Republic of Korea*
[2]*Samsung Medical Center, Department of Radiology-Imaging Center- Heart- Vascular- Stroke Institute, Seoul, Republic of Korea*

Background: Vasoconstriction and breakdown of the blood-brain barrier (BBB) have been postulated as the pathophysiology of reversible cerebral vasoconstriction syndrome (RCVS). We documented the presence and diagnostic role of BBB breakdown in patients with RCVS.

Methods: We prospectively recruited patients presenting with thunderclap headache who visited Samsung Medical Center between Apr 2015 and Mar 2016. Patients with aneurysmal subarachnoid hemorrhage were excluded. Evidence of BBB breakdown was investigated with a focal/multifocal leptomeningeal enhancement in Gadolinium-enhanced FLAIR imaging (Figure 1). When RCVS is suspected, MR angiogram was performed after 3–6 months to confirm the diagnosis. We defined a typical RCVS manifestation if patients met ICHD-3b criteria for RCVS at the initial visit.

Results: Among 50 patients included in the study, RCVS was confirmed in 23 (46.0%) patients. Fourteen (60.9%) patients with RCVS and one (3.7%) patient without RCVS showed leptomeningeal enhancement ($p < 0.001$). Leptomeningeal enhancement in RCVS were multifocal (92.9%) and located around midline (100%), convexity (71.4%), Sylvian fissure (28.6%), tentorium (14.3%) and cerebellum (7.1%). In patients without a typical manifestation initially ($N = 9$), leptomeningeal enhancement was present in 5 (55.6%), with a sensitivity of 55.6% and specificity of 96.3%.

Conclusion: BBB breakdown is present in about 60% of RCVS patients and highly specific for the diagnosis even when initial manifestation was not typical for RCVS. This finding would help to understand the pathophysiology of RCVS and lead to early diagnosis.

EHMTC-0246
POSTER SESSION D

NEW DAILY HEADACHE PRIOR TO ISCHEMIC STROKE IN ADULT MOYAMOYA DISEASE

Y.C. Lee[1], H.C. Huang[2], B.L. Tee[1]

[1]*NTUH Hsin-Chu, Neurology, Hsinchu, Taiwan*
[2]*NTUH Hsin-Chu, Medical Imaging, Hsinchu, Taiwan*

A 37-year-old woman had acute onset of new daily headache 4 days prior to her first visit at neurology clinic. She described the headache as severe throbbing pain around right temporal area without autonomic feature. Headache lasted for 30 ~ 60 minutes each and occurred 3 ~ 5 times per day. The headache had no response to indomethacin, and would be shortened by ergotamine. The frequency and severity of attack remained similar after 2-week of propranolol and flunarizine. Brain CT showed negative finding.

3 months after headache onset, she had sudden loss of bilateral vision during headache attack with incoherent speech. She was taken to emergency department where brain CT revealed right MCA territory infarction with mild mass effect. Subsequent head MRI showed nearly total occlusion of right MCA, segmental stenosis at proximal left MCA, bilateral PCA and bilateral ACA with increased small collateral circulations over bilateral basal ganglia. The followed angiography confirmed the diagnosis of Moyamoya disease.

Although most of the Moyamoya patients have presenting symptoms as ischemic or hemorrhagic stroke, headache associated with moyamoya disease (HAMD) is not uncommon. Typically, headache is episodic, migraine-like or tension type headache-like in quality, and is refractory to medical therapies. Our patient had no prior headache history. Her headache had a distinct and clearly remembered time of onset and was daily since then. It didn't fulfill the ICHD-III criteria of "New daily persistent headache" or any other primary headache. Brain CT alone is not sufficient to exclude secondary cause of headache in such patients.

EHMTC-0154
POSTER SESSION D

EFFECTS OF NON-INVASIVE VAGUS NERVE STIMULATION ON ATTACK FREQUENCY OVER TIME AND RESPONSE RATES IN PATIENTS WITH CHRONIC CLUSTER HEADACHE

C. Gaul[1], E. Liebler[2], C.K. McClure[3], A. Straube[4]

[1]*Migraine and Headache Clinic, Department of Headache and Facial Pain, Königstein, Germany*
[2]*electroCore- LLC, Scientific- Medical and Governmental Affairs, Basking Ridge, USA*
[3]*North American Science Associates Inc., Biostatistics, Northwood, USA*
[4]*Ludwig Maximilian University of Munich, Department of Neurology, Munich, Germany*

Background: In the PREVA study of chronic cluster headache (cCH) prophylaxis, attack frequency reductions from baseline were significantly more pronounced with non-invasive vagus nerve stimulation (gammaCore®) plus standard of care (nVNS + SoC) than with SoC alone.

Aim: To evaluate the time to and magnitude of nVNS benefits in PREVA ad hoc analyses.

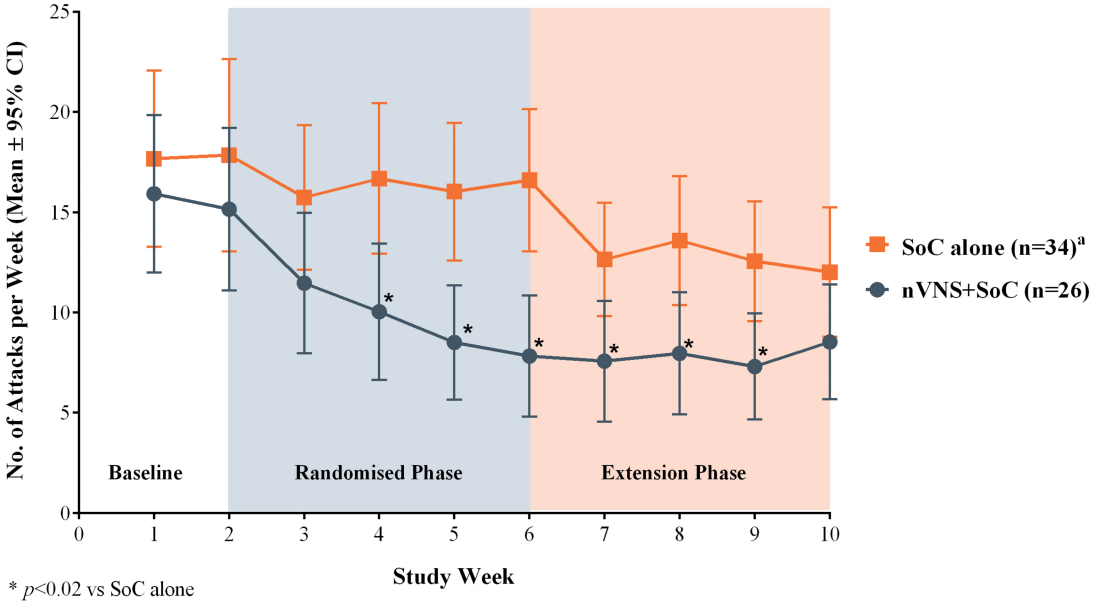
Methods: Subjects received SoC during the 2-week baseline period followed by nVNS + SoC or SoC alone during the 4-week randomised phase (RP). In the optional 4-week extension phase (EP), all subjects received nVNS + SoC. The nVNS treatment comprised three 2-minute stimulations administered twice daily (6 stimulations total per day).

Results: Mean weekly attack frequency was significantly lower with nVNS + SoC than with SoC alone from RP week 2 through EP week 3; this difference diminished by EP week 4 (Figure). For the nVNS + SoC group, attack frequency was significantly lower at RP week 1 through EP week 4 than at baseline and was relatively stable during the EP. Response rates were significantly greater with nVNS + SoC than with SoC alone when *response* was defined as attack frequency reductions of ≥25%, ≥50%, and ≥75% from baseline ($P \leq 0.01$).

Conclusions: Prophylactic nVNS led to rapid, significant, and sustained reductions in cCH attack frequency as early as 2 weeks after addition to SoC and was associated with significantly higher ≥25%, ≥50%, and ≥75% response rates vs SoC alone.

Conflict of interest
Disclosure statement:
Dr. Charly Gaul, MD, has received honoraria from Allergan plc, Autonomic Technologies, Inc., Bayer AG, Boehringer Ingelheim GmbH, Desitin Arzneimittel GmbH, electroCore, LLC, Grünenthal GmbH, Hormosan

***Figure*: Mean Attack Frequencies (mITT Population)**



* $p<0.02$ vs SoC alone

Abbreviation: mITT, modified intent-to-treat.
[a] Subjects received SoC alone in the RP and nVNS+SoC in the EP.

Pharma GmbH, Medical Specialties Distributors, LLC, and St. Jude Medical, Inc. Dr. Gaul has no ownership interests and does not own any pharmaceutical company stocks. Eric Liebler is an employee of electroCore, LLC, and receives stock ownership Candace K. McClure, PhD, is an employee of North American Science Associates Inc. Prof. Andreas Straube, MD, has received honoraria from Allergan plc, Berlin-Chemie AG, Boehringer Ingelheim GmbH, Desitin Arzneimittel GmbH, electroCore, LLC, Medical Specialties Distributors, LLC, Pfizer Inc., and St. Jude Medical, Inc. He has also received grants from the German Council of Science and Humanities, the German Secretary of Education, the Else Kröner-Fresenius Foundation, and the Ludwig-Maximilians-Universität München.

EHMTC-0367
POSTER SESSION D

CLINICAL AND PARACLINICAL FEATURES OF HEADACHE SECONDARY TO NONTRAUMATIC SUBARACHNOID HAEMORRHAGE – 10 YEARS EXPERIENCE OF OUR UNIVERSITY CLINICAL CENTRE

S. Ljubisavljevic[1], V. Milosevic[1], A. Stojanov[1], M. Ljubisavljevic[2]

[1]*Clinical Center of Nis, Clinic for Neurology, Nis, Serbia*
[2]*Clinical Center of Nis, Institute for Mental Health Protection, Nis, Serbia*

Objective: The study was designed to identify the clinical and paraclinical features associated with acute nontraumatic headache among patients with confirmed subarachnoid haemorrhage (SAH) attending our university clinical centre from January 2005 to December 2015.

Patients and methods: The study is a retrospective cohort study based on data collected from an individual medical record for each one of SAH patients.

Results: Among more than 250000 patients with wide neurological pathology, there were 431 (167 men, 264 women, age range from 19 to 91 years) with confirmed nontraumatic SAH, 104 (24%) patients had confirmed arterial-venous malformation. Among all SAH patients, 303 (70%) (116 men, 187 women, median age 59 years) had headache as a leading clinical presentation, with time to maximal intensity greater than a few minutes (∼60%) or with gradual onset within 1 hour (∼20%). The pain localization was referred more diffuse than localized (∼90%), accompanied with vomitus and nausea (∼70%), stiffness or limited flexion in neck (∼45%), loss of consciousness (∼37%), positive neurological findings (∼18%), neck pain (∼7%) or onset during exertion (6%). Majority of SAH patients presented with headache had two or more mentioned features (∼38%), without previous headache history (∼80%), while arterial hypertension was detected as previous co morbidity in ∼62% of them.

Conclusion: It can be concluded that each, new onset, nontraumatic, abrupt headache accompanied with loss of consciousness and/or stiffness or limited flexion in neck must be considered as a headache secondary to nontraumatic SAH.

EHMTC-0352
POSTER SESSION D

EFFECT OF CERVICAL PARAVERTEBRAL BLOCK COMBINED WITH OZONE INJECTION IN THE TREATMENT OF CERVICOGENIC HEADACHE

J. Ma[1], H. he[1], H. sun[1]

[1]*Beijing An Zhen Hospital Affiliated to Capital Medical University, Center for Anesthesiology, Beijing, China*

Objective: To investigate the clinical effect of cervical paravertebral block combined with ozone injection in the treatment of cervicogenic headache.

Methods: 40 patients suffered with cervicogenic headache were randomly divided into cervical paravertebral block combined with ozone injection group(group 1) and cervical paravertebral block group (group 2). The treatment effect was evaluated as the visual analogue scale (VAS) before the treatment, 1 and 7 days, 1 and 3 months after the treatment.

Results: The VAS scores before treatment, 1 and 7 days, 1 and 3 months after treatment were (7.0 ± 1.2), (4.2 ± 1.5), (1.5 ± 0.9), (0.6 ± 0.7)and (0.8 ± 0.6) in group 1, respectively. Whereas,in group 2, VASs were (7.2 ± 1.5), (4.0 ± 0.8), (5.0 ± 1.2), (5.4 ± 1.2) and (5.6 ± 1.0) respectively.Compared with group 2, the VASs were significantly lower in 7 days, 1 and 3 months after the treatment in group 1.

Conclusion: Cervical paravertebral block combined with ozone injection may play a complementary role in the treatment of cervicogenic headache.

EHMTC-0309
POSTER SESSION D

IDIOPATHIC INTRACRANIAL HYPERTENSION: A RETROSPECTIVE STUDY IN 40 PATIENTS

M. Bernal Sanchez-Arjona[1], C. Mendez del Barrio[1], E. Murillo Espejo[1], L. Lebrato Hernandez[1], J.H. Maria Dolores[1], C. Gonzalez Oria[1]

[1]*Hospital Virgen del Rocio, Neurosciences, Sevilla, Spain*

Objective: To describe demographic and clinical characteristics, workup, management and outcome of a population with Idiopathic Intracranial Hypertension (IIH) in South of Spain.

Method: Retrospective analysis of 40 patients with IIH attended in a Headache Clinic from January 2010 to December 2015. The diagnose was done according the International Headache Classification. All patients underwent MRI with angio and venography, lumbar punction and measure of CSF openning pressure, biochemical analyses, autoinmunity, serology and trombofilia studies. Ofthalmoscopy examination, perimetry and optical coherence peripapillary were done at the diagnosis and in the follow up. Clinical variables, medical treatment, surgical intervention and recurrence were reviewed.

Results: A total of 40 patients, 38 women, mean age $29 \pm 11{,}62$ were identified. Clinical presentation were bilateral papilledema (97%), headache (80%) and visual disturbances (70%). Primary headache, migraine and/or tensional headache was present in 64% of patients. One fourth of our patients had some grade of permanent visual loss, blindness in three of them, because of delayed diagnose. All patients were under lumbar puncture and evacuation of CSF, followed by diet and treatment with acetazolamida (500 mg-1500mg per day) and/or topiramate (50–150 mg per day). 8 patients needed ventriculoperitoneal shunt. Only 16 patients got weight loss. 24 patients had recurrence.

Conclusion: An early diagnosis in these patients is crucial to avoid permanent vision loss. Weight loss modifies the course of disease, therefore it is important to encourage our patients to make diet and exercise to prevent recurrences. Comorbidity with primary headaches complicates the diagnosis of disease recurrence.

EHMTC-0289
POSTER SESSION D

ASYMPTOMATIC SUPERFICIAL HEMOSIDEROSIS AFTER RESOLVED SPONTANEOUS INTRACRANIAL HYPOTENSION

M. Narring[1], J. Franc[2], C. Roos[1]

[1]*Hôpital Lariboisière- APHP, Centre d'Urgences Céphalées, PARIS, France*
[2]*Hôpital Lariboisière- APHP, Service de Neuroradiologie diagnostique, PARIS, France*

Superficial hemosiderosis syndrome (SHS) has been reported in rare patients diagnosed with spontaneous intracranial hypotension (SIH). All previously reported cases displayed a long term treatment-resistant ventral spinal CSF leak suggesting a related hypovolemia craniocaudal descent of the brain leading to a probable traction on vascular structures.

We monitored the neurological symptoms and brain MRI to determine recurrences and evolution of 80 SIH patients recruited between 2004 and 2009 in our Emergency Headache Center. We identified two 55 year-old men diagnosed with SHS. Their initial brain MRI showed a pachymeningeal enhancement and bilateral subdural fluid collections without subarachnoid haemorrhage. After the first few months, these abnormalities disappeared. Clinically, one of them reported a spontaneous improvement while the other needed an epidural blood patch. At the last evaluation, respectively seven and six years after the SIH diagnosis, none had presented documented recurrence, headache suggestive of SIH or other neurological symptoms. Both brain and spinal MRI did not display any sign of SIH, dural tear nor vascular malformation. However, we observed a posterior superficial hemosiderosis.

For the first time, we report a delayed brain hemosiderosis associated with mild forms of SIH. Because of the delay of several years, without symptoms, these observations differ from those previously reported. These two cases suggest that 1) a different mechanism from the severe ventral leak could be responsible for SHS; 2) a long-term brain MRI follow-up should be proposed in symptomatic and asymptomatic patients.

EHMTC-0307
POSTER SESSION D

MODIFIED STEP SCHEME WITH ACUPUNCTURE, FAN-SHAPED INFILTRATION FOR BLOCKADE OF NERVE OCCIPITAL FOR THE TREATMENT OF OCCIPITAL NEURALGIA, TO TRANG

T.X. Nguyen[1], T.T. Nguyen[2], H. Eckel[3], C. Pohl[4], W. Vogelsberger[5]

[1]*Praxis, Göttingen, Germany*
[2]*Praxis, pediatrics, Duderstadt, Germany*
[3]*Radiology Institute, radiology, Göttingen, Germany*
[4]*Practice, specialist for general medicine- nature treatments and particular pain therapy, Bochum, Germany*
[5]*Practice, Specialist for Anaesthesiology- Naturopathic, Freiburg, Germany*

In an occipital emerge from the Rami dorsalis of the spinal nerves C2 and nerve lesser occipital from the cervical plexus C1-C4 to pain in the coverage area of the occipital nerve. These nerves run along the back of the head towards the forehead, temples and skull page. They happen sometimes very deep muscle layers. By stimulating the nerve occipital headaches may occur. The pain can be affected both sides, but most is unilateral. The pain follows the course of the nerves and can radiate to the eyes, ears and arms. Often the scalp is extremely sensitive to touch. Some patients experience a worsening of pain when moving the head.

In the puncture technique with fan-shaped infiltration for blockade of nerve occipital et minor for the treatment of occipital neuralgia, ganglion stellate, cervical plexus C1 – C7/Th1, brachial plexus, accessory nerve, auricularis magnus nerve, transverse cervical nerve, suprascapular nerve without CT, fluoroscopy for treating intractable occipital neuralgia and cephalalgia, shoulder arm neck belt syndrome, armplexusneuritis, torticollis Spasticus.

In the occipital ganglion are pterygopalatinum blocked and performed a puncture technique with fan-shaped infiltration for blockade of N. infratrochealis, N. supratrochlear and supraorbital nerve.

The above therapeutic local analgesia in combination with the security acupuncture, complementary medicine can while reducing and after therapy to reach 0% even the strongest pain as occipital neuralgia, cephalalgia, shoulder arm neck belt area and armplexusneuritis so this a cure or alleviation of occipital neuralgia except for a large nucleus prolapses.

EHMTC-0339
POSTER SESSION D

SPONTANEOUS INTRACRANIAL HYPOTENSION

T. Ozbenli[1], B. Özberk[2]

[1]*Ondokuz Mayis University – Faculty of Medicine, Samsun, Turkey*
[2]*Ondokuz Mayis University – Faculty of Medicine, Neurology, Samsun, Turkey*

Spontaneous intracranial hypotension (SIH) is an important cause of thunderclap headache. SIH is being recognized with increasing frequency. Orthostatic headache, low cerebrospinal fluid opening pressure and diffuse meningeal enhancement on post-contrast brain MRI are the major features of classical syndrome. Some patients with SIH do not demonstrate typical postural headache.

We describe ten patients (7 female, 3 male) diagnosed with SIH, their presenting symptoms, clinical course, treatment and outcome. Six patients (60%) initially received an incorrect diagnosis. Seven patients had thunderclap headache. Our patients had orthostatic headache as defined by the International Headache Society, without lumbar puncture or trauma. Cerebrospinal fluid leakage sites were confirmed in two patients. The other patient were treated by epidural blood patch.

The diagnosis of SIH should be considered in patients who present with thunderclap headache. Most patients with SIH, the diagnosis is missed. SIH is a rare and treatable cause of secondary headaches. In SIH patients, early recognition is very important. In any suspicious case, brain MRI with gadolinium should be performed.

EHMTC-0237
POSTER SESSION D

IMPAIRED CEREBRAL VASOREACTIVITY IN MIGRAINE: A MARKER OF ENDOTHELIAL DYSFUNCTION NOT RELATED WITH FREQUENCY OF ATTACKS

D. Larrosa[1], C. Ramon[1], E. Cernuda[1], R. Alvarez[1], P. Martinez-camblor[2], J. Pascual[3]

[1]*Hospital Universitario Central de Asturias, Neurology, Oviedo, Spain*
[2]*Hospital Universitario Central de Asturias, Statistics, Oviedo, Spain*
[3]*UNIVERSITY HOSPITAL "MARQUES DE VALDECILLA", NEUROLOGY, SANTANDER, Spain*

Background: Endothelial dysfunction has been implicated in migraine. Cerebral CO2 vasoreactivity (CVR) reflects

the vasodilation of microvasculature mediated via endothelial pathway and its impairment is a marker of endothelial dysfunction.

Aim: To asses the presence of endothelial dysfunction in migraineurs and its relation with migraine frequency.

Methods: This series includes 33 women (age 39.02 ± 12.84) meeting diagnostic criteria for episodic migraine (EM) and 97 women (age 43.81 ± 11.43) for chronic migraine (CM) according to current IHS criteria. CVR was assessed by Breath Holding Index (BHI) on transcranial Doppler in middle cerebral arteries (MCA), posterior cerebral arteries (PCA) and in the basilar artery (BA).

Results: In EM, mean BHI was: MCA 1.623 ± 0.496, PCA 1.431 ± 0.431, BA 1.420 ± 0.453. In CM, mean BHI was: MCA 1.528 ± 0.408, PCA 1.528 ± 0.408, BA 1.450 ± 0.352.

When comparing CM and EM, there were no differences in mean BHI in any of the different arteries examined (MCA p = .323, PCA p = .908, BA p = .769).

When comparing different vascular territories, there was a significant reduced CVR in the posterior circulation both in EM (MCA vs. PCA p = .009, MCA vs. BA p = .005, BA vs. PCA p = .311) and CM (MCA vs. PCA p = .001, MCA vs. BA p = .003, PCA vs. BA p = .280).

Conclusion: Our results suggest an endothelial dysfunction in the posterior vascular territory linked to migraine but independent of the frequency of attacks. These findings could explain the underlying pathophysiology behind the higher prevalence of white matter lesions in the posterior circulation.

Conflict of interest
Disclosure statement:
Supported by the PI14/00020 FISSS grant (Fondos Feder, ISCIII, Ministry of Economy, Spain).

EHMTC-0238
POSTER SESSION D

NO SIGNS OF CEREBRAL SMALL-VESSEL DISEASE ON TRANSCRANIAL DOPPLER IN MIGRAINE PATIENTS

D. Larrosa[1], C. Ramon[1], N. Riesco[1], E. Cernuda[1], P. Martinez-camblor[2], J. Pascual[3]

[1]*Hospital Universitario Central de Asturias, Neurology, Oviedo, Spain*
[2]*Hospital Universitario Central de Asturias, Statistics, Oviedo, Spain*
[3]*NEUROLOGY, Spain*

Background: Pulsatility Index (PI) reflects the vascular resistance induced by cerebral small-vessel disease (CSVD). The increase of PI is a marker of estructural changes of the small vessels due to lipohyalinosis and microatherosclerosis. Data on PI in migraine are scarce and contradictory.

Aim: To asses the presence of CSVD in migraineurs and its relation with migraine frequency.

Methods: This series includes 51 women (age 38.69 ± 12.97) meeting diagnostic criteria for episodic migraine (EM) and 120 women (age 43.73 ± 11.76) for chronic migraine (CM) according to current IHS criteria. PI was measured on transcranial Doppler in both middle cerebral arteries (MCA), both posterior cerebral arteries (PCA) and in the basilar artery (BA) according to Gosling's formula.

Results: PI was within range in all arteries examined.

In EM, mean PI was: MCA 0.908 ± 0.109, PCA 0.916 ± 0.101, BA 0.920 ± 0.100. In CM, mean PI was: MCA 0.889 ± 0.131, PCA 0.910 ± 0.151, BA 0.882 ± 0.146.

When comparing CM and EM, there were no differences in mean PI in any of the different arteries explored ((MCA p = .309, PCA p = .770, BA p = .136).

When comparing different vascular territories, there were not significant differences between anterior and posterior circulation in EM (MCA vs. PCA p = .702, MCA vs. BA p = .395, BA vs. PCA p = .973) neither in CM (MCA vs. PCA p = .079, MCA vs. BA p = .252, PCA vs. BA p = .404).

Discussion: Our results do not suggest the existence of estructural changes of the small vessels linked to migraine neither to the frequency of attacks.

Conflict of interest
Disclosure statement:

Supported by the PI14/00020 FISSS grant (Fondos Feder, ISCIII, Ministry of Economy, Spain).

EHMTC-0242
POSTER SESSION D

CORRELATION BETWEN MORNING HEADACHE AND RESTLESS LEGS SYNDROME DETECTED ON POLYSOMNOGRAPHY

R. Moreira Pereira[1], V. Correia dos Santos Moraes[1], J.R. Gomes da Silva[1], L. Bastos Machado[1], L. Neves Reis[1], R. Leite Pontes[1]

[1]*UNIG – Universidade Iguaçu campus V Itaperuna, Faculdade de Medicina, Itaperuna, Brazil*

The restless leg syndrome (RLS) is characterised by Periodic legs movement and is associated with nocturnal sleep disturbances, arousals, excessive daytime sleepiness and has as an outcome, morning headache. This is a cross-sectional study with 32 patients with morning headaches and sleep complaints. They were seen at the "Sleep Institute" of Itaperuna, Rio de Janeiro, Brazil, and underwent a polysomnography exam. Statistical evaluation was performed using the frequencies, means and standard deviations. The Pearson's chi-square test assessed the variables; Statistical significance was estimated at $p < 0.05$. All subjects signed the "Consent and Informed term". The mean age was 42.75 ± 12.64 years. Among the samples, 75% ($n = 24$) were men and, coincidentally, the same 75% was presented with Obstructive sleep apnea (OSA) and morning headache. The mean BMI was 30.33 ± 6.17. Moreover, 90% ($n = 21$) of patients were sedentary, 74% ($n = 23$) were hypertensive and 93% ($n = 29$) presented snoring problems. A highly significant link was found between restless legs syndrome (RLS) and morning headache ($p < 0.044$). It was also noted that a sedentary lifestyle is the most expressive association flag in relation to restless legs syndrome ($p < 0.009$). In multivariate analysis, surmised-correlation between morning headache and a sedentary lifestyle can be suggested (image 1).

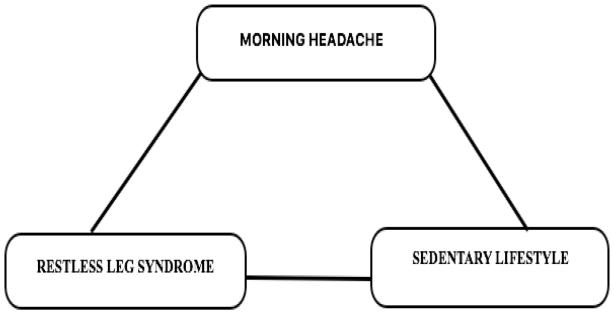


Image 1: Multivariate Correlation between morning headache, Restless legs Syndrome and sedentary lifestyle. Itaperuna, Rio de Janeiro, Brazil, 2016.

EHMTC-0349
POSTER SESSION D

THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE AND ITS EXPENDITURE BY A SAMPLE OF TURKISH HEADACHE PATIENTS

B. Polat[1], O. Saatci[2], N. Helvaci Yilmaz[1], O. Arici Duz[1], L. Hanoglu[1]

[1]*istanbul medipol university, Neurology, İstanbul, Turkey*
[2]*Uskudar State Hospital, ENT, İstanbul, Turkey*

Complementary and alternative medicine (CAM) use is widespread in patients with common neurological disorders despite little scientific evidence suggesting its efficacy. Results from large cohort/population studies indicate that CAM use is common among headache and migraine patients. However there is limited data regarding the cost of regular CAM use. The aim of this study was to provide 12 month prevalence and expenditure of CAM use in patients with headache who were evaluated in our neurology out-patient clinic.

All patients attending our neurology out-patient clinic were asked to complete a structured questionnaire with accompany health professional which included demographic information, details on the use and cost of CAM.

Four hundred and twenty five patients (316 F/109 M) completed the questionnaire. Over 50 % of the patients had used CAM, while 29.6 % of these patients had used mix type of CAM (i.e herbs + cupping or herbs + acupuncture. etc) and %9.4 had used only herbs. From the patients who used CAM the mean annual cost was changed between 30–1000 Turkish Lira(TL). Men patients with have high income (>5000 TL) tended to use more CAM.

Headache patients attending our neurology out-patient clinic used frequently CAM (%52) which is in line with other studies. According to our data patients spend substantial amount of personal income on CAM. These findings underline the importance of a regular questionnaire for CAM use that every headache specialist should have in routine use. Moreover physicians and stakeholders should be aware of behaviour and choices of headache patients.

EHMTC-0337
POSTER SESSION D

CLINICAL CHARACTERIZATION OF VISUAL SNOW

F. Puledda[1,2], C. Schankin[3], P.J. Goadsby[1]

[1]*King's College London, Basic and Clinical Neuroscience, LONDON, United Kingdom*
[2]*Sapienza University of Rome, Neurology and Psychiatry, Rome, Italy*
[3]*University Hospital Bern – Inselspital University of Bern Bern Switzerland, Neurology, Bern, Switzerland*

Introduction: Patients with Visual Snow suffer from pan-field, dynamic visual disturbance. Proposed diagnostic criteria require at least two additional visual symptoms from: palinopsia, entoptic phenomena, photophobia and nyctalopia (1).

Methods: We characterized patients' clinical symptoms with regard to the current criteria (1). An online survey was prepared in collaboration with the patient group Eye-on-Vision. Patients were directed to the site after they contacted us by email asking to be involved in research. The study has been approved by the KCL Research Ethics Panel.

Results: Of patients ($n = 184$) replying and fitting the diagnostic criteria by presenting at least two additional symptoms (1), 116 were male, with a mean cohort age of 29 ± 9 years. They presented with black and white ($n = 99$), colored ($n = 71$), flashing ($n = 77$) *and transparent* ($n = 94$) static. They experienced between one ($n = 104$) and all types ($n = 37$) of static. Floaters ($n = 155$) were the most common associated symptom, followed by afterimages ($n = 147$) and photophobia ($n = 144$).

Conclusions: The data confirm earlier work (1) and extend the analysis of the overlapping symptoms. Visual Snow can be a highly disabling syndrome that is now becoming better understood as it is recognized and systematically studied.

References

1. Schankin CJ, Maniyar FH, Digre KB and Goadsby PJ. Visual snow- a disorder distinct from persistent migraine aura. *Brain*. 2014; 137: 1419–28.

EHMTC-0338
POSTER SESSION D

TREATMENT EFFECT IN VISUAL SNOW

F. Puledda[1,2], C. Schankin[3], P.J. Goadsby[1]

[1]*King's College London, Basic and Clinical Neuroscience, LONDON, United Kingdom*
[2]*Sapienza University Hospital, Neurology and Psychiatry, Rome, Italy*
[3]*University Hospital Bern – Inselspital University of Bern, Neurology, Bern, Switzerland*

Introduction and aims: Patients with Visual Snow suffer from pan-field, dynamic visual disturbance. Proposed diagnostic criteria require two additional visual symptoms from: palinopsia, entoptic phenomena, photophobia and nyctalopia (1). Little is known regarding useful pharmacological treatments for patients. The aim of this study was to gain knowledge on the effect of a number of commonly used medications on visual snow, as well as to monitor the phenotype and severity of the disease through a daily diary.

Methods: Two questionnaires were prepared in collaboration with the patient group Eye-on-Vision and were sent to subjects who had expressed an interest in research. The first required to select from a list of drugs, including antiepileptics, antidepressants and benzodiazepines, treatments that when used in the past had caused a change in Visual Snow symptoms. The second asked subjects to fill in a symptom scale and a diary over 30 days. The study was approved by KCL Research Ethics Panel.

Results: Of patients ($n = 36$) replying, 18 were male, with a mean cohort age of 32 ± 11 years. The effect for forty-eight drugs was recorded in 131 reports. Antidepressants and antiepileptics were the most commonly used drugs; they showed no effect on visual snow in 52% of reports.

Conclusions: Visual Snow is a highly disabling syndrome, for which there is no widely accepted treatment. More effort needs to be made in understanding its pathophysiology to allow focused treatment strategies.

References

1. Schankin CJ, Maniyar FH, Digre KB and Goadsby PJ. Visual snow- a disorder distinct from persistent migraine aura. *Brain*. 2014; 137: 1419–28.

EHMTC-0106
POSTER SESSION D

DISABILITY FROM POST-TRAUMATIC HEADACHE IS COMPOUNDED BY POST-TRAUMATIC STRESS DISORDER

L. Roper[1], P. Nightingale[2], Z. Su[3], A. Belli[3], A. Sinclair[3]

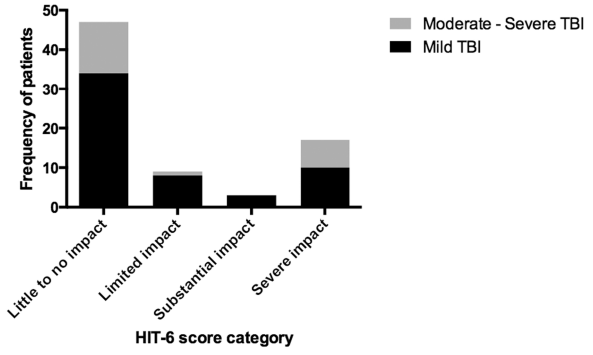
[1]*University of Birmingham, Neurometabolism- Institute of Metabolism and Systems Research, Birmingham, United Kingdom*
[2]*University Hospitals Birmingham, Wolfson Computer Laboratory, Birmingham, United Kingdom*
[3]*University of Birmingham, Wellcome Trust Clinical Research Facility, Birmingham, United Kingdom*

Background: Post-traumatic headache (PTH) occurs in up to 82% of patients with traumatic brain injury (TBI)(1,2,3). Post-traumatic stress disorder (PTSD) occurs in 39% of those with TBI (3, 4, 5). This study evaluates whether PTSD affects PTH disability.

Methods: 151 consecutive patients with TBI were evaluated from a secondary care trauma centre. Headache disability was assessed using the Headache Impact Test version 6 (HIT 6) and PTSD using PTSD Check List Civilian version (PCL-C).

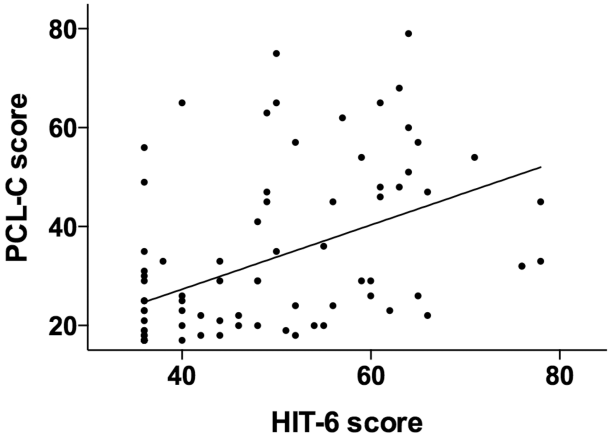
Results: In patients with chronic PTH, increased PTSD symptoms were significantly associated with increased headache disability ($p < 0.001$), as were employment status and loss of consciousness ($p = 0.049$ and 0.016, respectively). Age was negatively correlated with headache disability (Spearman's correlation -0.361, $p = 0.001$).

Conclusion: Increased PTSD severity is significantly associated with increased headache disability in patients with chronic PTH. Managing PTSD in patients with chronic PTH may facilitate headache management.

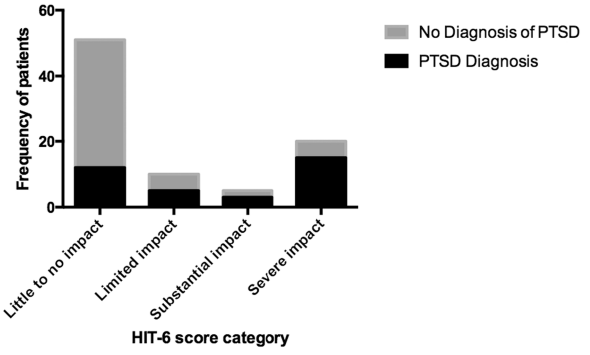


Normal 0 false false false EN-GB JA X-NONE

Figure 2A. Thenumber of patients with little, limited, significant and severe impact fromPTH, defined by their HIT-6 score. Each category is broken down in to thenumber of patients with mild or moderate-severe TBI in each. B. Thenumber of patients with little, limited, significant and severe impact fromPTH, defined by their HIT-6 score. Each category is broken down in to thenumber of patients diagnosed with PTSD or not, based on their PCL-C scores.



Normal 0 false false false EN-GB JA X-NONE Figure3. Linear regression for HIT-6 scores and PTSD scores. $r = 0.583$, $p < 0.001$



EHMTC-0253
POSTER SESSION D

PREDICTORS OF DROPOUTS FROM A DETOXIFICATION PROGRAMME FOR (MOH): RESULTS FROM A MULTICENTRIC MULTINATIONAL STUDY (THE COMOESTAS PROJECT)

P. Rossi[1], C. Di Lorenzo[2], M. Allena[3], G. Nappi[3], R. Jensen[4], C. Tassorelli[3]

[1]*INI, Grottaferrata Rome, Italy*
[2]*INI, Headache Centre, Grottaferrata, Italy*
[3]*"C. Mondino" National Neurological Institute, Headache Science Centre, Pavia, Italy*
[4]*Glostrup Hospital, Danish Headache Centre, Copenaghen, Denmark*

Detoxification from the overused drug considered as the core of the management of MOH patients. This strategy may be complicated by a high rate of low compliance to treatment. The aim of the present analysis was to evaluate the predictors of dropouts from drug withdrawal intervention in MOH.

The present study was part of a larger study with the main aim to compare relapse rates after detoxification between MOH patients using an electronic and a paper headache diary. Patients seen in six headache centres in Europe and Latin America were recruited consecutively for a period of 18 months. Detoxification was performed either as inpatient or outpatient detoxification. Dropouts were defined as those patients who failed to accomplish the detoxification protocol or did not return to the follow-up visits.

A total of 668 MOH patients were evaluated. At two months, 102 were considered as dropouts (15.2%.). Binary logistic regression analysis was performed. Only two variables emerged as significant predictors of dropouts: the recruiting headache centre [OR ratio (OR) −0.2, *P = 0.002], and answering never to "do you feel in control of your headache?" of the HURT questionnaire (OR 1.25,* $P = 0.02$).

Dropout rate is a critical point in the management of MOH. The present findings suggest that it is not related to the clinical characteristics of MOH or to the type of detoxification programme while it is associated to the expertise of the headache centre or negatively influenced by the low level of self-efficacy reported by the patient.

EHMTC-0275
POSTER SESSION D

PERSONALITY PROFILES OF MIGRAINE HEADACHE PATIENTS AS COMPARED TO MEDICATION-OVERUSE HEADACHE PATIENTS

L. S. Mose[1], S. S. Pedersen[2], R. H. Jensen[3], B. Gram[4]

[1]*Institute of Regional Health Research- University of Southern Denmark, Department of Neurology Hospital Southwest Jutland, Esbjerg, Denmark*
[2]*University of Southern Denmark, Department of Psychology, Odense, Denmark*
[3]*University of Copenhagen, Danish Headache Centre- Department of Neurology- Rigshospitalet-Glostrup-, Copenhagen, Denmark*
[4]*Institute of Regional Health Research, University of Southern Denmark/Center Southwest Denmark- Hospital Southwest Jutland, Esbjerg, Denmark*

Background: The exact mechanisms leading to the transformation of primary headaches to medication-overuse headache (MOH) remain unclear. Neither intensity of headache nor frequency is significantly associated with relapse rates, but studies suggest that psychological features may be crucial. Knowledge about the personality of patients at risk of developing MOH could be useful in order to develop individually tailored treatment. The aim of this study is to compare personality profiles of patients with migraine headaches (MH) to patients with MOH.

Methods: This questionnaire survey is conducted at the Hospital of Southwest Jutland. The personality traits among MH patients and patients with MOH were assessed by the NEO five-factor Inventory (NEO-FFI-3) personality questionnaire that contain five facets; Neuroticism, Extroversion, Openness, Agreeableness and Conscientiousness.

Results: Preliminary results on MH ($n = 59$) and MOH ($n = 20$) are presented. Mean (SD) age (years) in MH was 40.7 ± 13 and in MOH 45 ± 9; the gender distribution (male/female) was MH: 11/48 and MOH: 7/13. There were no statistically significant differences between the groups with respect to Neuroticism (mean ± SD): MH 34.7 ± 10.1, MOH 34.2 ± 10.5 ($p = 0.84$), Extroversion: MH 39.0 ± 7.9, MOH 39.4 ± 11.2 ($p = 0.89$), Openness: MH 37.8 ± 6.5, MOH 37.2 ± 6.3 ($p = 0.68$), Agreeableness: MH 44.2 ± 6.7, MOH 43.9 ± 6.2 ($p = 0.86$), and Conscientiousness: MH 47.2 ± 6.2, MOH 47.4 ± 6.5 ($p = 0.91$).

Conclusion: The preliminary results of this study indicate that patients with MOH do not differ from MH patients with respect to personality. As the study is ongoing,

inclusion of more patients into the study will show whether this is a power issue or whether these two patient groups are similar in their psychological profile.

EHMTC-0184
POSTER SESSION D

DIAGNOSTIC LUMBAR PUNCTURES IN IIH: WHAT IS THE PATIENT EXPERIENCE?

W. Scotton[1], T. Walters[2], S. Doughty[3], S. Williams[4], P. Nightingale[5], H. Botfield[1], K. Markey[1], A. Sinclair[6]

[1]*Neuro-metabolism, Institute of Systems and Metabolism Research- University of Birmingham, Birmingham, United Kingdom*
[2]*Neuro-metabolism, nstitute of Systems and Metabolism Research- University of Birmingham, Birmingham, United Kingdom*
[3]*Idiopathic Intracranial Hypertension UK, Registered Charity in England & Wales No. 1143522 & Scotland SC043294., UK, United Kingdom*
[4]*Idiopathic Intracranial Hypertension UK, Registered Charity in England & Wales No. 1143522 & Scotland SC043294, UK, United Kingdom*
[5]*Wellcome Trust Clinical Research Facility, University of Birmingham- Birmingham- United Kingdom., Birmingham, United Kingdom*
[6]*Neuro-metabolism, Institute of Systems and Metabolism Research- University of Birmingham, Birmngham, United Kingdom*

Idiopathic intracranial hypertension (IIH) is characterised by raised intracranial pressure (ICP) of unknown cause. Diagnostic lumbar puncture (LP) is an unavoidable procedure for most patients. Many patients report significant emotional distress associated with LPs.

We aimed to assess the patient's experience of LPs in IIH. In collaboration with the patient charity IIHUK an online questionnaire was distributed to IIH patients (age $>$ 16).

502 patients responded, due to incomplete date only 463 were analysed (mean age 33, BMI 36 with 98% female). Using a verbal rating score (VRS) 0–10, 41% of patients experienced severe pain ($>$8) during LP (median pain score 7). 85% stated they did not receive adequate analgesia. Patients VRS of fear associated with diagnostic LP was 8/10 and anxiety about future LP 7/10. 72% of diagnostic LPs were performed in the emergency setting, and were associated with more pain than the non-emergency setting LPs ($p = 0.012$). Only 36% of patients felt well informed pre-procedure, with increasing pain being significantly ($p < 0{,}001$) correlated with poorly informed patients. Patients felt significantly more informed when the LP was performed by an SpR or Consultant, compared to a junior doctor ($p = 0.001$, $p < 0.001$), as well as suffering less severely from post-LP headaches. The median number of LPs experienced was 4 (IQR 1–11).

This survey indicates that patients are experiencing significant morbidity from pain and anxiety related to LPs. Patient experience maybe improved though enhanced pre-procedure information, moving emergency department LPs to dedicated day-case units and greater physician training.

EHMTC-0342
POSTER SESSION D

PREVALENCE RATE AND RISK FACTORS OF CERVICOGENIC HEADACHE IN PATIENTS WITH NECK DISEASES WHO NEED NECK SURGERY

K. Shimohata[1], T. Shimohata[2]

[1]*Kameda- Daiichi hospital, Department of Anesthesiology, Niigata, Japan*
[2]*Brain Research Institute- Niigata University, Department of Neurology, Niigata, Japan*

Objective: The aim of the present study was to determine the prevalence rate and risk factors of "cervicogenic headache (CH)" in patients with neck diseases.

Methods: We enrolled patients with neck diseases such as cervical spondylotic myelopathy (CSM), ossification of posterior longitudinal ligament (OPLL), cervical spondylotic radiculopathy (CSR), and cervical spondylotic myeloradiculopathy (CSMR), who were scheduled for cervical surgeries between June 2014 and December 2015. All patients were assessed preoperatively and followed prospectively at 3, 6 and 12 months postoperatively with the ICHD3β, the neck disability index (NDI) score, and range of motion (ROM) of the neck.

Results: We enrolled 70 patients (M:F = 46:24; 64.5 ± 11.5 years old) with CSM (53 patients), OPLL (7 patients), CSM (5 patients), and CSMR (5 patients). Fifteen patients (21%) had a headache, and 12 patients were diagnosed with CH, 2 with CH + tension-type headache, and 1 with CH + psychogenic disorder. Frequencies of CH in patients with CSM, OPLL, CSR. CSMR were 19%, 14%, 20%, and 60%, respectively. The visual analogue scale (VAS) was 32 ± 11. The NDI score and degree of decreases in ROM in patients with CH was higher than those without CH ($P < 0.001$ and $p = 0.049$, respectively). The VAS at 3 and 6 month after surgery ($8 \pm 15, 11 \pm 18$) was lower than that before surgery ($P = 0.001$ and $P = 0.005$, respectively).

Conclusion: We demonstrated that the prevalence rate of CH (21%) was much lower than the previous report and that the risk factors of CH may include CSR and severe disability and ROM limitation of the neck.

EHMTC-0406
POSTER SESSION D

GLUCAGON LIKE PEPTIDE-1 REDUCES RAISED INTRACRANIAL PRESSURE: A POTENTIAL TREATMENT FOR IDIOPATHIC INTRACRANIAL HYPERTENSION

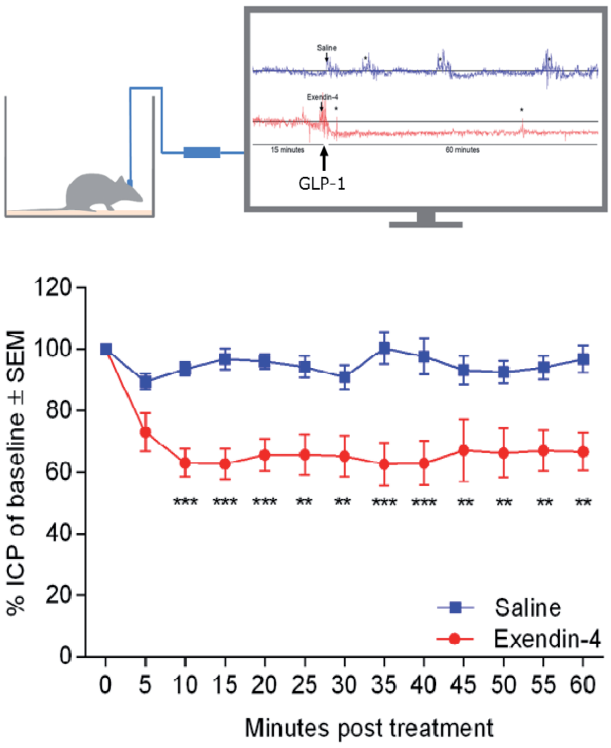
H. Botfiled[1], J. Mitchell[1], C. Westgate[1], S. Hagen[2], A.M. Gonzalez[1], R. Jensen[2], A. Sinclair[1]

[1]*University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom*
[2]*University of Copenhagen, Danish Headache Centre, Copenhagen, Denmark*

Current therapies to reduce intracranial pressure (ICP) in conditions such as idiopathic intracranial hypertension (IIH) have limited efficacy and tolerability consequently novel therapies are needed. Glucagon-like peptide-1 receptor (GLP-1R) agonists are currently used to treat diabetes and obesity, but also affect fluid homeostasis in the kidney. We investigated whether Exendin-4, a GLP-1R agonist, is able to modulate cerebrospinal fluid (CSF) secretion at the choroid plexus and reduce ICP.

We demonstrated GLP-1 receptor mRNA and protein in the choroid plexus which were localised to the cytoplasm and apical surface of the epithelial cells. Exendin-4 treatment significantly increased, GLP-1 receptor mRNA and protein levels ($p < 0.05$) compared to baseline. Evaluation of downstream signalling in primary choroid plexus epithelial cells identified a 2.14 ± 0.61 fold increase in cAMP after Exendin-4 treatment ($P < 0.01$). Exendin-4 significantly reduced Na^+K^+ATPase activity, a marker of CSF secretion ($-39.3 \pm 9.4\%$; $P < 0.05$). In vivo ICP recording in adult rats demonstrated that Exendin-4 significantly reduced ICP ($65.2 \pm 6.6\%$ of baseline ($P < 0.01$)). This was replicated in hydrocephalic rodents (ICP $62.6 \pm 5.1\%$ of baseline ($P < 0.0001$)).

We demonstrate that Exendin-4 reduces CSF secretion at the choroid plexus and ICP in rats. Repurposing existing GLP-1 drugs may represent a novel therapeutic strategy for conditions of raised ICP such as IIH. Additionally, GLP-1 therapy promotes significant weight loss which would be advantageous in IIH.



EHMTC-0090
POSTER SESSION D

ERGOTAMINE RESPONSIVE OPHTHALMOPLEGIC MIGRAINE LIKE HEADACHE

B.L. Tee[1]

[1]*National Taiwan University Hospital – Hsinchu branch, Neurology, Hsinchu, Taiwan*

Background: Ophthalmoplegic migraine (OM) was renamed as "recurrent painful ophthalmoplegic neuropathy" (RPON) in the International Classification of Headache Disorders 3(ICHD3). Its pathophysiology remained elusive. Typically, headache precedes diplopia and pain is unilateral. Most individuals exhibit nausea, vomiting, photophobia and phonophobia. Unlike migraine, headache lasted days or weeks and no aura was reported. Some literatures support steroid use but there is no treatment consensus.

Case report: A 39 year-old lady developed headache followed by binocular diplopia 2 days later. Headache was excruciating sharp pain over right periorbital area with phonophobia, photophobia and aggravated upon motion. There was nausea and vomiting. Pain was VNRS 10. She had rhinorrhea and sore throat 2 weeks ago. No

migraine noted previously. Neurological examination demonstrated right oculomotor palsy. Brain MRI showed no mass lesion or abnormal enhancement. Cerebrospinal fluid analysis was unremarkable. Blood data was normal for fasting glucose, HbA1c, autoimmune markers but revealed subclinical hypothyroidism and elevated anti-*thyroid peroxidase antibody. Acetaminophen and* non-steroidal anti-inflammatory drug were partially responsive. Ergotamine was given and headache abolished 30 minutes later. After 5 dosage, patient's opthalmoplegia resolved.

Conclusion: OM/RPON is a rare form of headache accompanied by ophthalmoplegia. We demonstrated a case of OM like individual that responded well with Ergotamine. As a first attack, she is not qualified for RPON yet. However her treatment response suggests that OM/RPON may be attributed to vascular dysregulation. In addition, she has elevated anti-TPO level. This correlation remained inconclusive. Yet antiTPO level may help identifying Ergotamine responsive OM/RPON individuals.

EHMTC-0057
POSTER SESSION D

RELATIONSHIP BETWEEN HEADACHE AND ANGIOARCHITECTURAL PARTICULARITIES OF BRAIN ARTERIOVENOUS MALFORMATIONS

O. Tsurkalenko[1], L. Dzyak[1]

[1]*Public institution "Dnipropetrovsk medical academy Ministry Health of Ukraine", neurology and neurosurgery, Dnipropetrovsk, Ukraine*

Background: It has been widely described that headache occurs in almost half of patients with arteriovenous malformations (AVM) and could be the first manifestation of the disease. However, the specific characteristics of AVM-assotiated headache, the mechanisms of it occurrence depending on the features of AVM are still poorly described. The purpose of this study was analyse the relationship between clinical features of headache and angioarchitectural particularities of AVM.

Methods: Between 2005 and 2015 years 355 consecutive patients with brain AVM were treated in Dnepropetrovsk regional hospital. We conducted a comprehensive clinical, neuropsychological and neuroimaging examination of this subjects. Headache was characterized according to ICHD-II criteria.

Results: Among the studied patients headache was found in 65% (230), in 52% (184) it was the first symptom of the disease. Clinical and radiological findings of AVM images showed that headache occurred significantly more frequently among larger AVM (with vs. without headache, 12.7 vs. 5.1 ml, $p = 0{,}002$), diffuse AVM (78.5 vs. 24.3%, $p = 0.002$), AVM with transdural arterial communication (84.6 vs. 29.7%, $p = 0.001$), occipital AVM (69.5 vs. 29.1%, $p < 0.001$), older patients (43.1 vs. 36.6 years, $p = 0.037$). CT-spectrography patients with headache showed reduced flow through structurally normal brain region remote from AVM. These changes were accompanied by cognitive impairment.

Conclusions: Intractable, unilateral migraine-like headache should increase suspicion for brain AVM and prompt neuroimaging. The pathogenesis of headache in AVM patients may involve several mechanisms and demonstrate general lesion of the brain vessels caused by arteriovenous shunting.

EHMTC-0056
POSTER SESSION D

NEW DAILY PERSISTENT HEADACHE:A CLINICAL STUDY WITH DIAGNOSTIC AND TREATMENT IMPLICATIONS

M. Wang[1], E. Cittadini[2], A. Bahra[3]

[1]*Shanxi Province People's Hospital, Department of Neurology, Taiyuan, China*
[2]*Springfield University Hospital, Wandsworth Complex Needs Service, London, United Kingdom*
[3]*National Hospital for Neurology and Neurosurgery, Institute of Neurology, London, United Kingdom*

Background: New daily persistent headache (NDPH) is characterized by headache which is daily from onset, for at least three months. There are a limited number of observational cohorts published in this field. This study retrospectively assessed patients with NDPH seen at a tertiary centre. Based upon the observations we suggest revision of the current classification.

Methods: Patients with NDPH seen at the National Hospital for Neurology and Neurosurgery from March 2005 to April 2015 were identified. All fulfilled criteria of the International Classification for Headache Disorders 3-Beta (ICHD-3) for NDPH. Clinical features and treatment responses were documented.

Results: Of 159 patients identified, 86.8% had a clinical syndrome consistent with ICHD-3 chronic migraine, 7.5% chronic tension-type headache and 5.7% could not be classified. In the latter group there was no consistent syndrome type. Most patients were resistant to treatment. The most consistent responses were seen with Topiramate and local nerve blockade.

Conclusions: We conclude that NDPH is not a phenotypic entity which warrants a unique classification. Furthermore the current classification does not inform treatment, which for most primary headache disorders is guided by clinical syndrome. We propose reclassification of NDPH as a subtype of clinical syndrome, differentiated by mode of onset. Such a classification already exists for the trigeminal autonomic cephalalgias.

The proposed classification would allow comparison of more homogenous headache phenotypes and provide guidance for management, both key objectives of the ICHD.

Conflict of interest
Disclosure statement:
I applied for IHS Junior Travel Grant of the 5th EHMTIC.

EHMTC-0400
POSTER SESSION D

LUMBAR PUNCTURE IN PATIENTS WITH SPONTANEOUS INTRACRANIAL HYPOTENSION

H. Yokota[1], K. Yokoyama[2], T. Yonezawa[3], H. Nakase[1]

[1]*Nara medical university, Neurosurgery, kashihara, Japan*
[2]*Higashiosaka City General Hospital, Neurosurgery, HIgashiosaka, Japan*
[3]*Osaka Police Hospital, Neurosurgery, Osaka, Japan*

Background: A lumbar puncture (LP) for patients with spontaneous intracranial hypotension (SIH) may be difficult due to low cerebrospinal fluid (CSF) pressure.

Methods: In this study, we retrospectively evaluated LP procedures performed in 7 patients with SIH.

Results: We performed at least 2 LP procedures as part of radioisotope cisternography and computerized tomography myelography (CTM) examinations in all patients after obtaining a diagnosis of SIH, while 2 underwent an additional LP in order to reach a diagnosis. One had a history of multiple LP procedures at another institution. A Queckenstedt test in the lateral decubitus position was used to confirm subarachnoid space in patients with extreme low CSF pressure. Two patients received epidural injections during a CTM examination and a re-examination was performed for each with the LP procedure performed in a sitting position.

Conclusion: Difficulties may be encountered during a LP procedure to precisely confirm subarachnoid space in patients with SIH. A Queckenstedt test in the lateral decubitus position and LP in a sitting position may be helpful for obtaining success with the LP procedure in patients with SIH.

EHMTC-0191
POSTER SESSION D

PHARMACOTHERAPY OF PERSISTENT IDIOPATHIC FACIAL PAIN – ARE TRIGEMINAL NEURALGIA MEDICATIONS EFFICACIOUS?

J. Zidverc-Trajkovic[1], A. Radojicic[1]

[1]*Neurology Clinic, Headache Center, Belgrade, Serbia*

Persistent idiopathic facial pain (PIFP), coded as 13.11 by ICHD-III is chronic neuropathic pain condition with still unknown prevalence in the general population. Unlike trigeminal neuralgia (TN), there is a lack of recommendation for pharmacological treatment of PIFP.

The aim of this study was to compare the efficacy of medications that are used for treatment of TN in patients with PIFP.

From January 2005 to April 2016 PIFP were diagnosed in 35 and TN in 98 patients. Due to incomplete follow-up data analysis was performed in 33 PIFP and 92 TN patients. More females (78.8% vs. 56.5%), younger age at disease onset (45.2 ± 17.9 vs. 53.4 ± 16.0), as well as unremitting course of disorder (92.0% vs. 62.3%) were noted in PIFP patients than in TN group. Pain was localized on both sides of the face in 45.2% PIFP patients involving more than one branch of trigeminal nerve in half of them and was unilateral in all TN patients, involving more branches in only 17.7%.

Decrease of pain intensity, frequency and/or duration of 50% or more was considered as treatment efficacy. The most commonly used drugs were carbamazepine and gabapentin, both efficacious in less patients with PIFP than with TN, 3/14 vs. 51/71 and 3/15 vs. 28/44 respectively. Pregabalin (5/16 vs. 10/19), lamotrigine (2/4 vs. 6/9), and amitriptyline (1/9 vs. 1/7) demonstrated similar efficacy. Baclofen, valproic acid, phenitoin, and opioids were prescribed only in a few patients. Similar adverse events were presented in both groups equally.

EHMTC-0315
POSTER SESSION E

VAGUS NERVE STIMULATION (VNS) INHIBITS ACUTE INTRACRANIAL-DURAL AND TRIGEMINO-AUTONOMIC NOCICEPTIVE ACTIVATION OF TRIGEMINOCERVICAL NEURONS

S. Akerman[1], B. Simon[2], M. Romero-Reyes[1]

[1]*New York University, College of Dentistry, New York, USA*
[2]*ElectroCore LLC, -, Basking Ridge, USA*

Introduction: Non-invasive cervical vagus nerve stimulation is reported to be efficacious in the acute treatment of both migraine and cluster headache, but its effects in animal models of acute head-pain are unknown.

Objective: To determine the effects of invasive (i)VNS in animal models of acute intracranial (migraine headache) and trigemino-autonomic (cluster headache) head-pain.

Method: Rats were anesthetized and prepared for physiological measurements. Electrophysiological techniques were used to record trigeminocervical neurons in response to noxious dural-(intracranial) or superior salivatory nucleus (SuS; trigemino-autonomic) stimulation. Neuronal responses were measured after iVNS (25 Hz, 1 ms pulse of 5KHz, 2 min) using a custom-built hook electrode (Dr. Matthew Ward, Purdue University).

Results: Single dose ipsilateral and contralateral iVNS caused significant inhibition of spontaneous ongoing (both $P < 0.05$) and dural-evoked (both $P < 0.001$) neuronal firing, for up to 45mins. Two 2 min iVNS stimulus trains, separated by 5 minutes, produced a similar inhibition of neuronal responses, prolonged for 2 hrs. Also, two doses of ipsilateral iVNS inhibited spontaneous ongoing ($P = 0.001$) and SuS-evoked ($P = 0.007$) neuronal responses, prolonged for 3 hrs.

Conclusion: iVNS dose-dependently inhibits acute nociceptive activation of trigeminocervical neurons in animal models of acute intracranial and trigemino-autonomic head pain, translating to nVNS effects in migraine and cluster headache, respectively, validating these preclinical approaches. Further, we may begin to hypothesise the neurobiological mechanisms for the efficacy of nVNS in the treatment of primary headaches. Firstly, modulating nociceptive activation of trigeminocervical neurons via direct projections, but also (via the efficacy of contralateral stimulation) by engaging bilateral structures involved in descending modulation of nociceptive inputs.

Conflict of interest
Disclosure statement:

This work was funded, in part, by an unrestricted research gift by Electrocore LLC

EHMTC-0317
POSTER SESSION E

TRANSCRANIAL MAGNETIC STIMULATION MAY MODULATE CORTICAL NEURONAL ACTIVITY BY INFLUENCING INTRACELLULAR CALCIUM ELEVATIONS IN EXCITABLE NEURONS

A.P. Andreou[1], A.A. Miedzik[1], I. Nagy[2], M. Jones[1], S.P. Antreou[1], G. Lambru[1], A. Al-Kaisy[3]

[1]*Guy's and St. Thomas' NHS Foundation Trust & King's College London, Academic Headache Centre, LONDON, United Kingdom*
[2]*Imperial College London, Section of Anaesthetics- Pain Management & Intensive Care, LONDON, United Kingdom*
[3]*Guy's and St. Thomas' NHS Foundation Trust, Pain Management & Neuromodulation Centre, LONDON, United Kingdom*

Introduction: Clinical trials demonstrated that single pulse transcranial magnetic stimulation (sTMS) can be a promising novel treatment in migraine. We have previously shown that sTMS could inhibit cortical spreading depression (CSD). However, its actual effect on cortical neuronal activity remains to be investigated.

Objectives: To investigate the potential effects of sTMS on cortical neuronal activity.

Methods: Single neurons were identified in the occipital cortex of adult male rats ($n = 6$) by means of in-vivo electrophysiology. The effects of a single pulse of TMS (170 μs rise time), delivered over the ipsilateral occipital cortex, were studied on spontaneous neuronal activity over a range of magnetic field intensities. In isolated cortical neuronal cultures, neuronal activity was recorded in-vitro using the calcium indicator dye, Fura-2, and calcium fluorescence imaging post-sTMS application and in response to K^+ stimulation.

Results: sTMS did not depolarise cortical neurons for any of the magnetic fields tested, however at 1.1–1.3 Tesla it decreased spontaneous neuronal firing in 5/6 cortical neurons ($P < 0.05$). At lower magnetic field intensities, sTMS had no effect on spontaneous neuronal activity. Similarly, *in-vitro*, sTMS at 1.1Tesla did not depolarise cultured cortical neurons ($n = 1102$), however it reduced the concentration of intracellular calcium following K^+ stimulation (50% $\Delta F/F$).

Conclusions: The data demonstrate that although sTMS delivered at the clinically used magnetic fields may not depolarise cortical neurons, it could reduce spontaneous neuronal activity, potentially through interactions with intracellular calcium elevations in excitable neurons. The potential role of calcium channels as a molecular target of sTMS warrants further investigation.

EHMTC-0373
POSTER SESSION E

NON-PARALYTIC BOTULINUM MOLECULES FOR THE CONTROL OF MIGRAINE

M. Paraskevopoulou[1], J. Torres Perez[2], A. Miedzik[1], J. Chamberlain[1], G. Lambru[1], B. Davletov[3], A.P. Andreou[1]

[1]*Guy's and St. Thomas' NHS Foundation Trust & King's College London, Academic Headache Centre, LONDON, United Kingdom*
[2]*Imperial College London, Section of Anaesthetics- Pain Management & Intensive Care, London, United Kingdom*
[3]*University of Sheffield, Department of Biomedical Sciences, Sheffield, United Kingdom*

Background: *Botulinum* toxin is an established preventive treatment for migraine. However, its toxicity and the unwanted muscle paralysis are major limitations of the administrated dose and achieved efficacy. Recently, Clostridial chimeras that lack this paralytic effect have been developed. These novel *recombinant* molecules can selectively target sensory over motor neuronal fibres.

Aim: To investigate the efficacy of Bitox, a Clostridial chimera with reduced paralytic activity in the migraine animal model of trigeminovascular activation.

Methods: In male rats, Bitox (200 ng) was injected over one peri-orbital area (100 nl), while saline was injected contralaterelly. Forty-eight to 72 hours later, the animals were tested for blink reflex, as an indication of muscle paralysis. Following, mechanical (von Frey) and electrical trigeminovascular activation thresholds were assessed bilaterally on second order neurons in the trigeminocervical complex by a researcher blinded to experimental groups.

Results: None of the animals demonstrated muscle paralysis during the blink reflex test. Bitox significantly increased the mechanical thresholds compared to the control side ($P < 0.005$). Activation thresholds of second order neurons, assessed as the minimum voltage required to induce evoked action potentials, were significantly increased following treatment with Bitox compared to saline ($P < 0.005$). No differences in the basal levels of spontaneous neuronal activity were observed between the two treatments ($P = 0.45$).

Conclusion: Non-paralytic botulinum-like molecules can be important modulators of trigeminovascular nociceptive processing, potentially offering a significant advancement in the preventive therapeutic options for patients.

EHMTC-0224
POSTER SESSION E

CHANGES IN CORTICAL SPREADING DEPRESSION INITIATION AND TERMINATION IN CORTICAL BRAIN SLICES FOLLOWING ASTROCYTE-SPECIFIC GLUTAMATE TRANSPORTER BLOCKADE

S. Baca[1], C. Dulla[2], M. Mostamand[1], A. Charles[1]

[1]*UCLA, Neurology, Los Angeles, USA*
[2]*Tufts University, Biomedical Sciences, Boston, USA*

Cortical spreading depression (CSD) is a pathological brain phenomenon observed in humans and in animal models used for migraine research. In animal models, CSD can be elicited in multiple ways and profoundly disrupts ionic homeostasis, affecting extracellular potassium, sodium, calcium, and glutamate. Although neuronal hyper-excitation or blood-flow reductions are thought to precipitate CSD, astrocytes are also likely involved in the process. but their specific role(s) in CSD remain unclear. We examined the potential role of astrocytes in CSD generation by pharmacologically blocking astrocyte-specific glutamate transporters using TFB-TBOA. Using local field potential recordings and the FRET-based glutamate biosensor FLII81E in cortical brain slices, we observed the following: 1. CSDs were spontaneously initiated in the presence of TFB-TBOA; 2. Electrophysiologically, both spontaneous and KCl-elicited CSDs in the presence of TFB-TBOA were much larger in amplitude but similar in waveform to those observed in normal solutions; 3. Using the glutamate biosensor, we optically observed glutamate level changes propagate across the cortex following CSD initiation. The propagating changes in glutamate levels were of similar velocity to CSD waves as measured by optical intrinsic signal (OIS) in previous reports. Unlike OIS, the glutamate wave did not preferentially spread in superficial cortical layers and we sometimes observed small and focal changes in glutamate levels that appeared ahead of the main wave front. These *in vitro* results suggest that astrocytes can be involved in both the initiation and the termination/recovery phases of CSD and even when intrinsic neuronal excitability is normal.

EHMTC-0379
POSTER SESSION E

CRITICAL ROLE OF SRC FAMILIY KINASES IN CORTICAL SPREADING DEPRESSION

F. Bu[1], J. Quinn[2], M. Wang[1]

[1]*Xi'an Jiaotong-Liverpool University, Biological Sciences, Suzhou, China*
[2]*Translational Medicine- Liverpool University, Molecular and Clinical Pharmacology, Liverpool, United Kingdom*

NR2A-containing NMDA receptors contribute to genesis and propagation of cortical spreading depression (CSD), the underlying cause of migraine pain. Src family kinases (SFKs) can potentiate NR2A-containing receptors current by phosphorylating NR2A subunit in the C-terminal tail. In this project, we aimed to understand whether SFKs are involved in migraine mechanism by examining how SFKs interact with CSD in rats. The results demonstrated that repeated CSD markedly increased phosphorylation of Src at amino acid Y416 in the ipsilateral cortex. The elevated Src activation can be suppressed by application of SFKs inhibitor PP2 at 2.5 nmol via intracerebral ventricle injection. Furthermore, the result also demonstrated that PP2 markedly reduced cortex susceptibility to CSD and the magnitude of CSD. In particular, PP2 prolonged CSD latency by 142.7 % and reduced magnitude of CSD by 67.9 % when compared with the negative control, PP3. This study reveals a previously unknown migraine mechanism involving SFKs and helps to identify novel target for prophylactic migraine treatment. Whether Src activation regulates NR2A mediated CSD requires further investigation.

EHMTC-0254
POSTER SESSION E

CILOSTAZOL INDUCES C-FOS EXPRESSION IN THE TRIGEMINAL NUCLEUS CAUDALIS AND BEHAVIOURAL CHANGES SUGGESTIVE OF HEADACHE WITH MIGRAINE-LIKE MANIFESTATIONS IN RATS

S.L.T. Christensen[1], S. Petersen[1], D.B. Sørensen[2], J. Olesen[3], I. Jansen-Olesen[1]

[1]*Glostrup Research Institute, Danish Headache Center, Glostrup, Denmark*
[2]*University of Copenhagen, Experimental Animal Models, Frederiksberg C, Denmark*
[3]*Rigshospitalet, Danish Headache Center, Glostrup, Denmark*

Introduction: Research in migraine therapeutics is hindered by the lack of knowledge on migraine pathophysiology and suitable predictive animal models. As headache and migraine can be provoked in healthy humans and migraine patients the aim of this study was to see if it can also provoke headache in rats. Also, we tested the response to sumatriptan in order to evaluate the predictive properties of the model.

Methods: The effect of cilostazol (125 mg/kg p.o.) was evaluated on a range of spontaneous behavioural parameters, light sensitivity and mechanical sensitivity thresholds. To assess headache specificity we evaluated the c-fos expression in the trigeminal nucleus caudalis. All experiments were done in female Sprague Dawley rats and the oestrous cycle was included in the analyses.

Results: We found that cilostazol increased the light sensitivity and grooming behaviour of the rats and decreased their head twitching. These manifestations were not inhibited by sumatriptan. Cilostazol also induced c-fos expression in the trigeminal nucleus caudalis. Locomotion, rearing, eating and drinking activity as well as the amount of wet dog shakes and mechanical sensitivity thresholds were unaltered.

Discussion: The altered behaviours are suggestive of headache with migraine features, but not specific. The c-fos response in the trigeminal nucleus caudalis implies that the rats had pain originating from the head. The lack of response to sumatriptan disqualifies the model as predictive, but confirms the translation of the human findings into rats.

EHMTC-0391
POSTER SESSION E

PERIPHERAL VAGAL NERVE STIMULATION MODULATES THE NOCICEPTIVE WITHDRAWAL REFLEX IN HEALTHY SUBJECTS: A CROSS-OVER PLACEBO-CONTROLLED STUDY

R. De Icco[1], D. Martinelli[1], G. Sandrini[1], E. Liebler[2], C. Tassorelli[1]

[1]*Headache Science Centre- "C. Mondino" National Neurological Institute, Department of Brain and Behavior- University of Pavia, Pavia, Italy*
[2]*electroCore LLC, Basking Ridge- 07092, NJ, USA*

Peripheral non-invasive vagal nerve stimulation (nVNS) has become a target for the treatment of primary headaches, though its exact mechanisms are unclear. The nociceptive flexion reflex paradigm is widely used to investigate modulation of nociception.

The aim of our study is to evaluate the effect of nVNS on the nociceptive withdrawal reflex in healthy subjects.

Seven healthy subjects were evaluated in a cross-over placebo-controlled study and randomly assigned to a) nVNS: one 120-s electrical stimulation on each side of the neck using the gammaCore device and b) active placebo stimulation (PS): one 120-s electrical stimulation of the median nerve on each wrist. Nociceptive withdrawal reflex was investigated at baseline (T0), 5' minute after stimulation (T5) and 30' after stimulation (T30).

nVNS caused a significant increase in the reflex threshold (RTh) and in the temporal summation threshold (TST) 30 minutes after the stimulation (Figure 1); PS did not cause any significant modification on the reflex parameters. When analyzing percent changes from baseline, nVNS caused a significant increase in RTh already at 5' as compared to PS. At T30 nVNS also induced a significant increase in TST as compared to PS.

nVNS induces a rapid onset analgesia in healthy subjects, which likely affects pain facilitation mechanisms in the spinal cord, as suggested by the increase in the threshold of temporal summation.

EHMTC-0123
POSTER SESSION E

INFLUENCE OF MIGRAINE-RELATED SUBSTANCES ON MAST CELL DEGRANULATION IN A MIGRAINE MOUSE MODEL

E. Dlugosch[1], H. Lübbert[1]

[1]*Ruhr University Bochum, Animal Physiology, Bochum, Germany*

Background: It is indicated that the serotonin 5-HT_{2B} receptor, different histamine receptors and mast cells are involved in the neurogenic inflammation of the dura mater. The 5-HT_{2B} receptor or the H1 receptor is hypothesized to induce a cascade of events which triggers vasodilation and plasma protein extravasation (PPE) through mediators like calcitonin gene related peptide and substance P. Further contribution to their process may stem from activated mast cells which release pro-inflammatory substances which trigger than further inflammation. In a chronic migraine model, mice become sensitized by hypoxic treatment towards a migraine-related state in which the drug meta-chlorophenylpiperazine (a partial 5-HT_{2B} agonist) can induce dural PPE. (Hunfeld et al., 2015) Little is known about the role of mast cell activation in the induction of PPE and the sensitization process. Here, we aim at investigating the role of mast cells in these processes.

Aim: Elucidation of the role of dural mast cells in neurogenic inflammation and hypoxia-induced facilitation of PPE induction.

Methods: Half skull ex vivo experiments with histological examination.

Results: Mast cells in the dura mater of mice are not activated by all pharmacological substances used. mCPP and histamine act differently on mast cell degranulation, partly depending on the pretreatment performed and might influence the facilitation of a PPE induction.

Conclusion: Histamine and mast cell activation thus seems to contribute to the neurogenic inflammation in the mouse model.

EHMTC-0206
POSTER SESSION E

THREE DIMENSIONAL ORGANOID MODELLING TO INDUCE DIRECTED DIFFERENTIATION OF HUMAN INDUCED PLURIPOTENT STEM CELLS TOWARDS A PEPTIDERGIC TRIGEMINAL NEURONAL FATE

G. Duggal[1], P. Pettingill[1], S. Chintawar[1], Z. Cader[1]

[1]*Weatherall Institute of Molecular Medicine, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom*

Currently, there is no well-established methodology for successful differentiation of induced pluripotent stem cells (iPSCs) towards peptidergic neuronal fate. These are of great interest to the neuroscience community as it is the trigeminal (TG) peptidergic sensory neurons that release neuropeptides such as calcitonin gene-related peptide (CGRP), which plays a critical role in the pathophysiology of migraine and other primary headache disorders.

We have established functional TG-nociceptors *in vitro* and have extrapolated the knowledge gained to develop TG-organoids. This is because organoid modelling is emerging as a new and more efficient differentiation strategy to recapitulate mammalian organogenesis *ex vivo* due to the possibility of controlled niche signalling and efficient cell-cell interaction. We attempted to develop 3D model by isolating the TG placodes at day 13–15 of differentiation (postmitotic stage) and plating them in low-attachment dishes with our optimised TG neuronal maintenance media. As well, we supplemented floating TG-placodal cultures with 1% matrigel in the optimised TG media, to facilitate neurogenesis. By day 28, we observed increased

expression of nociceptor markers in organoid cultures supplemented in 1% matrigel. Upon re-plating these 3D organoids on matrigel followed by monolayer culture, peptidergic cMET$^+$ nociceptors were present only in cultures supplemented in 1% matrigel in the media, whereas as those cultured in its absence were of non-peptidergic RUNX1$^+$/cMET$^-$ identity.

Hence, we have successfully established peptidergic neuronal fate in TG-organoid cultures and this data serves as a strong baseline to further develop our 3D nociceptor organoid strategy, in conjunction with enhancing peptidergic neuronal population.

EHMTC-0333
POSTER SESSION E

VAGAL NERVE STIMULATION INHIBITS ACTIVATION OF TRIGEMINAL NOCICEPTIVE NEURONS IN A MODEL OF TRIGEMINAL SENSITIZTION

P. Durham[1], J. Hawkins[1], L. Cornelison[1]

[1]*Missouri State University, Biology, Sprinfield, USA*

Aim of Investigation: To determine if vagal nerve stimulation could repress activation of sensitized trigeminal nociceptive neurons, which are implicated in the underlying pathology of migraine and temporomandibular joint disorders (TMD).

Methods: Mechanical nocifensive thresholds were determined in Sprague Dawley male rats in response to von Frey filaments applied to the skin over the eyebrow (V1) and masseter (V3) areas. To promote sensitization of trigeminal neurons, animals were injected with CFA in the neck muscles, and 8 days later subjected to a pungent extract from California Bay leaves, which then triggered trigeminal activation. To stimulate the vagal nerve, electrodes were placed over the cutaneous area directly above the nerve and a 1 ms pulse of 5 kHz sine waves, repeated at 25 Hz for 2 minutes was administered to the animal.

Results: Exposure to a pungent extract from California Bay leaves (trigger), which is known to stimulate TRPA1 in V2 neurons, significantly increased the number of nocifensive withdrawals in response to mechanical stimulation of sensitized V1 and V3 trigeminal ganglion neurons mediated by neck muscle inflammation (risk factor) for at least 24 hrs. VNS prior to trigeminal nerve activation did not block increased nocifensive responses. However, VNS administered 2 hours after the initial pungent odor exposure significantly inhibited the nocifensive response 100% of the time.

Conclusions: Our findings provide evidence that VNS can abort V1 and V3 trigeminal nociception and thus may be useful as a nonpharmacological therapy for treating episodic migraine and inhibiting pain associated with TMD pathology.

Conflict of interest
Disclosure statement:
This study was supported by a grant awarded from electroCore.

EHMTC-0334
POSTER SESSION E

VAGAL NERVE STIMULATION INHIBITS EXPRESSION OF PROTEINS IMPLICATED IMPLICATED IN SENSITIZATION AND EXCITATION OF TRIGEMINAL NOCICEPTIVE NEURONS

P. Durham[1], J. Hawkins[1], C. Hyde[1], B. Blankenship[1]

[1]*Missouri State University, Biology, Sprinfield, USA*

Aim of Investigation: To investigate the cellular mechanisms by which vagal nerve stimulation represses activation of sensitized trigeminal nociceptive neurons, which are implicated in the underlying pathology of migraine.

Methods: To promote sensitization of trigeminal neurons, Sprague Dawley male rats were injected with the inflammatory agent CFA in the neck muscles, and 8 days later subjected a pungent extract from California Bay leaves, which then triggered trigeminal activation. To stimulate the vagus nerve, electrodes were placed over the cutaneous area directly above the nerve and a 1 ms pulse of 5 kHz sine waves, repeated at 25 Hz for 2 minutes was administered to the animal. Changes in cellular expression in trigeminal ganglia and upper spinal cord tissue were investigated using immunohistochemistry.

Results: Exposure to a pungent extract from California Bay leaves (trigger), which is known to stimulate TRPA1 in V2 neurons, significantly increased the expression of calcitonin gene-related peptide (CGRP), protein kinase A (PKA), and P-ERK, a marker of biomarker of activated nociceptors, in V1/V2 region of the trigeminal ganglion. Exposure also increased levels of PKA as well as Iba1, a biomarker of activated microglia, and GFAP, a biomarker of activated astrocytes, in the spinal trigeminal nucleus. VNS administered 2 hours after pungent odor exposure caused a transient decrease in the levels of these proteins.

Conclusions: Our findings provide evidence that the inhibitory effects of VNS in our model of trigeminal pathology

involve repression of proteins in neurons and glial associated with sensitization and excitation of trigeminal nociceptive neurons.

Conflict of interest
Disclosure statement:
This study was supported by a research grant awarded from electroCore.

EHMTC-0240
POSTER SESSION E

EFFECTS OF ADENOSINE AND CAFFEINE ON MIGRAINE-RELATED NEUROVASCULAR ACTIVITY

S. Eftekhari[1], I. Keselman[1], J. Zyuzin[1], A. Charles[1]

[1]*University of California- Los Angeles, UCLA Goldberg Migraine Program- David Geffen School of Medicine, Los Angeles, USA*

Objectives: Caffeine has traditionally been considered to be a vasoconstrictor based upon its effects on isolated blood vessels. The effects of caffeine may be different, however, when the caliber of cerebral vessels is controlled primarily by normal coupling between neuronal and vascular activity.

Methods: Confocal videomicroscopy was used to quantify the effects of adenosine and caffeine on the activity of mouse cortical neurons in cell culture. Optical intrinsic signal imaging and local field potential recordings in anesthetized mice were used to investigate the effects of caffeine on cortical spreading depression (CSD) evoked by KCl.

Results: Adenosine inhibited spontaneous neuronal calcium transients, which was blocked by A1 antagonist (DPCPX) whereas A1 agonist (CCPA) inhibited the calcium transients. Application of A2 receptor agonist (CGS21680) activated neurons.

Caffeine activated firing of neurons while systemic administration of caffeine increased burst activity and dilated cortical surface blood vessels. Caffeine attenuated the initial vasoconstriction associated with the CSD wave, but increased and prolonged the vasoconstriction that occurred during the sustained period of neurovascular uncoupling.

Conclusions: Adenosine has an inhibitory effect on cortical neuronal firing. The effects of caffeine on vascular caliber are different under conditions of normal neurovascular coupling as compared with the "uncoupled" state that occurs following CSD. The effects of drugs on isolated cerebral blood vessels may therefore not reflect their effects on the cerebral vasculature under normal conditions *in vivo*. Furthermore, CSD may alter the vascular effects of medications, a factor that may be important in migraine and other conditions in which CSD occurs.

Conflict of interest
Disclosure statement:
I have received grants from Swedish Migraine Society, The Royal Physiographic Society in Lund, Sweden, The Swedish Society of Medicine, The Segerfalk foundation, Lund, Sweden and The Brain Foundation Sweden.

EHMTC-0241
POSTER SESSION E

CHANGES IN THE CONTRALATERAL CEREBRAL HEMISPHERE IN RESPONSE TO CORTICAL SPREADING DEPRESSION

S. Eftekhari[1], S.M. Baca[1], A. Charles[1]

[1]*University of California- Los Angeles, UCLA Goldberg Migraine Program- David Geffen School of Medicine, Los Angeles, USA*

Rationale: It is often assumed that cortical spreading depression (CSD) is a unilateral event, affecting only the hemisphere in which it is evoked. The effects of CSD on neurovascular activity in the contralateral hemisphere have not been well characterized.

Methods: Vascular and parenchymal responses to CSD in mice were recorded using optical intrinsic signal (OIS) and field potential recording techniques. Two thinned skull windows were prepared to visualize both hemispheres. Burrholes were made on each side. An electrode for measurement of local field was placed on the contralateral side to the burrhole for KCl injection. Single or repetitive CSD events were evoked with transient or continuous application of 1 M KCl. In control animals, saline was injected instead of KCl.

Results: A multiphasic deflection in local field potential was consistently observed in the contralateral hemisphere with a delay of 60–120 seconds following initiation of CSD. This was accompanied by a transient change in parenchymal OIS and vascular caliber. Sustained changes (30–60 minutes) in cortical burst activity and associated vascular responses were also observed in the hemisphere contralateral to CSD initiation. Saline injections evoked no CSD or any change in local field potential or OIS on either the ipsilateral or contralateral side.

Conclusion: The contralateral cerebral hemisphere can be affected in response to CSD with both rapid and sustained electrophysiological and vascular changes.

Conflict of interest
Disclosure statement:
I have received grants from Swedish Migraine Society, The Royal Physiographic Society in Lund, Sweden, The Swedish Society of Medicine, The Segerfalk foundation, Lund, Sweden and The Brain Foundation Sweden.

EHMTC-0265
POSTER SESSION E

VISUAL PROCESSING IN MIGRAINE: FACE AND SHAPE PERCEPTION

G. Gordon[1], A. Logan[2], J. Greene[1], M. Griffin[1], G. Loffler[1]

[1]*Glasgow Caledonian University, Life Sciences, Glasgow, United Kingdom*
[2]*Bradford University, Optometry and Vision Science, Bradford, United Kingdom*

Migraineurs show subtle defects, even interictally, in a range of visual tasks compared to non-migraineurs, including judgment of shape. A recent study suggested that face processing may also be affected. In order to determine the generality of a deficit in visual processing in migraine, we measured sensitivity for shape and face perception in migraineurs and compared that to a control group.

Discrimination thresholds were measured using a memory-free "odd-one-out" task on 10 migraineurs (8 migraine with aura) and 10 age-matched controls. Observers were presented with complete synthetic faces, isolated internal features (eyes, nose, mouth, eyebrows) or isolated external features (head-shape).

We found no significant difference in the mean thresholds between the migraineurs versus the control group for the full-face test (6.43 ± 0.53 v's 6.26 ± 0.66), internal features tasks (13.02 ± 1.98 v's 13.32 ± 0.68) or external shape (10.02 ± 0.78 v's 7.97 ± 0.70). Migraineurs showed a similar pattern of sensitivities to controls with full faces yielding best, head shape intermediate and internal features poorest performance. Pairwise comparison, however, showed a difference between groups: controls performed as well for the head shape as for the full faces whereas migraineurs performed significantly better for the full faces than either the head shape or the internal features ($p < 0.005$).

These results suggest intact holistic face processing in migraine. The poorer face-outline performance is in line with earlier findings of decreased sensitivity for visual shape. This supports a specific rather than a general processing deficit of visual processing in migraine.

EHMTC-0287
POSTER SESSION E

PURINERGIC RECEPTORS AS POTENTIAL ANTI-MIGRAINE TARGETS

K.A. Haanes[1], A. Labastida-Ramirez[1], C.M. Dirven[2], A.H.J. Danser[1], A. MaassenVanDenBrink[1]

[1]*Erasmus MC, Division of Vascular Medicine and Pharmacology- Department of Internal Medicine, Rotterdam, Netherlands*
[2]*Erasmus MC, Dept. of Neurosurgery, Rotterdam, Netherlands*

Nucleotides act as short term signals being released from cells in physiological and pathophysiological situations. They activate purinergic receptors that can be expressed both on arteries and nerves. We investigated whether purinergic receptors could be potential anti-migraine targets. The vasoactive compound-screening on the human middle meningeal artery has proven a good model for detecting anti-migraine candidates. We therefore first embarked on characterizing the purinergic receptors on the human middle meningeal artery, using enzymatically stable analogues and a wire myograph setup. UTPγS (P2Y2 receptor agonist) and ATPγS (P2Y2/P2X receptor agonist) caused strong contractions, whereas UDPβS (P2Y6 receptor agonist) caused minor contractions. However, as for 5-$HT_{1B/1D}$ receptors mediating the action of the triptans, all these receptors are expressed in the coronary or cerebral circulation and would cause constrictive side effects. Surprisingly, ADPβS (P2Y1/P2Y12/P2Y13 receptor agonist), which is not expressed in the coronary circulation, caused moderate contractions (E_{max} $20 \pm 5\%$ of K^+ response, $n = 4$) which, were completely inhibited by the P2Y13 selective antagonist MRS2211 (10 μM). Interestingly, P2Y13 and 5-$HT_{1B/1D}$ receptors have similar intracellular signaling. We therefore followed up by investigating if ADPβS could inhibit CGRP release from the sensory neurons surrounding the rat middle meningeal artery, similarly to triptans. Our preliminary data suggest that ADPβS indeed negatively modulates CGRP release, as observed using periarterial electrical nerve stimulation during closed skull videomicroscopy. In conclusion, the P2Y13 receptor appears to be an interesting and unexplored target with potential anti-migraine effects that seems cardiovascularly safe. Further involvement in the trigeminovascular system remains to be explored. Funding: International Headache Society.

EHMTC-0180
POSTER SESSION E

PAC-1 RECEPTOR ANTIBODY MODULATES NOCICEPTIVE TRIGEMINAL ACTIVITY IN RAT

J. Hoffmann[1,2], M. Martins-Oliveira[1,3], S. Akerman[1], W. Supronsinchai[1], C. Xu[4], P.J. Goadsby[1,3]

[1]*University of California, San Francisco, Headache Group – Department of Neurology, San Francisco, CA, USA*
[2]*University Medical Center Hamburg-Eppendorf, Department of Systems Neuroscience, Hamburg, Germany*
[3]*King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, United Kingdom*
[4]*Amgen Inc., Department of Neuroscience, Thousand Oaks, CA, USA*

Objective: To study the efficacy of a PAC-1 receptor antagonist antibody on nociceptive trigeminovascular activity in an *in vivo* model of migraine.

Background: Pituitary adenylate cyclase-activating polypeptide (PACAP) may play a role in migraine given PACAP38 is elevated in migraineurs during attacks, and infusion of PACAP38 induces migraine-like attacks attenuated by sumatriptan. Moreover, recent data indicate that migraine-relevant action may be mediated by PAC-1 receptors.

Methods: In anesthetized Sprague-Dawley rats, electrical stimulation was performed on the intact dura mater above the middle meningeal artery and nociceptive neuronal activity was recorded within the trigeminocervical complex (TCC). A PAC-1 antibody (10 $mgkg^{-1}$) or its vehicle were administered intravenously followed by a resting period of 2.5 hours. Sumatriptan (10 $mgkg^{-1}$) or its vehicle were then administered intravenously followed by a resting period of 30 minutes. Post-stimulus histograms and background activity were then recorded in the TCC over 45 minutes.

Results: PAC-1 receptor antibody induced an inhibition of stimulus-evoked nociceptive activity in the TCC ($-40 \pm 11\%$, $p = 0.016$, $n = 8$) when compared to its baseline. Likewise, sumatriptan, induced neuronal inhibition ($-30 \pm 11\%$, $p = 0.020$, $n = 8$), whereas vehicle control did not affect stimulus-evoked neuronal activity ($18 \pm 9\%$, $p = 0.136$, $n = 8$). A significant effect on spontaneous background activity was not observed.

Conclusions: The results show that targeting the PAC-1 receptor with a specific antibody reduces nociceptive neuronal activity in the TCC. The findings suggest a potential utility in the treatment of migraine.

EHMTC-0071
POSTER SESSION E

ACID SENSING ION CHANNEL 3 INHIBITERS REDUCE TRIGEMINOVASCULAR ACTIVATION

C. Holton[1], P. Goadsby[1], P. Holland[1]

[1]*King's College London, Basic and Clinical Neuroscience, LONDON, United Kingdom*

Introduction: Blockade of acid sensing ion channel-1 (ASIC1) with amiloride inhibits trigeminovascular nociceptive firing in preclinical models of migraine and may be useful in migraine with aura. Similar to ASIC1, ASIC3 is expressed in human and rodent nociceptive trigeminal fibres. ASIC3-expressing neurons project to the trigeminal nucleus caudalis (TNC) and are sensitive to changes in pH.

Aim: To establish the role of ASIC3 in a model of trigeminovascular nociception.

Method: Male Sprague-Dawley rats were anaesthetised and the parietal bone partially removed to enable electrical stimulation of the dura mater surrounding the middle meningeal artery (MMA). Extracellular recordings of neurones in the TNC were conducted in response to activation of trigeminal afferents via MMA stimulation.

Results: Intravenous infusion of 100 μg/kg APETx2 reduced nociceptive firing in the TNC in response to MMA stimulation after 30 minutes compared to saline infusion (data normalised to baseline: vehicle, 97 ± 5 %; drug, 65 ± 9; $n = 6$, $p = 0.01$), lasting for at least 60 minutes. In comparison the lower dose of 50 μg/kg did not have any significant effect on nociceptive firing.

Conclusion: ASIC3 blockade inhibits trigeminovascular nociception, building on the previously reported ASIC1 data. Taken together the data suggests the potential utility of targeting ASICs as novel migraine therapeutics.

This work is supported by FP7 project EUROHEADPAIN (no. 602633) and The Wellcome Trust.

Conflict of interest
Disclosure statement:
CH, PH have nothing to declare. PJG reports grants and personal fees from Allergan, grants and personal fees from eNeura, personal fees from Autonomic Technologies Inc, grants and personal fees from Amgen, personal fees from Bristol-Myers Squibb, personal fees from AlderBio, personal fees from Pfizer, personal fees from Impax, personal fees from Dr Reddy, personal fees from Zosano, personal fees from Colucid, personal fees from Eli Lilly, personal fees from Medtronic, personal fees from Avanir,

personal fees from Gore, personal fees from Heptares, personal fees from Nupathe, personal fees from Teva, personal fees from MedicoLegal work in headache, personal fees from Journal Watch, and personal fees from UpToDate, outside the submitted work.

EHMTC-0113
POSTER SESSION E

EFFECT OF CHRONIC ASPIRIN AND ACETAMINOPHEN ADMINISTRATIONS ON ACTIVATION OF AMYGDALA NEURONS PROVOKED BY CORTICAL SPREADING DEPRESSION

U. Jansri[1], A. Wanasuntronwong[2], A. Srikiatkhachorn[1]

[1]*Chulalongkorn University, Physiology- Faculty of medicine, Bangkok, Thailand*
[2]*Mahidol University, Oral Biology- Faculty of Dentistry, Bangkok, Thailand*

Background: Psychiatric comorbidities are common in patients with medication-overuse headache (MOH). Previous studies have demonstrated that chronic analgesic exposure can lead to an increase in cortical excitability which may increase tendency to have cortical spreading depression (CSD). The objective of this study is to investigate whether chronic analgesic exposure can also increase excitability in amygdala in CSD model.

Methods: Adult male Wistar rats were divided into three groups (10 rats each) receiving aspirin (100 mg/kg), acetaminophen (200 mg/kg) or normal saline for 30 days. Twenty-four hours after the last administration, CSD was induced by cortical application of crystals of potassium chloride. Fos expression in amygdala and trigeminal nucleus caudalis was studied by immunohistochemistry.

Results: Chronic administration of aspirin and acetaminophen led to an increase in the number of Fos-positive cells in amygdala and trigeminal nucleus caudalis. In amygdala, the Fos-positive cells were confined in the capsular region of central nucleus. An increase in the frequency of CSD waves were demonstrated in acetaminophen-treated group.

Conclusion: Our study shows that chronic analgesic exposure can increase the excitability of neurons in the capsular regions of amygdala and trigeminal nucleus caudalis. Since amygdala plays a major role in the process of emotion, the enhancement of amygdala neurons may result in the negative emotion. This process may underlie the development of psychiatric comorbidities seen in patients with medication-overuse headache.

EHMTC-0134
POSTER SESSION E

PERIPHERAL AND CENTRAL DISTRIBUTION OF THE CGRP NEUTRALIZING ANTIBODY [125I]-LY2951742 IN MALE RATS

K. Johnson[1], B. Ellis[1], D. Maren[1], S.M. Morin[1], V. Wroblewski[1], M. Johnson[1]

[1]*Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, USA*

Background: Recent clinical studies have shown that CGRP neutralizing antibodies such as LY2951742 are efficacious for migraine prevention. As such, the distribution of LY2951742 into peripheral and central tissues was determined to characterize potential sites of action. In order to determine this experimentally, radiolabelled CGRP neutralizing antibody (LY2951742) and a control IgG4 antibody were injected and their biodistribution measured.

Methods: LY2951742 and a control IgG4 antibody were radioiodinated to give specific activities of 0.11 mCi/mg and 0.16 mCi/mg, respectively. At 24, 72 and 168 hours following subcutaneous injection of either antibody (4 mg/kg) into rats, cerebrospinal fluid (CSF) and plasma were collected, followed by whole body perfusion to remove residual blood and dissection of selected tissues for quantitation of wet weight and [125I] present.

Results: No significant differences in distribution were seen for [125I]LY2951742 versus [125I]IgG4 control at any time point. The rank order of tissue levels was: dura mater = spleen > trigeminal ganglia > > hypothalamus = spinal cord = prefrontal cortex = cerebellum = CSF. [125I]LY2951742 peripheral tissue levels (dura mater, spleen and trigeminal ganglia) averaged 4–11% of plasma while all of the CNS tissues had levels that were <0.4% of plasma.

Conclusions: Distribution of the antibodies into the dura mater and the trigeminal ganglia of rats was similar to that observed in the spleen, and significantly greater than exposure in the brain or spinal cord. Although central levels of LY2951742 were relatively low, a central site of action for the observed clinical efficacy cannot be excluded.

Conflict of interest
Disclosure statement:
All authors are full-time employees of Eli Lilly and Company

EHMTC-0151
POSTER SESSION E

INVESTIGATION OF GENE-EXPRESSION PATTERN IN A CHRONIC MIGRAINE MOUSE MODEL

M. Josten[1], M. Kremser[1], H. Luebbert[1]

[1]*Ruhr-University Bochum, Animal Physiology, Bochum, Germany*

Introduction: Migraine is a chronic neurological disorder, which is thought to arise in the dura mater through sterile inflammatory processes. Research showed that the 5-$HT_{2B/2C}$ agonist meta-Chlorophenylpiperazine induces a migraine-like headache in migraineurs and that the 5-HT_{2B} receptor is present in murine dura mater. Therefore we have established a chronic migraine mouse model in which 5-HT_{2B} agonists/antagonists are able to induce/block a neurogenic inflammation in hypoxic mice. This model also serves as an animal model for pulmonary hypertension.

Further research about the behaviour of the 5-HT_2 receptors under normoxic and hypoxic conditions may lead to new insights regarding the hypoxia-induced migraine mouse model.

Aim: Characterization of the gene expression pattern of 5-$HT_{2A/2B}$ receptors in a chronic migraine mouse model.

Methods: Quantitative real time PCR of murine hypoxic and normoxic tissue.

Results: The 5-HT_{2B} receptor is significantly higher expressed ($p < 0{,}05$; $n = 50$) in dural tissue of normoxic mice compared to hypoxic mice, whereas the expression of the 5-HT_{2A} receptor is significantly elevated in lung, but not in dural tissue, of hypoxic mice.

Marker for hypoxic conditions as Angiopoietin-2 and Vascular Endothelial Growth Factor A show significantly elevated expression level in hypoxic tissue.

Conclusion: The variations of gene expression of the 5-$HT_{2A/2B}$ receptors in murine dural and lung tissue may depict an altered receptor demand under hypoxic conditions. Taken together with our findings that hypoxic mice are more sensitive to substances which induce a migraine-like headache, these results provide a promising basis for further research on the 5-$HT_{2A/2B}$ receptors in our chronic migraine mouse model.

EHMTC-0150
POSTER SESSION E

TEMPORAL PROFILES OF TRPM8 AND TRPV1 EXPRESSION IN THE TRIGEMINAL GANGLION NEURONS AFTER CFA-INDUCED INFLAMMATION

Y. Kayama[1], M. Shibata[1], T. Takizawa[1], T. Shimizu[1], H. Toriumi[1], T. Ebine[1], N. Suzuki[1]

[1]*Keio University, Neurology, Tokyo, Japan*

Background: TRPM8 (transient receptor potential melastatin subfamily member 8) is a menthol-sensitive cation channel and recent GWAS (genome-wide association study) data have disclosed that the *TRPM8* gene is related to susceptibility to develop migraine. We previously found a functional interaction between TRPM8 and TRPV1(transient receptor potential vanilloid subfamily member 1) in a cell-based experiment. Here we aim to explore the effect of inflammation on the TRPM8 and TRPV1 expression levels in the trigeminal ganglion neurons.

Methods: Twelve male C57BL/6 mice were used. Complete Freund's adjuvant (CFA, 100 μl) was applied to the bilateral whisker pads to induce local inflammation. Mice were sacrificed at 1, 3, and 7 days after the induction of inflammation. We performed *in situ* hybridization and immunohistochemistry for TRPM8 and TRPV1 using trigeminal ganglion sections. Untreated mice were used as controls.

Results: The proportions of neurons positive for *TRPM8* and *TRPV1* mRNA were 10.6 ± 6.2(mean $\pm$ SD)% and 6.5 ± 1.1% in Control, 8.0 ± 1.7% and 8.1 ± 0.3% at Day1, 6.6 ± 0.7% and 7.9 ± 2.5% at Day3, 9.2 ± 0.2% and 8.9 ± 1.3% at Day 7, respectively. The proportions of TRPV1-positive cells in the entire TRPM8-positive neurons (double-immunoreactive for TRPM8 and TRPV1) were 36.5 ± 16.1% in Control, 17.9 ± 16.7% at Day1, 13.9 ± 13.5% at Day3, and 19.5 ± 0.8% at Day7. There were no statistically significant differences in between-groups comparisons.

Discussion: The results imply that the CFA-induced local inflammation in the trigeminal area does not significantly affect the transcriptional activity or co-expression state of TRPM8 and TRPV1 in the trigeminal ganglion neurons.

EHMTC-0200
POSTER SESSION E

SODIUM CHANNEL ROLES IN ATTENUATION OF CORTICAL SPREADING DEPRESSION RELATED NEUROLOGICAL CHANGES

B. Khodaie[1,2], A.A. Iotfinia[1,2], M. Ahmadi[1,2], M. Iotfinia[1,3]

[1]*Shefa Neuroscience Research Center, Neuroscience, Tehran, Iran*
[2]*Islamic Azad university, pathology, Karaj, Iran*
[3]*Shahid Beheshti university, medicine, Tehran, Iran*

Introduction: Cortical spreading depression (CSD) refers to waves of mass cellular depolarization associated with distribution of ion and water, which followed by a massive depression of neuronal bioelectrical activity. CSD is described as a self-maintained cycle of depolarization, which is initiated by elevated potassium and/or glutamate in the extracellular space. Both activation of Na+ channel current induced action potentials and NMDA-controlled ion channels are involved in pathophysiology of CSD. CSD plays a dramatic role in migraine and epilepsy, and repetitive CSD can induce neural cell injuries in different brain regions, followed by cognitive defects.

Materials and Methods: In the present study, 36 Wistar rats were treated with intraperitoneal injection of Carbamazepine as Na+ channel blockers before induction of SD by direct injection of KCl through guide cannula to investigate the role of sodium channels in chains of responses, which lead to SD-induced cell damages and memory impairment. Shuttle test and histological assessment on Hippocampal region was used to assess behavioural and neurobiological effects of treatment.

Results: Data from the histopathological study showed significant reduction in mean number of necrotic and apoptotic cell in the hippocampal region. Shuttle test revealed that sodium channel blockade could prevent SD induced memory impairment.

Conclusion: We conclude that action potentials play a significant role in SD wave generation and/or depolarization wave propagation, as blocking sodium channels attenuated the neurological and behavioural effects of SD. Blockade of Na+ channel could interfere with CSD, and may have efficacy as a therapeutic agent for related neurological disorders such as epilepsy.

EHMTC-0359
POSTER SESSION E

CHARACTERIZATION OF THE BINDING OF THREE ANTI-CGRP ANTIBODIES EFFECTIVE IN PREVENTING MIGRAINE: A COMPARATIVE CASE STUDY OF ALD403, LY-2951742, TEV-48125

J. Latham[1], C. Karasek[2], E. Ojala[3], D. Allison[2]

[1]*Alder Biopharmaceuticals Inc, Research, Bothell, USA*
[2]*Alder Biopharmaceuticals, Research, Bothell, USA*
[3]*Alder Bopharmaceuticals, Research, Bothell, USA*

Monoclonal antibodies have emerged as an important new mode in preventive treatment of migraine. As part of expanding our understanding of the differentiation of CGRP-directed antibodies, we have characterized the CGRP binding kinetics of three monoclonal antibodies (ALD403, TEV-48125, and two versions of LY-2951742, a & b), shown to be effective in migraine prevention. To directly compare the intrinsic CGRP binding features of these antibodies, all were formatted using the same IgG1/kappa constant regions and expressed using mammalian protein production techniques. Using well-established technology (surface plasmon resonance) for characterizing the binding of these antibodies to CGRP, our studies established that these antibodies have very differentiated characteristics from one another that may contribute to their observed clinical efficacy. In our head to head studies of ALD403 versus TEV-48125, we found that ALD403 engages CGRP twice as rapidly as TEV-48125 and has a comparable off-rate. On the other hand, LY-2951742a/LY-2951742b both display fast association with CGRP but have markedly faster rates of dissociation compared to both ALD403 and TEV-48125, leading to higher steady state levels of free CGRP ligand.

These studies show that ALD403 displays a rapid engagement of CGRP to inactivate the peptide and an extremely slow dissociation, properties that we believe contribute to the rapid onset and long-lived clinical activity we observe in an on-going single dose trial of ALD403 in chronic migraine. The data support our conclusion that not all antibodies directed against CGRP are equal and that with optimized properties clinical differentiation can be observed.

Conflict of interest
Disclosure statement:
I am an employee and shareholder in Alder Biopharmaceuticals

EHMTC-0326
POSTER SESSION E

PROPHYLACTIC EFFECT OF SODIUM VALPROATE ON SPREADING DEPRESSION INDUCED BY KCL IN JUVENILE RATS

A.A. Lotfinia[1,2]

[1]*shefa neuroscience research center, neuroscience, Tehran, Iran*
[2]*Iranian headache association- Sina hospital, headache, Tehran, Iran*

Background: Cortical spreading depression (CSD) is a transient depolarization of neurons and glial cells, which slowly propagate through the brain and cause cell damage when it chronically applies. Aim: In the present study the effect of repetitive SD induction before and after treatment with sodium valproate on hippocampal brain region were evaluated.

Materials and Methods: SD was induced by applying KCl (3 M) to the frontal cortex of right hemisphere without any perforation of Dura matter in male juvenile rats for four weeks. Saline solution was injected in a same manner in sham group. Also intraperitoneally treatment with sodium valproate (25 mg kg−1 I.P) one hour before induction of SD was performed in drug-treated group. KCl injection was monitored with electroencephalographic recording to confirm SD induction. After four weeks rats were decapitated and their brains were removed for histopathological assessment.

Results: Four weeks application of KCl in SD group induced necrotic or apoptotic cells and the number of dark neurons in SD group was significantly increased in comparison with drug-treated rats. And also the mean number of dark neurons in SD group was significantly increased in compare to sham group.

Conclusion: Repetitive SD induction could cause dark neuron in different brain region. Prophylactic administration of sodium valproate could effectively reduce propagation of SD wave and also cell damage in hippocampus. These data suggest the preventive effect of sodium valproate on neurons from cell injury.

EHMTC-0361
POSTER SESSION E

MIDBRAIN REWARD PATHWAY AND PREMONITORY FOOD CRAVING IN MIGRAINEURS: STUDIES IN AN ANIMAL MODEL

M. Martins-Oliveira[1,2], S. Akerman[1], P.R. Holland[2], P.J. Goadsby[1,2]

[1]*University of California San Francisco, Headache Group-Department of Neurology, San Francisco- CA, USA*
[2]*King's College London – UK, Department of Basic and Clinical Neuroscience- Institute of Psychiatry- Psychology and Neuroscience, London, United Kingdom*

Background: Imaging studies in migraineurs show increased brain activation including the ventral tegmental area (VTA) during the premonitory phase. Premonitory symptoms can include hunger or food craving and the dopaminergic neurons in the midbrain VTA are involved in hedonic feeding mechanisms and pain modulation.

Objective: To determine the effect of chemical manipulation of the VTA on the trigeminocervical complex (TCC) neuronal activity in response to nociceptive activation, as well as the effect on glucose homeostasis following the stimulation.

Methods: Rats were anesthetized and the parietal bone was removed over the midbrain and the middle meningeal artery for dura mater electrical stimulation. Using *in vivo* electrophysiology, TCC neurons were recorded before and after microinjection into the VTA with a $GABA_A$ receptor antagonist, glutamate, naratriptan or sterile water as vehicle control. Glycemic levels were measured before and after microinjection of drugs.

Results: Stimulus-evoked neuronal firing in the TCC was significantly reduced by $GABA_A$ receptor antagonist ($p < 0.001$, max inhibition 22%), glutamate ($p < 0.001$, max inhibition 38%) and naratriptan ($p < 0.01$, max inhibition 39%). Local VTA microinjection of a $GABA_A$ receptor antagonist, glutamate and naratriptan significantly decreased blood glucose levels after 60 minutes ($p < 0.05$). Vehicle control alone had no significant effect on TCC neuronal firing or blood glucose levels.

Conclusion: These results show that reward-related pathways including the VTA are involved in modulating the transmission of trigeminal nociceptive inputs, as well as central glucose homeostasis. Disrupted appetite regulation may occur during the premonitory phase through dysfunctional VTA activity, which could potentially affect downstream pain modulation pathways.

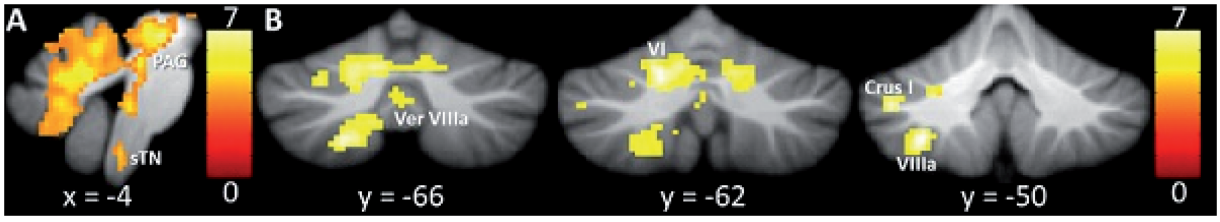
EHMTC-0160
POSTER SESSION E

THE ROLE OF THE CEREBELLUM IN TRIGEMINAL NOCICEPTION

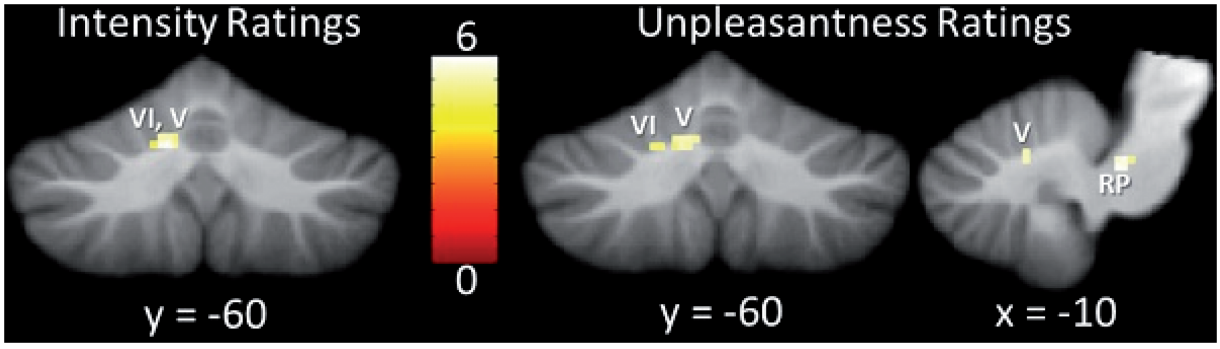
J. Mehnert[1], A. May[1]

[1]*University Medical Center Hamburg-Eppendorf, Institute of Systems Neuroscience, Hamburg, Germany*

Pathologies involving the trigeminal nervous system like migraine might be influenced by cerebellar modulation, known to play a crucial role in nociception [1]. To analyze cerebellar activation, modulation and connectivity during trigeminal pain, 54 healthies underwent fMRI while 15 chemosensory, nasal, painful stimuli were applied [2]. Subjects rated intensity and unpleasantness of each trial and their data was analyzed according to a brainstem and cerebellar specific atlas and protocol [3] leading to activations in the spinal trigeminal nucleus (sTN), periaqueductal gray (PAG) and >5% of the cerebellum, primarily regions V, VI, Crus_I and Vermis_IIIa (Figure 1).



Intensity and unpleasantness modulated VI, V and the rostral pons (Figure 2).



Brainstem-cerebellar coupling was increased between sTN and VI, as well as I_IV; cerebellar coupling increased to PAG, substantia nigra and thalamus.Our results underpin the cerebellar involvement in trigeminal nociception due to its vigorous activation, potential of modulating sensation, and increased coupling with important nociceptive hubs.

References:

1. Ruscheweyh (2014). Altered experimental pain perception after cerebellar infarction. Pain.
2. Stankewitz (2010). A new trigemino-nociceptive stimulation model for event-related fMRI. Cephalalgia.
3. Diedrichsen (2009). A probabilistic MR atlas of the human cerebellum. Neuroimage.

EHMTC-0284
POSTER SESSION E

CGRP RELEASE AND VASODILATORY ACTIONS IN THE TRIGEMINOVASCULAR SYSTEM

K. Messlinger[1], M. Dux[2], C. Will[1], M.M. Fischer[1]

[1]*Institute of Physiology & Pathophysiology, University of Erlangen-Nürnberg, Erlangen, Germany*
[2]*Institute of Physiology, University of Szeged, Szeged, Hungary*

Primary headaches are accompanied by the release of calcitonin gene-related peptide (CGRP) from activated meningeal afferents increasing intracranial blood flow. We aimed to localize the sites of CGRP release, record meningeal and medullary blood flow and measure intracranial arterial diameter in anaesthetized rats.

The exposed cranial dura mater was stimulated by electrical pulses of C-fiber strength or by 60 mM KCl or sodium sulfide inducing nitroxyl formation. Blood flow in the dura mater and the medullary brainstem was recorded by laser Doppler flowmetry. The diameter of dural and medullary blood vessels was monitored by video microscopy and measured using a plugin for ImageJ. Samples of femoral arterial plasma and cerebrospinal fluid (CSF) collected from the cisterna magna were analyzed for CGRP concentrations using an ELISA.

Electrical stimulation elevated meningeal and medullary blood flow and increased the diameter of arteries, which was abolished after application of the CGRP receptor antagonist olcegepant. Electrical stimulation and KCl increased CGRP in femoral plasma and CSF. Intravenous infusion of sodium sulfide also induced blood flow increases and vasodilatation in medullary arteries. After injection of lidocaine into the trigeminal ganglion electrically evoked medullary blood flow increases were reduced.

The methods allow estimating peripheral and central trigeminal activity by observing CGRP release and concomitant vasodilatory actions, which are increased upon stimulation of meningeal afferents. CGRP in plasma may mainly originate from the dura mater, while CGRP in the CSF is likely released from central terminals of trigeminal afferents.

EHMTC-0026
POSTER SESSION E

MODULATORY EFFECT OF NITROGLYCERIN ON THE TRYPTOPHAN 2,3-DIOXYGENASE AND INDOLAMINE 2,3-DIOXYGENASE EXPRESSION IN THE RAT CERVICAL SPINAL CORD

G. Nagy-Grocz[1], Z. Bohár[2], K.F. Laborc[3], E. Spekker[3], A. Fejes-Szabó[3], L. Vécsei[4], Á. Párdutz[3]

[1]*University of Szeged, Department of Neurology and Faculty of Health Sciences and Social Studies, Szeged, Hungary*
[2]*University of Szeged, MTA-SZTE Neuroscience Research Group, Szeged, Hungary*
[3]*University of Szeged, Department of Neurology, Szeged, Hungary*
[4]*University of Szeged, MTA-SZTE Neuroscience Research Group and Department of Neurology, Szeged, Hungary*

Migraine belongs to the group of primary headaches, and it is one of the most prevalent neurological diseases, which affects 16% of the total population. Despite the intensive research, the exact pathomechanism is not known, but the role of glutamate seems pivotal. One of the endogenous glutamate receptor antagonist is kynurenic acid (KYNA), which is synthesized from L-kynurenine (L-KYN). Tryptophan 2,3-dioxygenase (TDO) and indolamine 2,3-dioxygenase (IDO) are the key enzymes in the kynurenine pathway, converting L-tryptophan to N-Formylkynurenine – a precursor of L-KYN.

Administration of nitroglycerin (NTG) is one of the human and animal models of migraine, which leads to activation and sensitization of the trigeminal system. Our previous findings showed that NTG influences the kynurenine-system.

The aim of our experiments was to determine the possible modulatory role of NTG on the other metabolizing enzymes of L-KYN: TDO and IDO.

Half of the animals ($n = 5$) received intraperitoneal NTG-injection (10 mg/kg), the remaining rats ($n = 5$) got the vehicle of the drug. Four hours later the animals were perfused transcardially and the cervical part of spinal cord (C1-C2) was removed for Western blotting.

Four hours after the NTG-injection of rats, the expression of TDO and IDO 1 and 2 in the C1-C2 was decreased.

Our data shows, that the NTG is able to decrease the initiating enzymes of the kynurenine pathway and thus possibly influencing the downstream events of the cascade, modifying endogenous glutamate agonists and antagonists

levels. This phenomenon might play a role in the development of trigeminal activation and sensitization in animals.

EHMTC-0203
POSTER SESSION E

MODELLING MIGRAINE USING INDUCED HUMAN PLURIPOTENT STEM CELLS

P. Pettingill[1], G. Weir[1], G. Duggal[1], T. Lalic[1], Z. Cader[1]

[1]*Weatherall Institute of Molecular Medicine, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom*

Migraine is a complex and disabling headache disorder that affects 15% of the population. It is characterised by severe episodes of throbbing headache pain which are often accompanied with autonomic symptoms. The mechanisms of migraine pathophysiology are complex and involve multiple brain structures and pathways. Activation of the trigeminovascular system is a central step in the development of migraine. In particular it is nociceptors residing in the trigeminal ganglia that innervate the head and face that are activated during a migraine attack.

We have identified a rare loss-of function mutation in TRESK (F139WfsX24), a two-pore potassium channel in patients with migraine and aura. TRESK is highly expressed in nociceptors which are over active in migraine. We hypothesise that TRESK is responsible for modulating the resting membrane potential and dampening neuronal responsiveness to stimuli and that this mutation leads to nociceptors to become hyper-excitable.

We have established an *in vitro* model of migraine using human induced pluripotent stem cells (iPSC) differentiated into functional nociceptors to represent a novel platform for disease modelling. Nociceptors derived from migraine-F139WfsX24 lines have reduced outward potassium currents and exhibit features of hyper-excitability including reduced rheobase and increased repetitive firing to a supra-threshold stimulus. We have generated an isogenic line, correcting the F139WfsX24 mutation, which we hope will reverse the hyper-excitable phenotype observed in this study. This will confirm that neuronal-hyperexcitability in these patients is attributed to a loss of TRESK activity.

EHMTC-0319
POSTER SESSION E

DELTA OPIOID RECEPTOR AS A TARGET FOR MIGRAINE – CGRP CO-EXPRESSION AND INHIBITION OF MEDICATION OVERUSE HEADACHE

A. Pradhan[1], L. Segura[1], A. Tipton[1]

[1]*University of Illinois at Chicago, Psychiatry, Chicago, USA*

Migraine is an extraordinarily common brain disorder for which therapeutic options continue to be limited. We have previously demonstrated that in preclinical animal models, delta opioid receptor agonists may be promising targets for the treatment of migraine. Delta agonists effectively inhibit cortical spreading depression, as well as nitroglycerin-induced hyperalgesia and negative affect. A better understanding of how delta opioid receptor modulates migraine mechanisms would encourage future development of this target. The neuropeptide, calcitonin gene related peptide (CGRP) plays a pivotal role in the induction and maintenance of migraine, primarily through the peripheral afferents projecting from the trigeminal ganglia. The aim of this study was to characterize the expression of delta opioid receptor in trigeminal ganglia, and on CGRP-expressing neurons specifically. To visualize the delta opioid receptor, we used knockin mice in which the endogenous receptor was replaced by a fluorescent tagged delta opioid receptor (DOR-eGFP). We observed a significant population of trigeminal ganglia which co-expressed CGRP with DOR-eGFP. This data suggests that delta agonists may produce their anti-migraine effects by directly modulating CGRP-expressing ganglia. As a further goal of this study we also tested delta agonists in a model of sumatriptan-induced medication overuse headache (MOH). In this case, C57BL6 mice were treated chronically with sumatriptan for 11 days, which produced severe mechanical hypersensitivity. The delta agonist, SNC80, inhibited this hyperalgesia, and suggests that delta agonist could be an effective strategy for managing MOH. Together, this work provides further evidence that delta opioid receptors are promising targets for migraine treatment.

Conflict of interest
Disclosure statement:
I have a contract with Trevena Inc.

EHMTC-0101
POSTER SESSION E

CHARACTERIZATION OF A NOVEL MOUSE MODEL OF POST-TRAUMATIC HEADACHE

L. Segura[1], H. Krishnan[1], S. Pandey[1], A. Pradhan[1]

[1]*University of Illinois at Chicago, Department of Psychiatry, Chicago, USA*

Mild traumatic brain injury (mTBI) impacts millions of people worldwide causing behavioral, cognitive, and emotional deficits. Post-traumatic headache (PTH) is the most common and long-lasting impairment observed following mTBI. Often persisting for up to a year, PTH is most frequently associated with migraine characteristics. The mechanisms underlying the progression of mTBI to PTH are not fully understood. The aim of this study was to develop a novel mouse model of PTH, by combining the closed head weight drop mTBI method and the nitroglycerin chronic migraine model. To induce mTBI, a 30 gram weight was dropped onto intact crania of mildly-anesthetized C57Bl6/J male mice. Mechanical responses to chronic-intermittent administration of nitroglycerin was determined 2, 4, and 12 weeks post-mTBI. Low (0.1 mg/kg) and high (10 mg/kg) doses of nitroglycerin were used, as only the high dose has been reported to produce basal hypersensitivity in naïve mice. The mTBI group showed basal hypersensitivity to both low and high doses of nitroglycerin, unlike sham controls which were only sensitive at the high dose. Additionally, following the last injection of nitroglycerin, the time to recover mechanical responses to control levels was significantly longer in the mTBI group compared to shams. mTBI in mice appears to produce increased sensitivity to migraine-associated pain induced by nitroglycerin, and this procedure may be used to model PTH. Gene expression studies are underway to explore changes in CGRP and PACAP associated with mTBI and chronic nitroglycerin.

EHMTC-0220
POSTER SESSION E

GASTROINTESTINAL MOTILITY IN FAMILIAL HEMIPLEGIC MIGRAINE MICE

A. Sprouse Blum[1], B. Lavoie[1], K. Eikermann-Haerter[2], E. Tolner[3], A. van den Maagdenberg[3], S.P. Chen[2], G. Mawe[1], R. Shapiro[1]

[1]*University of Vermont, Department of Neurological Sciences, Burlington, USA*
[2]*Massachusetts General Hospital, Department of Radiology, Massachusetts, USA*
[3]*Leiden University Medical Center, Departments of Human Genetics & Neurology, Leiden, Netherlands*

Background: Migraine is associated with nausea, vomiting, and early satiety, and is co-morbid with multiple functional bowel disorders including gastroparesis. We sought to determine if Familial Hemiplegic Migraine type 1 is associated with upper gastrointestinal dysmotility in a monogenic migraine mouse model.

Methods: Familial Hemiplegic Migraine type 1 female homozygous CACNA1A S218L knock-in mice (FHM1), and their wild-type littermates (WT) were studied. Upper gastrointestinal motility was measured by gavage of a bolus of non-absorbable fluorescent tracer into the stomach, euthanizing the animal fifteen minutes later, and then quantifying fluorescence in the stomach and in the small intestine dissected into ten segments of equal length. Primary endpoints were: 1) percentage of tracer bolus that progressed from the stomach into the small intestine (gastric emptying) and 2) small intestinal segment containing the mode fluorescence of the progressed bolus (geometric center). In further experiments, we repeated this protocol following pretreatment with subcutaneous nitroglycerin (or vehicle), an established migraine trigger.

Results: No difference in gastric emptying was observed between FHM1 mice and WT littermates ($p = 0.13$). However, geometric center of the gavaged bolus occurred more proximally in FHM1 vs. WT mice (1.77 vs. 2.26; $p = 0.037$) indicating possible impairment of small bowel motility. No difference in gastric emptying or geometric center was found following subcutaneous pretreatment with nitroglycerin vs. saline.

Conclusions: There is minimal evidence for a delayed gastrointestinal motility phenotype in FHM1 mice, and no evidence that a delay can be induced using nitroglycerin with this assay.

Conflict of interest
Disclosure statement:

Grants from Association of Migraine Disorders/Migraine Research Foundation, EUROHEADPAIN, American Heart Association, Massachusetts General Hospital (Claflin Distinguished Award)

EHMTC-0032
POSTER SESSION E

SUBSTANCE P (NK1) RECEPTOR INHIBITION DOES NOT PREVENT CORTICAL SPREADING DEPRESSION IN A RODENT MODEL OF MIGRAINE AURA

L. Strother[1], C. Holton[1], P. Holland[1], P.J. Goasby[2]

[1]*King's College London, Basic and Clinical Neuroscience, LONDON, United Kingdom*
[2]*King's College London, NIHR-Wellcome Trust Clinical Research Facility, LONDON, United Kingdom*

Migraine aura is a parallel neurological phenomenon to migraine and manifests commonly as visual disturbances. Cortical spreading depression (CSD) is accepted as the preclinical correlate of migraine aura and is characterised by a wave of spreading cortical excitation followed by a cortical depression. Early clinical trials with Substance P (NK1) receptor antagonists failed to treat acute migraine; however, its potential in migraine aura is unclear. As such, we investigated the effect of the specific NK1 receptor antagonist fosaprepitant on CSD in rats.

Male Sprague-Dawley rats ($N = 17$) were anesthetized using isoflurane and surgically prepared for monitoring steady state cortical potentials (DC) and cerebral blood flow (CBF) changes representative of CSD. Anaesthesia was maintained via propofol (12.5–15 mg/kg/hr). CSDs were induced subdurally by mechanical (needle prick) or chemical (1 M KCl) application. Rats received either fosaprepitant (1 mg/kg, i.v.) or saline control 20 minutes prior to CSD induction and were then monitored for a further one hour period.

CSDs triggered by both mechanical and chemical means were not significantly reduced by fosaprepitant. Fosaprepitant failed to inhibit mechanically induced CSDs in 5 out of 6 animals tested ($x^2 = 1.00$; $p > 0.05$), while chemical induction produced an average of 8 versus 9 CSD events in treated or saline control animals respectively ($t_7 = 0.53$; $p > 0.05$).

In conclusion, acute blockade of Substance P (NK1) receptors has no impact on mechanically or chemically induced CSD in a rat model of migraine aura.

This work is supported by FP7 project EUROHEADPAIN (no. 602633) and The Wellcome Trust.

Conflict of interest
Disclosure statement:
PJG reports, unrelated to this report, grants and personal fees from Allergan, grants and personal fees from eNeura Inc, personal fees from Autonomic Technologies Inc, grants and personal fees from Amgen Inc, personal fees from Alder Biopharmaceuticals, personal fees from Pfizer Inc, personal fees from Dr Reddy's Laboratories, personal fees from Zosano Pharma Corporation, personal fees from Colucid Pharmaceuticals, Ltd, personal fees from Eli-Lilly and Company, personal fees from Avanir Pharmaceuticals, personal fees from WL Gore & Associates, personal fees from Heptares Therapeutics, personal fees from Nupathe Inc, personal fees from Teva, personal fees from Cipla Ltd, personal fees from Ajinomoto Pharmaceuticals Co, personal fees from Akita Biomedical, personal fees from Wells Fargo, personal fees from Ethicon, US, personal fees from EMKinetics, personal fees from Promius Pharma, personal fees from Supernus, personal fees and other from Trigemina, personal fees from MedicoLegal work, personal fees from Journal Watch, personal fees from Up-to-Date, outside the submitted work In addition, Dr. Goadsby has a patent Magnetic stimulation for headache pending

EHMTC-0258
POSTER SESSION E

INFLUENCE OF CRANIOFACIAL NOCICEPTIVE PROCESS ON DEVELOPMENT OF CORTICAL SPREADING DEPRESSION

W. Supronsinchai[1], N. Puttasanakul[1], N. Khanoowatthana[2], A. Srikiatkhachorn[1]

[1]*Chulalongkorn University, Physiology, Bangkok, Thailand*
[2]*Chulalonkorn University, Physiology, Bangkok, Thailand*

Background: Intense sensory stimulation especially bright light is a known trigger for migraine attack. Although, the role of other sensory modalities in triggering migraine is not well understood, clinical observations demonstrate the possible link between craniofacial nociception and migraine attacks.

Objective: To demonstrate the relationship between craniofacial nociception and development of cortical spreading depression.

Methods: The study comprised two experiments. In the first experiment, formalin was subcutaneously injected at forehead of Wistar rats. One hour after injection, CSD was elicited in rat brains using cortical application of KCl. Electrocorticogram and cortical blood flow was recorded. Saline injection was used as a control group. In the second

experiment, lidocaine was microinjected into ventral posteromedial nucleus of thalamus, the principle nucleus conveying the information concerning craniofacial nociception, prior to CSD induction.

Results: Injection of formalin led to a significant increase in CSD frequency as compared to the control group. The number of depolarization shift in the formalin and control groups were 15 + 2 and 12 + 2, respectively. On the contrary, inhibition of somatosensory thalamic neurons resulted in a reduction in CSD frequency. The number of depolarization shift in the lidocaine and control groups were 9 + 2 and 12 + 2, respectively. Parallel changes in cortical blood flow were observed.

Conclusion: Our results show that input from somatosensory thalamus has influence on cortical excitability. Activation of somatosensory thalamus via craniofacial nociception can increase the susceptibility while inhibition of this nucleus can decrease the susceptibility.

EHMTC-0351
POSTER SESSION E

EFFECTS OF A KYNURENIC ACID (KYNA) ANALOGUE IN NITROGLYCERIN-INDUCED HYPERALGESIA: POTENTIAL ANTI-MIGRAINE MECHANISMS

C. Tassorelli[1], R. Greco[2], C. Demartini[3], A.M. Zanaboni[4], E. Redavide[5], S. Pampalone[5], F. Blandini[5], L. Vecsei[6], G. Nappi[7]

[1]*C. Mondino National Neurological Institute and University of Pavia, Headache Science Centre and Dept. of Brain and Behavioral Sciences, Pavia, Italy*
[2]*"C. Mondino" National Neurological Institute, Laboratory of Neurophysiology of Integrative Autonomic Systems-Headache Science Centre-, Pavia, Italy*
[3]*C. Mondino National Neurological Institute and University of Pavia, Laboratory of Neurophysiology of Integrative Autonomic Systems- Headache Science Centre, Pavia, Italy*
[4]*University of Pavia, Dept. of Brain and Behavioral Sciences, Pavia, Italy*
[5]*"C. Mondino" National Neurological Institute, Laboratory of Neurobiology, Pavia, Italy*
[6]*Albert Szent-Györgyi Clinical Center and University of Szeged, Department of Neurology, Szeged, Hungary*
[7]*"C. Mondino" National Neurological Institute, Headache Science Centre-, Pavia, Italy*

Trigeminal sensitization represents a major mechanism underlying migraine attacks and their recurrence. Systemic nitroglycerin (NTG) administration provokes spontaneous-like migraine headaches and the facilitation of pain transmission at the spinal level witnessed by a hyperalgesic behavioural response to the formalin test. Kynurenic acid (KYNA), an endogenous regulator of glutamate activity, and its analogues attenuate NTG-induced activation of neurons in the trigeminalis caudalis (NTC). In this study, we investigated the effect of a KYNA analogue, SZR-72, on NTG-induced hyperalgesia at the plantar and the orofacial formalin tests. SZR-72 abolished NTG-induced hyperalgesia in the hindpaw and in the trigeminal area. NTG-induced hyperalgesia in the trigeminal area was associated to the transcriptional activation of CGRP, nNOS and cytokines in the trigeminal ganglion, cervical spinal cord and medulla. In addition, NTG administration was linked to a decrease in CGRP-positive fibers and an increase in nNOS protein in the NTC, both of which were blocked by SZR-pretreatment. These findings demonstrate that glutamate activity is involved in mediating hyperalgesia in an animal model specific for migraine. Its inhibition blocks the release of CGRP and the synthesis of endogenous NO and of cytokines.

EHMTC-0185
POSTER SESSION E

CHRONIC SYMPATHETIC ACTIVATION IN MIGRAINE HEADACHE: UNIQUE TO MIGRAINE OR COMMON TO SYMPATHETIC NERVOUS SYSTEM DISORDERS?

M. Thomas[1]

[1]*Whitby, Canada*

The mechanisms of autonomic nervous system dysfunction in migraine are not well understood. It has been proposed that chronic/excessive SNS activation contributes to migraine episodes by rapidly depleting norepinephrine stores while increasing the release of dopamine, adenosine triphosphate, adenosine and prostaglandins. Evidence for chronic/excessive SNS activation in migraineurs has been demonstrated by research showing significantly colder hands in female migraineurs between headaches than healthy controls.

A recent audit of standardized clinical assessment data collected over several years during a 26 minute psychophysiological stress assessment revealed interesting results which shed light on this dilemma. Data included hand skin temperature (HST), frontal sEMG, HR, SCR, respiration rate and the Anxiety Sensitivity Index. Ten female migraineurs (MH), 10 females with muscle contraction headache (MCH) and 10 females with panic disorder (PD) were compared.

MCH controlled for the effects of having a distressing non-migraine/non SNS headache disorder. PD controlled for

the effects of having a distressing, non-headache, SNS disorder.

Between-group differences for age and most test scores were non-significant.

A repeated measures ANOVA showed a significant between-groups difference for HST. The MCH group was in the normal range while the MH and PD groups were well below normal and significantly colder than the MCH group.

The MH group results suggest chronic SNS arousal. However the PD group's similar result and the MCH normal result suggests that chronic SNS arousal is a characteristic of SNS disorders and is not unique to migraine. Alone, it appears insufficient to explain migraine episodes. Additional factors are proposed.

EHMTC-0121
POSTER SESSION E

THE ROLE OF THE LOCUS COERULEUS IN REGULATING TRIGEMINOVASCULAR NOCICEPTION

M. Vila-Pueyo[1], L. Strother[1], P.J. Goadsby[1], P.R. Holland[1]

[1]*King's College London, Basic and Clinical Neuroscience-Institute of Psychology- Psychiatry and Neuroscience, London, United Kingdom*

The noradrenergic locus coeruleus (LC) is involved in arousal and may play a role in migraine.

We aimed to test whether the LC could modulate neurons responsive to trigeminovascular nociceptive activation.

Sprague-Dawley rats ($n = 24$) were anesthetized with isoflurane and maintained with propofol infusion (33–50 mg/kg/h). The interparietal bone was drilled for electrical stimulation or lesioning of the LC, the parietal bone was removed for electrical stimulation of the dura mater overlying the middle meningeal artery and a C1 laminectomy was performed to record from trigeminocervical complex (TCC) neurons. Following baseline responses to dural stimulation, the LC was electrically stimulated or lesioned and TCC neural responses recorded for up to 1 hour.

Stimulation of the LC significantly reduced nociceptive dural-evoked Aδ-fiber neuronal firing in the TCC ($F_{6,90} = 4.361$, $p = 0.001$), reaching a maximum reduction to 67% at 15 minutes. However, control LC electrode placement significantly reduced TCC neuronal responses to 75% ($F_{6,90} = 4.361$, $p = 0.001$), indicating a potential mechanical disruption of the LC. To test further the impact of disrupted LC signaling, the LC was lesioned resulting in a significant reduction of TCC neuronal responses to 42% from initial baseline 60 minutes post-lesion ($t_5 = 4.223$, $p = 0.008$).

The results demonstrate a role for the LC in the modulation of trigeminal nociceptive processing that may provide a potential mechanistic link between sleep-wake disruption and migraine.

Conflict of interest
Disclosure statement:
MV-P, LS and PRH report no conflict of interest. PJG reports, unrelated to this abstract, grants and personal fees from Allergan, grants and personal fees from eNeura Inc, personal fees from Autonomic Technologies Inc, grants and personal fees from Amgen Inc, personal fees from Alder Biopharmaceuticals, personal fees from Pfizer Inc, personal fees from Dr Reddy's Laboratories, personal fees from Zosano Pharma Corporation, personal fees from Colucid Pharmaceuticals, Ltd, personal fees from Eli-Lilly and Company, personal fees from Avanir Pharmaceuticals, personal fees from WL Gore & Associates, personal fees from Heptares Therapeutics, personal fees from Nupathe Inc, personal fees from Teva, personal fees from Cipla Ltd, personal fees from Ajinomoto Pharmaceuticals Co, personal fees from Akita Biomedical, personal fees from Wells Fargo, personal fees from Ethicon, US, personal fees from EMKinetics, personal fees from Promius Pharma, personal fees from Supernus, personal fees and other from Trigemina, personal fees from MedicoLegal work, personal fees from Journal Watch, personal fees from Up-to-Date, outside the submitted work In addition, Dr. Goadsby has a patent Magnetic stimulation for headache pending.

EHMTC-0434
POSTER SESSION E

LASMIDITAN INHIBITS TRIGEMINOVASCULAR NOCICEPTIVE TRANSMISSION

M. Vila-Pueyo[1], L. Strother[1], K. Page[2], H. Loaraine[2], J. Kovalchin[3], P.J. Goadsby[4], P.R. Holland[1]

[1]*Headache Group, Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology and Neuroscience, King's College London. UK*
[2]*Asterand Bioscience, Hertfordshire. UK*
[3]*Colucid Pharmaceuticals Inc., Cambridge. USA*
[4]*NIHR-Wellcome Trust Clinical Research Facility, King's College London. UK*

Targeted 5-HT1F receptor agonists have emerged as potential centrally acting therapeutic agents for migraine.

Lasmiditan is a novel highly specific 5-HT1F receptor agonist currently undergoing Phase 3 pivotal clinical trials for the acute treatment of migraine.

We have studied the effects of intravenous (IV) lasmiditan on dural-evoked trigeminovascular nociception and have mapped the tissue specific expression of the 5-HT1F receptor mRNA.

Male adult Sprague Dawley Rats (N = 16) were randomly divided into two groups, anaesthetised with isoflurane (5%) and cannulated for measurement of blood pressure, administration of experimental drugs and supplementary anaesthesia (propofol; 33–50 mg/kg/hr). A craniotomy provided access to the underlying dura mater surrounding the middle meningeal artery and a hemi-laminectomy provided access to the trigeminocervical complex (TCC). Trigeminovascular afferents responsive to stimulation of the ophthalmic dermatome were activated via a bipolar stimulating electrode placed on the dura mater and the TCC neural responses recorded via a microelectrode following lasmiditan (5 mg/kg) IV administration or vehicle. 5-HT1F receptor mRNA-expression was measured in multiple human tissues via qRT-PCR.

Lasmiditan significantly inhibited TCC dural-evoked responses demonstrating clear efficacy for the inhibition of trigeminovascular nociception ($F(3.7, 51) = 4.95$; $P = 0.002$) compared to vehicle. Investigation of receptor mRNA levels in human tissues revealed highest expression in multiple cortical regions followed by subcortical nuclei suggesting potential central sites of action.

The results support the CNS mechanism of action and anti-migraine therapeutic potential of lasmiditan. We further highlight several potential central sites of action based on lasmiditan's brain penetrability that demonstrate robust 5-HT1F expression including cortical, hypothalamic and brainstem regions.

Conflict of interest
The study was conducted in collaboration with Colucid Pharmaceuticals Inc. for whom JK is an employee

EHMTC-0075
POSTER SESSION E

THE EFFECT OF CHRONIC ACETAMINOPHEN AND ASPIRIN ON ANXIETY-LIKE BEHAVIOR AND AMYGDALA ACTIVITY

A. Wanasuntronwong[1], U. Jansri[2], A. Srikiatkhachorn[2]

[1]*Mahidol University, Oral Biology, Bangkok, Thailand*
[2]*Chulalongkorn University, Department of Physiology-Faculty of Medicine, Bangkok, Thailand*

Background: Anxiety and depression are common comorbidities in patients with medication-overuse headache. Although the mechanisms underlying these psychiatric comorbidities are still unknown, alteration of amygdala function is one possible explanation. This study was conducted to investigate the relationship between amygdala activity and anxiety-like behaviours in animals chronically treated with acetaminophen or aspirin.

Methods: Wistar rats were divided into three groups receiving daily dose of either aspirin (100 mg/kg), acetaminophen (200 mg/kg) or normal saline. Anxiety-like behaviours were measured using open field and elevated plus maze tests. The neuronal activity on central nucleus of amygdala was examined by whole cell patch-clamp recording.

Results: Our study showed that chronic analgesic exposure increased anxiety-like behaviors in both elevated plus maze and open field tests. The duration in the close arms of elevated plus maze were significantly longer in acetaminophen and aspirin treated groups as compared to the control group ($214.2 + 55.8$, $172.2 + 55.1$ and $101.5 + 14.2$ seconds, respectively, $p < 0.001$). The duration on periphery area of open field test in acetaminophen and aspirin treated groups was statistically greater than that of the control group ($221.1 + 34.4$, $239.7 + 28.4$ and $145.1 + 19.0$ seconds, respectively, $p < 0.001$). Acetaminophen and aspirin also decreased the threshold of neurons in central nucleus of amygdala ($-55.17 + 0.97$, $-54.6 + 5.01$ and $-31.5 + 5.34$, mV, respectively, $p < 0.001$).

Conclusion: Our study showed that chronic administration of acetaminophen and aspirin can increase excitability of amygdala neuron which may lead to the development of anxiety-like behaviors. The hyperexcitability of central amygdala neuron may underlie the pathogenesis of these psychiatric comorbidities observed in patients with medication-overuse headache.

EHMTC-0108
POSTER SESSION E

NR2A MEDIATES CSD-INDUCED PANX1 CHANNELS OPENING VIA SRC FAMILY KINASES

M. Wang[1], F. Bu[1], J. Quinn[2]

[1]*Centre for Neuroscience, Department of Biological Sciences, Suzhou, China*
[2]*Institute of Translational Medicine, Department of Pharmacology, Liverpool, United Kingdom*

NR2A-containing NMDA receptors contribute to genesis and propagation of cortical spreading depression (CSD), the underlying cause of migraine aura, which may also lead to migraine headache through Pannexin1 (Panx1) channels activation. In this project, we aimed to explore the molecular mechanism of migraine by investigating whether NR2A could regulate CSD-induced Panx1 opening involving Src family kinases. The results firstly showed that repeated CSD significantly induced Src phosphorylation at Y416 site but also increased the interaction of Src and Panx1 in ipsilateral cortex of rats. These elevated of Src phosphorylation and Src-Panx1 interaction as well as Panx1 channel opening induced by CSD were markedly suppressed the NR2A inhibitor, NVP-AAM077, at 0.3 nmol injected through intracerebral ventricle (i.c.v). Furthermore, similar to NVP-AAM077, Src inhibition by PP2 (2.5 nmol, i.c.v) markedly suppressed cortex susceptibility to CSD and prevented CSD-induced Src activation as well as Panx1 opening. These data demonstrates that NR2A regulates CSD-triggered neuronal Panx1 channels opening via activation of Src family kinases and reveals a previously unknown NR2A-Src-panx1 pathway in migraine pathophysiology.

EHMTC-0365
POSTER SESSION F

CHARACTERS OF MIGRAINE AND TREATMENT OPTIONS IN KUWAIT-HOSPITAL BASED STUDY

J. Al-Hashel[1,2], S. Farouk Ahmed[3,4], W. A. Kamal[1,5], R. A. Alroughani[6,7]

[1]*Ibn sina hospital- Neurology- Kuwait, Neurology, Kuwait, Kuwait*
[2]*Kuwait University- Faculty of medicine, Medicine, Kuwait*
[3]*Ibn Sina Hospital- Neurology, K, Kuwait*
[4]*Al-Minia University- Faculty of medicine- Neurology, Al-Minia, Egypt*
[5]*Beni-Suef University- Neurology, Beni-Suef, Egypt*
[6]*Amiri Hospital-Neurology, K, Kuwait*
[7]*Neurology Clinic, Kuwait*

Background: Epidemiological studies of migraine in Kuwait are scarce.

Aim: To assess the clinical characteristics and management of migraine in Kuwait.

Methods: A cross-sectional hospital-based study was conducted between 1st. January 2015 up to 31st. December 2015 to assess patients aged 12–65 years who were referred to the neurology tertiary hospital. The International Classification of Headache Disorders, 3rd edition-beta, was used to diagnose headaches.

Results: A total of 3215 patients were diagnosed as primary headache while 2063 (64.17%) patients were diagnosed as migraine. Mean age of migraine patients was 41.32 ± 11.92 years with female predominance (75.9%). Migraine without aura represented 60.4%, followed with chronic migraine 22.5%, migraine with aura 12.2% and medication over used headache 4.7%. Topiramate was the most common used drug for episodic migraine (54.2%) while boutilinium toxin A was commonly used for medication overuse headaches (53.6%) and chronic migraine (28.7%). With respect to abortive medication, triptans were the most regularly prescribed medications (50.7%). The longer the time to seek neurologist opinion, the more liable the patient was to have transformed into chronic migraine and medication overuse headache (chronic migraine 8.46 ± 2.10; medication over used headache 9.37 ± 0.77 versus 3.41 ± 1.75 in episodic migraine, $p < 0.0001$)

Conclusions: Migraine is the most frequent primary headache disorder in our cohort. Topiramate and Boutilinium toxin A were the most common used prophylactic drugs while triptans were commonly used as abortive medications. Delay in referring patients to neurology

services results in transformation into chronic migraine and medication overuse headache.

EHMTC-0366
POSTER SESSION F

PREVALENCE OF PRIMARY HEADACHE DISORDERS IN KUWAIT- HOSPITAL BASED STUDY

J. Al-Hashel[1,2], S. Farouk Ahmed[3,4], W. A. Kamal[5,6], R. A. Alroughani[7,8]

[1]*Ibn sina hospital- Neurology- Kuwait, Neurology, Kuwait, Kuwait*
[2]*Kuwait University- Faculty of medicine, Medicine, Kuwait*
[3]*Ibn Sina Hospital-Neurology, Kuwait*
[4]*Al-Minia University- Faculty of medicine- Neurology, Al-Minia, Egypt*
[5]*Ibn Sina Hospital- Neurology, Kuwait*
[6]*Beni-Suef University- Neurology, Beni-Suef, Egypt*
[7]*Amiri Hospital- Neurology, Kuwait*
[8]*Dasman Diabetes Institute- Neurology clinic Kuwait, Neurology, Kuwait*

Background: Data on the prevalence of primary headaches in Kuwait is scarce.

Aim: To determine the prevalence of primary headaches at a tertiary center in Kuwait.

Methods: A cross-sectional hospital-based study was conducted between 1st. January 2015 up to 31st. December 2015 to assess patients aged 12–65 years who were referred to neurology tertiary hospital. The International Classification of Headache Disorders, 3rd edition-beta, was used to determine the types of headache. Patients with secondary headache were excluded.

Results: A total of 27825 patients were referred to the tertiary hospital; in 2015; of whom 3215 were diagnosed as primary headache disorder. Primary headache prevalence was 11.55% with female predominance 71.7%. Prevalence of primary headache in males was 7.38% versus 14.88%in females ($p < 0.0001$). Mean age was 39.28 ± 11.54 years. Most of them 37.7% in the age group 31–40 years. Episodic migraine was the most prevalent at 46.6% followed by tension-type headache (24.7%), chronic migraine (14.5%), cluster headache (7.4%), medication overuse headache (6.1%) and paroxysmal hemicranias (0.7%). Mean time for referral was 4.25 ± 2.85 years from headache onset, which was significantly longer among patients diagnosed with medication overuse headache (9.37 ± 9.77) and chronic migraine (8.45 ± 2.10) versus episodic migraine (3.41 ± 1.75); ($p < 0.0001$). Most patients were managed by either general practitioners (52.2%) or ENT specialists (30.5%) prior to their referral.

Conclusions: Primary headache prevalence in Kuwait is comparable to international figures. Improving the awareness of the general practitioners and other specialists may reduce the chronicity of headache.

EHMTC-0147
POSTER SESSION F

PREVALENCE OF MIGRAINE AMONG MEDICAL STUDENTS IN SOKOTO

S. Balarabe[1], Y. Mufutau[2]

[1]*Usmanu Danfodio university Teaching Hospital, Department of Medicine, Sokoto, Nigeria*
[2]*Usmanu Danfodio university Teaching Hospital, Department of Psyciatry, Sokoto, Nigeria*

Background: Migraine is a common neurological disorder and is characterized by debilitating head pain and other symptoms such as nausea, vomiting, photophobia, phonophobia, and occasionally, visual or sensory disturbances. Due to its negative effects on quality of life, it becomes especially considerable among university students, who require constant concentration and performance. Headaches have a profound impact on school performance among university students. The aim of this study is to determine the prevalence of migraine among medical students in sokoto

Methods: This was a prospective cross sectional study. Two hundred students were recruited for this study. Self administered questionnaire was used to assess for sociodemographic variables and the presence of migraine.

Results: One hundred and twenty three of the subjects responded to the questionnaire corresponding to 61.5%. The male students were 72 (59.5%) while the female students were 49 (40.5%). The mean age of the subjects was 23.03 ($\pm$2.99). All the level of medical students were represented however with more representation from 400 level, 57 (46.7%) and 500 level 29 (23.8%). The prevalence of migraine among the subjects was 31 (28.7%). The frequency of the migraine varied with some as frequent as 3 times a week. Fourteen (45.2%) reported the presence of aura including visual, and olfactory hallucination.

Conclusion: The present study suggested that migraine is not uncommon among the medical students in Sokoto. About one third of the subjects reported previous history of migraine and left and both sided migraine were common. Least common was entire head migraine.

EHMTC-0222
POSTER SESSION F

ADOLESCENT PERSPECTIVES ON THE BURDEN OF THEIR PARENT'S MIGRAINE: RESULTS FROM THE CHRONIC MIGRAINE EPIDEMIOLOGY AND OUTCOMES STUDY

D.C. Buse[1], S.W. Powers[2], A.A. Gelfand[3], J. VanderPluym[4], K.M. Fanning[5], M.L. Reed[5], A. Manack Adams[6], R.B. Lipton[1]

[1]*Montefiore Medical Center- Albert Einstein College of Medicine, Department of Neurology, Bronx, USA*
[2]*Cincinnati Children's Hospital- University of Cincinnati College of Medicine, Headache Center and Division of Behavioral Medicine and Clinical Psychology, Cincinnati, USA*
[3]*UCSF Medical Center, UCSF Pediatric Headache Center and Division of Child Neurology, San Francisco, USA*
[4]*Mayo Clinic Arizona, Neurology, Phoenix, USA*
[5]*Vedanta Research, Biostatistics, Chapel Hill, USA*
[6]*Allergan plc, Global Medical Affairs, Irvine, USA*

Background: We assessed the impact of parental migraine on adolescent children, from the perspective of the adolescent, for parents with chronic migraine (CM; ≥15 headache days/month) versus episodic migraine (EM; <15 headache days/month).

Methods: In the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study, respondents meeting modified ICHD-3 b migraine criteria, assessed using a validated questionnaire, invited their adolescent children (ages 13–21 years) living in their homes to complete surveys that assessed 4 domains validated with Confirmatory Factor Analysis (CFA).

Results: Among 1,411 parent-adolescent dyads, 168 parent probands (11.9%) had CM and 1,243 (88.1%) had EM. CFA identified 4 domains with good model fit. EM vs CM comparisons for representative items from each domain are presented in Tables 1–2. For example, in the Loss of Parental Support domain, 50% of adolescents of CM parents felt they could not get parental help they needed over the past month compared with 27% of those of EM parents.

Conclusions: Burden among adolescent family members mirrors that of their parents with migraine, with greater burden for adolescents of CM parents, suggesting broader clinical support may be warranted for many families with parental migraine.

Conflict of interest
Disclosure statement:
Dawn C. Buse, PhD, in the past 12 months, has received grant support and honoraria from Allergan, Avanir, and Eli Lilly. She is an employee of Montefiore Medical Center, which in the past 12 months, has received research support funded by Allergan, Alder, Avanir, CoLucid, Dr. Reddy's, and Labrys, via grants to the National Headache Foundation and/or Montefiore Medical Center. She is on the editorial board of Current Pain and Headache Reports, the Journal of Headache and Pain, Pain Medicine News, and Pain Pathways magazine.

Table 1. Adolescent Responses to Questions in Domains 1 and 2, by Parent Headache Status

	Parent with EM (%)	Parent with CM (%)	*P* value
Domain 1: Loss of Parental Support			
Because of your parent's headaches, how many TIMES during the past 30 days did you need help from your parent and couldn't get it?*	27.0	50.0	<0.001
Domain 2: Emotional Experience			
Parental Behavior Subdomain Because of your parent's headaches, during the past 30 days, how often did your parent get upset with you over something that was not important?†	39.4	54.2	<0.001
Adolescent Feelings Subdomain Because of your parent's headaches, during the past 30 days, how often did you feel that your parent was too "moody?"†	32.6	49.4	<0.001
Quality of Parenting Subdomain How much do you agree or disagree that you would get along better with your parent if they didn't have headaches?‡	21.5	43.5	<0.001

*Percent of adolescents reporting ≥1 time.
†Percent of adolescents reporting "a little" or "a lot."
‡Percent of adolescents reporting agree "somewhat" or "completely."

Table 2. Adolescent Responses to Questions in Domains 3 and 4, by Parent Headache Status

	Parent with EM (%)	Parent with CM (%)	*P* Value
Domain 3: Interference with School			
It bothers me that my parent cannot help with school activities like other parents because of headaches.*	9.5	17.9	0.001
Domain 4: Missed Activities/Events			
Missed Group Activities Subdomain Because of your parent's headaches, how many times during the past 30 days did you miss (not go to) a family outing (e.g., movie, game, dance, picnic)?†	22.6	46.5	<0.001
Missed Social Activities Subdomain Because of your parent's headaches, how many times during the past 30 days did you miss having friends over to visit at your house?†	22.0	48.1	<0.001
Missed Major Events Subdomain In the past 12 months, have your parent's headaches kept you from doing things you wanted to do while on vacation?‡	9.8	20.8	<0.001

*Percent of adolescents reporting agree "somewhat" or "completely."
†Percent of adolescents reporting ≥1 time.
‡Percent of adolescents reporting "yes."

Dr. Powers has received grant support from the National Institutes of Health, the National Headache Foundation, and the Migraine Research Foundation.

Dr. Gelfand has received research grant support from eNeura, Allergan, and EMKinetics. She has consulted for Eli Lilly.

Juliana VanderPluym, MD, has no disclosures to report.

Kristina Fanning, PhD, is an employee of Vedanta Research, which has received research funding from Allergan, CoLucid, Dr. Reddy's Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPathe, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation.

Michael L. Reed, PhD, is Managing Director of Vedanta Research, which has received research funding from Allergan, Colucid, Dr. Reddy's Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPathe, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc, and owns stock in the company.

Richard B. Lipton, MD, has received grant support from the National Institutes of Health, the National Headache Foundation, and the Migraine Research Fund. He serves as consultant, serves as an advisory board member, or has received honoraria from Alder, Allergan, American Headache Society, Autonomic Technologies, Boston Scientific, Bristol Myers Squibb, Cognimed, CoLucid, Eli Lilly, eNeura Therapeutics, Merck, Novartis, Pfizer, and Teva, Inc. He receives royalties from Wolff's Headache, 8th Edition (Oxford University Press, 2009).

EHMTC-0219
POSTER SESSION F

IMPACT OF ITALIAN-SISC GUIDELINES ON HEADACHE MANAGEMENT: ANALYSIS BASED ON 2455 "NAIVE CASES" OF THE VENETO REGION HEADACHE-CENTRE

M. Bellamio[1], M. Barp[2], A. Terrin[1], F. Mainardi[3], C. Lisotto[4], G. Zanchin[1], F. Maggioni[1]

[1]*University of Padua, Department of Neurosciences – Headache Centre, Padua, Italy*
[2]*University of Padua, School of medicine, Padua, Italy*
[3]*S.S. Giovanni and Paolo Hospital, Headache Centre, Venice, Italy*
[4]*S. Vito al Tagliamento Hospital, Headache Centre, Pordenone, Italy*

Introduction/Methods: The last version of italian guidelines (GL) on treatment of headache was revised in 2012. We assessed the impact of GL on the management of migraine in the last two decades analyzing the attack and

preventative drugs taken by a series of 2455 patients suffering from migraine without aura (ICHD criteria, 2013) divided in four cohorts (2014–15, n = 500; 2009–11, n = 1400 1995–98, n = 204; 1989–92, n = 351).

Results: The positive changes, in keeping with GL, were the reduction of combination drugs (from 79% to 22%) and ergotamine (from 37% to less than 1%); important were the spreading of triptans (from 17% to 22,2%) and the confirmation of NSAIDs as first-line therapy of migraine attack (by an average of 65,5%). Focusing on the preventative drugs, it was very relevant the high percentage of patients who had not received a therapy even if it was necessary (almost two-thirds); however, in accordance with GL, it was ameliorated the percentage of patients who were receiving drugs without having any therapeutic indications (from 30% to less than 2%).

Conclusions: The current clinical management of migraine patients differs in many aspects from Italian GL even after the publications and the sponsorship of three versions in last 20 years. Headache is one of the most frequent neurological syndrome and not only neurologists have to learn how to treat it; a more adequate diffusion of the existing 2012-revised GL, especially among general practitioners, should be planned in order to impact effectively on current clinical practice.

EHMTC-0264
POSTER SESSION F

HEADACHE IN ELEMENTARY AND HIGH SCHOOL PUPILS

V Assmann[1], R. Berner[2], M. von der Hagen[2], R. Sabatowski[1], M. Richter[2], G. Gossrau[1]

[1]*University Hospital/TU-Dresden, University Pain Center, Dresden, Germany*
[2]*University Hospital/TU-Dresden, Department of Pediatrics, Dresden, Germany*

Headache is common among children and adolescents. Evidence for its increasing prevalence and earlier onset exists. Using anonymous questionnaires we investigated here the headache prevalence, its intensity and characteristics among 6–19-year-old children attending elementary or high schools in Dresden. Furthermore, we investigated the impact of headache on school attendance, frequency of medication intake and doctor visits, as well as the relationship of headache with sports and daily activities.

We received back filled questionnaires from 2,706 pupils, with a return rate of 63,7% for elementary school children and 42,1% for high school children. Headache was reported by 60,7% of elementary school children and by 72,2% of high school pupils, with its prevalence increasing with age. In general, 49,1% of 1st grade pupils suffered from headaches at least once per month, compared to 73% and 78,7% of the children in 4th grade and 10th grade, respectively. Girls experienced headaches more often than boys in total (73,3% vs. 63,3%), and at each class level. Furthermore we verified the negative influence of daily smoking and weekly alcohol consumption as well as coffeine on frequent headaches. Pupils with less than 1-hour usage of smart phone or computer per day suffered less from headaches than those with more than 1-hour use of these media. The high number of children and adolescents with headache shows the need of headache education concerning causes, prevention and therapies.

EHMTC-0335
POSTER SESSION F

THE ASSOCIATION BETWEEN TV NEWS VIEWING RATES AND FOLLOWING DAY HEADACHE RELATED EMERGENCY DEPARTMENT VISITS IN ISRAEL

A. Vodonos Zilberg[1], A. Guetta[2], I. Waismel-Manor[3], V. Novack[1], G. Ifergane[2]

[1]*Soroka University Medical Center and The Faculty of Health Sciences- Ben Gurion, Clinical Research Center, Beer Sheva, Israel*
[2]*Soroka University Medical Center and The Faculty of Health Sciences- Ben Gurion, Neurology, Beer Sheva, Israel*
[3]*University of Haifa- Israel., School of Political Science, Haifa, Israel*

Introduction: Stress is a well-known trigger for primary headache yet its impact is difficult to demonstrate in large epidemiological studies. Israeli national TV news is often referred to as the "tribal fire", as many Israelis watch national news coverage following stressful events. We evaluated the association between TV news viewing rates to headache related ED visits.

Methods: This retrospective cohort study included data on daily ED visits with a chief complaint of headache in Soroka University Medical Center (SUMC), 1,000 bed tertiary hospital during 2002–2012. Data on daily rating percentages were obtained from the Israeli audience research board, which electronically monitors TV activity in a sample of Israeli households. To estimate the short-term effects of news rating during 8:00–9:00 pm on number of daily headache ED visits, we applied generalized linear mixed models (GLMM) adjusted for daily temperature and relative humidity.

Results: 16,693 ED visits were included in the analysis. An increase in 5 units of daily rating percentages was associated with increase in ED visits the following day, relative

risk (RR) = 1.032, (95%CI 1.014; 1.050). This association increased with the age of the patients; RR = 1.119, (95%CI 1.014; 1.050) for older than 60 year old, RR = 1.044 (95%CI 1.010–1.078) for ages 40–60 and RR = 1.000 (95%CI 0.977–1.023) for younger than 40 year old.

Discussion: Higher rates of news watching were associated with increased ED headache related visits. Possibly, especially in older persons, news watching rates provide an indirect estimate of community stress, acting as a headache trigger for susceptible individuals.

EHMTC-0140
POSTER SESSION F

THE EFFECT OF PSYCHIATRIC SYMPTOMS ON HEADACHE-RELATED DISABILITY IN MIGRAINE: RESULTS FROM THE CHRONIC MIGRAINE EPIDEMIOLOGY AND OUTCOMES (CAMEO) STUDY

R.B. Lipton[1], M.K. Chu[2], E.K. Seng[3], M.L. Reed[4], K.M. Fanning[4], A. Manack Adams[5], D.C. Buse[1]

[1]*Montefiore Medical Center- Albert Einstein College of Medicine, Department of Neurology, Bronx, USA*
[2]*Kangnam Sacred Heart Hospital, Department of Neurology, Seoul, Republic of Korea*
[3]*Albert Einstein College of Medicine- Yeshiva University, Department of Neurology Einstein- Ferkauf Graduate School of Psychology Yeshiva University, Bronx, USA*
[4]*Vedanta Research, Biostatistics, Chapel Hill, USA*
[5]*Allergan plc, Global Medical Affairs, Irvine, USA*

Background: This CaMEO Study analysis examines the separate and joint influences of depression and anxiety symptoms on headache-related disability in people with migraine (episodic and chronic).

Methods: This cross-sectional analysis of data from CaMEO, a web-panel study, assessed sociodemographic and headache features, headache-related disability (Migraine Disability Assessment Scale [MIDAS]), migraine symptom severity (Migraine Symptom Severity Score), and cutaneous allodynia (Allodynia Symptom Checklist-12). Four groups were defined based on scores on validated psychiatric comorbidity screeners for symptoms of depression (Patient Health Questionnaire ≥ 10) and anxiety (Generalized Anxiety Disorder scale ≥ 10) as follows: depressive symptoms alone, anxiety alone, both, or neither. A negative binomial regression model investigated predictors of MIDAS score.

Results: Respondents (N = 16,789) were predominantly female (74.4%) and white (84.0%), with a mean age of 41.1 years. After adjusting for demographics and headache features, persons with both depressive and anxiety symptoms had the highest levels of disability followed by those with depression alone and anxiety alone, compared with those without depression or anxiety symptoms (Table).

Conclusions: Depressive symptoms alone and anxiety symptoms alone are associated with greater headache-related disability after controlling for sociodemographic and headache features. In combination, depression and anxiety affect disability more than either symptom alone. While this analysis cannot determine causation, interventions targeting depression and anxiety may help improve headache-related disability in persons with migraine.

Funding: Allergan

Table. Predictors of Mean MIDAS Score*

	P-value	Rate Ratio	95% CI
Intercept	<0.001	1.38	1.17–1.62
Male	<0.001	0.86	0.83–0.90
Age (10-y intervals)	<0.001	0.91	0.88–0.93
Depression/anxiety symptom status (vs neither anxiety nor depression)			
Both depression and anxiety	<0.001	1.79	1.71–1.87
Depression only (PHQ-9 ≥10)	<0.001	1.56	1.46–1.66
Anxiety only (GAD-7 ≥10)	<0.001	1.39	1.30–1.50
Allodynia (ASC-12 ≥3)	<0.001	1.35	1.30–1.41
Monthly headache-day frequency	<0.001	1.11	1.10-1.11

ASC-12=12-item Allodynia Symptom Checklist; GAD-7=7-item Generalized Anxiety Disorder scale; PHQ-9=9-item Patient Health Questionnaire.
*Adjusted for gender, age, body-mass index, race, income, and Migraine Symptom Severity Score.

Conflict of interest
Disclosure statement:
Richard B. Lipton, MD, has received grant support from the National Institutes of Health, the National Headache Foundation, and the Migraine Research Fund. He serves as consultant, serves as an advisory board member, or has received honoraria from Alder, Allergan, American Headache Society, Autonomic Technologies, Boston Scientific, Bristol Myers Squibb, Cognimed, CoLucid, Dr. Reddy's Laboratories, Eli Lilly, eNeura Therapeutics, Merck, Novartis, Pfizer, and Teva.

Min Kyung Chu, MD, PhD, in the past 12 months, has received grant support and honoraria from Allergan Korea and Yu Yu Pharma, Inc.

Elizabeth K. Seng, PhD, has received research support from the International Headache Academy.

Michael L. Reed, PhD, is Managing Director of Vedanta Research, which has received research funding from Allergan, Colucid, Dr. Reddy's Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPathe, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation. Vedanta Research has received funding directly from Allergan for work on the CaMEO Study.

Kristina Fanning, PhD, is an employee of Vedanta Research, which has received support funded by Allergan, CoLucid, Dr. Reddy's Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPathe, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc, and owns stock in the company.

Dawn C. Buse, PhD, in the past 12 months, has received grant support and honoraria from Allergan, Avanir, and Eli Lilly. She is an employee of Montefiore Medical Center, which in the past 12 months, has received research support funded by Allergan, Alder, Avanir, CoLucid, Dr. Reddy's, and Labrys, via grants to the National Headache Foundation and/or Montefiore Medical Center. She is on the editorial board of Current Pain and Headache Reports, the Journal of Headache and Pain, Pain Medicine News, and Pain Pathways magazine.

EHMTC-0272
POSTER SESSION F

DEMOgraphic, CLINICAL, AND TREATMENT CHARACTERISTICS OF PATIENTS WITH MIGRAINE IN JAPAN: A RETROSPECTIVE ANALYSIS OF HEALTH INSURANCE CLAIMS DATA

J. Meyers[1], K. Davis[1], R. Lenz[2], F. Sakai[3], F. Xue[4]

[1]*RTI Health Solutions, Health Economics, Research Triangle Park, USA*
[2]*Amgen, Neuroscience, Los Angeles, USA*
[3]*Saitama Neuropsychiatric Institute, Saitama International Headache Center, Saitama, Japan*
[4]*Amgen, Global Observational Research, Los Angeles, USA*

Objectives: To describe demographic, clinical, and treatment characteristics of migraine patients in the Japan Medical Data Center (JMDC) database.

Methods: Patients ≥18 years old with ≥1 inpatient or ≥2 outpatient migraine diagnoses, ≥1 outpatient diagnosis and ≥1 triptan/ergotamine prescription, or ≥2 triptan/ergotamine prescriptions from 5/1/2011–4/30/2014 were identified in the JMDC database. The first migraine diagnosis or triptan/ergotamine prescription defined the index date. Patients were required to have ≥12 months pre-index (baseline) and post-index date plan enrollment. Patients were stratified by the 1st observed migraine treatment (i.e., acute treat only [AT], any prophylactic treatment [PT], no treatment [NT]) during follow-up. Demographics, comorbidities, and migraine medications were described.

Results: 16,664 eligible migraine patients were identified, with mean (SD) age of 40.6(11.0) years, and approximately two-thirds as female. Among assessed comorbidities, COPD/asthma (21.0%), peptic ulcer disease (12.7%), diabetes (12.7%), and cancer (12.6%), were the most prevalent. AT patients (N = 10,510) were ~5 years younger on average and had a lower prevalence of most assessed comorbidities than PT patients (N = 2,472). Baseline use of NSAIDs/aspirin/caffeine was common (19.5%), and prophylactic treatment was low (7.2%). During follow-up, 18.3% of patients received prophylactic medication and a lower proportion of PT patients (20.8%) received NSAIDs/aspirin/caffeine than AT patients (27.8%). Treatment with opiates was low in both baseline (0.2%) and follow-up (0.3%).

Conclusions: Among Japanese migraine patients, the burden of comorbidities is high and prophylactic migraine medication use is low. Patients treated with prophylactic medications were older with a higher comorbidity burden, but required less acute treatment during follow-up.

Conflict of interest
Disclosure statement:
This study was funded by Amgen.

EHMTC-0280
POSTER SESSION F

TREATMENT PATTERNS OF PATIENTS WITH MIGRAINE IN JAPAN: A RETROSPECTIVE ANALYSIS OF HEALTH INSURANCE CLAIMS DATA

J. Meyers[1], K. Davis[2], R. Lenz[3], F. Xue[4]

[1]*RTI International, RTI Health Solutions, Washington- DC, USA*
[2]*RTI Health Solutions, Health Economics, Research Triangle Park, USA*
[3]*Amgen, Neuroscience, Los Angeles, USA*
[4]*Amgen, Global Observational Research, Los Angeles, USA*

Objectives: To describe treatment patterns of migraine patients in the Japan Medical Data Center (JMDC) database.

Methods: Patients ≥18 years with ≥1 inpatient or ≥2 outpatient migraine diagnoses, ≥1 outpatient diagnosis and ≥1 acute treatment (triptan or ergotamine), or ≥2 acute treatments from 5/1/2011–4/30/2014 were identified. Patients were required to have ≥1-year pre- and post-index date plan enrollment. The first migraine diagnosis or acute treatment defined the index date. Patients were stratified by the migraine treatments ever observed post-index date [i.e., migraine-specific acute treatment only (AT), prophylactic with or without acute treatment (PT), no treatment (NT)] and described regarding the first migraine treatment regimen and subsequent treatment pattern during up to 1-year of follow-up.

Results: A total of 16,443 patients met eligibility criteria (9,873 AT, 3,022 PT, and 3,548 NT). AT patients had mean (SD) 10.3 (20.5) acute treatment days during follow-up and 81.9% received triptans. When assessing the first migraine treatment regimen during follow-up in PT patients, 29.2% received prophylactic treatment only and 51.7% received both acute and prophylactic treatment. Calcium-channel blockers with or without concomitant triptans (34.4%) were the most common first regimen. Approximately 62.2% discontinued initial prophylactic treatment after an average of 61.2 days (STD = 65.3) of persistent treatment. Among discontinuers, 15.2% re-initiated original treatment and 7.0% switched treatment post-discontinuation within a year.

Conclusions: Among Japanese migraine patients, prophylactic use was low and associated with a high rate of discontinuation following a brief treatment period. Many patients re-initiated or switched treatment following discontinuation, suggesting a high unmet need.

Conflict of interest
Disclosure statement:
This study was funded by Amgen.

EHMTC-0127
POSTER SESSION F

WOMEN LIVING TOGETHER HAVE A HIGHER PREVALENCE OF MENSTRUAL MIGRAINE

V Ribeiro Faria[1], G. Guilherme[1], K. dos Santos Ferreira[1], A. Ayumi Tome Uchiyama[1], L. Mazini Borges[1]

[1]*University Center Barão de Mauá- Ribeirão Preto- São Paulo- Brazil., Faculty of Medicine, Ribeirão Preto, Brazil*

Justification and Objectives: Menstrual migraine is a highly prevalent disorder among adult women, resulting in disability and loss of quality of life. We report here the prevalence of menstrual migraine in a group of women living together compared to a control group of women living alone.

Methods: The study was conducted on female university students with a diagnosis of migraine. The subjects were divided into a group of women who lived together with two or more other students and a control group of age-matched students who lived alone, interviewed with a specific questionnaire and assessed for 3 months by means of a pain diary. The data evaluated included frequency of headache crises, presence of menstrual migraine, intensity of crises, medications used including contraceptives, and triggering factors such as diet, sleep deprivation and stress.

Results: We detected a higher prevalence of menstrual migraine among women living together (9, 50%) compared to women living alone (3, 16.7%) ($p = 0.03$). After binary logistic regression analysis, this finding was not related to the main influencing factors detected, i.e., use of a contraceptive, test stress or sleep deprivation ($p = 0.03$, adjusted odds ratio: 1.27; 0.02 −0.81). These women also showed menstrual cycle synchrony with their roommates (8, 44.4%) and the presence of headache crises during the menstruation of their colleagues (11, 61.1%).

Conclusion: The present findings have not been reported previously and no consensus exists about menstrual cycle synchrony among women. However, we believe that the present study could represent a step towads more elaborate investigations.

EHMTC-0137
POSTER SESSION F

EPIDEMIOLOGY OF MIGRAINE IN MEN: DISEASE PRESENTATION AND COMORBIDITIES FROM THE CHRONIC MIGRAINE EPIDEMIOLOGY AND OUTCOMES (CAMEO) STUDY

A. I. Scher[1], S.J. Wang[2], Z. Katsarava[3], D.C. Buse[4], K.M. Fanning[5], A. Manack Adams[6], R.B. Lipton[4]

[1]*Affiliated with Uniformed Services University of the Health Sciences USUHS, Department of Preventive Medicine and Biometrics, Bethesda, USA*
[2]*Faculty of Medicine- National Yang-Ming University School of Medicine, Department of Neurology, Taipei, Taiwan*
[3]*Evangelical Hospital Unna- University of Essen, Department of Neurology, Unna, Germany*
[4]*Montefiore Medical Center- Albert Einstein College of Medicine, Department of Neurology, Bronx, USA*
[5]*Vedanta Research, Biostatistics, Chapel Hill, USA*
[6]*Allergan plc, Global Medical Affairs, Irvine, USA*

Background: This analysis from the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study highlights migraine epidemiology in men by examining sex differences in migraine disease presentation and comorbidities.

Methods: CaMEO participants were recruited from a Web-panel using quota sampling and completed baseline and 3-month follow-up surveys. Sociodemographic and headache features, headache-related disability (Migraine Disability Assessment [MIDAS]), symptom severity (Migraine Symptom Severity Score [MSSS]), cutaneous allodynia (Allodynia Symptom Checklist), and comorbidities (self-reported healthcare professional diagnosis, Patient Health Questionnaire [PHQ-9], and Generalized Anxiety Disorder scale [GAD-7]) were assessed.

Results: Compared with women, men were slightly older at migraine onset and had fewer headache days/month, slightly less severe attacks (MSSS), lower MIDAS scores, and a lower prevalence of allodynia; CM was a lower proportion of all migraine for men than women (all $P < 0.001$; Table). Of the 5 most common comorbidities for each sex, all were reported by lower proportions of men than women (except depression, which was similarly prevalent; Table).

Table. Sex Differences in CaMEO Study Participant Disease Presentation and Comorbidities

Characteristic	Men (n=4,294)	Women (n=12,495)
Mean (SD) age at most severe headache onset, years*	24.1 (13.2)	22.3 (10.9)
Mean (SD) headache days/month*	4.3 (5.6)	5.3 (6.1)
Mean (SD) Migraine Symptom Severity Score (MSSS)*	21.6 (3.1)	22.6 (3.2)
Migraine Disability Assessment (MIDAS) score in the severe range (Grade IV), n (%)*	672 (15.7)	3004 (24.1)
Presence of allodynia, (ASC ≥3), n (%)*	1051 (32.6)	4769 (49.7)
Presence of CM, n (%)*	279 (6.5)	1197 (9.6)
Five most common comorbidities, respondents answering "yes," n (%)		
HCP-diagnosed sinusitis*	1230 (38.2)	4960 (51.7)
HCP-diagnosed allergies, hay fever, or allergic rhinitis*	1067 (33.1)	3875 (40.4)
HCP-diagnosed bronchitis*	911 (28.3)	3823 (39.9)
Moderate-to-severe depression (PHQ-9)†	1342 (31.3)	4083 (32.7)
Moderate-to-severe anxiety (GAD-7)*	1103 (25.7)	3919 (31.4)

ASC=Allodynia Symptom Checklist; CM=chronic migraine; EM=episodic migraine; GAD-7=Generalized Anxiety Disorder scale; HCP=healthcare professional; PHQ-9=Patient Health Questionnaire.
*$P<0.001$ for men vs women comparison.
†$P=0.09$ for men vs women comparison.

Conclusions: Results suggest sex differences in migraine disease presentation and comorbidities. Men had a lower attack frequency, less disability, and less allodynia than women and most comorbidities were reported by lower proportions of men than women. Nevertheless, migraine is disabling in men and the perception that migraine is a women's disease may contribute to migraine stigma and deny men access to treatment.

Funding: Allergan

Conflict of interest
Disclosure statement:
Ann I. Scher, PhD, in the past 12 months, has received honoraria from and is an advisory board member for Allergan, receives grant support from CDMRP and CNRM, and is on the editorial boards of Cephalalgia and Pain Medicine. The Views expressed are those of the author(s) and do not necessarily reflect the official views of the Uniformed Services University of the Health Sciences or the Department of Defense.

Shuu-Jiun Wang, MD, has received personal compensation for consulting, advisory boards, or speaker activities from Allergan, GlaxoSmithKline (Taiwan), and Eli Lilly, and has received research support from Novartis (Taiwan), Daiichi-Sankyo, and Eli Lilly.

Zaza Katsarava, Prof, Dr. med., MSc., has received personal compensation for consulting, advisory boards, or speaker activities from Allergan, Amgen, Biogen, and Boehringer-Ingelheim.

Dawn C. Buse, PhD, in the past 12 months, has received grant support and honoraria from Allergan, Avanir, and Eli Lilly. She is an employee of Montefiore Medical Center, which in the past 12 months, has received research support funded by Allergan, Alder, Avanir, CoLucid, Dr. Reddy's, and Labrys, via grants to the National Headache Foundation and/or Montefiore Medical Center. She is on the editorial board of Current Pain and Headache Reports, the Journal of Headache and Pain, Pain Medicine News, and Pain Pathways magazine.

Kristina Fanning, PhD, is an employee of Vedanta Research, which has received support funded by Allergan, CoLucid, Dr. Reddy's Laboratories, Endo Pharmaceuticals, GlaxoSmithKline, Merck & Co., Inc., NuPathe, Novartis, and Ortho-McNeil, via grants to the National Headache Foundation.

Aubrey Manack Adams, PhD, is a full-time employee of Allergan plc, and owns stock in the company.

Richard B. Lipton, MD, has received grant support from the National Institutes of Health, the National Headache Foundation, and the Migraine Research Fund. He serves as consultant, serves as an advisory board member, or has received honoraria from Alder, Allergan, American Headache Society, Autonomic Technologies, Boston Scientific, Bristol Myers Squibb, Cognimed, CoLucid, Eli Lilly, eNeura Therapeutics, Merck, Novartis, Pfizer, and Teva, Inc. He receives royalties from Wolff's Headache, 8th Edition (Oxford University Press, 2009).

EHMTC-0270
POSTER SESSION F

CHRONIC AND EPISODIC MIGRAINE IN RUSSIA: SOCIODEMOgraphic ANALYSIS IN A CHOSEN MEGAPOLIS

A. Artemenko[1], V. Shevchenko[1], V. Tsivileva[1], K. Tatarinova[1], N. Yahno[1]

[1]*I.M.Sechenov First Moscow State Medical University, Neurological Department Scientific-Research Centre, Moscow, Russia*

Introduction: Moscow is the city with more than 12 million inhabitants was chosen as megapolis for the socio-demographic analysis of migraine. The aim of the study is to provide a sociodemographic data of patients with CM and EM live in Moscow.

Methods: 362 subjects with CM (n = 183) and with EM (n = 179) who were patients in the Moscow University neurological clinic within 2014–2015 years were taken into retrospective study. The diagnoses were established according to ICHD-III beta criteria. Patient's age, gender, marital status, education level, occupational status were accessed.

Results: All patients were Russian Federation residents, and vast majority of all interviewers with CM vs EM were women – 92,9% vs EM – 84,4%, average age 40,9 ± 12,3 vs 36,3 ± 8,2; married – 73% vs 75%;having children – 85% vs 72%; single or divorced -22% vs 24,5%; 5% vs 0,5% were widowed; 95% of CM patients had the highest educational level (HEL) and 5% had completed only secondary school; 98% of EM patients had HEL and the rest 2% – completed had secondary school.In a group with CM patients 93% were employed full time with medium and high income, the rest 7% were unemployed. In EM, patients group 90% were employed full time and 10% are unemployed.

Conclusion: Thus, the classic portrait of a patient with CM as a person with low socio-economical status was not confirmed in our study. We found that identified socio-demographic characteristics of the patients with CM in

Russian population are different from the data of similar investigations in the USA and Europe.

EHMTC-0348
POSTER SESSION F

DRUG ABUSE IN CHRONIC MIGRAINE AND STATE RESTRICTION OF PAINKILLERS SALES IN RUSSIA

A. Artemenko[1], V. Shevchenko[1], V. Tsivileva[1], K. Tatarinova[1], A. Kurenkov[2]

[1]*1 st Moscow State Medical University, Neurological department Scientific Research Centre, Moscow, Russia*
[2]*Scientific Centre of Children's Health of the Ministry of Health of the Russian Federation, Neurology, Moscow, Russia*

Introduction: Patients with chronic migraine (CM) have excessive consumption of painkillers. Russian CM patients usually are overused with non-prescribed painkillers and for a long time the combined analgesics, including low dosage codeine phosphate containing drugs (CAC) were the most popular self-treatment method. Since 1 June 2012, the State restriction of painkillers sales (SRS) resulted in changes of the medication profile overuse in CM, which was not analyses for the last 4 years.

Methods: This retrospective observational study included 208 medication-overused patients with CM referred to headache specialist in Moscow University neurological clinic: group 1 – 103 patients checked before SRS in 2010–2011 and group 2 – 105 patients checked in 2014–2015 after the SRS was introduced. The diagnosis was established according to ICHD-III beta criteria. Information about taking acute medication were collected by questionnaires and supplemented with structured patient interviews.

Results: The number of overused patients with CM taking acute painkillers was different in groups: combined analgesics – 64% in group 1 and 5% in group 2 ($p \leq 0{,}01$); simple analgesics – 21% in group 1 and 59% in group 2 ($p \leq 0{,}01$); triptans were taken by 15% and 36% of patients.

Conclusion: The profile of drug overuse in CM has changed from the previously high number of patients taking CAC towards the increased number of patients with triptans abuse after the introduction of the SRS in Russia.

EHMTC-0354
POSTER SESSION F

PARANASAL SINUS OPACIFICATION IN HEADACHE SUFFERERS: A POPULATION-BASED IMAGING STUDY (THE HUNT STUDY-MRI)

L.J. Stovner[1], A.G. Hansen[2], K. Hagen[3], A.S. Helvik[3], W.M. Thorstensen[3], S. Nordgård[1], V. Bugten[1], H.B. Eggesbø[4]

[1]*NTNU- Norwegian University of Science and Technology, Neuroscience, Trondheim, Norway*
[2]*Norwegian University of Science and Technology, Neuroscience, Trondheim, Norway*
[3]*NTNU. Norwegian University of Science and Technology, Neuroscience, Trondheim, Norway*
[4]*Oslo Universily Hospital, Department of Radiology and Nuclear Medicine-, Oslo, Norway*

Background: The association between headache and paranasal sinus disease is still unclear. Because of symptom overlap, the two conditions cannot be easily studied on the basis of symptoms alone. The aim of the present study was to investigate if paranasal sinus opacification at magnetic resonance imaging (MRI) was associated with migraine, tension type headache (TTH) or unclassified headache.

Methods: 844 participants (463 women) in a large population study (HUNT) between 50–65 years (mean 57.7) had been randomly selected for an MRI of the head. Based on 14 headache questions, participants were allocated to four mutually exclusive groups: migraine, TTH, unclassified headache or headache free. At MRI, opacifications as mucosal thickening, polyps/retention cysts and fluid in the five paired sinuses were measured and recorded if ^{3} 1 millimetre. For each participant, opacification thickness was summed for each sinus and in addition, a total sum of all sinuses was calculated.

Opacification in each sinus was compared between headache free participants and the headache groups using non-parametric tests, and the total sum by logistical regression.

Results: No significant association was found between paranasal sinus opacification and being a headache sufferer. Conclusion: Migraine, TTH and unclassified headache were not associated with an increased degree of paranasal sinus opacification at MRI.

EHMTC-0212
POSTER SESSION F

CLINICAL FEATURES OF MIGRAINE AURA: RESULTS FROM A PROSPECTIVE DIARY-AIDED STUDY

M. Viana[1], G. Sances[1], M. Linde[2], N. Ghiotto[1], E. Guaschino[1], M. Allena[1], S. Terrazzino[3], G. Nappi[1], P.J. Goadsby[4], C. Tassorelli[1]

[1]*C. Mondino National Neurological Institute, Headache Science Center, Pavia, Italy*
[2]*Norwegian University of Science and Technology, Department of Neuroscience, Trondheim, Norway*
[3]*Universita' del Piemonte Orientale "A. Avogadro", Department of Pharmaceutical Sciences-, Novara, Italy*
[4]*King's College, Headache Group – NIHR-Wellcome Trust King's Clinical Research Facility, London, United Kingdom*

Background: A detailed evaluation of migraine aura symptoms is crucial for classification issues and pathophysiological discussion. Few studies have focused on the detailed clinical aspects of migraine aura.

Methods: We conducted a prospective diary-based study of migraine aura features including presence, quality, laterality, duration of each aura symptom, their temporal succession; presence of headache and its temporal succession with aura.

Results: Seventy-two patients completed the study recording the characteristics of three consecutive auras ($n = 216$ auras). Visual symptoms occurred in 212 (98%), sensory symptoms in 77 (36%), dysphasic symptoms in 22 (10%). Most auras had more than one visual symptom (median 2, IQR 1–3, range 1–4). The majority of patients (56%) did not report a stereotyped aura on the three attacks with respect to visual features, the combination and/or temporal succession of the three aura symptoms. Fifty-seven percent of patients also reported a different scenario of temporal succession between aura and headache in the three attacks. Five per cent of auras were longer than four hours.

Conclusion: These findings show a high inter and intra-variability of migraine with aura attacks. Furthermore, they provide reliable data to enrich and clarify the spectrum of the aura phenotype.

EHMTC-0228
POSTER SESSION F

MIGRAINE IS ASSOCIATED WITH BETTER COGNITION IN THE MIDDLE-AGED AND ELDERLY: THE ROTTERDAM STUDY

K.X. Wen[1], N.T. Nguyen[1], A. Hofman[1], M.A. Ikram[1], O.H. Franco[1]

[1]*Erasmus MC University Medical Centre, Epidemiology, Rotterdam, Netherlands*

Background: Converging evidence suggests that migraine partly has a vascular basis. In turn, vascular pathology is a strong risk factor for cognitive decline. In this population-based study, we studied cognition amongst individuals with and without migraine.

Methods: In 6708 participants of the Rotterdam Study, migraine was assessed using a validated questionnaire. Cognition was assessed by the Mini-mental state exam (MMSE) and a dedicated cognitive test battery. Participants were classified as non-migraineurs ($n = 5399$), migraineurs ($n = 1021$) or probable migraineurs ($n = 288$). Multivariable linear regression was used to cross-sectionally evaluate the association between migraine and cognition, adjusting for age, sex and cardiovascular risk factors. Additionally, we stratified the analysis by sex and by migraine subtype.

Results: Migraineurs had higher mean MMSE score (unstandardized regression coefficient 0.21, 95%CI 0.08, 0.34) and global cognition (0.10, 95%CI 0.04, 0.15) than non-migraineurs. This difference was particularly marked for migraineurs with aura (MMSE: 0.40, 95% CI 0.13, 0.66; global cognition: 0.13, 95% CI 0.01, 0.24). Amongst specific cognitive domains migraineurs performed better on tests of executive function and fine motor skills. The difference in MMSE between migraineurs and non-migraineurs was greater in women (0.25, 95% CI 0.10, 0.40) than in men (0.13, 95% CI −0.15, 0.40), while the difference in global cognition was similar in men and women (0.15, 95% CI 0.04, 0.27 and 0.09, 95% CI 0.02, 0.15, respectively).

Conclusions: Migraineurs, particularly migraineurs with aura, tend to score higher in cognition tests than non-migraineurs. More studies are needed to corroborate these findings.

Conflict of interest
Disclosure statement:
Ke-xin Wen is funded by a grant by Metagenics Inc.

EHMTC-0229
POSTER SESSION F

MIGRAINE IN WOMEN IS ASSOCIATED WITH SMALLER RETINAL ARTERIOLAR CALIBER: THE ROTTERDAM STUDY

K.X. Wen[1], U. Mutlu[1], M.K. Ikram[1], A. Hofman[1], C. Klaver[1], M. Kavousi[1], O.H. Franco[1], M.A. Ikram[1]

[1]*Erasmus MC University Medical Centre, Epidemiology, Rotterdam, Netherlands*

Background: Migraine is more frequent among women and has been associated with increased risk of cardiovascular disease. Considering the potential role of microvascular pathology in cardiovascular disease, especially among women, we investigated the association between migraine and retinal microvascular caliber.

Methods: In 2944 participants of the Rotterdam Study, migraine was assessed using a validated questionnaire. Retinal microvascular caliber was measured by semi-automatic assessment of digitized retina images. Participants were classified as non-migraineurs (n = 2439) or migraineurs (n = 505). Generalized linear regression models were used to evaluate the association between migraine and retinal vessel caliber, adjusting for the other vessel, age, sex, education and cardiovascular risk factors. In addition, we performed stratified analyses by sex and migraine subtypes.

Results: In overall analyses, we did not find differences in retinal calibers between migraineurs and non-migraineurs. However, after stratification by sex, among women we found smaller arteriolar calibers in migraineurs compared to non-migraineurs (mean difference in adjusted caliber in women: −1.70 (95% CI −3.06, −0.34) μm, and 2.34 (95% CI −0.15, 4.83) μm in men, *p*-interaction = 0.004). When comparing migraine with and without aura to non-migraineurs, no differences were found.

Conclusions: Amongst women, migraineurs have smaller mean arteriolar caliber than non-migraineurs. More studies are needed to verify these findings.

Conflict of interest
Disclosure statement:
Ke-xin Wen is funded by a grant from Metagenics inc.

EHMTC-0210
POSTER SESSION F

MIGRAINE RADAR – A NOVEL APPROACH COLLECTING MIGRAINE ATTACK DATA USING SMARTPHONE APPS AND WEB FORMS

F. Wogenstein[1], J. Drescher[1], J. Scheidt[1], C. Gaul[2], P. Kropp[3]

[1]*University of Applied Sciences Hof, Institute of Information Systems, Hof, Germany*
[2]*Migraine and Headache Clinic, Migraine and Headache Clinic, Königstein, Germany*
[3]*University of Rostock, Institute of Medical Psychology and Medical Sociology, Rostock, Germany*

About 10% of the population suffers from migraine. Nevertheless, despite this large number of affected persons, most of the traditional epidemiological studies, analyzing triggers of migraine, are based only on small groups of patients – usually up to 200 participants. Furthermore, these studies are often limited in relation to regional extensions as well as to the time periods of the surveys. These limitations become a disadvantage when analyzing migraine triggers which affect only a small group of patients, e.g., different levels of stress between full-time workers and unemployed people.

In this work we introduce a newly developed system for the collection of migraine attack data. Migraine patients – the migraine type is diagnosed by a standard questionnaire or a qualified doctor – have to register and afterwards submit information about their migraine attacks using a smartphone or a PC. In order to cluster patients later on, we collect demographic information as well as spatial data for each migraine attack. To respect the patients' privacy, all data are saved in pseudonymized form – only information necessary for our analyses are requested.

This new approach helped us to recruit about 3,000 (April 2016) migraine patients, within Germany, Austria and Switzerland, participating in our project. After a period of only 10 months the participants reported nearly 20,000 migraine attacks. With this large quantity of data, we will be able to identify and evaluate groups of patients with very specific triggers causing their migraine attacks, e.g., certain weather conditions, geomagnetic activity or other environmental impacts.

EHMTC-0304
POSTER SESSION F

ACUTE HEADACHE MANAGEMENT

M. Allam[1], C. Spence[1], E. Newman[2], J.P. Leach[2]

[1]*University of Glasgow, School of Medicine, Glasgow, United Kingdom*
[2]*Queen Elizabeth University Hospital, Department of Neurology- Institute of Neurological Sciences, Glasgow, United Kingdom*

Introduction: The Scottish Intercollegiate Guidelines Network's (SIGN) guideline 107 outlines the management of acute headache. The aim of this project was to assess potential over or under investigation of patients admitted with acute headache. Furthermore, we are trying to clarify if a specialist headache service would change management by reducing investigations, and decrease future referrals to outpatient neurology.

Methods: 37 patients admitted with headache to a large teaching hospital, over a period of three months, were identified using the computer database system, Trakcare. Data was collected retrospectively using: neurology clinic and discharge letters, inpatient notes, as well as biochemistry and radiology records.

Results: Over 45 days, 37 patients were admitted with acute headache, accounting for 42 admissions. Average length of stay was two days. 40% of admissions were due to sudden onset headache. 30 patients received a computerised tomography (CT) scan (10% abnormal). Lumbar puncture (LP) was performed for 16 patients (0% abnormal). Six patients had a CT Venogram (17% abnormal). Sudden onset, gradual onset and known headache sufferers were investigated equally. Five patients were seen by neurology as an inpatient. Seven patients were referred to neurology outpatient clinic. No formal diagnosis on discharge was noted in 31 patients.

Conclusion: Headache is a common area of diagnostic uncertainty. It relies on accurate neurological assessment to avoid over investigation. The results highlight diagnostic uncertainty among general physicians dealing with headache and suggested over investigation with LP. Both of these findings would suggest that formal specialist headache services would therapeutically and financially benefit patients and NHS services.

EHMTC-0300
POSTER SESSION F

TYPICAL VISUAL AURA WITHOUT HEADACHE. CLINICAL DESCRIPTION OF A SERIES OF 27 PATIENTS

R. Belvis[1], A. Aceituno[1], N. Mas[1], N. Morollon[1], S. Yagüe[1]

[1]*DEXEUS UNIVERSITY HOSPITAL, NEUROLOGY, Barcelona, Spain*

Episodes of typical visual aura without headache (TVAWH) may appear occasionally in 33% of patients with migraine with aura(MA), but approximately 3–6% of migraine patients present exclusively TVAWH, and they never suffer the migraine headache in their lifes.

Patients with TVAWH (ICHD-3 beta Code:1.2.1.2): A. Fulfils criteria 1.2.1 for MA; and B. No headache accompanies or follows the aura within 60 minutes in patients without migraine previously known.

We include 27 patients (average age–42.2 years,85.6%-women). The 59.2% had a family history of migraine. The debut of the TVAWH was the cause of the visit in 15 patients-55.5%. The rest suffered from TVAWH for an average of 18.8 years with an average of 6.9 episodes/year (1–18). The average duration of the TVAWH was 27.7 minutes (5 to 60 minutes) and the 100% appeared and disappeared progressively (no ictal presentations). The clinical picture was: sparkling scotoma-10, photopsies-8, spectral fortification-4, water vision-2, glare-1, revealed filter-1, scotoma-2. Only 2 patients(7.4%) presented negative visual phenomena. The 'VARS scale was suggestive of 'aura (more than 5 punts) in 100% of cases with a mean value of 6.1 points(5–8). All the patients had normal brain MRI and cardiovascular studies; and negative thrombophilia tests. No treatment was started during a 22.6 months follow-up.

The typical visual 'aura without headache is uncommon. Although the 'TIA is the main differential diagnosis there are several items that suggest aura: duration of 5–60 minutes, progressive development, visual positive phenomenon, a family history of migraine, absence of vascular risk factors and suggestive VAR scale score.

EHMTC-0360
POSTER SESSION F

THE ASSESSMENT OF HEADACHES ON THE ACUTE MEDICAL UNIT: IS IT ADEQUATE AND HOW COULD IT BE IMPROVED?

S. Binks[1], J. Ganesalingam[2], A. Ratnarajah[1]

[1]*Brighton and Sussex University Hospitals NHS Trust, Acute medicine, Brighton, United Kingdom*
[2]*Brighton and Sussex University Hospitals NHS Trust, Neurology, Brighton, United Kingdom*

Introduction: Neurological emergencies are common and represent 15–25% of the medical take, second only to cardiac and respiratory cases. However, the UK has a low number of neurologists compared to comparable nations.

Method: This quality improvement project aimed to explore and optimise acute headache management in our institution. We carried out an on-line survey of doctors' knowledge of acute headache presentations and an audit of current clinical practice. Using this information and literature review, we developed a comprehensive acute headache guideline for the hospital's clinical handbook for doctors.

Results: 62 doctors, from pre-registration house officers to consultants, responded to our survey, of whom 32 (51.6%) saw 1–2 headache patients per week. 53/56 (94.6%) agreed a guideline would be useful. Only 40.3% (25/62) agreed they would do fundoscopy, with availability of equipment a key barrier. Knowledge of some important causes of headache was high, but was lower for others, including cerebral venous sinus thrombosis, cervical artery dissection, carbon monoxide poisoning and acute glaucoma. A consultant neurologist deemed 14/27 (51.9%) of acute headache presentations audited to have an entirely appropriate management. Our guideline, written by acute medicine in conjunction with senior clinicians from neurology and stroke, is now in use.

Conclusion: We conclude there is room for improvement in the investigation and management of acute headache and a guideline may be a cost-effective method to achieve this.

Conflict of interest
Disclosure statement:
Dr Binks currently holds an NIHR academic clinical fellowship

EHMTC-0087
POSTER SESSION F

THEORY OF MIND IN CHRONIC MIGRAINE

S. Bottiroli[1], S. Negro[1], E. Cavallini[2], S. Lecce[2], G. Sances[1], M. Allena[1], N. Ghiotto[1], E. Guaschino[1], G. Sandrini[1], C. Tassorelli[1], G. Nappi[1]

[1]*National Neurological Institute C. Mondino, Headache Science Center HSC, Pavia, Italy*
[2]*University of Pavia, Department of Brain and Beavioural Sciences, Pavia, Italy*

Background: Theory of Mind (ToM) is the ability to infer mental states and to use them in order to understand, predict and affect other's behaviour. ToM is fundamental for individual's wellbeing as it allows social competent behaviours. Evidences have shown an association between ToM and Alexithymia (A), which refers to the inability to identify and express emotions. Since previous studies have showed pathological scores of A in chronic migraine, ToM could be low in this population.

Aim: To evaluate whether chronic migraine is associated to deficit in ToM and in other aspects of social functioning.

Method: 67 patients suffering from chronic migraine (CM) (80.6% female, Age: 42.9 ± 8.8) and 60 healthy controls (HC) (65.0% female; Age: 37.9 ± 12.3) were evaluated using a battery of tests of ToM (Strange Stories task and the Animation task) and questionnaires on their social functioning. Chronic migraine diagnosis was operationally defined according to ICHD-IIIβ. Data were analyzed with analysis of variance.

Results: Compared with HC, CM patients had significantly lower scores in both ToM tests: the Strange Stories task ($CM = 5.8 \pm 1.6$, $HC = 6.7 \pm 1.3$, $p < .001$) and Animation Task ($CM = 14.6 \pm 3.3$, $HC = 16.5 \pm 4.1$, $p = .008$). Healthy controls also reported to be part of broader social networks and believed to be abler to understand others' feelings in comparison to chronic migraineurs.

Conclusions: Our results indicate that CM patients have more difficulties in understanding others' mental states than healthy controls. This evidence suggests the existence of a link between this chronic condition and ssocial competent behaviours and abilities.

EHMTC-0088
POSTER SESSION F

STUDY OF THE RELATION BETWEEN ALEXITHYMIA AND CHRONIC MIGRAINE WITH MEDICATION OVERUSE

S. Bottiroli[1], F. Galli[2], M. Viana[1], G. Sances[1], M. Allena[1], N. Ghiotto[1], E. Guaschino[1], G. Sandrini[1], C. Tassorelli[1], G. Nappi[1]

[1]*National Neurological Institute C. Mondino, Headache Science Center HSC, Pavia, Italy*
[2]*University of Milan, Dept of Health Sciences, Milan, Italy*

Background: Alexithymia (A) describes the inability to identify and express emotions. Neuroimaging studies showed specific neural correlates in alexithymic subjects and pathological scores in several chronic pain populations and in episodic migraine. It is unclear whether there is a role for A in the evolution from episodic Migraine (MIG) into Medication Overuse Headache (MOH).

Aim: To evaluate whether MOH individuals differ from MIG as regards alexithymia scores and to investigate the association of alexithymia with headache characteristics.

Method: 101 patients suffering from MOH ($N = 56$; 78.6% female, Age: 42.0 ± 11.0) evolved from migraine (chronic migraine + MOH) or MIG ($N = 45$; 74.5% female; Age: 40.9 ± 9.2) were evaluated using the Toronto Alexithymia Scale (TAS-20), which has a three-factor structure consisting of (F1) Difficulty in identifying feelings, (F2) Difficulty in describing feeling and (F3) Externally oriented thinking. Diagnosis in the 2 groups was operationally defined according to ICHD-IIIβ.

Results: MIG and MOH patients were comparable in terms of demographic characteristics. MOH patients scored higher than MIG on two of the three alexithymia factors: (F1) difficulties in identifying (MOH $= 19.2 \pm 6.6$, MIG $= 13.8 \pm 6.6$, $p < .001$) and (F2) describing feelings (MOH $= 14.4 \pm 4.4$, MIG $= 11.7 \pm 4.8$, $p = .003$). Groups were comparable in term of (F3) externally oriented thinking (MOH 18.7 ± 4.2, MIG $= 18.2 \pm 4.3$, $p = .50$). Significant correlations resulted between A and illness characteristics.

Conclusions: Results show a specific alexithymic profile in MOH population, suggesting that alexithymia could represent a risk factor in the transformation from episodic migraine into the chronic subtype with medication overuse.

EHMTC-0288
POSTER SESSION F

HEADACHE SELF-ADMINISTERED QUESTIONNAIRE IN THE WAITING ROOM, A USEFUL AND EASY TOOL FOR HEADACHE CENTRES

T. Catarci[1]

[1]*Rome, Italy*

The diagnosis of headache rely mostly upon patient's history, but second level headache centres of the Italian NHS have to face the difficulty of a shorter availability of time. Therefore, we elaborated a self-administered questionnaire to be filled-in while patients are in the waiting room. It was decided to study patient's compliance and comprehension of any single item, in order to finally reshape a more informative questionnaire. Most of ICHD-II criteria for primary headache were transformed in questions, formulated in such a way that they could be self-administered, easily understood, and quickly filled out. Patients consulting for headache for the first time were asked to fill in a 16-item questionnaire in an outpatient neurology clinic of the Italian NHS, between October 2014 and June 2015.

One-hundred and twenty patients were admitted to the outpatient clinic, 90 females and 30 males, mean age 41 years $+14.7$, mostly suffering from primary and episodic headaches. Twenty-seven patients only, out of 120, did not fill in the questionnaire: they were significantly older than those who filled in the questionnaire ($46.2 + 15.4$ vs $39.5 + 14.3$, $p < 0.05$), there were more females than males (27% vs 13%, $p < 0.05$) and more secondary headaches (50% vs 18% $p < 0.001$). This self-administered tool was well accepted by the patients, it was not intended to be a screening or a diagnostic tool, simply it allowed the patients to better focus on informative items of their headache and the Clinician to reduce visit time.

EHMTC-0161
POSTER SESSION F

CHARACTERISTICS OF HYPERTROPHIC PACHYMENINGITIS IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS

H.A. Choi[1], M.J. Lee[1], C.S. Chung[1]

[1]*Samsung Medical Center- Sungkyunkwan University School of Medicine, Department of Neurology, Seoul, Republic of Korea*

Objective: Hypertrophic pachymeningitis (HP) is an important neurologic complication of granulomatosis with polyangiitis (GPA; formerly Wegener's

granulomatosis). The aim of this study is to investigate clinical features, radiological findings, and diagnostic pitfalls of GPA-related HP.

Methods: Retrospective chart review was performed to screen patients who were diagnosed with GPA at Samsung Medical Center between 1997 and 2016. Neurologic symptom manifestation, brain imaging, and clinical course were evaluated in all patients. Characteristics of patients with HP were compared with those of patients without HP.

Results: A total of 65 patients with GPA were identified in the study period. Among them, 25 patients who presented neurologic symptoms underwent brain imaging, HP was second most common neurologic complication (N = 9, 36%), compared to inflammatory pseudotumor (N = 16, 64%) and stroke (N = 7, 28%). Patients with HP showed more p-type ANCA positivity (N = 6 vs N = 17 in non-HP controls, p = 0.065), longer interval from symptom onset to diagnosis (median 246 days, IQR [223–924] vs median 80.5 days, IQR [39–199.5] in non-HP controls, p = 0.002), and less systemic manifestation (N = 1, 11.1% vs N = 37, 67.3%, p = 0.002 in lower airway; N = 0, 0% vs N = 26, 47.3%, p = 0.002 in kidney) than non-HP patients. HP patients presented with headache (N = 8, 88.9%), which was similar with primary headache disorders (migrainous N = 1, 12.5%, tension-type N = 1, 12.5%, stabbing N = 3, 37.5%) and other secondary headache disorders (postural-type N = 1, 12.5%, meningitis N = 1, 12.5%) while they rarely had neurologic deficits (N = 3, 37.5%).

Conclusion: HP can be the first clinical manifestation of GPA. Different clinical-radiologic features can be presented in GPA-related HP.

EHMTC-0157
POSTER SESSION F

MIGRAINE WITH CRANIAL AUTONOMIC SYMPTOMS TREATED AT A TERTIARY HEADACHE CENTER IN JAPAN: PRELIMINARY STUDY OF 138 MIGRAINE PATIENTS

D. Danno[1], S. Kikui[2], K. Ishizaki[2], T. Takeshima[2], H. Yoshikawa[1]

[1]*Hyogo College of Medicine, Neurology, Nishinomiya, Japan*
[2]*Tominaga Hospital Headache Center, Department of Neurology, Osaka, Japan*

Background: Migraine with cranial autonomic symptoms (CAS) has been reported in 26.9% of migraine patients in a population-based study, and in 37.4% in patients presenting at tertiary headache centers. However, there have so far been no reports on migraine with CAS in Japan.

Aim: To clarify the prevalence of migraine with CAS (CAS+) and without CAS (CAS-) in patients presenting at a tertiary headache center in Japan, and to investigate the clinical phenotype.

Method: We studied 138 consecutive episodic and chronic migraineurs who presented at the Tominaga Hospital Headache Center and Hyogo College of Medicine Hospital with face-to-face interviews, while carefully noting the detailed migraine characteristics from April 2015 until March 2016.

Results: According to our findings, 49 out of 138 cases (35.5%) had CAS. The CAS+ cases had a longer average disease duration compared to the CAS- cases (19.5 years vs 17.4 years), more strictly unilateral headache (65.3% vs 50.6%), more severe headache pain (NRS 8.24 vs 7.78), a longer attack duration (34.9 hours vs 29.5 hours), and more frequent allodynia (30.6% vs 16.9%), however, the differences did not reach the statistically significant level.

Discussion: Migraine with CAS is relatively common in Japan. It is estimated that the hyperactivity of the trigemino-autonomic reflex due to central sensitization plays a role in this, because there were longer and more severe headache attack cases in the CAS+ patients. The accumulation of further such cases is therefore needed in the future to better elucidate the mechanism of action in such cases.

EHMTC-0255
POSTER SESSION F

CLINICAL USE OF THE HURT QUESTIONNAIRE IN MANAGEMENT OF MEDICATION OVERUSE HEADACHE

M.K. Danoe[1], A. V. Rasmussen[1], A.F. Jonasson[1], H. Rasmussen[1], N.L. Find[1], R.H. Jensen[1]

[1]*Rigshospitalet, Danish Headache Center, Glostrup, Denmark*

Background & Aim: Medication-overuse headache (MOH) is a wide-spread and potentially treatable headache with a world-wide prevalence of 2%. MOH is disabling and cause a significant impact on patients' lives. At the Danish Headache Center, a tertiary specialized center, all patients diagnosed with MOH are referred to headache nurses for detoxification.

The HURT (Headache Under-Response to Treatment) Questionnaire, a validated and easy applicable instrument,

involves headache frequency and related disability, medication use and efficacy and patients' experience of treatment and self-efficacy.

The aim of this study is to evaluate the patient experiences of the treatment and to compare self-efficacy before and after treatment of MOH by means of HURT.

Design & Methods: Throughout 2 years data was systematically collected on all newly diagnosed MOH patients. The headache nurses gave detailed information to each patient for decision-making according to the treatment plan. Patients answered HURT at baseline and after 1 year.

Primary Endpoints: The change in medication use, disability and self-efficacy related to headache measured by HURT.

Results: In total 407 patients (110 M/297F, mean age of 45 years) were diagnosed with MOH – close to 25% of all newly referred patients. Of the 407 patients 80% completed the detoxification program.

So far 51 patients answered HURT both at baseline and follow-up. They experienced significant improved treatment, less disability and a lower number of days using acute medication ($p < 0.001$*). Furthermore, a significant improvement of the patients' self-efficacy was noted.

Conclusions: We find that HURT is a useful clinical instrument to survey headache management for patients with MOH.

EHMTC-0402
POSTER SESSION F

ANXIETY AND DEPRESSIVE SYMPTOMS IN HEADACHE SUFFERERS VS. HEADACHE FREE PATIENTS

C. Deligianni[1], E. Kasioti[1], E. Mitropoulou[1], I. Belesioti[1], D.D. Mitsikostas[1]

[1]*ATHENS NAVAL HOSPITAL, Neurological department, ATHENS, Greece*

Background: Primary headache syndromes are often comorbid with affective disorders.

Aim: To evaluate the frequency of anxiety and depression symptoms in a large sample of headache sufferers' population compared to a headache free population.

Methods: Patients seeking consultation at the Athens Naval Hospital Headache Clinic were prospectively screened using a specific questionnaire that included the Hamilton rating scales for anxiety (HAM-A) and depression (HAM-D).

Results: 545 headache sufferers (333 females and 212 males; mean age 39.9 ± 14.9 years) and 150 headache free patients (94 females and 56 males; mean age 33.5 ± 4.3 years) completed the two interviews. The average scores of the Hamilton rating scales for anxiety and depression were significantly higher in headache sufferers (18.6 ± 8.2 and 14.7 ± 8.6, respectively) than in headache-free people (6.8 ± 4.0 and 5.7 ± 3.3, respectively). Table 1 shows the mean scores (±SD of HAM-A and HAM-D scales by headache disorder.

Conclusion: Patients suffering from medication overuse and chronic headache subtypes are suffering from anxiety and depressive symptoms very often, indicating specific management and treatment.

HEADACHE SUBTYPE	N (%)	HAM-A	HAM-D
Episodic MwoA	101(18.5)	15.7±7.6	11.6±6.8
Episodic MwA	25(4.6)	16.9±7.8	13.6±6.9
Chronic Migraine	172(31.6)	20.7±7.6	16.3±7.3
Episodic TTH	59(10.8)	18.0±8.0	13.4±6.1
Chronic TTH	99(18.2)	21.0±8.7	18.1±11.7
Episodic Cluster H	26(4.8)	13.5±8.0	12.2±8.1
Chronic Cluster H	8(1.5)	11.8±3.5	9.1±3.2
Other primary H	15(2.8)	20.3±6.9	18.1±5.8
Medication Overuse H	42(7.7)	26.9±8.1	21.0±8.1

EHMTC-0415
POSTER SESSION F

CHARACTERIZATION OF NECK AND SHOULDER PAIN IN SELF-TREATING PATIENTS WITH HEADACHE

H. Gräter[1], T. Weiser[1], C. Gaul[2]

[1]*Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany*
[2]*Migraine and Headache Clinic Königstein, Königstein, Germany*

Background: Acute headache or migraine attacks -widely self-treated with over-the-counter-analgesics, are commonly associated with neck and shoulder pain (NSP). Further understanding of NSP in headache patients may help to reduce suffering.

Aim: To better characterize self-diagnosing and self-treating patients, and to evaluate the effect of age, gender, physical activity and stress on NSP.

Methods: In this pharmacy-based survey, patients filled in a questionnaire about demographics, pain characteristics and treatment effect after use of fixed dose combinations of acetylsalicylic acid, paracetamol and caffeine (Thomapyrin®).

Results: 72% of 1298 participants were females. Headaches were assigned to tension-type headache TTH; n = 828) or migraine (n = 206) according to IHC-II diagnosis criteria. 54% females and 44% males reported NSP – with no difference between TTH and migraine. Presence of NSP increased with age (18–29y: 46%; 30–49y: 53%; >50y: 55%), stress level (relaxed 47%; slightly stressed 52%, extremely stressed 58%), and was positively correlated with the number of days with pain during the last 30 days (mean change 1.2; 95%CI 0.518-1.793, p = 0.0004; mean 5.4 (TTH 4.8; migraine 6.7)). No/little stress was negatively correlated. No consistent trend was evident for physical activity. More than 90% rated efficacy and tolerability of treatment to be "good" or "very good".

Conclusions: The risk factors NSP and stress are associated in self-treating headache patients. Patients' assessment of efficacy of acute medication is good; strategies to prevent headache could be more beneficial if they include NSP therapies and stress management.

Conflict of interest
C Gaul has potential conflict of interest to disclose.
C Gaul received honoraria for advise, oral presentations or contributions to clinical trials from Allergan, Berlin-Chemie, MSD, electroCore, St. Jude Medical, Grünenthal, Desitin, Bayer, Boehringer Ingelheim, Autonomic Technologies and Hormosan. C Gaul has no ownership interests and does not own any pharmaceutical company stocks.

HG and TW are employed at Boehringer Ingelheim.

EHMTC-0387
POSTER SESSION F

MIGRAINE, HEADACHE AND COGNITION. A FOLLOW-UP STUDY ON COGNITIVE DECLINE

R. Gil-Gouveia[1], C. Loureiro[2], I. Martins[2]

[1]*Headache center- Hospital da Luz, Neurology, Lisboa, Portugal*
[2]*Instituto de Medicina Molecular IMM- Lisbon Faculty of Medicine, Department of Clinical Neurosciences UNIC, Lisboa, Portugal*

Objectives and Background: Cognitive performance of older adults and elderlies with persisting headaches and migraine has been shown to differ from control individuals in some aspects of executive functioning yet the influence of persisting migraine and non-migraine headache on cognitive decline is controversial.

Design and Method: Older (>50 years) adults with migraine, non-migraine headache and healthy controls had an extensive neuropsychological evaluation at baseline and after 5 years, to screen for cognitive decline in memory and/or executive functions.

Results: From the original 478 individuals, 275 (57.5%) were evaluated, with an age average of 70.40 + 8.34 years, 64% being females. Cognitive decline occurred in 14.9% of the sample, yet neither migraine nor non-migraine headache influenced the odds of decline. In migraine patients, decline was not consistently associated with migraine characteristics.

Conclusion: Persisting migraine and non-migraine headache at old age is not associated with an increase in probability of cognitive decline. Although chronic pain and aging are able to influence cognitive function, pain-related changes are probably due to pain adaptation mechanisms and not degenerative processes.

EHMTC-0403
POSTER SESSION F

VALIDATION OF THE COMPREHENSIVE HEADACHE-RELATED QUALITY OF LIFE QUESTIONNAIRE (CHQQ) IN THE ACTIVE PERIOD OF CLUSTER HEADACHE

T. Gyüre[1,2], M. Magyar[1], É. Csépány[1], Á. Palásti[1], G. Bozsik[1], C. Ertsey[1]

[1]*Semmelweis University, Department of Neurology, Budapest, Hungary*
[2]*Semmelweis University, János Szentágothai Doctoral School of Neurosciences, Budapest, Hungary*

Background: Cluster headache (CH) is one of the most intense human pain syndromes. Despite this, information about its effect on the quality of life (QOL) of patients is relatively scarce.

The Comprehensive Headache-related Quality of life Questionnaire (CHQQ) is a new headache-specific QOL questionnaire, developed at the Department of Neurology, Semmelweis University.

Aim: To present the psychometric properties of the CHQQ in cluster headache (CH).

Patients and methods: 60 CH patients (age 39.2 ± 13.3 years; 21 females and 39 males) suffering from episodic CH (N = 57) or chronic CH (N = 3) completed the CHQQ and the SF-36 questionnaires. The clinical characteristics of the headaches were collected using a structured interview. We assessed the reliability (internal consistency) as well as the criterion, convergent and discriminative validity of the CHQQ. To examine the discriminative validity of the instrument, CH patients' data were compared to those of 177 migraineurs (age: 34.9 ± 11.2 years; 156 females and 21 males).

Results: The CHQQ showed excellent reliability: Cronbach's alpha was 0.922 for the whole instrument, and 0.765–0.843 for its dimensions. CHQQ's dimensions and total score showed significant negative correlations with headache severity and attack frequency (criterion validity), and showed significant positive correlations with most of the the SF-36 domains (convergent validity). Most of the items as well as the total score and all dimensions were significantly ($p < 0.05$) lower in the CH group than in the migraine group (discriminative validity).

Conclusion: The CHQQ showed adequate psychometric properties in this group of cluster headache patients.

EHMTC-0259
POSTER SESSION F

THE LAST TEN HEADACHE PATIENTS' AN EVALUATION OF ACUTE HEADACHE CARE FOR THE WEST MIDLANDS STRATEGIC CLINICAL NETWORK

E. Brown[1], T. Hayton[1]

[1]*University Hospital Birmingham, Neurology, Birmingham, United Kingdom*

Background: Strategic Clinical Networks (SCN) have been established to bring together clinicians, commissioners and service users with the aim of improving the complex patient care pathways. The care of patients with acute severe headache in particular has been identified as one such pathway, requiring input from a number of different specialities. The West Midlands SCN for Mental Health, Dementia and Neurological Conditions has commissioned an evaluation of the acute severe headache pathway, staring with a 'last ten patient' study at the regional neurosciences centre.

Methods: The case notes of ten consecutive patients with acute severe headache who presented to and were admitted from the emergency department at UHB were reviewed and the nature of every documented interaction with a medical professional assessed. Data collected included the personnel involved, the time and what change, if any, to the diagnosis or plan was made.

Results: Six patients were felt to have primary headache syndromes; one had a blocked shunt; and one an acute stroke. There were two patients with post-LP headaches. These latter were the only patients who did not have a CT brain scan. None of the patients were seen by a neurologist. The longest avoidable delay was due to an error with processing a CSF sample.

Discussion: There are areas for improvement in terms of resource use and length of stay. Input from neurologists or other headache specialists, both at a strategic level and through direct input is urgently needed and strategies have been proposed to achieve this.

EHMTC-0130
POSTER SESSION F

FACTORS INFLUENCING PROGRESSION OF EPISODIC TO CHRONIC HEADACHES IN SOUTH INDIAN POPULATION

V Karthikeayan[1], G. Shankar[1], C. Venkatraman[1]

[1]*Madras Medical College, Institute of Neurology, Chennai, India*

Objectives: To investigate the factors influencing the progression of episodic headaches to chronic headaches in a Tertiary care centre of South India

Methods: Seventy one patients diagnosed with primary headaches using ICHD-3(beta) classification were enrolled and interviewed face to face. They were classified into two groups, episodic (group1) and chronic headaches(group 2) based on the frequency of headache. 32 parameters, including employment status, duration of headaches, prophylactic dose titration, drug compliance, abortive therapy, comorbid illness, life style factors and headache characteristics were compared between the two groups. The study used Microsoft SPSS for statistical analysis. The parameters were grouped categorically and the results were analysed for statistical significance (p value $< .05$) using Chi-square test.

Results: 38 patients (53.5%) had episodic headaches and 33 patients (46.5%) had chronic headaches. Duration of headache, inadequate prophylactic drug dosing, drug in compliance,delayed intake of abortive drug during headaches, inadequate relief of headache following abortive therapy, high coffee intake, employment in females were significantly associated with chronic headaches. Hypertension, Diabetes, Obesity were not significant in influencing the progression of Episodic to Chronic

headaches. Disability and Depression were significantly higher in the chronic headaches. Medication overuse headache was significantly associated with chronic headaches.

Conclusion: Our study found high coffee intake and delayed intake of abortive drugs as new risk factors associated with chronic headaches. A proper follow up, regular drug dose titration, patient education and counselling can reduce the progression to chronic headache.

EHMTC-0131
POSTER SESSION F

PREVALENCE OF MULTIPLE HEADACHES IN PATIENTS TREATED FOR PRIMARY HEADACHE

V Karthikeayan[1], B. Kesavamurthy[1], C. Venkatraman[1]

[1]*Madras Medical College, Institute of Neurology, Chennai, India*

Objectives: To estimate the prevalence of multiple headaches in patients diagnosed with primary headache in South Indian population.

Methods: Seventy one patients who were enrolled for a comparative study between episodic and chronic primary headaches were diagnosed on the type of headache using the ICHD-3 (beta) version. Patients were grouped into patients with isolated primary headache (group 1) and patients with multiple headaches(group 2). The prevalence of multiple headaches was estimated. Comparison was made between the two groups on the basis of MIDAS, HIT-6 scores and Patient Health Questionnaire for depression.The parameters were grouped categorically and the results were analysed for statistical significance(p value $<$ .05) using Chi-square test.

Results: Of the 71 patients diagnosed and treated as primary headaches, 30 patients(42.3%) had isolated primary headache and 41 patients(57.7%) had multiple headaches. In the multiple headache group 34 patients and 7 patients had a total of two and three headache types respectively. 8 patients(11.3%) had another primary headache and rest had secondary headaches in addition to their primary headache for which they were treated. Medication overuse headache was the most prevalent secondary headache(24 patients-33.8%).MIDAS and HIT-6 score were significantly higher in the multiple headache group. Multiple headache group had moderate to severe depression compared to the isolated headache group.

Conclusions: It is essential to investigate for the presence of multiple headaches in patients treated for primary headache. Addressing each headache type individually would create a positive impact in patient outcomes.

EHMTC-0132
POSTER SESSION F

CLINICAL PROFILE OF MALE HEADACHE PATIENTS IN A SAMPLE SOUTH INDIAN POPULATION

V Karthikeayan[1], C. Venkatraman[1], G. Shankar[1]

[1]*Madras Medical College, Institute of Neurology, Chennai, India*

Objectives: To study the clinical profile of male primary headaches cases attending the headache outpatient service of the Institute of Neurology, Madras Medical College, Chennai, India.

Methods: Male patients (study group) who were enrolled for a comparative study between episodic and chronic primary headaches were selected. 32 parameters, including duration of headaches, prophylactic dose titration, drug compliance, abortive therapy, co morbid illness, life style factors headache characteristics, headache impact scores and sexual dysfunction were analyzed in the study group.Sexual dysfunction was compared between age matched healthy male volunteers and headache patients using International index of erectile function(IIEF) -5 score.

Results: A total of 31 male patients were studied. 16(51.6%) and 15(48.4%) had episodic and chronic headaches respectively.Average duration of headache was 4 years.15 patients had multiple headache(48.4%) of which 11 patients(35.5%) had medication overuse headache.11 patients(35%) had a moderate to severe erectile dysfunction.Erectile dysfunction was statistically significant in headache patients compared to the volunteers. Statistically significant erectile dysfunction were observed in chronic headache cases, multiple headaches and increased frequency of headache (p value $<$ .05).Erectile dysfunction was significantly associated with high MIDAS score and high Patient Health Questionnaire score(p value $<$ .05).

Conclusions: Erectile dysfunction is significantly associated with headache and remains to be an unaddressed issue.Multiple factors including chronic pain, depression, side-effects prophylactic drugs plays a role in erectile dysfunction of these patients. This study highlights the need for a consensus statement with regards to sexual dysfunction in males.

EHMTC-0273
POSTER SESSION F

PREMONITORY SYMPTOMS OF KOREAN MIGRAINEURS

B. KIM[1]

[1]*EUlji Hospital, Neurology, Seoul, Republic of Korea*

Some migraineurs can predict their headache attacks. The detection of premonitory symptoms has the potential to treat their attacks more effectively. However, published data show very diverse prevalence rate and different symptoms depending on the study designs. In addition, there have been few studies in Asian migrainueurs. We retrospectively studied the prevalence of self reported premonitory symptoms, which precede the aura and/or headache by 1 to 48 hours, in a clinic-based population. We consecutive collected 180 patients migraine without aura fulfilling the ICHD, 3rd beta criteria. 62 % of them can predict upcoming migraine attacks. However, symptoms other than dull head and/or neck pain were reported by 70 (39%). The most frequently reported premonitory symptoms were vague feeling that migraine attack is impending, indigestion, fatigue and concentration difficulties. Premonitory symptoms were more frequent in patients with female gender and longer duration of disease. In conclusion, many migraineurs feel that they can predict their attacks. However, many of them are dull aches, which are probably beginning of headache phase. Prospective study using diary is needed to differentiate premonitory symptoms from early phase of headache.

EHMTC-0247
POSTER SESSION F

PROFILE OF CHRONIC MIGRAINE PATIENTS FROM NEUROLOGY OUTPATIENT SERVICES OF A TERTIARY CARE NEUROLOGICAL UNIVERSITY TEACHING HOSPITAL FROM INDIA

G.B. Kulkarni[1], A.P. Kulkarni[1], G.N. Rao[2], G. Desai[3]

[1]*National Institute of Mental health & neurosciences, Neurology, Bangalore, India*
[2]*National Institute of Mental health & neurosciences, Epidemiology, Bangalore, India*
[3]*National Institute of Mental health & neurosciences, Psychiatry, Bangalore, India*

Background: Migraine in general and chronic form (CM) in particular are associated with significant disability in patients. There is lack of data from India.

Objective: To describe the, clinical profile and disability of CM patients attending OPD services our hospital.

Materials and Methods: It was a prospective study of patients (>18 years) satisfying ICHD-3(beta) criteria for CM attending general neurology outpatient dependent. Clinical profile, disability, quality of life and comorbidities were assessed. Ethical clearance and informed consent were taken.

Results: There were 49 (14.2%) patients of CM (M: F:: 1:9, mean age 32.2 ± 9.6years, urban: rural::7:3, 24(49%) poor,25(53%) unemployed and 26% illiterate) in a cohort of 315 patients of Migraine seen over 2 years. Mean duration of Migraine was 9.4 ± 7.0 years, 95% had MWoA, and 98% of attacks were rated as severe. Clinical features seen were-phonophobia (100%), photophobia (98%), nausea (79%), vomiting (39%). Family history of migraine seen-33%. Common triggers were emotional stress (71%), sleep deprivation (64%), travel (65%), hunger/fasting (57%). Disability according to MIDAS grade were -1 (2%), 2-(4%), 3(8%) and 4(86%). Quality of life assessed with MSQ showed mean of score-55.47 ± 9.1. Psychiatric comorbidy of anxiety(GAD7) (seen in 80%,mild-47%, moderate-27%, severe-6%)and depression(PHQ9) (seen in 76%,mild-43%, moderate-25%, moderately severe-2 severe-6%) were common. Medical comorbidities were comparable with non-migraine patients. For acute attacks 94 % were using analgesics, 86% CAM methods. Only 36% used prophylactic treatments. 36% patients knew about migraine.

Conclusion: CM is associated with significant disability, impaired quality of life, high prevalence of anxiety and depression and 2/3rd not receiving prophylactic treatment.

EHMTC-0393
POSTER SESSION F

PREVALENCE OF MEDICATION OVERUSE HEADACHE AMONG NEW NEUROLOGY REFERRALS WITH HEADACHE

V Little[1], J. Vanderpol[1]

[1]*Cumbria Neurology, Neurology, Penrith, United Kingdom*

Background: Headaches represent a significant proportion of neurology referrals. Medication Overuse Headache (MOH) is a recognized contributing factor of chronic headaches, particularly tension-type headaches and migraine. Management of MOH involves withdrawal of the suspected causative agent. This could be implemented in Primary Care.

Method: We performed a retrospective review of all new neurology patients seen over a 10-week period. 336 new patients were assessed during the period, of which 88

were referred with headache (26.2%). For all patients with headache we noted the diagnosis (following International Classification of Headache Disorders 3rd edition, beta version), and also if medication overuse headache was diagnosed or suspected as a contributory factor.

Results: 55 patients were diagnosed with primary headache. Of the patients with primary headache, 19 (34.5%) were identified as having an analgesia overuse, causing MOH, contributing to their headache.

Conclusion: 34.5% of primary headache patients had a suspected medication overuse headache contributing to their clinical picture. We believe if this was dealt with in primary care, this could significantly reduce referrals to neurology thus reducing burden to the neurology service and cost to Primary Care and the Clinical Commissioning Group.

EHMTC-0095
POSTER SESSION F

10-MINUTE-TRIAGE FOR ACUTE HEADACHE WITH KANPO MEDICINE (JAPANESE TRADITIONAL MEDICINE)

T. Matsuda[1], M. Takiguchi[2]

[1]*Misato Family Clinic, Family Medicine, Misato-shi, Japan*
[2]*Misato Family Clinic, Pediatrics, Misato-shi, Japan*

Background: We have investigated effectiveness of Kanpo medicine with Goreisan (Poria Powder with Five Hurbs; GR) and Goshuyutou (Evodia Decoction; GS) for acute headache in order to triage secondary headache.

Methods: Subjects had visited our clinic with acute headache from January 5th to October 31st in 2015. Cases with focal sign, meningeal sign, frequent vomiting or high fever were excluded, 101 patients were eligible for this study.

Age: 7- 74y.o (32.3 ± 17.1). Female/male = 78/23. GR and GS were given simultaneously orally, then numerical rating scale (NRS) of each headache had been obtained 10 minutes after intervention. GR and GS have been produced by Tsumura & Co. (Japan).

Results: GR and GS have shown effective in 85 patients (84.2%) within 10 minutes.

NRS 3/10 or less; 40/85 (47.1%). NRS 4-5/10; 33/85 (38.8%).

NRS 6–8/10; 12/85 (14.1%), who had given another GR and GS 15 minutes later after first intervention, subsequently all NRS had dropped below 3/10 after second intervention.

Non-responders (n = 16): Dissection of basilar artery, brain tumor, cervical disc herniation, and 2 cases of sinusitis found by MRI or MRA. 4 cases were due to mental disorders. 5 cases were idiopathic.

As to residual 2 cases, one was effective to triptan, and the other was effective to second intervention with GR & GS despite of first intervention failure.

Conclusions: No response to combination therapy with GR and GS for acute headache allows us easily to find patients with secondary headache, suggesting would be useful not only for general practitioners but also emergency medical care.

EHMTC-0100
POSTER SESSION F

HEADACHES: CLINICAL FORMS AND ELECTROENCEPHALOGRAPHIC STUDY IN THE NEUROLOGY UNIT OF CONAKRY TEACHING HOSPITAL

M. Mohamed Lelouma[1], H. Moriba[2]

[1]*cheikh anta diop university, Teaching Hospital in Fann, Dakar, Senegal*
[2]*Conakry University Teaching Hospital, Neurology Unit, Conakry, Guinea Republic*

Headaches are a subject of concern and effort consuming within neurology. Electroencephalography stands as the reference method to investigating brain function, readily available in routine medical practice.

The goal of this single center study was to determine its frequency in a neurology unit and to study the EEG profiles obtained during headache events.

Among 2139 outpatients the study recruited 144 consulting for headaches in the unit over 12 months. Thirty patients were lost after the first consultation. The EEG was performed on all patients but only 52 upon agreed to conduct a second check. The Research and Study Group on Headaches' classification (Brest 1985) was used to distributing them into five groups. They were analyzed according to the conventional method of interpretation and gathered in two groups considered normal and abnormal.

Headaches accounted for 6.73% of the main reason for consulting. The distribution of collected cases is shown below.

Headache	Frenquency	Single check	Double check Normal	Double check Abnormal
Mixed	40.36	46	04	01
Organic Neurological	28.95	33	29	02
Psychogenic	17.54	20	04	–
Migraine	11.40	13	12	–
Organic Non Neurological	1.75	02	–	–
Total	100	114	49	03

In our cohort, a significant correlation index between the types of headaches collected and the abnormal EEG profiles analyzed was not established. However, for three cases referred the traces were quite instrumental for diagnostic orientation. Multiple checks on the same patient may help for diagnostic consolidation during headaches crisis thus contributing to the dynamic classification of headaches. Further multicenter studies are needed.

EHMTC-0269
POSTER SESSION F

DEVELOPMENT OF AN EDUCATIONAL AND SELF-MANAGEMENT INTERVENTION FOR CHRONIC HEADACHE – CHRONIC HEADACHE EDUCATION AND SELF-MANAGEMENT STUDY (CHESS)

S. Patel[1], D. Carnes[2], M. Matharu[3], T. Pincus[4], H. Sandhu[1], M. Underwood[1], K. Probyn[4]

[1]*University of Warwick, Medical School, Coventry, United Kingdom*
[2]*University of Applied Sciences and Arts Western Switzerland, School of Health Sciences, Fribourg, Switzerland*
[3]*Institute of Neurology and The National Hospital for Neurology and Neurosurgery, Headache Group, London, United Kingdom*
[4]*Royal Holloway- University of London, Department of Psychology, London, United Kingdom*

Purpose: To develop and evaluate an education and self-management support intervention for the management of chronic headaches, specifically, migraine, tension type headache and medication overuse headaches.

Methods: The development of the intervention has been informed by a systematic review of educational and/or self-management interventions for chronic headache, qualitative literature and interview material on the lived experiences of chronic headache, a review of the predictors of poor outcomes from headache disorders, and our knowledge from an existing intervention package for people living with chronic musculoskeletal pain. These data were bought together at an intervention development meeting comprising of the academic team, clinical team and lay people living with chronic headaches.

Results: The CHESS intervention comprises self-management and education topics including acceptance, mood and headache, recognising unhelpful thought patterns and behaviours, stress management, sleep management, medication management, communication and mindfulness. This will be a group intervention where participants will attend a two day programme delivered by a nurse and lay person with chronic headaches. Each participants will subsequently attend a one to one consultation with the nurse to diagnose their headache and discuss medication, lifestyle management and goal setting. Following this the group of participants will come back for a follow-up session. Each participant will also be provided with ongoing telephone or email support for up to eight weeks.

Conclusion: We have developed an intervention package from the evidence base with the aim to pilot this before going onto a randomised controlled trial.

EHMTC-0271
POSTER SESSION F

ASSESSING THE IMPACT OF CHRONIC AND EPISODIC HEADACHE AND TREATMENT OUTCOMES: A SYSTEMATIC REVIEW OF PATIENT-REPORTED OUTCOME MEASURES (PROMS)

K.L. Haywood[1], T.S. Mars[2], R. Potter[2], S. Patel[2], M. Underwood[2]

[1]*University of Warwick, Royal College of Nursing Research Institute, Coventry, United Kingdom*
[2]*University of Warwick, Medical School, Coventry, United Kingdom*

Purpose: To critically appraise, compare and synthesise the quality and acceptability of headache-specific multi-item PROMs evaluated following completion by people with chronic or episodic headache (including migraine).

Methods: Systematic literature searches of major databases (1980–2015) to identify published evidence of measurement and practical properties of clearly defined PROMs. Data was extracted and assessed against accepted standards for study and measurement quality to inform an evidence synthesis.

Results: 36 articles provided evaluative evidence for 11 headache (5) and migraine (6)-specific PROMs. Evidence of

structural validity and internal consistency was mixed: the strongest evidence was for the MSQ v2.1 and the HIT-6. Evidence of temporal stability was limited, but acceptable for the HIT-6. Evidence of construct validity was also mixed: strong and modest evidence was reviewed for the HIT-6 and MSQ v2.1 respectively. Responsiveness was rarely evaluated; but estimates of the minimal important difference were reviewed for the MSQ v2.1 and HIT-6. The contribution of patients in PROM development and evaluation is limited and often poorly reported.

Conclusion: Despite the large number of PROMs, evidence for the majority is limited. However, two high quality measures were reviewed – the 6-item HIT-6 and 14-item MSQ v2.1. The HIT-6 is recommended where a short but comprehensive assessment of headache impact is required for completion by a mixed population of headache patients. However, the relevance and acceptability of these measures to patients must be explored and robust evidence of responsiveness to important change is required.

EHMTC-0266
POSTER SESSION F

STYLE AND CONTENT OF EDUCATIONAL AND SELF-MANAGEMENT INTERVENTIONS FOR CHRONIC HEADACHE – A SYSTEMATIC REVIEW

K. Probyn[1], F. Caldwell[1], H. Bowers[1], M. Matharu[2], S. Patel[3], H. Sandhu[3], M. Underwood[3], T. Pincus[1]

[1]*Royal Holloway University of London, Psychology, Egham, United Kingdom*
[2]*The National Hospital for Neurology and Neurosurgery, Headache Group- Institute of Neurology, London, United Kingdom*
[3]*University of Warwick, Warwick Medical School- Warwick Clinical Trials Unit, Coventry, United Kingdom*

Aim: To identify components of non-pharmaceutical educational and self-management interventions for chronic headache and the style of delivery to inform the development of the intervention for CHESS (Chronic Headache Education and Self-management Study).

Methods: We included studies published in English, validating one or more educational and/or self-management intervention for chronic headache. The interventions had to be directed at patients, and we excluded any invasive treatments such as acupuncture and interventions involving apparatus such as TENS machines or biofeedback interventions. We also excluded interventions purely focusing on physical exercise. We excluded studies with participants' <18 years old, dissertations and conference proceedings.

We searched MEDLINE, Embase, Web of Knowledge and PsycINFO using free text and MeSH terms based on NICE headache guidelines 2012.

Two reviewers independently extracted data using a predetermined pro-forma; and assessed the risk of bias in RCTs.

Results: We identified 15.332 titles, removed 3669 duplicates, and reviewed 145 papers, of which 44 were included in the review.

Included studies comprised 28 RCTs and 16 uncontrolled experimental or observational studies.

The majority of studies featured a relaxation component (n = 34) and/or a psychological component (n = 26); headache information was featured in 17 studies and mindfulness in five.

Most intervention were delivered in group-sessions (n = 21), 19 in individual sessions, and 10 studies featured remote delivery of the intervention. Homework practice was part of 18 interventions and email/telephone support was available in 5 interventions.

Conclusions: We have found a reasonable number of studies validating non-pharmaceutical self-management and/or educational interventions featuring various components.

EHMTC-0404
POSTER SESSION F

MENTAL DISORDERS, HEADACHE AND PAIN IN PRIMARY CARE

J. Peceliuniene[1], I. Zukauskaite[2], A. Karvela[3], R. Bunevicius[4]

[1]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*
[2]*Vilnius University, Faculty of Philosophy, Vilnius, Lithuania*
[3]*Klinikum Darmstadt, Neurologie Dpt., Darmstadt, Germany*
[4]*Lithuanian University of Health Sciences, Bahavioral Institute, Palanga, Lithuania*

The aim of the study was to evaluate mental disorders in relation to pain, particularly headache, in primary care (PC).

Methods: a cross-sectional study with 496 adult consecutive PC patients was performed. Patients' mental status

was evaluated twice, by using MINI international Neuropsychiatric Interview (MINI) and Hospital Anxiety and Depression Scale (HADS). McGill Pain self-assessment Questionnaire was filled in by patients.

Results: There were 264 patients having mental disorders, according MINI with the high rates of major depressive episode (MDD) (N = 40), generalized anxiety disorder (GAD) (N = 52), suicide ideation (SI) (N = 42) and pathological alcohol use (N = 131). 187 patients indicated having pain and most of them – 45 patients(24%) had headache. Headache was found more often for those having problems with alcohol use by MINI compared with those, who had headache but did not use alcohol pathologically (19 (9.9%) vs.16 (5.2%) p = 0.037), and no associations were found between MDD, GAD, SI and headache. Patients having depression or anxiety diagnosed by HADS, more often felt pain in general 37 (53,6%) compared with those who had no mental diagnosis 152 (35.6%) (p = 0.004). However pain in other body parts was related with HADS diagnosis more often than with headache (torso 33.3% vs 17.6%, p = 0.003; legs 15.9% vs 6.3%, p = 0.009; dorsum 8.7% vs 3.3%, p = 0.046; head p > 0.05).

Conclusions: Mental disorders are prevalent and associated with pain in primary care. Headache is associated with pathological alcohol use in PC.

EHMTC-0076
POSTER SESSION F

SURFACE-BASED MORPHOMETRY REVEALS GRAY MATTER ABNORMALITIES IN MIGRAINE WITH AURA

I. Petrusic[1], M. Dakovic[2], J. Zidverc[3,4]

[1]*Faculty of Medicine, Radiology, Belgrade, Serbia*
[2]*Faculty of Physical Chemistry, Physical Chemistry, Belgrade, Serbia*
[3]*Neurology Clinic- Clinical Center of Serbia, Center for headaches, Belgrade, Serbia*
[4]*Faculty of Medicine, Neurology, Belgrade, Serbia*

Objective: Previous studies have reported gray matter alterations in migraineurs. We aimed to explore cortical thickness abnormalities in migraineurs with aura and to delineate possible relationships between cortical thickness changes and clinical variables.

Methods: Forty-eight migraineurs with aura and 30 healthy controls were selected for the study. All participants were scanned on a 1,5T magnetic resonance imager. Surface-based morphometry was used to segment each brain volume, reconstruct and inflate the cortical sheet, and estimate gray matter thickness. Correlation analysis was conducted between cortical thickness of significant clusters and clinical variables.

Results: Migraineurs did not differ significantly from controls in relation to age and gender (39,3 ± 11,2 vs. 39,6 ± 12; 75% vs. 76% females). Compared to controls, migraine patients had cortical thinning in left rostral-anterior cingulate gyrus, entorhinal gyrus, precuneus, and middle-temporal gyrus; also in right medial-orbitofrontal cortex, insula, fusiform gyrus, caudal-anterior cingulate gyrus, inferior parietal gyrus, pars triangularis and bilateral inferior temporal gyrus, post-central gyrus and lateral orbitofrontal cortex. Monte-Carlo simulation yielded left inferior temporal gyrus, lateral orbitofrontal cortex and right medial orbitofrontal cortex and insula, as significantly differ in migraineurs. Considering all the migraine patients, we did not find a significant correlation between gray matter reduction and frequency of migraine attacks, duration of migraine aura or duration of disease.

Conclusions: We have provided evidence for interictal cortical abnormalities in migraineurs with aura. Our findings of greater gray matter reduction in insula, temporal and orbitofrontal cortex support the concept that migraine may be a progressive disorder with complex pathophysiology.

EHMTC-0278
POSTER SESSION F

DEVELOPMENT OF A CHRONIC HEADACHE CLASSIFICATION INTERVIEW – CHRONIC HEADACHE EDUCATION AND SELF-MANAGEMENT STUDY (CHESS)

R. Potter[1], K. Dodd[1], M. Matharu[2], K. Probyn[3], M. Underwood[1]

[1]*University of Warwick, Clinical Trials Unit, Coventry, United Kingdom*
[2]*Institute of Neurology and The National Hospital for Neurology and Neurosurgery, Headache Group, London, United Kingdom*
[3]*Royal Holloway- University of London, Department of Psychology, London, United Kingdom*

Purpose: To develop and validate a telephone classification interview that can be used by a non-headache specialist to classify common chronic headache types in primary care.

Methods: The development of the classification interview has been informed by a systematic review of evidence on diagnostic tools for headache disorders; and a chronic headache classification consensus conference held at University of Warwick in October 2015. Conference

delegates were randomly allocated to multidisciplinary groups and a nominal group technique used to reach consensus on the key questions to be included in the classification interview.

Results: 26 delegates attended the conference, 5 headache specialist nurses, 13 neurologists (10 with a special interest in headache), 7 lay representatives (people living with headache) and 1 GP with a specialist interest in headache. Informed by evidence from the systematic review and delegate expertise, consensus was gained on key questions to:

- Confirm the diagnostic criteria for chronic headache
- Exclude secondary headaches (other than medication overuse)
- Exclude primary headache disorders other than migraine and tension type headache
- Distinguish between chronic migraine, probable chronic migraine, and chronic tension type headache
- Identify medication overuse headache

We used findings from the consensus conference to develop a logic model to underpin the content and structure of the telephone classification interview.

Conclusion: We have developed a telephone classification interview that can be used by a non-headache specialist to classify common chronic headache types in primary care which will be validated as part of the Chronic Headache Education and Self-management Study (CHESS).

EHMTC-0268
POSTER SESSION F

PREDICTORS OF CHRONIC HEADACHE – A SYSTEMATIC REVIEW

K. Probyn[1], F. Caldwell[1], H. Bowers[1], M. Matharu[2], H. Sandhu[3], M. Underwood[3], T. Pincus[1]

[1]*Royal Holloway University of London, Psychology, Egham, United Kingdom*
[2]*The National Hospital for Neurology and Neurosurgery, Headache Group- Institute of Neurology, London, United Kingdom*
[3]*University of Warwick, Warwick Clinical Trials Unit-Warwick Medical School, Coventry, United Kingdom*

Aim: Identify predictors of poor outcome from chronic headache disorders to identify potentially modifiable risk factors from prospective studies.

Methods: We included RCTs and prospective cohort studies of chronic headache, published in English, since 1980. Participants must be adults with chronic migraine, chronic tension-type headache with or without medication overuse headache disorders. We excluded studies with participants' <18 years old, dissertations and conference proceedings.

We searched key databases: Cochrane, Medline/Pub Med, Embase, Psychinfo, Web of science, ASSIA and Econlit.

Two reviewers independently extracted data and assessed the methodological quality.

RCTs were only included if subgroup analysis or predictor analysis reported or enough data to perform subgroup analysis – the adequacy of subgroup analyses was assessed.

Results: We identified 14803 titles, removed 663 duplicates, and reviewed 198 papers, of which 31 were included in the review – 21 prospective cohorts and 10 RCTs with subgroup analysis.

It wasn't possible to combine data in meta-analysis or perform subgroup analysis because of heterogeneity among studies. We categorised predictors in disease predictors and treatment predictors.

Predictor analyses in included studies comprised various demographics (Body Mass Index, sex, age, income, mental health, work status), headache characteristics (headache frequency, headache related disability, headache intensity and medication use) and sleep with mixed findings.

Conclusions: Despite a number of papers published on prognostic factors for headache in general or episodic headache– there is less evidence on prognostic factors explicitly for chronic headache.

EHMTC-0252
POSTER SESSION F

"WHAT'S UNDER THE HAT?" EXAMINING PATIENTS' STORIES ABOUT HEADACHE. A QUALITATIVE RESEARCH OF IMPLEMENTING A PUBLIC AWARENESS CAMPAIGN

P. Rossi[1], M.T. Aquilano[2], E. Ruiz De La Torra[3], J. Whelan[4], A. Craven[4]

[1]*INI, Headache Centre, Grottaferrata Rome, Italy*
[2]*European Headache Alliance, European Headache Alliance, Rome, Italy*
[3]*European Headache Alliance, European Headache Alliance, Valencia, Spain*
[4]*European Headache Alliance, European Headache Alliance, Dublin, Ireland*

Background: "What's under the hat?" a headache awareness story-telling campaign launched by the European Headache Alliance, aims a) to increase awareness of and compassion for the real and everyday impact of headache disorders amongst the general public; b) to help those affected to know that they are not alone and that headache disorders are treatable.

Aim of the study: We evaluated if the stories posted online reached campaign objectives. Methods. We conducted a qualitative analysis of patient stories posted during the first 4 months of the campaign and asked a selected team to rate the stories on their appropriateness, appeal and clarity.

Results: 30 stories were analyzed. Most patients described the dramatic impact of headache on their working and private life. Predominant feelings portrayed were anger, unhappiness and resignation. A lack of empathy from social groups and colleagues was reported. Appropriateness and clarity of patients' stories were rated as 'very good' whereas their appeal was scored as 'sufficient'.

Conclusions: Stories posted online reached the campaign aims, representing a potential powerful educational tool on the burden and impact of headache disorders,. The hopelessness evident in the stories however may wrongly suggest that headache disorders whilst common and disabling cannot be treated.

EHMTC-0020
POSTER SESSION F

HOW TO MEASURE HEADACHE SERVICE QUALITY: EVALUATION OF QUALITY INDICATORS IN 14 EUROPEAN SPECIALIST-CARE CENTRES

S. Schramm[1], D. Uluduz[2], R. Gil Gouveia[3], R. Jensen[4], A. Siva[2], U. Uygunoglu[2], G. Gvantsa[5], M. Maka[5], M. Braschinsky[6], E. Filatova[7,8], N. Latysheva[7,8], V. Osipova[8,9], K. Skorobogatykh[9], J. Azimova[9], A. Straube[10], O.E. Eren[10], P. Martelletti[11], V. De Angelis[11], A. Negro[11], M. Linde[12,13], K. Hagen[12,13], A. Radojicic[14], J. Zidverc-Trajkovic[14], A. Podgorac[15], K. Paemeleire[16], A. De Pue[16], C. Lampl[17], T. Steiner[18,12], Z. Katsarava[19,20]

[1]*University of Duisburg-Essen, Institute of Epidemiology-Biometry and Statistics, Essen, Germany*
[2]*Cerrahpasa School of Medicine- Istanbul University, Department of Neurology, Istanbul, Turkey*
[3]*Hospital da Luz, Hospital da Luz Headache Centre-Neurology Department, Lisbon, Portugal*
[4]*University of Copenhagen- Rigshospitalet-Glostrup, Danish Headache Centre- Department of Neurology, Copenhagen, Denmark*
[5]*Aversi Clinic, Department of Neurology, Tbilisi, Georgia*
[6]*Tartu University Clinics, Department of Neurology, Tartu, Estonia*
[7]*Alexander Vein Headache Clinic, Alexander Vein Headache Clinic, Moscow, Russia*
[8]*First Sechenov Moscow State Medical University, Moscow, Russian Federation*
[9]*Mowcow University, University Headache Clinic, Moscow, Russia*
[10]*Ludwig-Maximilians-University Munich- Klinikum Großhadern, Department of Neurology, Munich, Germany*
[11]*Sapienza University of Rome- Regional Referral Headache Centre- Sant'Andrea Hospital, Department of Clinical and Molecular Medicine, Rome, Italy*
[12]*Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway*
[13]*St Olavs University Hospital, Norwegian Advisory Unit on Headaches, Trondheim, Norway*
[14]*Clinical Centre of Serbia, Neurology Clinic, Belgrade, Serbia*
[15]*University of Belgrade, Faculty of Medicine, Belgrade, Serbia*
[16]*Ghent University Hospital, Department of Neurology, Ghent, Belgium*
[17]*Headache Medical Center Linz Seilerstätte, Headache Medical Center Linz Seilerstätte, Linz, Australia*
[18]*Imperial College London, Division of Brain Sciences, London, United Kingdom*

[19]*Evangelical Hospital Unna, Department of Neurology, Unna, Germany*
[20]*Medical Faculty, University of Duisburg-Essen, Germany*

Objective: The study was a collaboration between *Lifting The Burden* (LTB) and the *European Headache Federation* (EHF). Its aim was to evaluate the implemetation of quality indicators for headache care Europe-wide in specialist headache centres (level-3 according to the EHF/LTB standard).

Methods: Employing previously-developed instruments, we made enquiries in each of 14 specialist headache centres of health-care providers (doctors, nurses, psychologists, physiotherapists) and 50 patients, and analysed the medical records of 50 patients. Enquiries were in 9 domains: diagnostic accuracy, individualized management, referral pathways, patient's education and reassurance, convenience and comfort, patient's satisfaction, equity and efficiency of the headache care, outcome assessment, and safety.

Results: Our study showed that highly experienced headache centres treated their patients in general very well. Health-care staff were content with their work and their patients were content with their treatment. Including quality-of-life evaluation and protocols regarding safety proved problematic: better standards for these are needed. Some centres had difficulties with follow-up: many specialised centres operated in one-touch systems, with no possibility of controlling long-term management or the success of treatments dependent on this.

Conclusion: This first Europe-wide quality study showed that the quality indicators were workable in specialist care. They demonstrated common trends, producing evidence of what is majority practice. They also uncovered deficits that might be remedied in order to improve quality. They offer the means of setting benchmarks against which service quality may be judged. The next steps are to take the evaluation process into non-specialist care (EHF/LTB levels 1 and 2).

Conflict of interest
Disclosure statement:
RJ, AS, VO, PM, KP and ZK are Board members of the European Headache Federation. RJ, PM, TJS and ZK are directors and trustees of Lifting The Burden. No author has other conflicts of interest relevant to the subject matter of this manuscript.

EHMTC-0281
POSTER SESSION F

NEUROLOGICAL AND INSTRUMENTAL ASPECTS OF HEADACHES IN YOUNG INDIVIDUALS OF KYRGYZ REPUBLIC

C. Shambetova[1], T. Musabekova[1], S. Schleifer[1], N. Rsalieva[1]

[1]*Kyrgyz-Russian Slavonic University, Neurology, Bishkek, Kyrgyz Republic*

Due to high prevalence of headaches in young individuals, pathogenic mechanisms research is becoming increasingly relevant. With accordance to high intellectual and physical activity, psychological tension, student lifestyle, highlands conditions, neurological and instrumental aspects of headache in students are researched.

Methods: 69 KRSU students at the age of 19 to 25 years old were examined: 35 females (50.7%), 34 males (49.3%). Survey, neurological examination, neuropsychological examination: trait and situational anxiety (Spielberger) and depression (Zung V), Mini Mental Scale Examination (MMSE), Multidimensional Fatigue Inventory (MFI); and cardiointervalography were used. Statistical analysis conducted with SPSS.

Results: 30 (43.5%) out of all students suffered cephalalgia of primarily vascular-dystonic nature and tension. 30% out of above mentioned students had dizziness during the examination. More than half of the students with headache didn't have meals on regular basis (63.3%) and had sleep/wake disorders (56.6%). In 43.3% of the examined water consumption deficit was indicated. Daily walk within 1–2 km was mentioned by 15 (50.0%) students. During results comparative analysis, mentioned disorders were identified in individuals with headaches. Intense lifestyle is reflected in high and mild trait anxiety – 17 (56.7%) and 12 (40%) accordingly, and in increased level of situational anxiety – 80.0%. Mild depressive disorders were more often observed in students with cephalalgia (40.0%), than in total amount of students. More than 1/3 with headaches indicated below-normal MMSE. In 40% of the cases, according to cardiointervalography, parasympathetic influences at rest predominated.

Conclusion: Revealed vegetative, emotional and neuropsychological disorders may cause and aggravate primary headaches.

EHMTC-0223
POSTER SESSION F

CLINICAL PROFILE, TRIGGERS FOR CHRONIFICATION AND TREATMENT OUTCOME IN CHRONIC MIGRAINE: A CLINIC BASED STUDY FROM NORTH INDIA

S. Sharma[1], D. Chowdhury[1], G. Khwaja[1]

[1]*Govind Ballabh Pant Institute Of Post Graduate Medical Education And Research Gipmer, Neurology, New Delhi, India*

Introduction: Data on clinical profile, triggers for chronification and treatment of chronic migraine (CM) are sparse from India. This report presents the data on these aspects of CM.

Methods: Patients diagnosed as CM by ICHD3β were prospectively evaluated at the headache clinic of a tertiary care centre with a structured questionnaire. Demography, clinical features and treatment outcomes were analyzed.

Results and discussion: 235/1000 consecutive patients (24%) were diagnosed as CM over a period of 1.5 years. 221(96%) patients had episodic migraine (EM) and 14(6%) had de-novo CM. Mean age of onset of EM was 26.2 years with M:F ratio 4.34:1. Mean duration of EM before transformation was 7.8 years. Mean duration of CM was 14.3 months. 92.5% patients transformed to CM abruptly. Mean attack frequency of CM was 22.4 days/month. Identifiable triggers were seen in 30% (family stressors, blunt head injury, exams, social stressors and weight gain). Allodynia was present in 51%. Medication overuse headache (MOH) occurred in 26% (96% NSAIDs and 4% triptans). 70% of MOH responded to withdrawal.

Six months follow up data in 218 patients showed reversal to EM in 78.5%. Divalproex, topiramate/amitriptyline combinations provided best results. Treatment response was better in women (82.87% vs 56.76%; $p < 0.001$) but not influenced by the duration ($p = 0.280$) or attack frequency ($p = 0.34$) of CM.

Conclusion: One in four patients attending headache clinic has CM. It is more frequent in women and 50% had allodynia. Chronification triggers were seen in 1/3rd and MOH in 1/4th. Majority reverted to EM on optimum treatment.

EHMTC-0230
POSTER SESSION F

A COMPARATIVE STUDY OF CRANIAL AUTONOMIC DYSFUNCTIONS IN ADULT MIGRAINE AND CLUSTER HEADACHE PATIENTS

A.S. Singh[1], D. Chowdhury[1], G.A. Khwaja[2]

[1]*GB Pant Institute of Post Graduate Medical Education and Research, Headache Clinic- Department of Neurology-, New Delhi, India*
[2]*GB Pant Institute of Post Graduate Medical Education and Research, Department of Neurology-, New Delhi, India*

Introduction: Very few studies have compared head to head the cranial autonomic symptoms/signs (CAS) in cluster headache (CH) and migraine.

Aim of study: To study and compare CAS in migraine and cluster headache patients.

Material and methods: We analyzed following 10 features of CAS in migraine and CH patients (diagnosed by ICHD3β): lacrimation, conjunctival injection, eyelid edema, nasal congestion, rhinorrhea, facial/forehead sweating, facial/forehead flushing, drooping of eyelid, aural fullness and miosis. We noted their occurrence, laterality and extent of involvement.

Results: 41 CH patients [28 episodic and 13 chronic] were studied. Ipsilateral autonomic dysfunction was present in all (100%). Most common CAS was lacrimation (39/41; 95%) Bilateral CAS was seen in 21 patients (51%), commonest being facial/forehead sweating. Degree of involvement varied from 1 CAS feature in 2% to 7 in 4% patients. Majority (21%) had a combination of 4 CAS features.

50 migraine patients [39 episodic and 11 chronic] were studied. 2 (4%) patients had migraine with aura. 5 patients had side locked headaches (10%). CAS was present in 24 (48%) patients. Ipsilateral CAS was present in 9/24 (38%) and bilateral in 15/24 (62%). Most common CAS was lacrimation (23/50; 46%). Degree of involvement varied from 1 CAS feature in 12% to 7 in 2% patients. Majority (50%) had a combination of 2 CAS features.

Conclusion: All CH patients had ipsilateral while half had bilateral CAS in addition. In contrast, CAS was seen in only half of migraine patients. Of these, two thirds had bilateral involvement. CH patients had more extensive involvement of CAS.

EHMTC-0181
POSTER SESSION F

OSMOPHOBIA AS A CLINICAL MARKER OF MIGRAINE: A PROSPECTIVE STUDY

A. Terrin[1], M. Bellamio[1], F. Mainardi[2], G. Zanchin[1], F. Maggioni[1]

[1]*University of Padua, Neurosciences, Padova, Italy*
[2]*Ospedale SS. Giovanni e Paolo, Neurology, Venice, Italy*

During a migraine attack, an unbearable perception of odours that are non-aversive or even pleasant outside the attack is often reported by migraineurs. This study analyses osmophobia as regards its characteristics and its possible role in the differential diagnosis between migraine and Episodic Tension-Type Headache (ETTH). For the first time, a prospective evaluation followed the retrospective investigation of this symptom: we analysed four consecutive attacks through a semi-structured questionnaire. We recruited from our Headache Centre 193 patients (140 female, 53 male, age 39.6 ± 12.5 years) of whom 128 suffered Migraine without Aura (MO), 5 Migraine with Aura (MA), 31 ETTH, 21 MO and ETTH, 7 MO and MA, 1 MA and ETTH. We studied 772 attacks. Among patients with MO, 67.2% (86/128) reported osmophobia in at least one of four attacks. This percentage raises to 75.8%, if we consider also those 11 patients who reported osmophobia during their headache history, without confirming it during the four prospectively studied attacks. As a whole, osmophobia was present in 75.8% of MO (97/128). The presence of osmophobia correlates with a higher number of accompanying symptoms, and a more typically migrainous pain pattern. Most frequently offending odours were scents (69.1%), cigarette and/or cigar smoke (57.2%) and food (56.4%). This prospective study shows that osmophobia is a frequent symptom of MO, present in about ¾ of these patients, whereas none of the 31 patients with ETTH suffered this symptom. Its high specificity is useful in the differential diagnosis between MO and ETTH.

EHMTC-0082
POSTER SESSION F

VISUAL AND POSTURAL MOTION EVOKED DIZZINESS SYMPTOMS DOMINATE IN VESTIBULAR MIGRAINE PATIENTS

D. Vuralli[1], F. Yildirim[1], D. Akcali[2], M. Ilhan[3], N. Goksu[4], H. Bolay[1]

[1]*Gazi University Faculty of Medicine, Department of Neurology and Algology, Ankara, Turkey*
[2]*Gazi University Faculty of Medicine, Department of Anesthesiology and Reanimation and Algology, Ankara, Turkey*
[3]*Gazi University Faculty of Medicine, Department of Public Health, Ankara, Turkey*
[4]*Gazi University Faculty of Medicine, Department of Otolaryngology, Ankara, Turkey*

Background and Objective: Vestibular migraine (VM) is one of the most common and underdiagnosed causes of vertigo. We aim to define characteristic vestibular symptoms of VM patients in whom peripheral causes of vertigo were excluded.

Methods: Vestibular symptoms of 101 VM patients who were referred to headache clinic by otolaryngology were retrospectively reviewed.

Results: The mean age of VM onset was 34.7 ± 11.0 years and VM diagnosis was delayed for 5.4 ± 5.2 years. Patients defined vestibular symptoms mainly as ground slipping under the feet (40.6%), feeling like there is an earthquake or swaying (27.7%), rocking on a boat (26.7%) and stepping on empty space (24.8%). In 60.4% patients, vestibular symptoms lasted seconds, in 32.7% lasted minutes and in 6.9% lasted hours. Eventhough vestibular symptoms were comprised of brief attacks, they occurred with every movement during migraine attack. 71.3% of the patients defined visually induced vestibular symptoms and 82.2% complained of positional vestibular symptoms. Trigger factors and accompanying diseases are similar with other migraine subtypes. 98.0% of the patients responded to migraine prophylaxis whereas 83.2% of the patients used vestibular suppresant drugs and only in 12.9%, these drugs were effective temporarily ($P = 0.003$).

Conclusion: In VM, vestibular symptoms seem to be defined with expressions similar to dizziness rather than internal or external vertigo. Visual and postural motion induced vestibular symptoms precipitated by migraine triggers and unresponsive to vestibular suppresant agents are highly suggestive of VM. Recognition of these typical vestibular symptoms by neurologists and ENT specialists would avoid the deferral of diagnosis of VM.

EHMTC-0324
POSTER SESSION F

VISUAL SNOW: A CASE SERIES OF 54 ADULTS

M. Weatherall[1]

[1]*Charing Cross Hospital, Department of Neurology, London, United Kingdom*

Visual snow is a condition characterised by the presence of continuous TV-static-like tiny flickering dots in the entire visual field. Many patients experience additional visual symptoms including palinopsia, entopic phenomena, photophobia, and nyctalopia, as well as other non-visual symptoms such as tinnitus. Neurological and ophthalmological investigations are normal. Only two limited cases series of this condition are currently available in the literature. The clinical characteristics of 54 adult patients (24 male, 30 female, aged from 17–64 years) seen between February 2013 and March 2016 are presented. The average age of onset was 25.5 years, with a mean duration of symptoms of 8.5 years prior to review. Two patients had other affected family members. 46% of patients experienced palinopsia, 44% entopic phenomena, 20% nyctalopia, and 15% photophobia. 93% of patients had a history of headaches, most commonly migraine (78% – 46% with aura), 41% experienced tinnitus, and 22% anxiety. A small proportion of cases (7%) experienced spontaneous remission of symptoms. Reduced intensity of symptoms was reported by 7/20 patients who took magnesium, riboflavin, and/or co-enzyme Q10. Small numbers of patients found acetazolamide, tinted glasses or overlays, or distraction techniques helpful.

EHMTC-0232
POSTER SESSION F

SPONTANEOUS CERVICAL EPIDURAL HAEMATOMA PRESENTING AS THUNDERCLAP HEADACHE – CASE PRESENTATION

B. Wysota[1], A. Williams[2], T. Hayton[2]

[1]*University Hospitals Birmigham, Neurology, Birmingham, United Kingdom*
[2]*University Hospitals Birmingham, Neurology, Birmingham, United Kingdom*

Thunderclap headache is most commonly associated with subarachnoid haemorrhage or other acute intracranial pathology. It's typically investigated with head imaging and lumbar puncture. We are presenting the case of spontaneous cervical epidural haematoma manifesting as thunderclap headache. This pathology could be missed by following standard investigations of thunderclap headache and highlighting importance of through clinical history.

86 year old man presented to Emergency Department with thunderclap headache and loss of consciousness. Patient developed severe occipital headache while leaving the bath than lost consciousness. After waking up he was unable to stand up, his lower legs felt numb and weak. Headache gradually improved within 30 min. His CT head after arrival to A&E didn't show any acute intracranial pathology. CSF was normal, xantochromia was negative. Within 48 hours patient recovered almost completely. Was able to mobilise independently and was considered fit for discharge by medical team. After neurology review MRI scan of cervical spine was organised revealing spontaneous cervical epidural haematoma.