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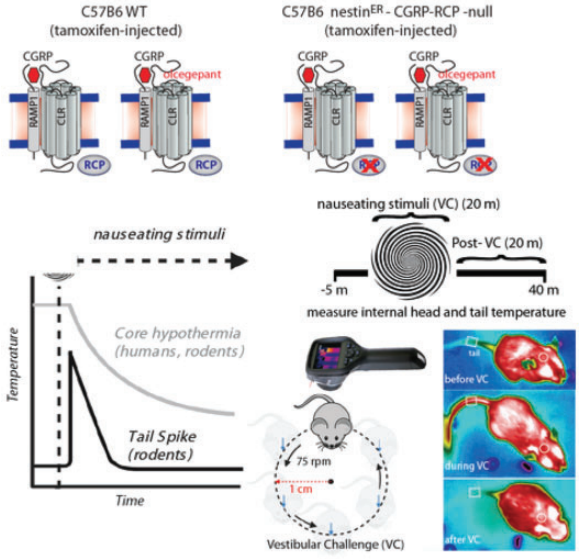
Headache pathophysiology – Basic science

IHC23-OR-001

The CGRP antagonist olcegepant does not block motion-induced nausea in mice lacking CGRP-Receptor Component Protein (CGRP-RCP)

Shafaqat Rahman, Ian Dickerson and Anne Luebke

University of Rochester, Rochester, NY, USA



Objective: Migraine and vestibular migraine (VM) are disorders associated with heightened motion sensitivity that lead to symptoms of motion-induced nausea. Monoclonal antibodies (mAbs) blocking CGRP and its receptor, as well as "gepants" antagonizing the CGRP receptor have been proven effective to reduce migraine nausea. However, 40% of patients are unresponsive to these new drugs, suggesting there may be other targets. The receptor for CGRP consists of three complexed proteins, i) CLR, ii) RAMP1, and iii) CGRP-Receptor Component Protein (RCP), an intracellular peripheral membrane protein required for signaling through the Gαs pathway. While current therapies have focused on antagonizing CGRP or CLR/RAMP1 complex we investigated what the loss of CGRP-RCP would have on a motion-induced nausea pain.

Methods: We have generated mice with a loxP conditional knockout of the 2nd exon of the Crcp gene. We then crossed these Crcp-loxP mice with nestin-CreER mice, resulting in mice with blocked neuronal RCP expression following tamoxifen induction. Tamoxifen-induced Crcp-loxP mice not expressing Cre served as controls. Both groups of mice were tested after tamoxifen induction in an assay of motion-induced nausea. Mice were assessed after intraperitoneal (IP) injections of: i) vehicle-PBS, ii) CGRP (0.1 mg/kg), or iii) CGRP (0.1 mg/kg) co-delivered with either olcegepant (1.0 mg/kg-CGRP-receptor antagonist) or rizatriptan (1.0 mg/kg-selective serotonin receptor agonists).

Results: We observed that CGRP increased motion-induced nausea, and that olcegepant (but not rizatriptan) was able to mitigate CGRP's effect in tamoxifen-treated control mice (n = 11F/11M). Interestingly, floxed CGRP-RCP null (-/-) mice responded similarly as controls to CGRP, yet neither olcegepant nor rizatriptan mitigated CGRP's effects (n = 11F/11M); suggesting that the absence of CGRP-RCP renders the receptor unresponsive to the antagonist olcegepant.

Conclusion: In summary, our findings show that: i) systemic CGRP increased motion-induced nausea in both control and mice lacking neuronal CGRP-RCP; and ii) loss of intracellular CGRP-RCP can render the CLR/RAMP1 complex insensitive to olcegepant, showing antagonist bias at the CGRP receptor.

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Disclosure of Interest: None Declared

Migraine preventive therapy

IHC23-OR-002

PACAP-targeted antibody Lu AG09222 inhibits vasodilation in healthy volunteers

Nadja Bredo Rasmussen[1,2], Christina Deligianni[1], Casper Emil Christensen[1], William Kristian Karlsson[1,2], Haidar Muhsen Al-Khazali[1,3], Tom Van de Casteele[4], Charlotte Granhall[4], Faisal Mohammad Amin[1,5] and Messoud Ashina[1,2]

[1]*Department of Neurology, Danish Headache Center, University of Copenhagen, Glostrup, Denmark*
[2]*Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Glostrup, Denmark*
[3]*Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Glostrop, Denmark*
[4]*H. Lundbeck A/S, Valby, Denmark*
[5]*Department of Neurorehabilitation/Traumatic Brain Injury, University of Copenhagen, Glostrup, Denmark*

Objective: To determine whether Lu AG09222—an investigational humanized monoclonal antibody directed against the pituitary adenylate cyclase-activating polypeptide (PACAP) ligand—would inhibit the PACAP-signaling cascade by abolishing its vasodilatory and headache-inducing abilities.
Methods: In a randomized, double-blind, parallel-group, single-dose, placebo-controlled study of Lu AG09222, healthy volunteers aged 18–45 years without history of headache disorders were randomly allocated to three treatment sequences (1:2:2) on two experimental infusion visits: placebo + saline + saline (n = 5), placebo + PACAP38 + vasoactive intestinal peptide (VIP) (n = 10), and Lu AG09222 + PACAP38 + VIP (n = 10). The primary outcome measure was area under the curve (AUC) of the change in superficial temporal artery (STA) diameter from 0 to 120 min after start of infusion of PACAP38. Secondary and exploratory outcomes analyzed changes in facial blood flow, heart rate, and headache. This study was conducted at the Danish Headache Center in Copenhagen, Denmark, and is registered with ClinicalTrials.gov (NCT04976309).
Results: In participants who received Lu AG09222 + PACAP38 infusion, there was a significantly lower STA diameter (mean (SE) [95% CI] AUC –35.4 (4.32) [–44.6, –26.3] mm × min; $P < 0.0001$) compared to participants who received placebo + PACAP38 infusion. Secondary and explorative analysis indicated LuAG09222 inhibited a PACAP38 infusion induced increase in facial blood flow, heart rate, and mild headache.
Conclusions: This proof-of-mechanism study demonstrates that Lu AG09222 inhibits PACAP38-induced cephalic vasodilation and increase in heart rate, and reduces concomitant headache. Lu AG09222 can be a potential therapy against migraine.

Headache and gender

IHC23-OR-003

Sex-dependent vascular effects of the endocannabinoid system and its regulation by TRPV1 channels

E. Rivera-Mancilla[1], A. van den Bogaerdt[2], A.H.J. Danser[1], C.M. Villalón[3] and A. MaassenVanDenBrink[1]

[1]*Erasmus University Medical Center, Division of Vascular Medicine and Pharmacology, Department of Internal Medicine, Rotterdam, Netherlands*
[2]*ETB-BISLIFE, Heart Valve Department, Beverwijk, Netherlands*
[3]*Cinvestav-Coapa, Department of Pharmacobiology, Mexico City, Mexico*

Objective: Endocannabinoids activate both cannabinoid (CB) receptors and transient receptor potential vanilloid 1 (TRPV1) channels to modulate vascular tone and pain pathways, including migraine. The contribution of TRPV1 channels in the sex-dependent modulation of vascular effects of endocannabinoids is not fully characterized. We investigated: (i) the vascular effect of anandamide (AEA, an endogenous $CB_{1/2}$ receptor/TRPV1 channel agonist) and N-arachidonoylethanolamine (ACEA, a synthetic CB1 receptor agonist); and (ii) the possible role of TRPV1 as modulator of the endocannabinoid system.
Methods: Human coronary artery segments [HCAs, (women n = 14, 50 ± 4 years; and men n = 9, 53 ± 3 years)] were used to evaluate the vasoactive effect of AEA (0.001–100 μM) or ACEA (0.01–10 μM). Therefore, concentration-response curves were constructed to obtain the maximum relaxant response (E_{max}). In a different setup of experiments, we evaluated the effect of 1 μM AM6545 (selective CB_1 receptor antagonist) in the E_{max} produced by AEA or ACEA in HCAs with or without capsaicin (TRPV1 activator, 10 μM) pretreatment.
Results: In HCAs from both women and men, AEA or ACEA induced concentration-dependent vasorelaxation. The E_{max} to AEA (women 59 ± 3% vs men 37 ± 4%) or ACEA (women 53 ± 3% vs men 34 ± 5%) was significantly higher in women than in men. Additionally, the E_{max} to AEA or ACEA was inhibited in the presence of AM6545: AEA, [women (control: 59 ± 3% vs AM6545: 29 ± 4%); men (control: 37 ± 4% vs AM6545: 20 ± 6%)]; and ACEA [women (control: 42 ± 5% vs AM6545: 17 ± 5%); men

(control: 22 ± 5% vs AM6545: 11 ± 5%)]. Moreover, TRPV1 desensitization produced a significant decrease in the E_{max} to AEA or ACEA in women (control: 59 ± 3% vs capsaicin: 42 ± 3%; and control: 42 ± 5% vs capsaicin: 21 ± 5%, respectively) but not in men (control: 37 ± 4% vs capsaicin: 29 ± 5%; and control: 22 ± 4% vs capsaicin: 20 ± 5%, respectively).

Conclusion: There is a differential vasoactive effect of the endocannabinoids between women and men, which is modulated by CB_1 receptors. Moreover, TRPV1 modulation of the endocannabinoid system might involve sex-dependent mechanisms. These findings suggest that the crosstalk between the endocannabinoid and vanilloid systems could represent a potential target for the treatment of neurovascular disorders, including migraine.

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Comorbidity of primary headaches

IHC23-OR-004

Abnormal serotoninergic and glutamatergic connectivity in visual snow syndrome and aura: evidence for 5-HT2A receptor dysfunction

Francesca Puledda[1,2], Ottavia Dipasquale[3], Benjamin Gooddy[3], Nazia Karsan[1,2], Ray Bose[4], Mitul Mehta[3], Steve Williams[3] and Peter Goadsby[1,2]

[1]*Headache Group, Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[2]*NIHR King's Clinical Research Facility, King's College Hospital, London, United Kingdom*
[3]*Centre for Neuroimaging Sciences, Department of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[4]*Greenlane Medical Specialists, Auckland, New Zealand*

Objectives: Here, we aimed to use receptor target maps combined with functional MRI data to identify neurotransmitters modulating brain circuit alterations in VSS, and to compare such changes with those shown by subjects with migraine.

Neuropharmacological changes in visual snow syndrome (VSS) are poorly understood. Involvement of glutamatergic networks is in line with evidence of hyperexcitability in the visual cortex, whereas hypotheses of dysfunctions of the serotoninergic (5-HT) system are based on cases of VSS being triggered by hallucinogenics, which target the 5-HT2A receptor. However, also dopaminergic, noradrenergic and gabaergic circuits might play a role in the pathogenesis of VSS.

Methods: We used Receptor-Enriched Analysis of Functional Connectivity by Targets (REACT) to estimate and compare the molecular-enriched functional networks of patients with VSS (n = 24), healthy controls (HCs, n = 24) and migraine patients (n = 25), both with (MwA n = 15) and without aura (MwoA, n = 10). Of the patients with VSS, n = 9 had no migraine (pure VSS), n = 14 had concomitant migraine, both with and without aura (VSS-MwA and VSS-MwoA).

For REACT we employed receptor density templates of the transporters of dopamine (DAT), noradrenaline (NAT) and serotonin (SERT), as well as the GABA-A and NMDA receptors, and estimated the subject-specific voxel-wise functional connectivity (FC) maps related to these molecular systems. We also ran a supplementary analysis focused on serotonin, exploring FC related to SERT, 5-HT1B and 5-HT2A.

For each system, we ran a one-way ANCOVA to compare the three groups (HC, VSS and migraine), including framewise displacement as a covariate of no interest. Additionally, to test if the changes found in the main analysis were unique to VSS, we ran sub-group one-way ANCOVAs comparing HC, pure VSS, MwoA; and HC, pure VSS, MwA.

Results: The ANCOVAs revealed significant differences in the SERT- and NMDA-enriched functional networks across the three main groups. Post-hoc analyses identified FC decreases in the SERT-enriched network between patients (both VSS and migraine) and HCs in the insula. In the NMDA-enriched network there was FC decrease in VSS with respect to HCs and migraine patients in the middle-posterior cingulate cortex.

In the 5-HT2A-enriched functional network, we found a bilateral area of decreased functional connectivity related to 5-HT2A in VSS and migraine as compared to HCs in the visual regions V5 and V3/V3A. The sub-group analysis showed similar decreased FC related to 5-HT2A in these areas in both pure VSS and MwA sub-groups, but not in MwoA.

Conclusions: Our results show that glutamate and serotonin are involved in brain connectivity alterations in areas of the limbic and visual systems in VSS. Importantly, decreased connectivity related to 5-HT2A in the visual network in VSS is independent of migraine biology, and shows a similar dysfunction to that of migraine with aura.

Disclosure of Interest: None Declared

Headache pathophysiology – Basic science

IHC23-OR-005

Proteomics profiling reveals mitochondrial damage in the thalamus in a mouse model of chronic migraine

Wei Xie[1], Ruibing Li[2], Yue Zhou[3] and Shengyuan Yu[1]

[1]*International Headache Center, Department of Neurology, Chinese PLA General Hospital, Beijing, China*
[2]*Department of Laboratory Medicine, the First Medical Center, Chinese PLA General Hospital, Beijing, China*
[3]*College of Life Science, Northwest University, Xi"an, China*

Background: Migraine, a complex brain disorder, is regarded as a possible clinical manifestation of brain energy dysfunction. The trigeminovascular system is considered the basis for the pathogenesis of migraine. We performed quantitative proteomics to analyse the protein signatures of certain regions in the trigeminovascular system, focusing on changes in mitochondrial function.
Methods: The mouse model of chronic migraine was established by repeated nitroglycerin (NTG) stimulation. The migraine-like behaviors were evaluated by von-Frey filament, hot plate instrument and light-dark box. Differential expressed proteins (DEPs) in some subcortical brain regions of trigeminovascular system were screened based on liquid chromatography-tandem mass spectrometry (LC-MS/MS). Compare the commonality and specificity of key signal pathways in different brain regions. Mitochondrial function was measured by Elisa, and mitochondrial morphology was observed by transmission electron microscope (TEM).
Results: The mouse central sensitization model of chronic migraine was successfully established by repeated NTG stimulation, which was characterized by periorbital and hind paw allodynia, and photophobia. The results of quantitative proteomics showed that 529,109,163,152 and 419 DEPs were detected between the NTG and control group in thalamus, hypothalamus, periaqueductal grey (PAG), trigeminal ganglion (TG) and trigeminocervical complex (TCC), respectively. No common key signal pathways were found across brain regions. The most significant change in the brain region-specific pathway was the thalamic mitochondrial dysfunction. Compared with the control group, the concentration of ATP and the activity of respiratory chain Complex I decreased ($P < 0.05$), and the number of abnormal mitochondria per unit area increased ($P < 0.01$) in thalamus in the NTG group.
Conclusion: Our findings highlight the involvement of mitochondrial damage in the thalamus in central sensitization of chronic migraine, which provide evidence of possible metabolic mechanisms in migraine pathophysiology.

Keywords: Chronic migraine; Thalamus; Mitochondrial damage; Proteomics.
Disclosure of Interest: None Declared

Headache classification

IHC23-OR-006

Are ICHD-3 criteria for headache attributed to Idiopathic Intracranial Hypertension (IIH) valid? Field-test and phenotyping in newly diagnosed IIH compared to clinical mimicries

Nadja Skadkær Hansen[1], Johanne Juhl Korsbæk[1], Hanne Maria Yri[2], Rigmor Højland Jensen[1] and Dagmar Beier[3,4]

[1]*Danish Headache Center, Department of Neurology, University Hospital Rigshospitalet, University of Copenhagen, Copenhagen, Denmark*
[2]*Department of Neurology, University Hospital Herlev, Herlev, Denmark*
[3]*Headache Clinic, Department of Neurology, Odense University Hospital, Odense, Denmark*
[4]*Department of Clinical Research, University of Southern Denmark, Odense, Denmark*

Objective: To field-test current International Classification of Headache Disorders version 3 (ICHD-3) criteria for headache attributed to Idiopathic Intracranial Hypertension (IIH) and to characterize headache phenotype in new-onset IIH compared to clinical mimicries.
Methods: In a prospective cohort of newly referred patients suspected of IIH at two tertiary headache centers applicability of the ICHD-3 was tested comparing patients with verified IIH to those in whom IIH was disproven (nonIIH). Headaches were also phenotyped according to resemblance of a primary headache disorder.
Results: In patients with IIH ($n = 140$), 72% had a new/worsened headache at time of diagnosis compared to 68% in the non-IIH group ($n = 99$, $p = 0.66$). Sensitivity of ICHD-3 criteria was 93%; specificity was 100%. Of all patients with headache, 65% and 0% fulfilled ICHD-3 criteria for IIH related headache in IIH and nonIIH, respectively. Comparing headache in IIH and nonIIH, it was migraine-like in 36% and 30%, tension type-like in 24% and 11%, and other/non-classifiable in 24% and 25% ($p = 0.35$), respectively. Pulsatile tinnitus accompanying headache was significantly more frequent in IIH vs. non-IIH (60% vs. 26%, $p < 0.0001$), but did not improve headache criteria applicability.
Conclusion: Current ICHD-3 headache criteria are sensitive and specific. Simplification may improve operationality without compromising accuracy; a new or worsened headache related to active IIH seem sufficient.
Disclosure of Interest: None Declared

Other secondary headache disorders

IHC23-OR-007

Long-Term Course of COVID-19 Vaccination-Related Headache: A Prospective Multicenter Follow-Up Study

Arife Çimen Atalar[1], Ayşe Nur Özdağ Acarlı[2], Betül Baykan[3,4], Hayrunnisa Bolay[5], Mustafa Ertaş[3], Esme Ekizoğlu[3], Ömer Karadaş[6], Paolo Marteletti[7,8], Burcu Polat[9], Işıl Yazıcı Gençdal[10], David Garcia-Azorin[11], Dimos Mitsikostas[12], Loukia Apostolakopoulou[12], Hamit Genç[13], Pınar Yalınay Dikmen[14], Rabia Gökçen Gözübatık[15], Javid Shafiyev Shafiyev[16], Bahar Taşdelen[17] and Aynur Özge[18]

[1]*Health Sciences University, Kanuni Sultan Süleyman Education and Research Hospital, Department of Neurology, Istanbul, Turkey*
[2]*Ermenek State Hospital, Department of Neurology, Karaman, Turkey*
[3]*Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, Headache Center, Istanbul, Turkey*
[4]*EMAR Medical Center, Department of Neurology, Istanbul, Turkey*
[5]*Gazi University, Medical Faculty, Department of Neurology and Algology, Istanbul, Turkey*
[6]*University of Health Sciences, Gulhane Training and Research Hospital, Department of Neurology, Ankara, Turkey*
[7]*Sapienza University, Department of Clinical and Molecular Medicine, Rome, Italy*
[8]*Sant"Andrea Hospital, Regional Referral Headache Centre, Rome, Italy*
[9]*Istanbul Medipol University, School of Medicine, Department of Neurology, Istanbul, Turkey*
[10]*Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatric, Neurologic and Neurosurgical Diseases, Istanbul, Turkey*
[11]*Hospital Clínico Universitario de Valladolid, Department of Neurology, Headache Unit, Valladolid, Spain*
[12]*First Neurology Department, Aeginition Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece*
[13]*University of Health Sciences, Van Training and Research Hospital, Van, Turkey*
[14]*Acibadem Mehmet Ali Aydinlar University, School of Medicine, Department of Neurology, Istanbul, Turkey*
[15]*Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatric, Neurologic and Neurosurgical Diseases, Istanbul, Turkey*
[16]*University of Health Sciences, Gulhane Training and Research Hospital, Department of Neurology, Istanbul, Turkey*
[17]*Mersin University School of Medicine, Department of Biostatistics and Medical Informatic, Mersin, Turkey*
[18]*Mersin University, Medical Faculty, Department of Neurology, Mersin, Turkey*

Objectives: Although headache related to COVID-19 vaccines is now well-recognized in the acute setting, little is known about its course and associated features in the long term. We aimed to investigate the course of prolonged/worsened COVID-19 vaccine-related headaches (PVRH).
Methods: We conducted a multinational, prospective study that included detailed questions about patients" pre- and post-vaccination headache conditions. In order to participate, patients must have experienced headache onset within the first 15 days after COVID-19 vaccination, and the headache starting within 0–72 hours after vaccination must have extended beyond this time. Standardized questionnaires were completed by headache experts at the first visit and at follow-up visits 3 and 6 months after vaccination to document the characteristics of PVRH. Cluster analysis was performed to define different patient clusters.
Results: The study included 174 patients (73.6% female) with a mean age of 45.2 ± 13.3 years. Among them, 107 (61.5%) had a pre-existing primary headache (PPH). We identified 2 clusters within patients with PVRH; Cluster 1 ($n = 86$) was composed of patients with PPH and more migrainous characteristics (throbbing, increase by physical activity, photo/phonophobia, osmophobia, nausea, frontal location, and more severe intensity) contrary to cluster 2 ($n = 88$) with stabbing, pressing quality and longer duration.
Conclusions: Patients with PVRH may show 2 separate clusters in the long-term independent of the type of COVID-19 vaccine type.
Disclosure of Interest: None Declared

Cluster headache and other trigeminal autonomic cephalalgias

IHC23-OR-008

Disease course and predictors of recurrence in patients with cluster headache: a prospective observation of 288 patients

Mi Ji Lee[1], Min Kyung Chu[2], Jae Myun Chung[3], Heui-Soo Moon[4], Pil-Wook Chung[4], Soo-Kyoung Kim[5], Jeong Wook Park[6], Byung-Kun Kim[7], Kyungmi Oh[8], Yun-Ju Choi[9], Jong-Hee Sohn[10], Byung-Su Kim[11], Dae Woong Bae[12], Daeyoung Kim[13], Kwang-Yeol Park[14] and Soo-Jin Cho[15]

[1]*Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*

[2]Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of
[3]Department of Neurology, Inje University College of Medicine, Seoul, Korea, Republic of
[4]Department of Neurology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of
[5]Department of Neurology and Institute of Health Science, Gyeongsang National University College of Medicine, Jinju, Korea, Republic of
[6]Department of Neurology, Uijeongbu St.Mary's Hospital, Catholic University of Korea College of Medicine, Uijeongbu, Korea, Republic of
[7]Department of Neurology, Eulji University School of Medicine, Seoul, Korea, Republic of
[8]Department of Neurology, Korea University College of Medicine, Seoul, Korea, Republic of
[9]Dr. Choi's Neurology Clinic, Jeonju, Korea, Republic of
[10]Department of Neurology, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea, Republic of
[11]Department of Neurology, Ewha Womans University Mokdong Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of
[12]Department of Neurology, The Catholic University of Korea, St Vincent's Hospital, Suwon, Korea, Republic of
[13]Department of Neurology, Chungnam National University Hospital, Chungnam National University College of Medicine, Daejeon, Korea, Republic of
[14]Department of Neurology, Chung-Ang University Hospital, Seoul, Korea, Republic of
[15]Department of Neurology, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of

Background: There has been no study investigating the disease course of cluster headache (CH) in a long-term prospective setting. We aimed to explore the disease course of CH and predictors of recurrence by prospectively following up unselected CH patients.
Methods: Patients with CH were recruited between September 2016 and January 2019 from 16 hospitals in Korea. We thoroughly collected patient demographics, disease characteristics, comorbidities, temporal changes of CH characteristics, and treatment response at baseline and follow-up visits. We prospectively followed up patients via clinic visit or telephone call at 3 months and yearly after baseline visit up to 5 years until January 2023. To represent the relative frequency of bout recurrence, the averaged between-bout interval was calculated by dividing the total length of follow up by the number of bouts observed. Univariable and multivariable linear regression analyses were performed to explore baseline factors predictive of the averaged between-bout interval in patients with episodic CH (ECH).
Results: A total of 295 patients completed mean 5.9 follow-ups (SD 1.39, range 1–7) during mean 4.2 years (SD 1.36). At baseline, 252 (85.4%) and 11 (3.7%) had ECH and chronic CH (CCH), respectively, while 32 (10.8%) were unclassified. After follow-up, 5 CCHs (2 De Novo CCH; 3 secondary CCH evolved from ECH) were newly identified. For 244 patients with ECH recruited during the active bout, a total of 298 recurrence (mean 1.2 [SD 1.44; range 0–9] per patient) were observed in 142 (58.1%) patients during prospective follow up. Multivariable linear regression showed higher number of lifetime bouts experienced (regression coefficient = −0.057, adjusted p = 0.003) and seasonal rhythmicity at baseline (regression coefficient = −0.682, adjusted p = 0.036) were associated with frequent bout recurrence, while older age, first-onset CH, and regular alcohol consumption were associated with less recurrence (regression coefficient = 0.057, 0.864, and 0.616, adjusted p = 0.003, 0.036, and 0.014, respectively).
Conclusion: This study was the first report of long-term, prospective, structured observation of bout recurrences in CH patients. While our ECH patients had relatively low incidence of bout recurrence, a small but significant proportion of chronification was also observed. Seasonal rhythmicity may be representative of CH disease activity, and aging may be associated with decline of disease activity.
Disclosure of Interest: None Declared

Headache epidemiology, outcomes and burden

IHC23-OR-009

Migraine in the Workplace: Why this is Important for Headache Specialists and What Can Be Done to Help

Olivia Begasse de Dhaem[1,2], Robert E Shapiro[3], Fumihiko Sakai[4] and David Dodick[5,6]

[1]Hartford Healthcare, Westport, USA
[2]University of Connecticut, Westport, USA
[3]University of Vermont, Burlington, USA
[4]Saitama International Headache Center, Saitama, Japan
[5]Mayo Clinic, Phoenix, USA
[6]Atria Academy of Science and Medicine, New York, USA

Introduction: Migraine is the second cause of disability (1). A 4-year study of nearly 8,000 employees found migraine to be the second cause of presenteeism, costing the employer 2million USD annually (2). Migraine is estimated to account for 157 million hours of lost work in the US and 16% of total workplace presenteeism, costing 240 billion USD annually. The cost of migraine-related presenteeism in Japan was estimated between 375 and 2,217

USD/year/person (3). Migraine impacts every aspect of one's professional life: 68% of workers with migraine had lower work productivity, 55% had to change their career goals, 39% missed work opportunities including promotions, and 38% missed out on additional earning potential due to migraine (4). People with chronic migraine have lower incomes and are less likely to be employed full time (35%) compared to people with low frequency episodic migraine (46%) (5). Absenteeism and presenteeism increase with migraine frequency from 4% and 30% respectively in people with low frequency episodic migraine to 6% and 50% in people with chronic migraine (6). The interictal burden of migraine is substantial; moderate-to-severe for 41.5% of workers (6).

Methods: Narrative Review

Results: Ways to help people with migraine in the workplace include social support, job satisfaction, autonomy, and migraine-friendly workplace accommodations (e.g., dimmed lights, noise reduction, scent free areas, regular breaks, air quality). Heighted demands (quantitative, emotional, social), lower job status, and shift work negatively impact productivity (7,8).

Migraine workplace education and management programs raise awareness and understanding, decrease stigma, improve diagnosis and treatment, and increase productivity (7). Five prospective cohort studies found that workplace education programs increased productivity by 29–36% (7). Five prospective cohort studies showed that workplace education plus management programs cut absences in half and increased productivity during migraine attacks by 36 to 59% (7,9). The Novartis Migraine Care program consisted of a company-wide migraine awareness and neurology care campaign combined with 6 months of individualized coaching sessions for those interested (9). It reduced migraine disability by 64% at 9 months (9). Participants gained 10.8 working and 13.6 migraine-free days/year for private/social life. Novartis" return-on-investment was 490% (9).

The largest migraine workplace education and evaluation program enrolled 73,432 (91%) Fujitsu employees in Japan (10). The prevalence of migraine was 17% but 70% of participants had some headaches (10). About 5% of total participants had moderate-to-severe headaches and 4% sought consultation through the program (10). The program improved the understanding of headache disorders of 73% of participants. It increased productivity for employees with headache disorders (1.2 fewer absentee and 14 fewer presentee days per employee per year) with a 32 fold return-on-investment (10). The success of the Fujitsu Headache Project relied on a relationship of trust between the organization and a headache specialist leader, an organizational culture emphasizing employee health, and inclusion of all employees and relevant stakeholders. The Fujitsu Headache Project emphasizes the need to educate the entire employee and c-suite population on headache disorders to increase understanding, decrease stigma, and improve health and productivity outcomes (10). Stigma towards migraine is pervasive and interferes with the ability to work of people with migraine (12–15). Only 22% of employers think that migraine is serious enough to justify a work absence (16). A little less than a third of people without migraine think that people with migraine make things difficult for their coworkers and use migraine as an excuse to get out of work commitments (13). More than half of workers do not disclose headache as a reason for their absences due to the stigma (17). The Fujitsu Headache Project, which included education of all employees had a dramatic effect on stigma; 83% of participants without headache changed their attitude towards colleagues with headache disorders (10).

Discussion: As workplaces are redesigned after the COVID19 pandemic, it is crucial to advocate for workplace education programs like the International Headache Society Global Patient Advocacy Coalition (IHS-GPAC) Migraine Fitness (18). Headache specialists should advocate and champion workplace programs since one of the main priorities, as ambassadors for the field, is to have a public health impact on the lives of people who are impacted by the diseases to which they have committed their professional lives to treat.

Disclosure of Interest: David Dodick serves as the Chair of the IHS-GPAC. Olivia Begasse de Dhaem and Fumihiko Sakai are members of the Executive Committee of the IHS-GPAC. Robert Shapiro is the Founding President of the Alliance for Headache Disorders Advocacy and is a member of the Steering Committee of Migraine at Work. Olivia Begasse de Dhaem receives a stipend for her contribution as Executive Editor of the Pain Medicine Journal. She received consulting fees from the virtual headache clinics NeuraHealth and Mable. Robert Shapiro has received, in the past 12 months, financial or editorial compensation as a research consultant for Eli Lilly and Lundbeck. David W Dodick, M.D.: Consulting: Amgen, Atria, CapiThera Ltd., Cerecin, Ceruvia Lifesciences LLC, CoolTech, Ctrl M, Allergan, AbbVie, Biohaven, GlaxoSmithKline, Lundbeck, Eli Lilly, Novartis, Impel, Satsuma, Theranica, WL Gore, Genentech, Nocira, Perfood, Praxis, AYYA Biosciences, Revance, Pfizer. Honoraria: American Academy of Neurology, Headache Cooperative of the Pacific, Canadian Headache Society, MF Med Ed Research, Biopharm Communications, CEA Group Holding Company (Clinical Education Alliance LLC), Teva (speaking), Amgen (speaking), Eli Lilly (speaking), Lundbeck (speaking), Pfizer (speaking), Vector Psychometric Group, Clinical Care Solutions, CME Outfitters, Curry Rockefeller Group, DeepBench, Global Access Meetings, KLJ Associates, Academy for Continued Healthcare Learning, Majallin LLC, Medlogix Communications, Medica Communications LLC, MJH Lifesciences, Miller Medical Communications, WebMD Health/Medscape,

Wolters Kluwer, Oxford University Press, Cambridge University Press. Non-profit board membership: American Brain Foundation, American Migraine Foundation, ONE Neurology, Precon Health Foundation, International Headache Society Global Patient Advocacy Coalition, Atria Health Collaborative, Domestic Violence HOPE Foundation/ Panfila. Research support: Department of Defense, National Institutes of Health, Henry Jackson Foundation, Sperling Foundation, American Migraine Foundation, Henry Jackson Foundation, Patient Centered Outcomes Research Institute (PCORI). Stock options/shareholder/patents/board of directors: Ctrl M (options), Aural analytics (options), Axon Therapeutics, ExSano (options), Palion (options), Man and Science, Healint (options), Theranica (options), Second Opinion/Mobile Health (options), Epien (options/board), Nocira (options), Matterhorn (shares/board), Ontologics (shares/board), King-Devick Technologies (options/board), Precon Health (options/board), AYYA Biosciences (options), Axon Therapeutics (options/board), Cephalgia Group (options/board), Atria Health (options/employee). Patent 17189376.1–1466:vTitle: Onabotulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (Non-royalty bearing). Patent application submitted: Synaquell® (Precon Health)

Other secondary headache disorders

IHC23-OR-010

Polysomnographic and clinical characteristics of sleep apnea headache patients

Esra Aydın Sünbül[1], Rahşan Karacı[2], Elif Gözde Türedi Karabulut[2], Hüseyin Güleç[1] and Füsun Mayda Domaç[2]

[1]*University of Health Sciences, Erenköy Mental and Nervous Diseases Training and Research Hospita, Pyschiatry Department, İstanbul, Turkey*
[2]*University of Health Sciences, Erenköy Mental and Nervous Diseases Training and Research Hospita, Neurology Department, İstanbul, Turkey*

Background: Sleep apnea headache is a recurrent universal pressing headache without accompanying symptoms at awakening that resolves within 4 h. The diagnosis requires polysomnography-verified apnea hypopnea index $\geq$5, that is, obstructive sleep apnea (OSA). The prevalence of sleep apnea headache is 10–15% in people with OSA, whereas morning headache occurs in 5%. The aim of the present study is to investigate the polysomnographic and clinical characteristics of sleep apnea headache among persons with PSG-verified OSA.
Method: The study was conducted in the sleep center of University of Health Science, Erenköy Mental and Nervous DiseaseTraining and Research Hospital. Clinical and polysomnographic data of the patients diagnosed as sleep apnea headache (SAH)according to IHS-3 criteria and who underwent polysomnography were collected retrospectively and were grouped as mild, moderate and severe OSA. Patients with morning headache expect sleep apnea headache and under PAP titration treatment were excluded. Macrostructure of sleep were investigated between patients with (WSAH) and without sleep apnea headache (WOSAH).
Results: There were 384 patients in WSAH and 294 WOSAH group with a mean age of 46.29 ± 12.18 and 45.08 ± 12.62, respectively. Eppworth scores and periodic limb movement index (PLMI) were significantly higher in WSAH patients ($p = 0.004$ and $p = 0.000$ respectively) while wake after sleep onset latency was shorter and sleep quality index was lower than patients WOSAH. There was a negative correlation between age and total sleep time ($p = 0.009$), wake after sleep onset latency ($p = 0.043$), sleep efficiency (0.000) and a positive correlation with AHI ($p = 0.009$) in WSAH. Eppworth scores were in a positive correlation with total wakefullnes time and AHI ($p = 0.008$ and $p = 0.000$, respectively) and in a negative correlation with Non REM 3% and average minimum O2 levels ($p = 0.001$ and $p = 0.020$ respectively) in WSAH group).
Conclusion: The etiology and pathophysiology of sleep apnea headache are largely unknown. Sleep apnea headache seem to be in association with disturbances of the preceding night's sleep and may be due to dysregulation in regions modulating sleep and nociception .

Headache pathophysiology – Imaging and neurophysiology

IHC23-OR-011

Abnormal thalamo-cortical communication patterns in overlapping communities of migraine: an edge-centric functional connectivity study

Wei Dai[1], Enchao Qiu[2], Shengyuan Yu[1] and Zhao Dong[1]

[1]*Department of Neurology, Chinese PLA General Hospital, Beijing, China*
[2]*Department of Neurology, Thomas Jefferson University, Pennsylvania, USA*

Objective: Migraine has been demonstrated with abnormal functional connectivity of intrinsic brain networks. However, the network interactions have not been investigated by edge-centric methods, which cluster brain regions with similar co-fluctuation patterns into the same community and evaluate overlap metrics. Here we applied a novel edge-centric functional connectivity to

investigate the time-varying co-fluctuations of brain networks in interictal migraine patients, and whether baseline and 3-month follow-up clinical features are associated with abnormal edge-centric functional connectivity results.

Methods: We investigated the edge-centric functional connectivity of brain networks in 108 interictal migraine without aura (MO) patients and 71 healthy controls (HC). The clinical features and resting-state functional MRI were collected at baseline, and patients were followed up at three months. We parcellated the brain into regions and networks using independent component analysis. We applied an edge-centric analysis by edge graph construction, k-means clustering, community overlap detection, and graph-theory-based evaluations. Relationships between clinical features and abnormal edge-centric results were evaluated. A 3-layer multi-layer perceptron-based deep model was applied for disease classification to testify the specificity of abnormal edge-centric functional connectivity results.

Results: We identified 49 independent components and categorized them into seven intrinsic connectivity networks. In edge functional connectivity analysis, we found the normalized entropy of lateral thalamus was significantly increased in MO patients compared with HC ($p = 0.0086$, $p_{FDR} < 0.05$). And the normalized entropy of lateral thalamus was significantly positively correlated with migraine headache duration in the last attack at baseline ($r = 0.332$, $p = 0.005$, $p_{FDR} < 0.05$), and negatively correlated with reduction of migraine headache duration after preventive medication ($r = -0.663$, $p = 0.007$, $p_{FDR} < 0.05$, $n = 15$) at 3-month follow-up. Network-wise entropy of the sensorimotor network was significantly higher in MO compared with HC ($p = 0.012$, $p_{FDR} < 0.05$) (Figure 1). The community similarity of lateral thalamus and postcentral gyrus was increased in MO compared with HC ($p = 0.0002$, $p_{FDR} < 0.05$), which was significantly positively correlated with migraine headache duration in the last attack at baseline ($r = 0.268$, $p = 0.025$, $p_{FDR} < 0.05$) (Figure 2). In disease classification, the normalized entropy of lateral thalamus achieved an accuracy of 65.48% with an F1 score of 75.66%, both of which ranked first among all the input variables.

Conclusion: Our results demonstrated the abnormal thalamo-cortical communication patterns in migraine, coupled with baseline headache duration, and predicted unsatisfactory treatment response. The impaired thalamo-cortical synchronization underlay a vast dysfunction in multi-sensory information processing and integration, which may be a major contributor for multimodal sensory symptoms in migraine. This interesting finding enriches our understanding of the dysrhythmia of thalamo-cortical network.

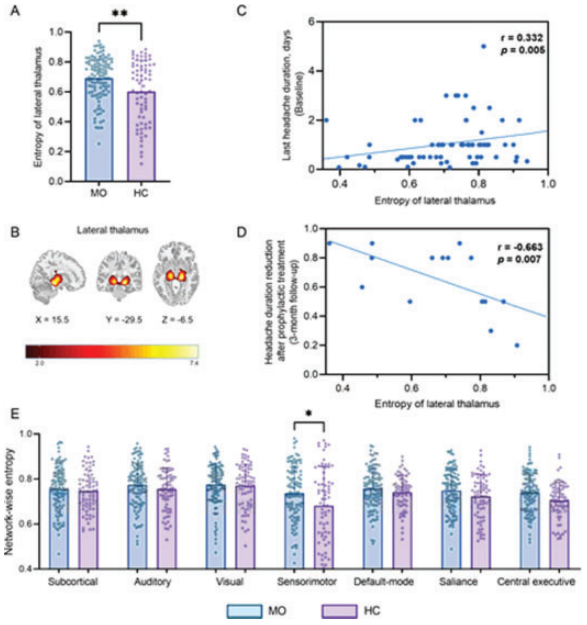

Figure 1. Component-wise and network-wise entropy and correlation analysis. A. Entropy of lateral thalamus in MO and HC. B. Spatial map of lateral thalamus. C. Correlation analysis between entropy of lateral thalamus and last headache duration at baseline. D. Correlation analysis between entropy of lateral thalamus and headache duration reduction after prophylactic treatment at 3-month. E. Network-wise entropy in MO and HC. MO: migraine without aura, HC: healthy controls.

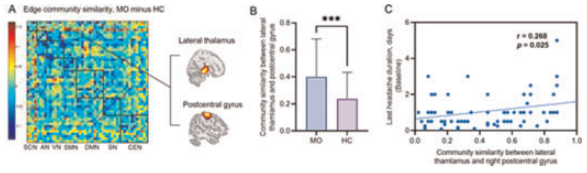

Figure 2. Community similarity and clinical correction analysis. A. Edge community similarity matrix (MO minus HC). B. Community similarity between lateral thalamus and postcentral gyrus in MO and HC. C. Correlation analysis between community similarity results and last headache duration at baseline. MO: migraine without aura, HC: healthy controls.

Disclosure of Interest: None Declared

Cluster headache and other trigeminal autonomic cephalalgias

IHC23-OR-012

Pre-cluster symptoms and treatment response in cluster headache: A large cohort in Taiwan

Shu-Ting Chen[1], Yu-Ching Lin[1,2], Hsin-Yi Tseng[3], Chia-Chun Chiang[4] and Jr-Wei Wu[3,2,5]

[1]*Department of Radiology, Taipei Veterans General Hospital, Taipei City, Taiwan*
[2]*Center for Quality Management, Taipei Veterans General Hospital, Taipei City, Taiwan*
[3]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei City, Taiwan*
[4]*Department of Neurology, Mayo Clinic, Rochester, Rochester, USA*
[5]*College of Medicine, National Yang Ming Chiao Tung University, Taipei City, Taiwan*

Background: Pre-cluster symptoms (PCS) are symptoms preceding the upcoming cluster headache (CH) bouts. Some patients could predict the CH bouts based on these symptoms and might have roles in pre-emptive treatment. This study analyzed the characteristic of PCS in a large cohort of CH patients in Taiwan. Also, we analyzed the linkage between PCS and the treatment outcome of CH.
Design/Methods: We prospectively collected consecutive data from patients with CH. Each patient completed semi-structured interviews during CH bouts, which included 50 questions about PCS, CH symptomatology, and severity. Also, we recorded the treatment response to acute and preventive treatments after the CH bout. The thirty-five PCS were divided into seven categories: local (head and neck pain) symptoms, general pain symptoms, fatigue and mood symptoms, sleep alternation, constitutional symptoms, cranial autonomic symptoms (CAS), and restlessness.
Results: A total of 131 CH patients (M: F = 98: 33) were recruited during the study period. The prevalence of PCS was 90.1%, and 64.9% had consistent PCS. The mean (SD) duration of PCS is 2.2 (3.9) days before the CH bout. Up to 64.1% of CH patients were able to predict upcoming bouts based on PCS. Among seven categories of PCS, head and neck pain symptoms are the most common (82.4%) and the best predictor for upcoming bouts (OR = 2.8 [95% CI 1.1–7.1]). The presence of PCS also links to treatment response to CH preventives, patients with sleep alternation (OR = 2.1 [95% CI 1.0–4.3]), restlessness (OR = 2.3 [95% CI 1.0–4.6]), and any CAS (OR = 2.3 [95% CI 1.0–4.3]) before upcoming bouts were more likely responsive to verapamil, but PCS were not associated with response to other acute or preventive treatments.
Conclusions: PCS is common among CH patients. Local (head and neck) pain-related symptoms are the most common PCS with the highest predictivity of the upcoming bout. There were three categories of PCS links to better response to verapamil, which provides insights into future CH preventive treatment.
Disclosure of Interest: 1. Speaker/speakers boards: -Biogen-Idec, Eli Lilly, Hoan Pharmaceuticals, UCB Pharmaceuticals & HAVA Bio-Pharma. Corp. -Taiwan Headache Society, Taiwan Stroke Society, & Neuroradiological Society of Taiwan 2. Grant support for research or education -Taiwan Ministry of Technology and Science (MOST) -Taiwan National Science and Technology Council -Taipei Veterans General Hospital 3. Travel reimbursement -American Academy of Neurology -International Headache Society -Taiwan Headache Society

Psychological and behavioural factors and management

IHC23-OR-013

Psychological profiles and clinical characteristics of migraine patients with early life traumas

Sara Bottiroli[1,2], Marta Allena[2], Roberto De Icco[3,2], Grazia Sances[2], Elena Guaschino[2], Natascia Ghiotto[2] and Cristina Tassorelli[3,2]

[1]*Giustino Fortunato University, Benevento, Italy*
[2]*IRCCS Mondino Foundation, Pavia, Italy*
[3]*University of Pavia, Pavia, Italy*

Objectives: To evaluate the impact of childhood traumas in a large sample of subjects with migraine in terms of psychological profiles and clinical characteristics.
Methods: A sample of patients with chronic migraine with medication overuse (CM + MO) (n = 200; age: 47.6 ± 10.9) or episodic migraine (EM) (n = 198; age: 39.1 ± 11.1) was enrolled and evaluated for migraine characteristics. Diagnosis was operationally defined according to the International Classification of Headache Disorders 3rd edition (ICHD-III). Patients received a psychological assessment including self-report questionnaires (Childhood Trauma Questionnaire, Stressful life-events Questionnaire, Hospital Anxiety and Depression Scale, and the Toronto Alexithymia Scale) and, for a subgroup, a clinical interview based on DSM-V criteria for psychopathologies and personality disorders.
Results: Thirty-five percent (n = 135) of participants reported childhood traumas (CT group), with a higher prevalence in the CM+MO (41%) than in the EM (28%) group (p = 0.006). CT individuals had significantly more days of migraine attacks per month (17.8 ± 11.3 vs 14.1 ± 10.7, p = 0.002), more days with medication intake (16.7 ± 12.4 vs 13.5 ± 10.1, p = 0.007) and more doses per month (26.5 ± 26.2 vs 20.4 ± 29.0, p = 0.04)

when compared with patients without CT (wCT group). The CT group was also characterized by a significantly higher anxious (8.0 ± 4.0 vs 5.9 ± 3.8, $p = 0.001$) and depressive (7.4 ± 4.8 vs 5.2 ± 4.0, $p = 0.001$) symptomatology, alexithymic levels (47.3 ± 12.7 vs 44.0 ± 12.9, $p = 0.04$), and a higher prevalence of severe (66% vs 34%, $p = 0.001$) and very severe (66% vs 34%, $p = 0.001$) current stressful life-events than the wCT group. Moreover, the CT group had a higher prevalence of patients with personality disorders (62% vs 40%, $p = 0.001$), specifically belonging to Cluster C (60% vs 34%, $p = 0.001$), as well as Axis I psychopathologies (94% vs 75%, $p = 0.001$) than the wCT group.

Conclusions: Childhood trauma can have a critical impact on the clinical and psychological characteristics of migraineurs. Patients with childhood trauma are characterized by a more complicated form of migraine associated with psychopathology and personality disorders. These findings have important practical implications and suggest that clinicians should treat patients who have experienced childhood trauma also from a psychological perspective because of the high risk of poor prognosis.

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Disclosure of Interest: None Declared

Headache pathophysiology – Basic science

IHC23-OR-014

Second messenger signaling bypasses calcitonin gene-relate peptide (CGRP) receptor blockade to provoke migraine attacks in humans

Thien Phu Do[1,2], Christina Deligianni[1], Sarkhan Amirguliyev[1], Josefin Snellman[3], Cristina Lopez Lopez[4], Mohammad Al-Mahdi Al-Karagholi[1], Song Guo[1] and Messoud Ashina[1,2]

[1]*Danish Headache Center, Copenhagen, Denmark*
[2]*University of Copenhagen, Copenhagen, Denmark*
[3]*3Novartis Pharma AG, Basel, Switzerland*
[4]*Roche Innovation Center Basel, Basel, Switzerland*

Objective: In a "migraine attack signaling cascade" model, calcitonin gene-related peptide (CGRP) acts via the downstream second messenger, cyclic adenosine monophosphate (cAMP). However, this model has never been tested directly in humans. Our purpose here is to ascertain whether treatment with erenumab (CGRP receptor blocker) can mitigate the migraine-inducing effects of administration of CGRP, but not those of cilostazol (an agent known to accumulate intracellular cAMP by inhibiting its degradation).

Methods: We enrolled adults with migraine in a randomized, double-blind, placebo-controlled, parallel trial. Participants were randomized to a 140 mg subcutaneous administration of erenumab or placebo followed by intravenous infusion of 1.5μg/min of CGRP over 20 minutes or oral intake of 200 mg cilostazol on separate study days. The primary endpoint was the incidence of migraine attacks in a 12-hour observational period after administration of experimental triggers.

Results: Between July 2020 and June 2021, 75 [mean age: 33.4 years, 66 (88%) were women] out of 80 randomized patients completed the study. After administration of CGRP, 10 of 37 (27%; 95% CI, 13%–41%) participants developed migraine attacks in the erenumab group compared with 20 of 38 (53%; 95% CI, 37%–69%) in the placebo group ($p = .024$). After administration of cilostazol, 28 of 37 (76%; 95% CI, 62%–90%) participants developed migraine attacks in the erenumab group compared with 31 of 38 (82%; 95% CI, 69%–94%) in the placebo group ($p = .533$).

Conclusions: Our findings provide clinical evidence of that cAMP-evoked migraine attacks act downstream of the CGRP receptor, and that these cAMP-evoked migraine attacks do not require CGRP receptor activation.

Disclosure of Interest: MA is a consultant, speaker, or scientific advisor for AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva and a primary investigator for ongoing AbbVie/Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva trials. MA has no ownership interest and does not own stocks of any pharmaceutical company. MA serves as associate editor of Cephalalgia, associate editor of the Journal of Headache and Pain, and associate editor of Brain. JS and CLL are full-time employees of Novartis Pharma AG, Basel, Switzerland. MA-MA-K has acted as an invited speaker for Novartis and received a travel grant from ElectroCore, LLC. TPD, CD, SA, and SG report no conflicts of interest.

Headache pathophysiology – Basic science

IHC23-JT-001

Neuropeptide Y regulates migraine-like behaviors through inhibiting habenula cholinergic neurons

Chunxiao Yang[1,2], Zihua Gong[2,3,4], Xiaochen Zhang[5], Hao Wang[6] and Shengyuan Yu[2]

[1]*School of Medicine, Nankai University, Tianjin, China*
[2]*Department of Neurology, the First Medical Center, Chinese PLA General Hospital, Beijing, China*
[3]*Medical School of Chinese PLA, Beijing, China*
[4]*Department of Medical Oncology, Bethune International Peace Hospital, Shijiazhuang, China*
[5]*Academy of Medical Engineering and Translational Medicine, Tianjin University, Tianjin, China*

[6]National Engineering Laboratory for Brain-inspired Intelligence Technology and Application, and School of Information Science and Technology, University of Science and Technology of China, Hefei, China

Background: Migraine is a disabling health condition with multiple symptoms; however, it remains undertreated because of the inadequate understanding of its neural mechanisms. Neuropeptide Y (NPY) has been demonstrated to be involved in the modulation of pain and emotion, and may play a role in migraine pathophysiology. Changes in NPY levels have been found in patients with migraine, but whether and how these changes contribute to migraine is unknown.
Methods: Here, we used intraperitoneal injection of glyceryl trinitrate (GTN, 10 mg/kg) as a migraine model to induce migraine-like behaviors in mice. To identify the critical regions expressing NPY in the brain that may be responsible for the migraine-like phenotypes, we then performed whole-brain imaging with NPY-GFP mice. Next, to determine the role of NPY and its underlying mechanisms in GTN-treated mice, we microinjected NPY or NPY receptor agonists into the medial habenula (MHb), and performed immunofluorescent double staining to determine the relationships between NPY receptors and cholinergic neurons of the MHb. Finally, we inhibited cholinergic neurons of the MHb using chemogenetic technique.
Results: Acute GTN administration effectively triggered allodynia, photophobia, and anxiety-like behaviors in mice. Analysis of whole-brain imaging showed a decreased level of GFP^+ cells in the MHb of GTN-treated mice. Further microinjection of NPY and Y1 receptor agonists into the MHb attenuated GTN-induced allodynia and anxiety without affecting photophobia. Moreover, we confirmed that the Y1 receptors were expressed on the cholinergic neurons of the MHb, and chemogenetic inhibition of cholinergic neurons mimicked the effects of Y1 receptor agonists.
Conclusion: Our data support that the NPY signaling in the MHb produces analgesic and anxiolytic effects through inhibiting habenula cholinergic neurons. These findings may provide new insights into novel therapeutic targets for the treatment of migraine.
Disclosure of Interest: None Declared

Headache pathophysiology – Basic science

IHC23-JT-002

Transient receptor potential melastatin 8 increases susceptibility to spreading depolarization and facilitates trigeminal neuroinflammation

Tzu-Ting Liu[1,2], Chyun-Yea Tseng[2], Yun-Ning Chen[2], Jian-Bang Chen[2], Shuu-Jiun Wang[1,3,4], Shih-Pin Chen[1,3,5,6] and Jiin-Cherng Yen[2]

[1]Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan
[2]Institute of Pharmacology, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan
[3]Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
[4]School of Medicine, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan
[5]Institute of Clinical Medicine, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan
[6]Division of Translational Research, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan

Objective: Genome-wide association studies have identified *transient receptor potential melastatin 8 (TRPM8)*, which encodes a nonselective cation channel sensitive to cold, to be a migraine susceptible gene. Yet, how TRPM8 contributes to migraine remains unclear. We herein characterized the expression of TRPM8 in the cerebral cortex and undertook functional analysis to address the role of TRPM8 in migraine pathophysiology.
Methods: Cortical TRPM8 expression was analyzed by immunostaining. The effect of TRPM8 on KCl-evoked spreading depolarization (SD) and SD-induced cortical inflammation was assessed using intracerebroventricular injection of TRPM8 specific agonist or antagonist in rats. We also examined the effects of TRPM8 activation on the expression level and the release of calcitonin gene-related peptide (CGRP) as well as trigeminal neuroinflammation in a primary culture of rat trigeminal ganglia (TG).
Results: TRPM8 was homogeneously distributed in the cerebral cortex and primarily co-localized with cortical neuron. Activation of cortical TRPM8 increased KCl-evoked SD frequency and enhanced SD-induced cortical inflammation, but inhibition of cerebral TRPM8 had no significant effects. In TG primary culture, TRPM8 activation increased the expression and the release of CGRP, and evoked cyclooxygenase-2 upregulation via calmodulin kinase 2-dependent mechanism.
Conclusion: TRPM8 activation increases SD susceptibility and facilitates the effect of CGRP as well as trigeminal neuroinflammation, suggesting that TRPM8 activation may play a detrimental role in migraine pathophysiology.
Disclosure of Interest: None Declared

Genetics and biomarkers of headache disorders

IHC23-JT-003

Expression of MicroRNA-155 in Migraine: association with migraine phenotypes and disease severity

Federico Bighiani[1,2], R. De Icco[1,2], F. Cammarota[1,2], M. Corrado[1,2], G. Vaghi[1,2], C. Brancaccio[1,2], M. Allena[2], V. Grillo[1,2], R. Greco[2], C. Demartini[1,2], A. Zanaboni[1,2], M. Francavilla[1,2], G. Sances[1], E. Guaschino[1], N. Ghiotto[1] and Cristina Tassorelli[1,2]

[1]*Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy*
[2]*Headache Science & Neurorehabilitation Center, IRCCS Mondino Foundation, Pavia, Italy*

Objectives: At present, there are no validated and reliable biomarkers of migraine, but the headache scientific community is intensely investigating the molecular signatures of migraine. microRNAs are small endogenous non-coding RNAs which operate as post-transcriptional regulator of gene expression. Several recent lines of preclinical evidence highlighted the role of MicroRNA-155 (miR-155) in inflammation, endothelium-dependent vasorelaxation, pain generation and maintenance. In the present study we aim to study the role of miR-155 in migraine, with a particular interest in its association with migraine phenotype and disease severity.
Methods: This is a cross-sectional and controlled study involving three study groups: healthy controls (HCs), episodic migraine (EM) and chronic migraine with medication overuse headache (CM-MOH). We assessed the expression of miR-155 measured as Relative Quantification (RQ) in peripheral blood monocytes. All determinations were performed in the inter-ictal migraine phase.
Results: Demographic features were comparable among the three study groups. Anxiety was more represented in CM-MOH when compared to EM ($p = 0.046$). Currently, we analysed miR-155 expression in 23 HCs (0.5 ± 0.16 RQ), 52 EM (1.73 ± 2.09 RQ), and 31 CM-MOH (2.65 ± 2.39 RQ) subjects. Migraine patients showed higher miR-155 expression when compared to HCs ($p = 0.001$). In addition, miR-155 expression was higher in CM-MOH patients when compared to EM group ($p = 0.002$). This finding was confirmed in a logistic regression (EM vs CM-MOH; $p = 0.019$), after controlling for age, sex, ongoing preventive treatment, and psychological comorbidities.
Conclusion: Our findings suggest that miR-155 is elevated in migraine patients, and associated with disease phenotype. The study of microRNAs may represent a useful tool to characterized different phenotypes across the migraine spectrum. Hopefully, microRNAs may represent novel molecular targets for drug development in the future ("agomir" & "antagomir").
Disclosure of Interest: None Declared

Headache pathophysiology – Imaging and neurophysiology

IHC23-JT-004

Behavioral response mechanisms in medication overuse headache: a study of thalamocortical activation and lateral cortical inhibition.

Gabriele Sebastianelli, Francesco Casillo, Chiara Abagnale, Cherubino Di Lorenzo, Mariano Serrao and Gianluca Coppola

Sapienza University of Rome, Polo Pontino, Latina, Italy

Objectives: It is unclear whether cortical hyperexcitability in medication overuse headache (MOH) is due to increased excitation of thalamocortical drive or to aberrant cortical inhibitory mechanisms.
Methods: Somatosensory evoked potentials (SSEP) were performed by electrical stimulation of the median nerve (M), ulnar nerve (U), and simultaneous stimulation of both nerves (MU) in 27 patients with MOH and for comparison in 23 aged and matched healthy volunteers (HVs). We calculated the degree of cortical lateral inhibition using the formula: [100–(MU/(M + U) *100)] and the level of thalamocortical activation by analyzing the high-frequency oscillations (HFOs) embedded in parietal N20 median SSEP.
Results: In comparison with HV, MOH patients showed: higher lateral inhibition (MOH $52.2\% \pm 15.4$ vs HV $40.4\% \pm 13.3$; $p = 0.005$) which positively correlated with monthly headache days, and greater amplitude of pre-synaptic HFOs ($p = 0.010$) but normal post-synaptic HFOs ($p = 0.122$).
Conclusion: Our findings showed that central neuronal circuits are highly sensitized in MOH patients, at both thalamocortical and cortical levels. The observed changes could be due to the combination of dysfunctional central pain control mechanisms, hyper-sensitivity, and hyper-responsiveness directly linked to the chronic administration of acute migraine treatment.
Disclosure of Interest: None Declared

Headache pathophysiology – Imaging and neurophysiology

IHC23-JT-005

Brain connectivity changes induced by monoclonal antibodies targeting the CGRP pathway in Migraine Patients: a prospective HD-EEG Study

Michele Corrado[1,2], Roberto De Icco[1,2], Gloria Vaghi[1,2], Federico Bighiani[1,2], Francescantonio Cammarota[1,2], Valentina Grillo[1,2], Alessia Putorti[1], Daniele Martinelli[1,2], Marianna Semprini[3], Marta Allena[2], Grazia Sances[2] and Cristina Tassorelli[1,2]

[1]Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy
[2]IRCCS Mondino Foundation, Pavia, Italy
[3]Italian Institute of Technology, Genova, Italy

Objective: Monoclonal antibodies targeting the calcitonin-gene related peptide pathway (CGRP-mAbs) proved effective and safe as migraine preventive treatment. Due to their molecular weight, mAbs act outside of the blood brain barrier, namely in the peripheral component of the trigeminovascular system. Nonetheless, a reduced sensitization of the first order neuron in the trigeminal ganglion may induce secondary effects at central level. Here we aim to study the cortical brain connectivity of migraine patients (MIG) and its changes during CGRP-mAbs therapy, recorded by means of high-density electroencephalography (HD-EEG).
Methods: This open-label study will involve five resting-state HD-EEG recordings: one at baseline (T0, before mAbs treatment) and one every three months for a year (T3, T6, T9, T12). We present data from 45 migraine (MIG) patients (age 44.3 ± 12.3, 39 females, 29 with chronic migraine) who completed the first six months of treatment (T0 to T6). We will examine changes in connectivity of the main resting state networks (RSNs): the default mode network (DMN), visual network (VN), dorsal attention network (DAN), ventral attention network (VAN), language network (LN), and somatomotor network (SMN). For every network, we assessed the seed-based connectivity for each frequency band (gamma, beta, alpha, theta, delta). We also compared MIG connectivity with the data from 30 healthy controls (HC, age 37.5 ± 14.0, 14 females).
Results: Compared to HC, MIG patients showed a significant increase in delta-band activity, which was robustly reflected as increased connectivity in the delta range between all RSNs ($p < 0.005$ for all RSNs). This difference with HC was preserved at subsequent visits during CGRP-mAbs therapy ($p < 0.005$ for all RSNs). At T6, there was also a decreased alpha activity of the VAN ($p = 0.01$), as well as a decreased connectivity in the beta-band between the VAN and VN ($p < 0.05$). MIDAS responder patients had a specific baseline brain connectivity pattern, characterized by enhanced connectivity between the DMN and DAN in the theta-delta bands ($p < 0.05$).
Conclusion: Our findings suggest that MIG patients consistently show an increased delta-band activity, which could possibly represent an electrophysiological signature of their disease. Moreover, the start of CGRP-mAbs therapy induces changes by modulating the VAN network. These changes may be related to a reduction in sensitization of the peripheral component of the trigeminovascular system. The specific connectivity pattern observed in Responders may provide insight into individual differences in treatment response.
Disclosure of Interest: None Declared

Comorbidity of primary headaches

IHC23-JT-006

A randomised cross-over study for assessment of cognitive dysfunction during migraine attack and interictal period in patients with episodic migraine without aura

Rahul Nagane, Debashish Chowdhury, Ashishkumar Duggal, Sanjay Rao Kordcal and Headache Group Gipmer

GB Pant Institute of Postgraduate Medical Education and Research(Gipmer), New Delhi, India

Objective: To compare the cognitive functions in episodic migraine without aura (E-MwA) patients during ictal (headache) and interictal (headache-free) states and to find out the impact of psychiatric comorbidities and sleep abnormalities on cognitive functions.
Methodology: This was a randomized, two-period cross-over study. E-MwA patients underwent two evaluations, first, during an untreated spontaneous attack of E-MwA and second during a headache-free interictal (IC) period with a minimum of 72 hours since the last attack. Evaluation order was randomized, half the patients underwent first evaluation while headache-free (Interictal-Ictal)) while another half underwent first evaluation during the attack (Ictal-Interictal)), with a minimum one-month interval between two evaluations. Assessment was done for clinical characteristics, psychiatric comorbidities [screened by patient health questionnaire-PHQ-9 and rated by Hamilton depression rating scale (HAM-D) and generalised anxiety disorder scale (GAD-7)] and sleep abnormalities [by Pittsburgh Sleep Quality Index (PSQI) and (Epworth Sleepiness Scale (ESS)]. Initially a migraine subjective cognitive impairment scale (MigScog) was administered followed by cognitive status assessment by a battery of 16 tests. The means between the two groups were compared by paired t-test. Post-hoc Bonferroni correction was applied. The level of significance was set at $p < 0.05$.
Results: The mean age of presentation was 30.3 ± 8.8 years and female: male ratio was 3.4:1. The mean attack frequency and VAS score were 5 attacks/month and 7.1 ± 1.2 respectively. Psychiatric co-morbidities found were depression (39.8%), anxiety (15.9%), and somatization disorder (4.5%). Sleep abnormalities were found in 20.5% of the patients.
Both the randomized groups consisting of 44 patients each, undergoing cognitive evaluation in two orders, had similar baseline variables. MigScore in patients was significantly higher during the ictal state versus the inter-ictal state (11.2 ± 3.4 vs.9.5 ± 3.6; $p < 0.001$). E-MwA patients showed significantly lower performance scores in all

Abstract number: IHC23-JT-006
Table 1.

Cognitive assessment tests	Ictal mean ± SD	Interictal mean ± SD	Mean difference ictal-interictal (95% CI)	p value
Montreal Cognitive Assessment test	26.1 ± 2.2	27.7 ± 2.8	−1.6 (−2.4, −0.8)	All p values: <0.001
Digit span forward	5.2 ± 0.9	6.2 ± 1.2	−0.9 (−1.1, −0.8)	
Digit span backward	3.7 ± 0.8	4.3 ± 0.9	−0.6 (−0.9, −0.3)	
Trail Making Test-A (seconds)	50.8 ± 19.0	40.3 ± 15.9	10.5 (8.9,12.1)	
Trail Making Test-B (seconds)	96.0 ± 32.7	75.9 ± 27.2	20.1 (16.9,23.3)	
Stroop test-Words (seconds)	61.1 ± 17.4	53.0 ± 15.7	8.0 (6.9,9.2)	
Stroop test-color (seconds)	89.1 ± 22.5	78.0 ± 17.0	11.1 (9.3,12.9)	
Stroop test-Interference (seconds)	139.2 ± 29.7	119.8 ± 27.7	19.4 (16.0,22.8)	
Errors-Stroop Words	0.9 ± 1.2	0.170 ± 0.5	0.7 (0.5,0.9)	
Errors-Stroop colors	2.2 ± 1.7	0.8 ± 1.0	1.4 (1.1,1.6)	
Errors-Stroop interference	4.8 ± 2.6	2.1 ± 1.9	2.8 (2.4,3.1)	
Phonemic fluency test	8.7 ± 2.7	10.8 ± 3.2	−2.1 (−2.5, −1.6)	
Semantic fluency test	14.9 ± 3.4	17.6 ± 3.7	−2.6 (−3.1, −3.2)	
Finger tapping test-right hand	35.6 ± 6.7	41.2 ± 7.3	−5.5 (−6.6, −4.5)	
Finger tapping test-left hand	32.2 ± 5.8	36.8 ± 6.5	−0.8 (−5.5, −3.5)	
Famous faces test	13.2 ± 1.7	14.0 ± 1.3	−0.8 (−1.0, −0.6)	

cognitive tasks, during ictal state compared to interictal state (all p values <0.001) (Table 1). There was no significant association between the cognitive scores and the presence or absence of psychiatric comorbidities and sleep abnormalities.

Conclusion: Our study shows that E-MwA patients during an ictal state not only have subjective complaints of cognitive dysfunctions but also have significant deficits in the domains of attention, vigilance, executive functions and language. Also, psychiatric comorbidities and sleep abnormalities didn"t have any significant impact on cognitive functions in E-MwA patients.

Comorbidity of primary headaches

IHC23-DP-001

Abdominal migraine symptoms persist into relatively old age in outpatients with migraine

Ryotaro Ishii[1], Ryosuke Fukazawa[1], Yuki Higashimoto[2], Makiko Shinomoto[1], Akihiro Fujii[3] and Toshiki Mzuno[4]

[1]*Kyoto Prefectural University of Medicine, Kyoo, Japan*
[2]*Okamoto memorial hospital, Kuze-gun, Japan*
[3]*Saiseikai Shiga hospital, Ritto, Japan*
[4]*JCHO Kyoto Kuramaguchi Medical Center, Kyoto, Japan*

Objective: Functional gastrointestinal disorders (FGID) are disorders in which abdominal symptoms occur paroxysmally without the presence of organic, systemic, or metabolic diseases and are reported to be associated with migraine. FGID includes abdominal migraine, irritable bowel syndrome, and cyclic vomiting syndrome. Typically, FGID start in children, improve with increasing age, and develop into migraine. However, FGID may not be accurately diagnosed, and its prevalence may be underestimated because most FGID improve without treatment. Therefore, we hypothesized that abdominal pain attacks caused by FGID in adult patients with migraine are underestimated in Japan.

Method: We retrospectively collected data from electronic medical records at the North Medical Center of Kyoto Prefectural University of Medicine, the only hospital providing emergency medical care in rural areas (population approximately 100,000, area 840 km2). There were 71 migraine patients who visited the hospital between April 2017 and March 2018. Seventy-one patients were divided into two groups: 1) the Case group: patients with a history of emergency visits due to attacks of abdominal pain not caused by organic disease over the past 10 years, 2) the Control group: else. We evaluated age, sex, aura, Medication-Overuse Headache, headache days per month, Numerical Rating Scale score, migraine trigger, age at onset of headache, symptoms associated with headache, family history of headache, age at onset of abdominal pain, and history of psychiatric visits.

Results: Among the 71 migraine patients, 25 (35%) had visited the emergency room (ER) for abdominal pain attacks not caused by organic disease in the past 10 years. Compared with the Control group, The Case group was significantly lower in age (median 20 y.o. [min 9-max 66 years] vs. 40.5 y.o. [min 10-max 72 years], p = 0.004), age at onset of headache (12 y.o. [min 5-max 65] vs. 16 y.o. [min 8-max 63], p = 0.00613), but no

significant differences were found in the other items. The median age of ER visits in the case group was 18 [min3-max59]. There was no record of another visit for at least one week thereafter.

Conclusion: Our study found that outpatients with migraine suffer from FGID even at a relatively old age. Considering that our data included abdominal pain requiring only an ER visit, we believe that more migraine patients are potentially suffering from FGID attacks. By clarifying the high frequency of FGID in migraine patients, the results suggest the need to screen for and develop treatments for functional gastrointestinal disorders in adult migraine patients, particularly in the ER. This study will contribute to reducing the decreased quality of life and socioeconomic burden of many people.

Disclosure of Interest: Ryotaro Ishi has served as a consultant for Amgen K.K., Eli Lilly Japan K.K., DAIICHI SANKYO COMPANY, LIMITED, and Otsuka Pharmaceutical Co., Ltd. He has received lecture fees from Amgen K.K., Eli Lilly Japan K.K., DAIICHI SANKYO COMPANY, LIMITED, Otsuka Pharmaceutical Co., Ltd, and Takeda Pharmaceutical Co., Ltd. Akihiro Fujii has served as a consultant for DAIICHI SANKYO COMPANY. Toshiki Mizuno has served as a consultant for DAIICHI SANKYO COMPANY. The other authors declare no conflicts of interest. No animals were used in this study.

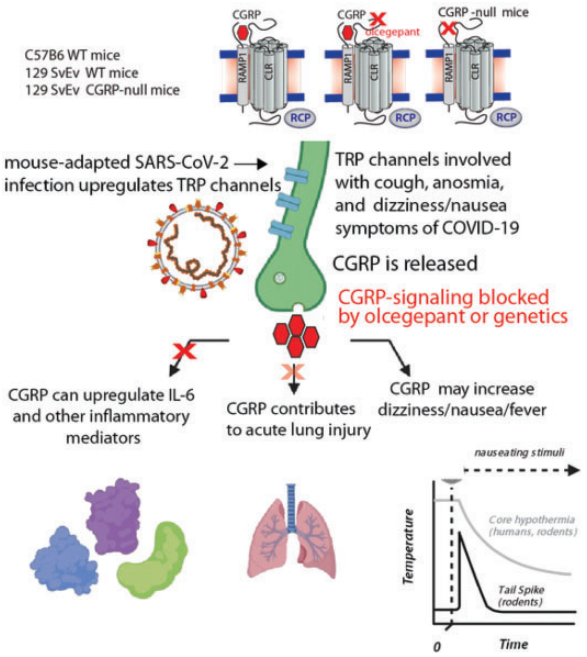
Headache pathophysiology – Basic science

IHC23-DP-002

Can antagonizing Calcitonin Gene-Related Peptide (CGRP) signaling mitigate neuroinflammatory and nausea-like responses to SARS-Cov-2 infection in preclinical mouse models?

Shafaqat Rahman[1], David Buchholz[2], Brian Imbiakha[2], Mason Jager[2], Justin Leach[1], Stephen Dewhurst[1], Hector Aguilar-Carreno[2] and Anne Luebke[1]

[1]*University of Rochester, Rochester, NY, USA*
[2]*Cornell University, Ithaca, NY, USA*



Objective: CGRP release in the CNS is implicated in COVID-19 neurological symptoms such as fever, headache, dizziness/nausea pain, and the subsequent release of interleukin 6 (IL-6). CGRP-receptor antagonists are known to have anti-inflammatory potential, and may mitigate the neuroinflammatory and nausea symptoms after SARS-CoV-2 infection. We were interested in testing if antagonizing CGRP signaling could mitigate COVID-19 neurological symptoms and reduce release of inflammatory cytokines.

Methods: We tested wildtype C57BL/6J and 129/SvEv mice, and a 129 αCGRP-null mouse line to infection using a mouse-adapted SARS-CoV-2 virus. As a control, we also assessed the K18-humanized ACE2 receptor mice to SARS-CoV-2 infection. As a readout of SARS-CoV-2 infection symptoms, we have assessed weight loss, O2 saturation, core temperature in either a) wildtype mice with the CGRP receptor antagonized by olcegepant (2 mg/kg/day/SQ) and b) mice lacking aCGRP. We also monitored the presence of a dizziness/nausea-like state by assessing hypothermic responses to provocative motion, and have collected BAL fluid from the lungs to determine if reduction of CGRP signaling reduces the subsequent release of IL-6, and performed lung histology to determine if there is a reduction in lung pathology.

Results: We have determined that CGRP receptor antagonism is only protective in older (>12 months) C57B6 and older 129Sv mice, as there was no significant difference between CGRP receptor antagonism and placebo controls in younger mice. Interestingly, there are no effects of CGRP antagonism against fever and dizziness/nausea-like symptoms as all infected mice were similarly

affected. However, CGRP antagonism in both 129 SvEv and C57B6 mice reduced IL-6 levels, with virtually no increase in IL-6 release in mice lacking αCGRP.
Conclusion: Findings suggest that blockage of CGRP signaling protects against acute IL-6 release after SARS-CoV-2 infection, but does not reduce acute fever or nausea-like symptoms, suggesting differences in CGRP receptor sensitivity to olcegepant.
Acknowledgements: This research is supported by a COVID-19 research supplement to NIH R01 DC017261 (AEL). We would also like to thank Dr. Ralph Baric (UNC) for the MA-10 SARS CoV-2 virus stock.
Disclosure of Interest: None Declared

Headache epidemiology, outcomes and burden

IHC23-DP-003

Overcoming Daily-Headache: Clinical Outcomes in Medication Overuse Headache Patients with NO Headache-Free Days

Hong-Kyun Park[1], Min Kyung Chu[2], Sun-Young Oh[3], Heui-Soo Moon[4], Tae-Jin Song[5], Mi ji Lee[6], Jin-Ju Kang[3], Yooha Hong[7] and Soo-Jin Cho[7]

[1]*Inje University Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea, Republic of*
[2]*Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of*
[3]*Chonbuk National University Hospital, Chonbuk National University School of Medicine, Jeonju, Korea, Republic of*
[4]*Kangbuk Samsung Hospital, Sungkyunkwan University College of Medicine, Seoul, Korea, Republic of*
[5]*Ewha Womans University Seoul Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of*
[6]*Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*
[7]*Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseoung, Korea, Republic of*

Background: Medication overuse headache (MOH) is a chronic medical condition that presents significant challenges in terms of disability and socioeconomic impact. Managing chronic daily headache (CDH) can be particularly complex in patients who do not experience headache-free days. However, these patients are often excluded from major clinical trials, resulting in limited data on treatment outcomes for this subgroup. Moreover, existing preventive treatments for CDH have shown limited efficacy. Therefore, there is a critical need for clinical data in patients who suffer from both MOH and CDH without any headache-free days. In this study, we aimed to address this knowledge gap by evaluating clinical outcomes in MOH patients without headache-free days after a 3-month treatment period using a prospective study using a nationwide multicenter MOH registry in Korea (RELEASE).
Methods: This is a retrospective, observational study using the RELEASE database. Patients followed up at 3 months were included. We divided the patients into two groups, depending on whether they had headache-free days (HFD [−] vs. HFD [+]) over the past month. Baseline characteristics were compared between HFD [–] and HFD[+]. Primary outcome was a $\geq$50% reduction (50RED) of monthly headache days at 3 months.
Results: A total of 309 patients were registered between April 2020 and October 2021. Among 228 patients (age, 45.7 ± 13.8; female, 84.6%; chronic migraine; 99.1%) followed up at 3 months, 105 (46.1%) patients did not have any headache-free days (HFD [−]) in the past 1 month at baseline. Compared to HFD [+] group, HFD [−] group more frequently had monthly headache days (30.0 ± 0.0 vs. 21.0 ± 4.2, $p < 0.001$), monthly headache days with severe intensity (12.8 ± 9.1 vs. 9.0 ± 5.4, $p < 0.001$), and days taking acute headache medications (25.3 ± 6.8 vs. 17.2 ± 5.9, $p < 0.001$). Only 13.3% of the HFD [−] and 7.3% of the HFD [+] decided to maintain the previously overused acute medications, and 3.8% of the HFD [-] and 8.1% of the HFD [+] refused to start preventive treatment. Proportion of calcitonin-gene related peptide monoclonal antibody therapy (34.3% vs. 24.4%, $p = 0.135$) and botulinum toxin type A (25.7% vs. 28.5%, $p = 0.753$) were comparable between two groups. At 3 months, 46.7% of the HFD [−] and 48.8% of the HFD [+] experienced the 50RED in monthly headache days. Changes in monthly headache days (12.2 ± 10.2 vs. 8.0 ± 7.6, $p = 0.001$) and with severe intensity (6.6 ± 9.4 vs. 3.2 ± 6.2, $p = 0.002$) in the HFD [−] and HFD [+], respectively.
Conclusion: Our study demonstrates that even patients without headache-free days can achieve comparable clinical outcomes to those with headache-free days. This underscores the potential for meaningful improvement in managing this challenging subgroup of patients.
Disclosure of Interest: None Declared

Headache pathophysiology – Basic science

IHC23-DP-004

Comparison of gepant effects at therapeutic plasma concentrations: connecting pharmacodynamics and pharmacokinetics

Deirdre M. Boucherie[1], Ruben Dammers[2], Arnaud Vincent[2], A.H. Jan Danser[1] and Antoinette MaassenVanDenBrink[1]

[1]*Division of Pharmacology and Vascular Medicine, Department of Internal Medicine, Erasmus MC University Medical Center, Rotterdam, Netherlands*
[2]*Department of Neurosurgery, Erasmus MC University Medical Center, Rotterdam, Netherlands*

Objective: The small-molecule calcitonin gene-related peptide (CGRP) receptor antagonists named gepants are making headway into the clinic for both the acute and prophylactic treatment of migraine. Here, we aimed to characterize the response to CGRP in the absence or presence of zavegepant in human middle meningeal arteries (HMMA). Furthermore, we aimed to compare the blocking effect of therapeutic gepant concentrations on CGRP-induced relaxation based on clinical gepant plasma levels. This method allows for the connection of *in vitro* pharmacodynamic data to clinical pharmacokinetics.
Methods: Upon precontraction with 30 mM KCl, concentration-response curves to CGRP (10 pM–1 μM) were constructed in HMMA segments from donors undergoing neurosurgery (n = 6, 52 ± 19 years, 33% women) in the presence or absence of 10 nM zavegepant, data on the potency of other gepants were obtained from our earlier studies.Furthermore, for all currently available gepants, we collected C_{max} values following therapeutic dosages from literature [1–7] and corrected these values for plasma-protein binding. Based on *in vitro* pharmacological gepant characterizations in HMMA, we calculated the effect of gepants on relaxation to 100 nM CGRP.
Results: A significant shift of the concentration-response curve to CGRP to the right was observed with 10 nM zavegepant (control pEC_{50}: 8.40 ± 0.09; 10 nM zavegepant pEC_{50}: 6.38 ± 0.07; p = 0.0001; Figure).Subsequently, we used *in vitro* pharmacological data to calculate the potency of gepants to inhibit responses to CGRP following therapeutic dosages. Relaxation to 100 nM CGRP would be between 4.4% (atogepant) and 52% (zavegepant) in the presence of therapeutic concentrations of gepants versus 100% in the absence of a gepant (Figure).

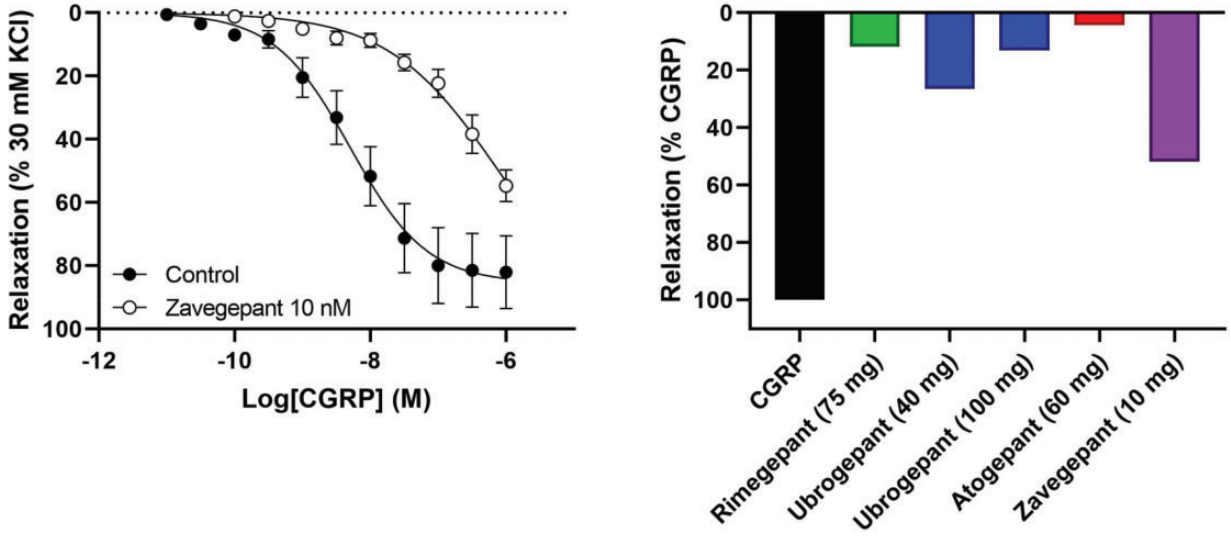


Figure: Concentration-response curve to CGRP in the absence or presence of 10 nM zavegepant in human middle meningeal arteries (left). Relaxation to 100 nM CGRP in the absence or presence of gepants (right).

Conclusion: All gepants are effective at inhibiting CGRP-induced relaxations at therapeutic concentrations, confirming the peripheral trigeminovascular system as the likely site of action of gepants. The relatively low *in vitro* efficacy of zavegepant compared with its good clinical efficacy may point to the relevance of local delivery through intranasal administration.

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Headache disorders in children and adolescents

IHC23-DP-005

HEY KIDS! LIFESTYLE AND HABITAT AFFECT YOUR FRAGILE ANALGESIA- EPIDEMIOLOGY 1992–2022

Maria Nicolodi[1], MariaStella Pinnaro[2] and Leonardo DiPuccio-Sicuteri[3]

[1]*Foundation for Headache and Stress, Firenze, Italy*
[2]*University of Florence, Firenze, Italy*
[3]*University of Padua, Padua, Italy*

Introduction: Headache is an ancient disease. The news is that it increased in evolutive age as well. Question: How is it that it has grown so much? If lately the disease increased, narrow-sense genetic heritability could be changed by epigenetic concurrent factors. So, we evaluated changes in pollution and lifestyle during the last three decades. Indeed, the mentioned epigenetic factors modify DNA expression through methylation, which alters pain processing. Since 1988 we has shown that methylation is a fragile point in biochemistry of M.

Methods: 1) Time-series observation. Descriptive Cross-Sectional Chronic headache in the 6–17 year-old general population. Data collection- Time series equally spaced times:one decade) 2) Analytical exams of correlation multiple variables Subjects: 1510 each decade from 35 Italian schools Exclusion: psychosis, mental retardation

Results: Prevalence chronic migraine under 18

Period 1991–1992N = 7 0.46% male:female ratio 1:1
Period 2001–2002N = 79 5.2% male:female ratio 1:2
Period 2021–2022N = 384 25.4% male:female ratio 1:4

Epigenetic: Global Environment

Nitrogen Oxide 1990–2020 European Agency-2022 Decrease
Global Data NS
Global CO2 increased since 1780, 1970–2022 (JRC) NS
Sub-data: Decrease in several EU-USA areas 1990–2022.
Water pollution (2018–2028 "decade of water" UN Organization) dramatic increase

Lifestyle: Modifiers of Epigenetic

Abuse of Psychoactive Substances included in List of Major Sanctions
1992 0
2002 4 5% $p > 0.01$ vs1992
2022 4 4.5% NS vs 2002
IAD Internet Addiction Disorder (Goldberg1995, DMS-5)
1992 NA
2002 7 9%
2022 39 10% $p > 0.001$ vs. 1992, 2002
PBI Parental-Bonding Instrument (overprotection)
1992 4 57%
2002 7 9%
2022 1 0.2% $p > 0.01$ vs. 1992, 2002
Authoritative-Parenting versus Neglecting-Permissive (Feehan 1991)
1992 Neglecting-permissive 0
2002 Neglecting-permissive 3 4%
2022 Neglecting-permissive 301 78% $p > 0.01$ vs. 1992–2002
Food
Interview by dietitian upon completion of a diary
Intake of saturated fatty acids
1992 vs. 2022 $p > 0.5$ increase varying in different areas of Italy from 12% to 4%
Refined-added sugar
1992 20.1gr/day
2002 23 gr/day
2022 54.4 gr/day $p > 0.01$ vs. 1992–2002
BMI for Child and Teen (5th percentile-above 85th percentile)
1992 0
2002 6 overweight 7% $p > 0.01$ vs1992
2022 19 underweight 26 overweight 12% NS vs. 2002

Biochemistry

Methylation 1992 vs. 2022 NS

Conclusion: The prevalence of chronic headaches in young people increased from 0.46% to 25.4% in 1992–2022, that is an increase of 500%. Correlations suggest water pollution, metals and lifestyle can be severe epigenetic modifiers and might pamper chronic headache as they do with other diseases. Even if present data are devoid of bias due to lack of individual level data and differences regarding ethnic group, environmental influences; this type of observation does not finally prove a single cause.

Disclosure of Interest: None Declared

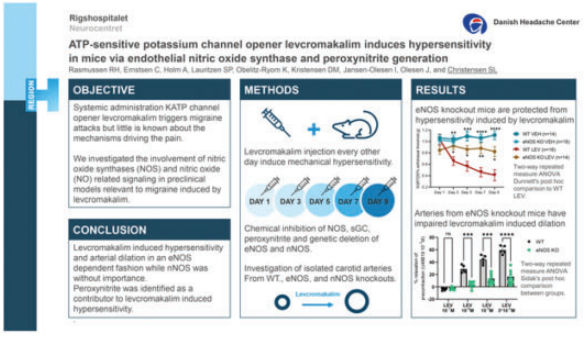
Headache pathophysiology – Basic science

IHC23-DP-006

ATP-sensitive potassium channel opener levcromakalim induces hypersensitivity in mice via endothelial nitric oxide synthase and peroxynitrite generation

Rikke Holm Rasmussen[1], Charlotte Ernstsen[1], Anja Holm[2,3], Sabrina Prehn Lauritzen[1], Karina Obelitz-Ryom[1], David M Kristensen[1,4,5], Inger Jansen-Olesen[1], Jes Olesen[1] and Sarah Louise Christensen[1]

[1]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Glostrup, Denmark*
[2]*Department of Clinical Experimental Research, Copenhagen University Hospital – Rigshospitalet, Glostrup, Denmark*
[3]*3Center for RNA Medicine, Aalborg University, Copenhagen, Denmark*
[4]*Department of Science and Environment Molecular and Medical Biology, Roskilde University, Roskilde, Denmark*
[5]*Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail, Rennes, France*



Objective: Systemic administration of ATP sensitive potassium (K_{ATP}) channel opener levcromakalim (LEV) potently triggers migraine attacks but little is known about the mechanisms driving the pain. We investigated the involvement of nitric oxide synthases (NOS) and nitric oxide (NO) related signaling in preclinical models relevant to migraine induced by LEV.

Methods: Mice (C57Bl/6 background) were injected systemically with LEV 1 mg/kg, i.p. every other day a total of five times. Hind paw sensitivity to stimulation with von Frey filaments was measured as a surrogate marker of migraine-like pain before and 2 h after injection. LEV induced hypersensitivity was tested with chemical inhibitors of NOS (non-selective) [L-NAME 100 mg/kg, i.p.], soluble guanylate cyclase (sGC) [ODQ 1–10 mg/kg, i.p.], and peroxynitrite (PN) [FeTPPS, 30 mg/kg, i.p.]. The role of endothelial (e) and neuronal (n) NOS were evaluated using specific knockout mice. LEV induced arterial dilation was tested in isolated carotid arteries from wild type, eNOS, and nNOS knockout mice. To identify possible location of NOS activity, different relevant tissues were analyzed for mRNA expression of NOS and other related targets. Von Frey data are presented as square root transformed (SQRT) 50% withdrawal thresholds. Vascular data are percentwise dilation. Data were analyzed by repeated measure two-way ANOVA with appropriate post hoc tests.

Results: Non-selective NOS inhibition prevented the development of tactile hypersensitivity in response to LEV ($P \leq 0.0004$). eNOS but not nNOS knockout mice were less sensitive to LEV induced hypersensitivity ($P \leq 0.03$ and $P = 0.02–0.77$). sGC inhibition did not alter the response to LEV ($P \geq 0.72$) but reducing PN was effective ($P = 0.008–0.06$) in the behavioral model. Arteries from eNOS deleted mice had compromised LEV induced dilation ($P \leq 0.0002$), whereas nNOS deleted arteries dilated normally ($P \geq 0.20$). mRNA data did not reveal any clear candidate genes as differentially regulated post LEV injections, but suggested targets in dura mater for further investigation. Neither inducible (i)NOS, nNOS, nor eNOS expression were altered.

Conclusion: Levcromakalim (K_{ATP} channel opener) induced hypersensitivity and arterial dilation in an eNOS dependent fashion while nNOS was without importance. We could not localize the NOS effect to trigeminal ganglia nor brain stem, but arterial eNOS activity induced by levcromakalim was found. Both NO and K_{ATP} channel opening are potent migraine provoking pathways in humans. Furthermore, identification of peroxynitrite as a contributor to levcromakalim induced hypersensitivity supports other preclinical studies suggesting that this and other reactive nitrogen species may be relevant in migraine pain generation and as a therapeutic target.

Disclosure of Interest: Contract research DSM Human nutrition and Health Cephagenix Consultant/advisor Y-mAbs Therapeutics

Headache classification

IHC23-DP-007

Functional connectivity-based diagnosis model for migraine

Jong Young Namgung[1], Yeong Jun Park[2], Bo-yong Park[1,3] and Mi Ji Lee[4]

[1]*Department of Data Science, Inha University, Incheon, Korea, Republic of*
[2]*Department of Computer Engineering, Inha University, Incheon, Korea, Republic of*
[3]*Center for Neuroscience Imaging Research, Institute for Basic Science, Suwon, Korea, Republic of*
[4]*Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*

Objective: We tested the reliability of the diagnostic model for migraine using functional MRI-based connectivity analysis combined with dimensionality reduction techniques.
Methods: We serially obtained resting-state fMRI of patients with episodic migraine and age-sex-matched healthy controls (HCs) at baseline and after one year for internal validation. We additionally recruited patients and HCs and obtained their resting-state fMRI data for external validation. We constructed a diagnostic model using migraine patients with interictal phase and matched controls at baseline using low-dimensional representations of functional connectivity (i.e., functional gradients). We selected functional connectivity features by assessing between-group differences in functional gradients, and trained the model with five-fold cross-validation. We repeated training 100 times with different training and test sets to mitigate subject selection bias. The final model was applied to the internal 1-year follow-up data as well as the external independent data.
Results: The model was trained using 16 pairs of patients and HCs ($n = 32$), and the diagnostic performance was $76.9 \pm 5.2\%$ across cross-validation and repetitions. The model was applied to the 21 interictal patient-control pairs ($n = 42$) of 1-year follow-up data, and it showed 64.3% of accuracy. However, diagnostic performance decreased to 48.4% in 32 interictal patient-control pairs ($n = 64$) for the external validation.
Conclusions: Utilizing dimensionality-reduced functional connectivity measures calculated from resting-state fMRI may be variable across time, phase, and individuals. A more robust and reliable diagnosis model is warranted.
Disclosure of Interest: None Declared

Headache pathophysiology – Imaging and neurophysiology

IHC23-DP-008

Impaired central parasympathetic modulation in patients with reversible cerebral vasoconstriction syndrome

Shih-Pin Chen[1,2,3,4,5], Chia-Hung Wu[6,1], Tun-Wei Hsu[6,1,7], Kuan-Lin Lai[2,3,1], Yen-Feng Wang[1,2], Jong-Ling Fuh[2,3,1], Hsiu-Mei Wu[6,1], Jiing-Feng Lirng[6,1] and Shuu-Jiun Wang[2,3,1]

[1]*School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[2]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[5]*Division of Translational Research, Department of Medical Research, Taipei, Taiwan*
[6]*Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan*
[7]*Department of Nuclear Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*

Objectives: To investigate the functional networks in subjects with reversible cerebral vasoconstriction syndrome (RCVS) using resting-state functional magnetic resonance imaging (rs-fMRI).
Methods: We prospectively recruited patients with RCVS and healthy controls (HCs) between February 2017 and April 2021. The acute stage of RCVS (aRCVS) was defined as RCVS patients with disease onset to MRI $\leq$30 days. The rs-fMRI data were analyzed using graph theory methods. We compared node-based global and regional topological metrics (Bundle 1) and network-based intranetwork and internetwork connectivity (Bundle 2) between RCVS patients and HCs. Exploratory investigations of associations of clinical parameters with significant rs-fMRI metrics were performed.
Results: A total of 197 subjects (104 RCVS patients and 93 HCs) were included in the final analysis. We identified significantly decreased local efficiency of the left dorsal anterior insula (dAI; $p = 0.0005$) in aRCVS patients, which was improved by 60 days after disease onset compared to HCs ($p = 0.075$, not significantly different from with HCs). Increased global efficiency ($p = 0.009$) and decreased average degree centrality ($p = 0.045$), clustering coefficient ($p = 0.033$) and assortativity values ($p = 0.003$) in node-based analysis were observed in RCVS patients compared to HCs. In addition, patients with RCVS had increased internetwork connectivity of the default mode network (DMN) with the salience ($p = 0.027$) and dorsal

attention ($p = 0.016$) networks but decreased connectivity with the visual and salience networks ($p = 0.044$). Interpretations: RCVS patients may have less clustered functional structures and higher global efficiency. The significantly lower local efficiency of the left dAI in aRCVS may imply impaired central parasympathetic modulation, which is highly plausible for the pathogenesis of RCVS.
Disclosure of Interest: None Declared

Other secondary headache disorders

IHC23-DP-009

Clinical and neuroradiological associates of recurrent headaches in patients with cerebral venous thrombosis

Esme Ekizoglu, Semih Taşdelen, Mine Sezgin, Nilüfer Yeşilot, Betül Baykan and Oguzhan Çoban

Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Turkey

Objective: Headache is one of the predominant symptoms of cerebral venous thrombosis (CVT). Our aim was to evaluate the clinical characteristics and risk factors of recurrent headaches (RHs) after CVT.
Methods: The study included patients diagnosed with CVT who presented with headache and had at least six months of follow- up. The clinical features of their previous headaches and new-onset headaches after CVT were investigated.
Results: Forty-two patients (27 females) with a mean age of 38.5 ± 10.4 years at diagnosis and a follow-up period of 4.4 ± 3.9 years were included. Of these patients, 26 (61.9%) had RHs after the acute stage of CVT, with headaches persisting for over one year in 21 of them (80.8%). These RHs were classified as tension-type headache-like in 10 patients, migrainous in 13 and symptomatic trigeminal autonomic cephalalgia in 3 patients. Thirteen patients (50%) with RHs described previous headaches, while only three patients (18.7%) in the group without RHs had history of headache. We found no associations between neurological findings, mode of onset, quality of headache, and the presence of phonophobia at CVT diagnosis of the patients with or without RHs. However, photophobia and thrombosis in multiple venous sinuses were more frequently observed in the group with RHs compared to those without RHs (25% vs 61.5%, $p = 0.029$ and 50% vs 80.1%, $p = 0.047$; respectively). Additionally, 7 patients in the RHs group described allodynia during their headache attacks, 2 of them did not have previous headaches and only one of the remaining five patients with allodynia reported previous allodynia.
Conclusion: Recurrent headaches with a protracted course were observed in nearly two-thirds of the patients with CVT; tension-type like headaches, migrainous headaches, and symptomatic trigeminal autonomic cephalalgia were the most common types. Involvement of multiple venous sinuses and the presence of photophobia were associated with RHs. Report of allodynia and autonomic symptoms in some cases with RHs may suggest central sensitization of the trigemino-cervical complex and the activation of the trigemino-autonomic reflex after CVT, which have not been previously noted in studies.
Disclosure of Interest: None Declared

Headache pathophysiology – Basic science

IHC23-DP-010

Development of an in vivo mouse model to study migraine related effects of the large conductance calcium-activated potassium channel

Karina Obelitz-Ryom, Jes Olesen and Sarah Louise Christensen

Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Glostrup, Denmark

Objective: Administration of maxipost, a known opener of the large conductance calcium-activated potassium (BK_{Ca}) channel, triggers migraine attacks in humans. To study mechanisms of BK_{Ca} induced migraine pain, we aimed to develop a mouse model where migraine-related effects were induced by opening of BK_{Ca}.
Methods: As a surrogate marker of migraine-like pain, hind-paw sensitivity was measured with von Frey filaments on mice (C5BL7/6JBomTac). Sensitivity was measured before and 2 hours after intraperitoneal (i.p.) injection of maxipost 1 mg/kg, 10 mg/kg or vehicle. Nitroglycerin 10 mg/kg was injected as positive control. Mice were injected and tested every other day for a total of five test days. BK_{Ca} channel specificity was investigated in a similar setup with i.p. dosing of NS11021 1 mg/kg, NS11021 10 mg/kg or vehicle. The Von Frey data were analyzed with repeated measure two-way ANOVA followed by Dunnet's post hoc comparison. Data is presented as square root transformed (SQRT) 50% withdrawal thresholds. Group size in all experiments were 12.
Results: Dosing with maxipost induced tactile hypersensitivity, both at baseline and 2 hours after injection (both $P \leq 0.0001$). The specific effect of the BK_{Ca} channel on the tactile hypersensitivity was validated by dosing with NS11021, which also led to increased tactile hypersensitivity both at baseline measurements and 2 hours after injection (both $P \leq 0.0001$). The response 2 hours after injection is presented in Figure 1.

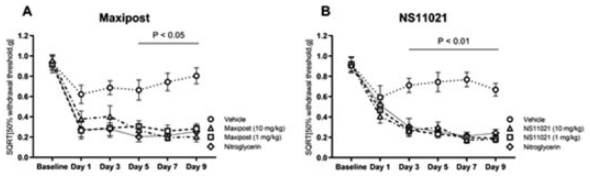


Figure 1. Tactile sensitivity 2 hours after injection. Both maxipost (A) and NS11021 (B) induces tactile hypersensitivity similar to the positive control, nitroglycerin. Data is presented as square root transformed (SQRT) 50% withdrawal thresholds. N = 12 in all groups.

Conclusion: The human migraine trigger maxipost induced hind-paw tactile hypersensitivity in mice. The induction of hypersensitivity was reproduced with the more specific BK_{Ca} channel opener NS11021. Thus, there is a strong indication that the BK_{Ca} channel is involved in the development of tactile hypersensitivity in mice relevant to migraine.

Disclosure of Interest: None Declared

Migraine acute therapy

IHC23-DP-011

Vaporized cannabis versus placebo for the acute treatment of migraine: a randomized, double-blind, placebo-controlled, crossover trial

Nathaniel Schuster[1], Mark Wallace[1], Dawn Buse[2], Euyhyun Lee[1], Lin Liu[1], Thomas Marcotte[1] and Michelle Sexton[1]

[1]*University of California, San Diego, San Diego, USA*
[2]*Albert Einstein College of Medicine, Bronx, USA*

Background: Preclinical and retrospective studies suggest anti-migraine effects of cannabinoids. However, despite broad patient interest and use, to date clinical trial data on the efficacy of cannabinoids for the acute treatment of migraine are lacking. This is the first randomized, double-blind, placebo-controlled trial testing the efficacy of cannabinoids for the acute treatment of migraine.

Methods: In this randomized, double-blind, placebo-controlled, crossover trial, adults (aged 21–65) with ICHD-3 defined migraine and 2–23 headache and migraine days per month were enrolled and randomized to treat moderate-to-severe migraine attacks within 4 hours of migraine onset with vaporized cannabis flower. Participants were instructed to treat up to 4 separate migraine attacks, 1 each with vaporized 1) THC dominant (6% THC), 2) CBD dominant (11% CBD), 3) THC/CBD mix (6% THC/11% CBD), and 4) placebo cannabis in a randomized, double-blind order. The washout period was ≥1 week between migraine attacks. The primary end point was pain relief at 2 hours post-vaporization. Key secondary end points were pain freedom and most bothersome symptom (MBS) freedom at 2 hours post-vaporization. Data were collected via a real-time, interactive smartphone application with push notifications. The association of outcomes with four different treatments were assessed using a generalized linear mixed effects model. A random intercept structure was included to account for the cluster effect of subjects going through the same trial multiple times. During the trials, some subjects filled out the survey before or after the expected timepoints. To minimize the loss of data due to the late/early responses, we performed a sensitivity analysis using a time window to retain as much subset of the data as possible without increasing possible exposure to retention bias. The protocol was registered at ClinicalTrials.gov (NCT04360044).

Results: 92 participants were enrolled and randomized and 71 participants treated at least one migraine attack. Median age was 41 and 82.6% were female. 27.2% had chronic migraine. For 234 migraine attacks, the participant entered 2 hour data, and for a subset of 202 migraine attacks the participant entered data time-stamped between 1.5 hours and 3 hours after the time 0 questionnaire. Sensitivity analyses were performed with both the total and subset populations with the same results. At 2 hours post-vaporization, THC/CBD mix was superior to placebo at achieving pain relief (n = 234 sample: 69.0% vs 48.3%, OR [95% CI]: 3.07 [1.26, 7.51], p = 0.014; n = 202 sample: 66.0% vs. 45.3%, 2.78 [1.13, 6.82], p = 0.026), pain freedom (n = 234 sample: 36.2% vs. 15.5%, 3.67 [1.36, 9.93], p = 0.010; n = 202 sample: 38.0% vs. 15.1%, 4.71 [1.54, 14.42], p = 0.007) and MBS freedom (n = 234 sample: 62.1% vs. 36.2%, 3.53[1.49, 8.35], p = 0.004; n = 202 sample: 62.0% vs 35.8%, 3.46 [1.40, 8.55], p = 0.007). THC dominant was superior to placebo at achieving pain relief at 2 hours (n = 234 sample: 70.5% vs. 48.3%, 3.417 [1.41, 8.29], p = 0.007; n = 202 sample: 70.0% vs. 45.3%, 3.40 [1.37, 8.43], p = 0.008) but was not significantly different from placebo for pain freedom or MBS freedom. CBD dominant was not significantly different from placebo for pain relief, pain freedom or MBS freedom. Sleepiness was the most common side effect, followed by euphoria. There were no serious adverse events.

Conclusion: Acute treatment of migraine with vaporized THC/CBD mix (6% THC/11% CBD) was superior to placebo for pain relief, pain freedom and MBS freedom at 2 hours. Future multi-center RCTs are needed and should examine pain freedom and MBS freedom as co-primary endpoints. Future research should examine whether frequent use of cannabinoids conveys risk of medication-overuse headache.

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partially supported by the UCSD Academic Senate and the National Institutes of Health, Grant UL1TR001442. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. Study drug was provided by the National Institute on Drug Abuse (NIDA). Vaporizers were donated by Storz & Bickel GmbH & Co. KG, which did not provide any financial support of this study and was not involved in the design or conduct of the study or manuscript preparation. NS has received <$5,000 for consulting services to Vectura Fertin Pharma and <$5,000 for consulting services from Schedule 1 Therapeutics; he has no stock or equity in these or any other related companies. DB has received research support and consulting honoraria from AbbVie, Amgen, Biohaven, Eli Lilly and Company, Lundbeck, and Teva and for work on the editorial board of Current Pain and Headache Reports. MW, TM, EL, LL, and MS report no relevant disclosures.

Psychological and behavioural factors and management

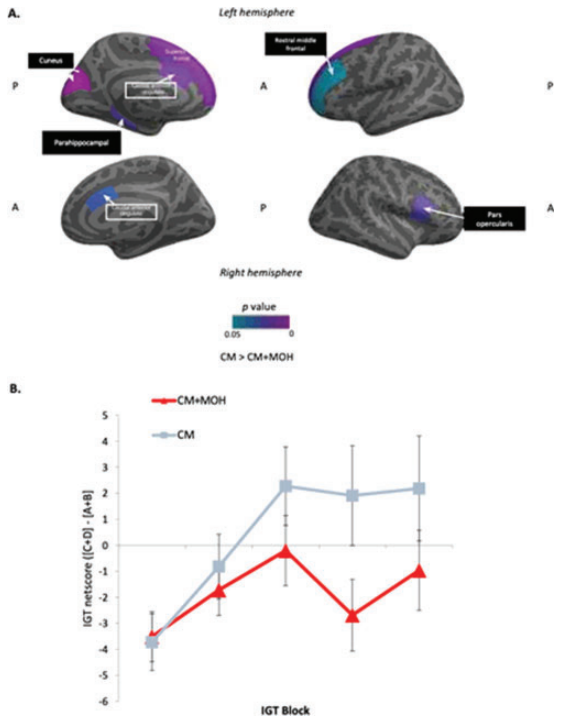
IHC23-DP-012

Dysregulated reward processing linked to medication overuse headache in chronic migraine

Chi Ieong Lau[1,2,3,4], Chi-Wen Jao[3], Wei-Hung Chen[1] and Vincent Walsh[2]

[1]*Department of Neurology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan*
[2]*Applied Cognitive Neuroscience Group, Institute of Cognitive Neuroscience Group, Institute of Cognitive Neuroscience, London, United Kingdom*
[3]*Institute of Biophotonics, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*College of Medicine, Fu-Jen Catholic University, New Taipei City, Taiwan*

Objective: Recent studies have linked brain changes in the mesocorticolimbic reward system to patients with chronic migraine and medication overuse headache (CM+MOH), although the mechanisms underlying their role in MOH development remain unclear. To address this question, we compared CM+MOH and CM patients on a decision-making task and correlated their performance with MRI measures of cortical thickness (CTh).
Methods: We recruited 60 patients with CM (82% female, 45.6 ± 11.6 years), of which 30 had comorbid MOH, and 60 age- and sex-similar healthy controls (HC). Using the automated surface-based analysis package FreeSurfer, we compared the cortical thickness (CTh) and subcortical nuclei volume between the groups. The patient groups also completed the Iowa Gambling Task (IGT) to evaluate decision-making under ambiguity and the substance dependence scale (SDS) questionnaire.
Results: Compared to CM patients, patients with CM+MOH showed a significant reduction in CTh in several key brain regions of the mesocorticolimbic reward circuity, including the bilateral anterior cingulate cortex (ACC), left superior and rostral middle frontal cortices, with the CTh of the left ACC being inversely correlated with SDS score($r = -0.41$, $p = 0.024$). We also observed reduced CTh in the left cuneus, parahippocampus, and right pars opercularis (Figure 1A). Additionally, decreased volume in subcortical regions associated with reward processing, including the left globus pallidum, right amygdala, and right cerebellum, was observed in patients with CM+MOH compared to CM patients.Furthermore, CM+MOH patients had poorer performance on the IGT, consistently making disadvantageous choices (lower net scores), whereas CM patients shifted to more advantageous strategies (Figure 1B). Interestingly, IGT performance showed a negative correlation with the CTh of the right ACC ($r = -0.41$, $p = 0.029$), as well as with analgesic consumption ($r = -0.53$, $p = 0.011$), suggesting a link between decision-making under ambiguity and MOH. While there was no significant difference in headache profiles, patients with CM+MOH reported more frequent analgesic use (22.96 ± 7.8 vs. 9.08 ± 7.01 days; $p < 0.001$) and higher SDS score (8.3 ± 3.3 vs. 4.2 ± 3.8; $p < 0.001$) compared to CM patients, with analgesic consumption being positively correlated with SDS score ($r = 0.402$, $p = 0.007$).
Conclusion: Our findings provide both imaging and behavioural evidence supporting the presence of a dysregulated reward processing mechanism in patients with CM+MOH.



Disclosure of Interest: None Declared

Headache classification

IHC23-DP-013

Vestibular migraine Vs Migraine: more the same than different

Eliseo Barral[1], David Moreno Ajona[1,2], María Dolores Villar Martínez[1], Francesca Puledda[1], Joseph Marshall[2] and Peter J Goadsby[1]

[1]*NIHR King's Clinical Research Facility & SLaM Biomedical Research Centre, and Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[2]*Neurology, Queen Elizabeth Hospital, London, United Kingdom*

Objective: Migraine with dizziness, migraine with prominent vertigo or vestibular migraine is a growing diagnosis. Indeed, a high proportion of patients with migraine complain of vestibular symptoms. Both the International Headache Society and the Barany Society agreed on diagnostic criteria for vestibular migraine. Whether the distinction between migraine and vestibular migraine is useful or not is a matter of debate. Our objective was to examine responses to migraine-specific preventive medications targeting the CGRP pathway in vestibular migraine patients, comparing them to migraine patients without vestibular symptoms.

Methods: We conducted an audit of consecutive patients attending the Headache Novel Therapies Clinic at King's College Hospital, London, UK. Patients on CGRP pathway monoclonal antibodies were included. Patients seen between January 2019 and March 2023 were included. History of migraine features and characteristics including vertigo were reviewed. Patients fulfilling ICHD-3 criteria for vestibular migraine were considered as such. Efficacy of treatment was compared between migraine and vestibular migraine patients at baseline, 6 and 12 months of treatment This was a convenience sample of treated patients. A sample size calculation estimated groups should involve at least 14 patients. Monthly migraine days and monthly headache days were used as efficacy variables. Median and interquartile range are used to describe headache frequency, Mann Whitney tests were used for comparison of medians and Chi-square for comparison of dichotomous variables. A generalized linear model with a negative binomial distribution and log link function was applied to identify predictor variables where change in headache days at 12 months was the dependent variable, this being baseline headache days minus headache days at 12 months plus 29 days to make all the values natural numbers in a scale of 0–57 as previously described (1). Sex, age, presence of vestibular symptoms, allodynia, change in headache at 6 months and migraine duration, as a marker of refractory status, were used as covariates. Statistical significance was established at $P < 0.05$ (IBM SPSS Statistics for Mac, Version 28.0. Armonk, NY: IBM Corp).

Results: One hundred and sixty-one migraine patients in total had been on the CGRP pathway monoclonal antibodies of which 20 were males, mean age was 46 (±15, SD) years old. Almost half of the patients (79/161) fulfilled the criteria for vestibular migraine. Eighty patients had been on fremanezumab and 81 on erenumab with similar distribution of vestibular migraine/migraine patients with each drug. No statistically significant difference between groups in the median of monthly migraine days was shown at baseline, 6 and 12 months (migraine vs vestibular migraine; baseline 15 vs 15 (IQR 25–28); 6 months 7 vs 8 (IQR 3–15); 12 months 5 vs 5 (IQR 3–10). Even if a a significant difference between groups in the median of monthly headache days was shown at 6 and 12 months (migraine vs vestibular migraine; baseline 28 vs 28 (IQR 25–28); 6-months 22 vs 28 (total IQR 11.5–28), $P = 0.006$; 12-months 11 vs 28 (total IQR 5.75–28), $P < 0.001$) the generalized linear model failed to show significant predictors of outcome. Of note, there was significantly more allodynia in the vestibular migraine group ($c2 = 6.53$, $P = 0.011$).

Conclusion: The response to CGRP-pathway antibodies is comparable between vestibular migraine and migraine

patients in terms of median monthly migraine days, median monthly headache days seem to respond less in vestibular migraine patients although the regression model did not show vestibular migraine or allodynia as predictors. A different biology mediating non-migraine headaches in vestibular migraine patients is possible although the presence of vestibular symptoms did not act as a predictor of such outcome.

Disclosure of Interest: PJG reports, over the last 36 months, a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly and Company, Epalex, GlaxoSmithKline, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer, and for medicolegal advice in headache, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee. DMA, EB, MDVM, FP and JM have no disclosures for the current work.

Reference

1. Villar-Martinez MD, Goadsby PJ. A simple method for transforming headache days to facilitate change modelling. *Cephalalgia*. 2021; 41(1S): 279.

Other secondary headache disorders

IHC23-DP-014

SIH-EBP Score for Evaluating the Response to Epidural Blood Patch in Patients with Spontaneous Intracranial Hypotension: a replication study

Tsung-Wei Hou[1], Shuu-Jiun Wang[2,3], Yen-Feng Wang[2,3] and Hung-Chieh Chen[4]

[1]*Department of Neurology, Neurological Institute, Taichung Veterans General Hospital, Taichung, Taiwan*
[2]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[3]*College of medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Department of Radiology, Taichung Veterans General Hospital, Taichung, Taiwan*

Objective: Spontaneous intracranial hypotension (SIH) is a unique headache disorder associated with postural changes, and spinal cerebrospinal fluid (CSF) leakage is considered the main pathogenic factor. Epidural blood patches (EBP) are the mainstay of treatment, especially after failure of conservative treatment, although the response to treatment could be variable. The SIH-EBP score was developed for prognostic purposes, and a cutoff score of $\geq$3 was predictive of treatment response to the first EBP. However, the grading system has not been validated. This study aimed to validate the SIH-EBP score in SIH patients in an independent patient cohort.

Methods: This was a retrospective study involving patients diagnosed with SIH and receiving at least one EBP in a tertiary medical center in central Taiwan. The SIH-EBP score (range 0–5) consists of two clinical and two radiological variables, including female sex [1 point], age $\geq$50 years [1 point], midbrain-pons angle $\geq$40° [1 point], and anterior epidural cerebrospinal fluid collections (<8 segments [2 points] or 8–18 segments [1 point]). The data mentioned above were independently assessed by a neuroradiologist and a neurologist, respectively. The cutoff score was determined by the receiver operating characteristic (ROC) curve, and the areas under the ROC curve (AUC) were calculated.

Results: In total, 96 patients with SIH were identified, and 49 (51.0%) received at least one EBP and were included in the analysis. The SIH-EBP score was positively associated with the response rate to the first EBP ($p = 0.006$). Based on the previous publication, an SIH-EBP score of $\geq$3 was associated with an accuracy of 69.40% in predicting the response to the first EBP (sensitivity = 73.70%, specificity = 66.70%). Based on the treatment outcome in our own patients ($n = 49$), the cutoff score predictive of the response to the first EBP was determined at $\geq$2 (accuracy = 75.5%, sensitivity = 52.60%, specificity = 90.00%, and AUC = 0.77, $p < 0.0001$).

Conclusion: The SIH-EBP score can be utilized as a predictor of the response rate to the first EBP in SIH patients. A higher SIH-EBP score is associated with a better response. However, in our study, a score of $\geq$2 was more accurate than a cutoff of $\geq$3. Therefore, differences in study populations, treatment strategies, definition of treatment response, image interpretation, and other factors could have contributed to the consistencies.

Disclosure of Interest: None Declared

Migraine preventive therapy

IHC23-DP-015

Real wold experience of Galcanezumab in 348 patients with chronic migraine and monthly daily headache (GalcaOnly Consortium).

Neus Fabregat[1], Víctor Obach[1], Santiago Fernandez-Fernandez[1], Teresa Marco[1], Ines Martin[1], Ana Rizo[1], Nuria Pola[1], Fernando Velasco[2], Maria Martin-Bujanda[3], Elisa Cuadrado[4], Antia Moreira[5], Sonsoles Aranceta[6], Marta Ruibal[7], Aintzine Ruisanchez[8], Nuria Riesco[9], Rocio Alvarez-Escudero[9], Alba Bravo[10], Ane Minguez[7], Amaya Echeverria[11], Izaro Kortazar[11], Antoni Suarez[4], Nuria Roncero[12], Juan Carlos Garcia. Monco[12], Angel Guerrero[13] and David Garcia-Azorin[13]

[1]*Hopital Clinic, Barcelona, Spain*
[2]*Hopital Cruces, Bilbao, Spain*
[3]*Hopital Navarra, Pamplona, Spain*
[4]*Hopital del Mar, Barcelona, Spain*
[5]*Hospital del Mar, Barcelona, Spain*
[6]*Hopital Parc Tauli, Barcelona, Spain*
[7]*Hopital Donosti, San Sebastian, Spain*
[8]*Hospital Galaakao, Bilbao, Spain*
[9]*H Asturias, Oviedo, Spain*
[10]*Hopital Tudela, Tudela, Spain*
[11]*Hospital de Alava, Alava, Spain*
[12]*Hospital Basurto, Bilbao, Spain*
[13]*Hospital Valladolid, Valladolid, Spain*

Objective: Chronic migraine patients with daily headache have been excluded from most of the randomized clinical trials assessing the efficacy of anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs). To date, there are few reports on the efficacy of CGRP-mAbs in patients with chronic migraine suffering Monthly Daily Headache (MDH). In the present sub-study, we analyzed the tolerability and effectiveness of galcanezumab in patients with chronic migraine and daily headache from a large multicentric registry.

Methods: Multicenter (n = 12) prospective cohort study. The study population were patients with diagnosis of chronic migraine, according to the International Classification of Headache Disorders, 3rd version. All consecutive patients that were treated with Galcanezumab were included. According to the local guidelines, Galcanezumab is approved in patients with prior failure to three or more migraine preventive drugs, including onabotulinumtoxinA. The study period was between November 15, 2019, to January 31, 2022. Patients were evaluated by headache experts by in-person evaluations and followed-up quarterly. A series of variables were routinely collected, including demographic variables, other psychiatric comorbidities and painful syndromes, clinical situation of migraine, and impact of migraine.Response to treatment was according to the 50% responder rate, defined as the proportion of patients with who achieved a reduction of at least 50% in the number of headache days per month, compared to the baseline period. Tolerability was assessed as the proportion of patients who discontinued the treatment due to inadequate tolerability. Data of follow-up at 12 months are presented.Patients with chronic migraine with daily headache were compared to patients with chronic migraine or high-frequency episodic migraine.

Results: In our registry of 1055 patients, 348 (33.0%) presented MDH. Differences between groups are shown in the table. Patients with MDH had fibromyalgia, other chronic pain and mood disorders requiring drug treatment more frequently.

At 12 month follow-up, patients with MDH has SR50 of 37.9% compared to 55.6% (p = 0.001) in non MHD. Moreover galcanezumab retention was 56.6% and 78.6% (p = 0001) and Galcanezumab was discontinued due to adverse events in 12.6% and 3.7% (P = 0.001), respectively.

Conclusion: Patients with Monthly Daily Headache had more systemic chronic pain and mental disorders and presented more adverse events to Galcanezumab treatment. Moreover, more than one third of patients with MDH had a good response to galcanezumab.

Disclosure of Interest: None Declared

Variables	DH patients (n = 348)	Non-DH (n = 707)	P value
Age, mean (SD)	50.9 (13.0)	49.2 (11.5)	0.2
Female, n (%)	299 (85.9)	576 (81.5)	0.1
Migraine worsening, years [IQR]	7 [4–13]	8 [4–14]	0.1
Chronic migraine, n (%)	334 (96.0)	472 (60.8)	0.001
Monthly headache days (MHDs), baseline [IQR]	30 [30–30]	16 [12–20]	0.001
HIT6 baseline, [IQR]	71 [67–74]	68 [65–72]	0.2
Mental disorders, n (%)	130 (43.9)	216 (37.0)	0.05
Fibromyalgia, n (%)	47 (15.9)	54 (9.2)	0.004
Other chronic pain, n (%)	91 (30.7)	115 (19.7)	0.001

Neuromodulation for headache

IHC23-DP-016

Efficacy of Kinetic Oscillation Stimulation for the preventive treatment of chronic migraine

Jan Hoffmann[1,2], Holger Kaube[3], Florian Rimmele[4], Tim P. Jürgens[4,5], Markku Nissilä[6], Charly Gaul[7], Mikko Kallela[8], Petra Keski-Säntti[9], Marja-Liisa Sumelahti[10], Andreas Straube[11], David Lewis[12] and Arne May[13]

[1]*Wolfson Centre for Age-Related Diseases, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom*
[2]*NIHR-Wellcome Trust King's Clinical Research Facility/SLaM Biomedical Research Centre, King's College Hospital, London, United Kingdom*
[3]*Neurologie und Kopfschmerzzentrum Münchner Freiheit, Munich, Germany*
[4]*Department of Neurology, Headache Center North-East, University Medical Center Rostock, Rostock, Germany*
[5]*Department of Neurology, KMG Hospital Güstrow, Güstrow, Germany*
[6]*Clinical Research and Biobank, Terveystalo Turku Pulsi, Turku, Finland*
[7]*Headache Center Frankfurt, Frankfurt am Main, Germany*
[8]*Department of Neurosciences, University of Helsinki, Helsinki, Finland*
[9]*Terveystalo Ruoholahti, Helsinki, Finland*
[10]*Terveystalo Tampere, Tampere, Finland*
[11]*Department of Neurology, University Hospital, LMU Munich, Munich, Germany*
[12]*Lewis Neurologie, Stuttgart, Germany*
[13]*Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*

Objective: The objective of the multicentre, randomised, sham-controlled clinical trial was the assessment of the therapeutic efficacy of Kinetic Oscillation Stimulation (K.O.S) of the nasal cavity as a preventive treatment for chronic migraine.

Methods: Patients with chronic migraine were randomised to either receive intranasal stimulation (85 Hz, 80 mbar, n = 67) or sham stimulation (no vibration, 30 mbar, n = 65) once per week for 10 minutes per nostril over a period of 6 weeks. The first two treatment weeks were considered as a run-in period whereas the 4-week treatment period between weeks 3–6 was defined as the performance assessment period. Primary outcome was the reduction of monthly headache days with moderate to severe intensity during the 4-week performance assessment period compared to the 4-week baseline period in the treatment group versus the sham group. Analysis was conducted using a group-sequential design applying the ÓBrien & Fleming alpha spending function which uses the updated boundaries of the interim analysis and the estimates from the ANCOVA model and provides an adjusted p-value from the final stage.

Secondary endpoints included the reduction of headache days with moderate to severe intensity during a 4-week follow-up period, the 30% response rate of the reduction of headache days of moderate to severe intensity, and the reduction of migraine days compared to baseline. Data was analyzed using ANCOVA or a van Elteren Test stratified for medication overuse. All statistical tests for secondary performance endpoints and sensitivity analyses are considered exploratory and no adjustment for multiplicity was made.

Results: Intranasal K.O.S significantly reduced the number of monthly headache days with moderate to severe intensity from baseline when compared to sham stimulation. The difference in least square means (LSQ) of the ANCOVA model, containing terms for treatment, baseline value, and medication overuse was 2.23 (CI95% = [–3.95; −0.51], p = 0.0132). The effect was sustained during the follow-up period with an LSQ difference of –2.68 (CI95% = [−4.32; −1.04], p = 0.0014). The number of patients with a 30% or greater reduction of headache days of moderate to severe intensity during the performance assessment period compared to baseline (30% response rate) was 47.1% in the active treatment vs. 25.4% in the sham group (p = 0.0102).

The analysis of the reduction in migraine days compared to baseline revealed an LSQ difference between active and sham treatment of –2.40 (CI95% = [–4.06; −0.73], p = 0.0048) during the performance assessment period and –2.87 (CI95% = −4.54; −1.20], p = 0.0008] during the follow-up period.

The treatment was well-tolerated with no treatment-related serious adverse events.

Conclusion: The findings of the clinical trial show that intranasal K.O.S is an effective, well tolerated, and safe option for the preventive treatment of chronic migraine. Efficacy was preserved in patients with medication overuse. Efficacy was sustained over the entire 4-week follow-up period which may suggest that once the treatment effect is established, the maintenance of the treatment effect may require less frequent stimulations. However, this aspect will need to be assessed and confirmed in future investigations as it was outside of the scope of this trial.

The non-pharmacological nature of the treatment positions K.O.S as a valuable expansion of the current therapeutic portfolio since most of the current preventive treatments have a significant risk of causing

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Pharma, Lundbeck, Novartis, Sanofi and Teva. He received personal fees for Medico-Legal work as well as from Oxford University Press, Quintessence Publishing, Sage Publishing and Springer Healthcare. He holds stock options from Chordate Medical AB. He also reports a research grant from Bristol Myers Squibb. Jan Hoffmann serves as Associate Editor for Cephalalgia, Cephalalgia Reports, Journal of Headache and Facial Pain, Journal of Oral & Facial Pain and Headache as well as for Frontiers in Pain Research. He is an elected member of the Board of Trustees of the International Headache Society (IHS) and serves as a Council Member and Treasurer of the British Association for the Study of Headache (BASH). Holger Kaube does not report a conflict of interest. Florian Rimmele has received honoraria for consulting and lectures from Abbvie/Allergan, Novartis, Teva, Lilly, Lundbeck, Ipsen. He has received royalties from Elsevier and serves as Editor for Frontiers in Neurology – Headache and Neurogenic Pain. Tim P. Jürgens reports honoraria for consulting activities and/or serving on advisory boards from Abbvie/Allergan, Autonomic Technologies Inc., Chordate Medical AB, Grünenthal, Lilly, Hormosan Pharma, Lundbeck, Novartis, Pfizer, Sanofi, and Teva. He received personal fees for medico-legal work, Elsevier and Springer. He does not hold any stock options. He also reports a research grant from EFRE, Innovationsfonds-Gemeinsamer Bundesausschuss and Novartis. He serves as Associate Editor for Frontiers in Neurology – Headache and Neurogenic Pain on the Editorial Board of the The Journal of Headache and Pain. He is currently President of the German Migraine and Headache Society. Markku Nissilä reports honoraria for consulting, lectures and serving on advisory boards within the past three years from Eli Lilly, Teva, Novartis, Pfizer, Lundbeck and AbbVie. He holds stocks of Orion Corporation and Faron Pharmaceuticals. Charly Gaul has received honoraria for consulting and lectures within the past three years from Abbvie, Lilly, Novartis Pharma, Hormosan Pharma, Grünenthal, Sanofi-Aventis, Reckitt, Chordate Medical AB, Lundbeck, Perfood, and TEVA. His research is supported by a grant of the German Research Foundation (DFG). He does not hold any stocks of pharmaceutical companies. He is honorary secretary of the German Migraine and Headache Society. Mikko Kallela has served on Advisory Boards for MSD, Allergan, TEVA, Lilly, Lundbeck, Pfizer and Orion; has received funding for travel and/or speaker honoraria from MSD, Allergan, TEVA, Novartis, Genzyme, Lundbeck, Lilly; has received compensation for producing educational material from TEVA and Allergan; has received research support from Helsinki University Central Hospital; and holds stock/stock options and/or has received Board of Directors compensation from Helsinki Headache Center. Petra Keski-Säntti has received honoraria from Allergan, Novartis, and Teva for lectures and for serving on advisory boards. Marja-Liisa Sumelahti reports honoraria for consulting activities and/or serving on advisory boardsas well as for lectures from Abbvie, Eli Lilly, Lundbeck, Pfizer, Novartis, and Teva. Andreas Straube reports honoraria for consulting activities and/or serving on advisory boards and/or lectures from Allergan, Allergosan, Eli Lilly, Novartis, Sanofi and Teva. David Lewis reports honoraria for consulting activities and/or serving on advisory boards, lectures from Allergan, Hormosan, Lilly, Lundbeck, Novartis and Teva. He does not hold any stocks of pharmaceutical companies. Arne May does not report a conflict of interest. He is the Editor-in-Chief of Cephalalgia.

Other secondary headache disorders

IHC23-DP-017

InfluenCef Study: Prospective cohort study on the clinical phenotype and duration of headache associated with Influenza infection (NCT05704335)

Laura Santana López[1], Jose Eugenio Lozano Alonso[2], Ana Ordax Díez[2], Ivan Sanz Muñoz[3], Yésica González Osorio[4], Silvia Rojo Rello[5], Javier Sánchez Martínez[6], Álvaro Sierra[1], Andrea Recio García[1], Ángel Guerrero Peral[1] and David García-Azorín[1]

[1]*Department of Neurology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[2]*Dirección General de Salud Pública/Consejería de Sanidad/ Junta de Castilla y León, Valladolid, Spain*
[3]*National Influenza Centre, Valladolid, Spain*
[4]*Instituto de Estudios de Ciencias de la Salud, Castilla y Leon, Valladolid, Spain*
[5]*Department of Microbiology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[6]*Centro Nacional de Gripe de Valladolid, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*

Objectives: Headache is one of the most frequent symptoms of acute systemic infections. We aimed to characterize the clinical phenotype and duration of headache experienced during the course of Influenza infection, and the need and response to acute treatment.
Methods: Observational analytic study with prospective cohort design. Adult patients with confirmed diagnosis of influenza virus infection were screened and included if they fulfilled the International Classification of Headache Disorders criteria for *9.2.2.1 acute headache attributed to systemic viral infection*. Patients were excluded if they had an unstable medical situation, cognitive impairment, speech disorders or declined to participate. The study

period was between 23rd January 2023 and 4th April 2023. Valladolid East Medical Review Board approved the study (PI 22–2884) and all participants gave informed consent form. The study protocol was published in ClinicalTrials.gov (NCT05704335).

Results: During the study period 103 patients were screened and 75 fulfilled the eligibility criteria, 42 (56%) males, aged 43 (standard deviation (SD): 15,9) years. Twenty (27%) patients had prior history of headache, and 46 (61%) had previously experienced headache during the course of other infections. All patients were managed in an outpatient setting.

Headache began within the first 24 hours in 51 (68%) patients. The median duration of the headache was 96 [IQR: 48–144] hours and lasted 10 or fewer days in 67 (89%) cases. Headache was bilateral in 39 (52%) cases, predominantly located in the frontal (n = 36, 48%) or temporal (n = 29, 39%) regions. Patients reported the quality of pain as pressing in 46 (61%) cases and stabbing in 16 (21%). The median intensity of headache was 7 [IQR: 6–8] out of 10. Patients associated photophobia (n = 44, 59%), phonophobia (n = 38, 51%), osmophobia (n = 8, 11%), nausea (n = 27, 36%), vomiting (n = 10, 13%), worsening with physical activity (n = 62, 83%).

All patients required acute medication, with paracetamol (n = 44, 59%) and non-steroidal anti-inflammatory drugs (n = 44, 53%) being the most frequently used drugs. The proportion of patients who responded to these was 55% and 70%, respectively.

Conclusion: The clinical phenotype of acute headache attributed to systemic Influenza infection was similar to other systemic infections, such as coronavirus disease 2019. In most cases, the headache was self-limited and lasted for ten days or less and responded to symptomatic treatment.

Disclosure of Interest: None Declared

Headache epidemiology, outcomes and burden

IHC23-DP-018

Characterizing family impact in a Danish population with headache: Results from the nationwide Headache in Denmark (HINDER) study

Thien Phu Do[1,2,3], August Dylander[1,2,3], Simon Stefansen[2], Mikala Dømgaard[2], Timothy Steiner[3,4,5] and Messoud Ashina[1,2,3]

[1]*Danish Headache Center, Copenhagen, Denmark*
[2]*Danish Knowledge Center on Headache Disorders, Glostrup, Denmark*
[3]*University of Copenhagen, Copenhagen, Denmark*
[4]*Norwegian University of Science and Technology, Trondheim, Norway*
[5]*Imperial College London, London, United Kingdom*

Objective: Our purpose here is better to characterize the family impact of headache disorders in Denmark by conducting a nationwide cross-survey.

Methods: The Headache in Denmark (HINDER) study is a nationwide cross-sectional survey of people with headache, conducted using SurveyXact (Rambøll Group A/S, Copenhagen). Family impact was assessed in a study sample generated by population screening and recruitment. Data collection occurred from November 30th, 2022, to December 13th, 2022. The study module enquired into a range of romantic and domestic domains, including child-care.

Results: Out of 4,436 respondents in the HINDER panel, 1,513 (82.6% female, 17.4% male; mean age 45.09 ± 11.71 years) completed the family impact study. Two thirds (66.0%) reported headache as a challenge in their current relationship, 56.0% agreed they would be a better parent without headache, and 39.0% agreed that their children would have a better quality of life. Headache influenced the decision to have children for 10.5% overall and 19.0% for those with daily headache. Headache affected recent activities, such as abstaining from domestic duties (81.7%), transferring parental responsibilities (69.1%), and diminishing participation, enjoyment, or mental presence (71.3–81.8%) in family time and activities.

Conclusions: There is a substantial family burden of headache disorders beyond the progenitor with negative impacts extending to partners and children. Our findings quantify the burden of headache disorders on individuals across several romantic and domestic domains, including child-care, and headache disorders were reported to have a negative impact across all assessed constructs.

Disclosure of Interest: Thien Phu Do has received honoraria or personal fees from Teva for lecturing. August Dylander reports no conflicts of interest. Mikala Dømgaard reports no conflicts of interest. Simon Stefansen reports no conflicts of interest. Timothy J. Steiner reports no conflicts of interest. Messoud Ashina is a consultant, speaker, or scientific advisor for AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva and a primary investigator for ongoing AbbVie/Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva trials. Messoud Ashina has no ownership interest and does not own stocks of any pharmaceutical company. Messoud Ashina serves as associate editor of Cephalalgia, associate editor of the Journal of Headache and Pain, and associate editor of Brain.

Migraine preventive therapy

IHC23-DP-019

Response Rates With Oral Atogepant in Participants With Prior Preventive Treatment Failure: Results From ELEVATE

Patricia Pozo-Rosich[1,2], Krisztian Nagy[3], Cristina Tassorelli[4], Michel Lanteri-Minet[5], Sara Sacco[6], Tomáš Nežádal[7], Michelle Finnegan[8], Lei Luo[8], Pranav Gandhi[8] and Joel M. Trugman[8]

[1]*Vall d"Hebron University Hospital, Barcelona, Spain*
[2]*Universitat Autonoma de Barcelona, Barcelona, Spain*
[3]*AbbVie, Budapest, Hungary*
[4]*Headache Science Centre, C. Mondino Foundation and University of Pavia, Pavia, Italy*
[5]*Pain Department and FHU InovPain, CHU Nice and Côte Azur University, Nice, France*
[6]*Director, Carolinas Headache Clinic, Matthews, NC, USA*
[7]*Neurology Department, Military University Hospital, 1st School of Medicine, Charles University, Prague, Czech Republic*
[8]*AbbVie, Madison, NJ, USA*

Objective: Atogepant is an oral calcitonin gene-related peptide receptor antagonist approved in the United States for preventive treatment of migraine in adults, and in Puerto Rico, Canada, and Israel for the preventive treatment of episodic migraine in adults. The objective of this analysis was to evaluate monthly migraine day (MMD) responder rates to further characterize the efficacy profile of atogepant.

Methods: ELEVATE was a randomized, double-blind, placebo-controlled trial conducted in Europe and North America. Adults (18–80 years) with 4–14 MMDs on average in the previous 3 months and during baseline who had previously failed 2–4 classes of conventional oral medications for preventive treatment of migraine were randomized to atogepant 60 mg once daily (QD) or placebo. This analysis evaluated the proportions of participants achieving ≥25%, ≥30%, ≥50% (alpha-controlled secondary endpoint [across 12 weeks]), ≥75%, and 100% reductions in mean MMDs across 12 weeks and at each 4-week interval.

Results: A total of 309 participants were included in the analysis population (placebo: n = 155; atogepant 60 mg QD: n = 154). Across the 12-week treatment period, a ≥50% improvement was achieved by 50.6% (78/154) of atogepant-treated participants vs 18.1% (28/155) of placebo-treated participants ($P < 0.0001$). Significant treatment effects were observed for the achievement of a ≥25%, ≥30%, ≥75%, and 100% reduction in MMDs across the 12-week treatment period in atogepant vs placebo-treated participants, respectively: 74.0% (114/154) vs 43.9% (68/155), $P < 0.0001$; 71.4% (110/154) vs 38.7% (60/155), $P < 0.0001$; 27.3% (42/154) vs 1.9% (3/155), $P < 0.0001$; 6.5% (10/154) vs 0.0%, $P < 0.05$. These significant treatment effects were observed as early as the first 4-week interval and maintained throughout the double-blind treatment period (**Table**). No new safety concerns were identified.

Conclusion: Treatment with atogepant 60 mg QD significantly increased the proportions of participants achieving ≥25%, ≥30%, ≥50%, ≥75%, and 100% reductions in MMDs compared with placebo.

Disclosure of Interest: This study was supported by Allergan (prior to its acquisition by AbbVie). Patricia Pozo-Rosich, MD, PhD, has received, in the last three

Table. Proportion of Participants Achieving ≥25%, ≥30%, ≥50%, ≥75%, and 100% Reductions in Mean Monthly Migraine Days Across Each 4-Week Interval (OTHE Population)

	Atogepant 60 mg QD (n = 154)			Placebo (n = 155)		
	Weeks 1–4	Weeks 5–8	Weeks 9–12	Weeks 1–4	Weeks 5–8	Weeks 9–12
≥25% Responders % (n/N)	77.6‡ (118/152)	73.3‡ (110/150)	73.0‡ (103/141)	39.6 (61/154)	45.5 (70/154)	49.7 (75/151)
≥30% Responders % (n/N)	73.0‡ (111/152)	72.0‡ (108/150)	68.8† (97/141)	31.2 (48/154)	38.3 (59/154)	46.4 (70/151)
≥50% Responders % (n/N)	54.6‡ (83/152)	52.7‡ (79/150)	56.7‡ (80/141)	14.9 (23/154)	26.6 (41/154)	32.5 (49/151)
≥75% Responders % (n/N)	29.6‡ (45/152)	31.3‡ (47/150)	36.2‡ (51/141)	1.3 (2/154)	7.8 (12/154)	8.6 (13/151)
≥100% Responders % (n/N)	13.8* (21/152)	14.0* (21/150)	15.6* (22/141)	0.0 (0/154)	2.6 (4/154)	4.6 (7/151)

*$P < 0.01$ vs placebo. †$P < 0.001$ vs placebo. ‡$P < 0.0001$ vs placebo.
Responders were defined as participants with ≥25%, ≥30%, ≥50%, ≥75%, or 100% reduction from baseline in mean monthly migraine days. For analysis purposes, 4-week interval was considered to be 28 days. OTHE, off-treatment hypothetical estimand.

years, personal fees for advisory boards and speaker panels from AbbVie, Amgen, Chiesi, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva Pharmaceuticals, and for serving on a Scientific Advisory or Data Safety Monitoring board for Lilly Foundation Spain. She is the principal investigator for clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva. Her group has received grants from AbbVie, EraNet Neuron, European Commission, Instituto Carlos III, Novartis, and Teva. She serves as an associate editor for Cephalalgia, Headache, Neurologia, and Revista de Neurologia. Cristina Tassorelli, MD, PhD, has participated in advisory boards for AbbVie, Dompé, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva. She has lectured at symposia sponsored by AbbVie, Eli Lilly, Novartis, and Teva. She is principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva. She has received research grants from the European Commission, the Italian Ministry of Health, the Migraine Research Foundation, and the Italian Multiple Sclerosis Foundation. She serves as an associate editor for Cephalalgia and The Journal of Headache and Pain. Michel Lanteri-Minet reports personal fees for advisory boards, speaker panels, or investigation studies from Allergan, Amgen, Biosavia Electronics, Boston Scientific, Eli Lilly, Grunenthal, IPSEN, Lundbeck, Medtronic, Novartis, Pfizer, ReckittBenckiser, Saint-Jude, Sanofi-Aventis, SUN Pharma, Teva, UPSA, and Zambon. He has received research grants from the French Ministry of Health, the French Pain Society, The APICIL Foundation, and the Migraine Research Foundation. He served as an associated editor for The Journal of Headache and Pain. Sara Sacco has participated in advisory boards and/or is a speaker for Allergan (now AbbVie), Amgen, BDSI, Biohaven, Eli Lilly, Impel NeuroPharma, and Teva. Tomáš Nežádal has received consulting fees, speaking fees, and travel grants from Eli Lilly, Glenmark, Lundbeck, Novartis, Pfizer, St. Jude Medical, Teva Pharmaceuticals, and UCB. He also has served on advisory boards or as a principal investigator in clinical trials for AbbVie, Amgen, Eli Lilly, Lundbeck, Neurocrine, Novartis, Teva Pharmaceuticals, and UCB. Krisztian Nagy, Lei Luo, Pranav Gandhi, and Joel M. Trugman are employees of AbbVie and may hold AbbVie stock. Michelle Finnegan was an employee of AbbVie at the time of the study and may hold AbbVie stock.

Headache pathophysiology – Basic science

IHC23-DP-020

Investigation of CGRP and AMY_1 receptor subunit expression using RNA-fluorescence in situ hybridization in migraine associated tissues.

Michael L Garelja[1], Tayla A Rees[2] and Debbie L Hay[1,3]

[1]University of Otago, Dunedin, New Zealand
[2]University of Auckland, Auckland, New Zealand
[3]Maurice Wilkins Centre for Molecular Biodiscovery, Auckland, New Zealand

Objectives: The calcitonin gene-related peptide (CGRP) pathway is therapeutically targeted for migraine treatment; however, there may be scope to improve upon current drugs. Current CGRP pathway-modulating therapeutics are designed to target either CGRP itself, or the canonical CGRP receptor, comprising the calcitonin-like receptor [CLR] and receptor activity-modifying protein 1 [RAMP1]). CGRP can, however, also activate the AMY_1 receptor, comprising the calcitonin receptor (CTR) and RAMP1. It is currently unclear whether both receptors contribute to migraine pathophysiology, and thus whether therapeutic gains could be made by targeting both receptors. Determining where each receptor is expressed in migraine-relevant locations is required to help address this question. Therefore, this project aimed to explore the expression of CLR, CTR, and RAMP1 in migraine-relevant tissues.
Methods: As antibodies to some receptor subunits have limitations, this study instead examined RNA expression in tissue sections. Regions were chosen based on previous evidence of migraine relevance, and previous reports of CGRP expression. RNA-fluorescence in situ hybridization (RNA-FISH) was performed to detect receptor subunit expression. RNA-FISH probes were first validated using transfected cell models. Tissue was then collected from adult male and female Sprague-Dawley rats, sectioned, and RNA expression probed. Fluorescence was visualized using confocal microscopy. Detection was multiplexed, enabling co-detection of multiple receptor subunits in single sections.
Results: Various migraine-relevant regions, such as the trigeminal ganglia, nucleus accumbens, caudate putamen, dorsolateral pons, and amygdala, were probed for receptor subunit expression. Some regions contained subunits for both receptors, such as the nucleus accumbens, and others predominantly expressed subunits for only one receptor, such as the caudate putamen. Each region displayed a unique combination of cells expressing subunits of the CGRP and AMY_1 receptors.
Conclusions: RNA-FISH offers a useful tool for comparing multiple receptor subunits in single sections. Detection of both CGRP and AMY_1 receptor subunits in

migraine-relevant sites suggests that CGRP could exert its effects through either or both receptors in individual locations. As such, further research should be performed to disentangle the roles of each receptor.
Disclosure of Interest: DLH has received research support from Living Cell Technologies and AbbVie, and has acted as an advisor, speaker or consultant for Amgen, Merck, Teva and Eli Lilly.

Other

IHC23-DP-021

Improving headache diagnosis and management in rural areas in Cameroon through a capacity-building strategy for primary healthcare nurses.

Mundih Njohjam

National University Teaching Hospital, Dakar, Senegal

Objective: Headaches remain one of the most common chief complaints amongst patients presenting to health facilities in rural areas in Cameroon and a major contributor to the burden of neurological disorders in Cameroon. The management of headache in rural areas in Cameroon is greatly hindered by a critical shortage of health personnel with training in headache management. In most rural areas in Cameroon, primary healthcare nurses act as the main consultants due to the scarcity of physicians in these areas. However, most of these primary healthcare nurses lack basic skills and knowledge on headache. This often results in misdiagnosis and mismanagement of headaches, inappropriate prescription of analgesics, increased rates of medication overuse headaches and late referrals of secondary headaches. The objective was to improve the diagnosis and management of headache in rural areas in Cameroon by offering a basic training on headache to primary healthcare nurses working in these areas.
Methods: We randomly selected 33 primary healthcare nurses working in rural areas in the North West, West and Adamawa regions of Cameroon. These nurses were the main consultants in their primary health centers. Prior to the training, a pre-training survey was conducted amongst the participants to assess their baseline knowledge and practices on headaches. The results of the survey were used to inform the content of the training. A basic training on headache was then given to the 33 primary healthcare nurses. The training was focused on basic anatomy of head and brain, definition of headache, differences between primary and secondary headaches, different types of primary headaches, red flags of headache, basic management of primary headaches and when to refer a patient with headache. Six months after the training, we conducted another survey to assess the impact of the training on the clinical practice of the nurses.
Results: Prior to the training, only 23.3% of the participants could accurately define headache; 27.4% could differentiate between primary and secondary headaches; only 15.2% could identify at least one red flag of headache; 28.2% could accurately prescribe medications for primary headaches. Additionally, there was a high rate of inappropriate prescription of opoids like codeine and corticosteroids (dexamethasone) as treatment for headaches. There was a significant improvement in the results six months after the training; 93.2% could now accurately defined headache; 89.7% could differentiate between primary and secondary headaches; 79.7% could identify major red flags of headache; 96.4% could accurately prescribed medications for primary headaches. Furthermore, all participants reported a significant improvement in outcomes of headaches managed by them and patient satisfaction rate after the training.
Conclusion: Training primary healthcare nurses on basic headache assessment and management can significantly reduce headache misdiagnosis, mismanagement, and inappropriate prescriptions of medications for headaches in resource-limited settings where there is a critical shortage of headache-trained physicians.
Disclosure of Interest: None Declared

Headache pathophysiology – Imaging and neurophysiology

IHC23-DP-022

Genetic mechanisms underlying local spontaneous brain activity in episodic migraine: a combined transcriptome and resting-state functional MRI study

Wei Gui[1,2], Ying Yang[3] and Yu Wang[2]

[1]*Department of Neurology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China*
[2]*Department of Neurology, Epilepsy and Headache Group, The First Affiliated Hospital of Anhui Medical University, Hefei, China*
[3]*Department of Radiology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China*

Background and Purpose: Advances in neuroimaging techniques during the past few decades have captured impaired functional brain activity in migraine disorders, yet the molecular mechanisms accounting for its alterations in migraine remain largely unknown.
Methods: 27 patients with episodic migraine (EM) and 30 sex-, age- and education-matched healthy controls (HCs)

underwent resting-state functional and structural magnetic resonance imaging (MRI) scans. Regional homogeneity (ReHo) of fMRI was compared between the two groups. Based on Allen Human Brain Atlas and risk genes in migraine, we identified gene expression profiles associated with ReHo alterations in EM.
Results: Compared with HCs, patients with EM showed increased ReHo in the left orbital part of superior frontal gyrus (ORBsup.L) ($P < 0.05$, cluster-level FWE-corrected). The expression profiles of 16 genes were significantly correlated with ReHo alterations in EM ($P < 0.05/5{,}013$, Bonferroni corrected). These genes were mainly enriched fortranscription regulation, synaptic transmission, energy metabolism as well as migraine disorders. Furthermore, the neural activation was positively correlated with Hamilton Rating Scale for Anxiety (HAMA) scores.
Conclusion: Overall, these findings not only demonstrated that the regional brain activity was increased in patients with EM, which was associated with illness duration and emotional regulation, but also provided new insights into the genetic mechanisms underlying these changes in migraine.

Genetics and biomarkers of headache disorders

IHC23-DP-023

"Dim Light Melatonin Onset" and chronotype profiling in patients with episodic and chronic migraine

Francescantonio Cammarota[1,2], Roberto De Icco[1,2], Silvia Cerri[2], Cristina Ghezzi[2], Gloria Vaghi[1,2], Elena Capriglia[1,2], Michele Corrado[1,2], Federico Bighiani[1,2], Valentina Grillo[1,2], Riccardo Cremascoli[2], Michele Terzaghi[1,2], Raffaele Manni[1,2], Grazia Sances[2] and Cristina Tassorelli[1,2]

[1]*Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy*
[2]*Headache Science & Neurorehabilitation Center, IRCCS Mondino Foundation, Pavia, Italy*

Objective: Chronic migraine with medication overuse headache (CM-MOH) represents one of the most disabling phenotypes across the migraine spectrum. Patients with CM-MOH suffer several comorbidities, including sleep disorders. The aim of this study is to better define the chronotype of migraine patients by means of subjective clinical scales and salivatory melatonin measurements.
Methods: We enrolled 40 patients with CM-MOH, 18 patients with episodic migraine (EM) and 32 healthy controls (HCs). All subjects completed the Morningness–Eveningness Questionnaire (MEQ), the Pittsburgh Sleep Quality Index (PSQI) and a prospective sleep diary, and underwent 5 saliva melatonin samplings (at hourly intervals with the first sample collected 3 h before the subject's regular bedtime). We calculated the "Dim Light Melatonin Onset" (DLMO), a well-known biological marker of circadian phase in humans. Furthermore, we considered the clinical and demographic features and the psychological profile of subjects enrolled.
Results: EM patients were younger when compared to CM-MOH patients and HCs. According to the PSQI, symptoms of depression and anxiety and sleep disturbances were more frequent in CM-MOH when compared to EM, as expected. MEQ score was higher in CM-MOH (59.6 ± 7.7) when compared to EM (53.3 ± 11.9, $p = 0.045$) and HCs (51.0 ± 10.1, $p = 0.001$). According to MED, a subjective morningness profile was more prevalent in CM-MOH (56.8%) when compared to EM (33.3%) and HCs (17.2%) ($p = 0.001$). DLMO occurred earlier in CM-MOH (20:31 $\pm$ 52 minutes) and in EM (20:28 $\pm$ 0:49 minutes) when compared to HCs (21:17 $\pm$ 63 minutes; $p = 0.05$ and $p = 0.014$, respectively). This was confirmed in a multinominal regression after correction for age and sex. DLMO did not differ between CM-MOH and EM groups ($p = 1.000$). According to DLMO, a biological morningness profile was more prevalent in CM-MOH (32.4%) and in EM (33.3%) when compared to HCs (7.4%) ($p = 0.019$).
Conclusion: Migraine patients showed a morning-oriented chronotype when compared to HCs. Chronotype evaluated according to DLMO did not differ between CM-MOH and EM, suggesting an endogenous phenotype of migraine biology without association with disease severity. By contrast, CM-MOH patients described themselves as more morning oriented, showing a role of behavioral aspects related to the more severe phenotype of disease.

Headache pathophysiology – Imaging and neurophysiology

IHC23-DP-024

Increased oscillatory activity in the parietal cortex and impaired habituation of somatosensory responses are measurable indicators of headache-related disability in patients with medication overuse headache

Francesco Casillo, Gabriele Sebastianelli, Chiara Abagnale, Cherubino Di Lorenzo, Mariano Serrao and Gianluca Coppola

Sapienza University of Rome, Latina, Italy

Objectives: Overuse of acute medications is one of the leading causes of the transition from episodic to chronic migraine. Chronic migraine is associated with greater

self-reported disability and impact on daily life compared to episodic migraine. Unknown is the connection between headache-related disability and persistent central sensitization, the presumed mechanism underlying the transformation process and daily recurrence of attacks.

Material and Methods: We prospectively enrolled 22 medication overuse headache (MOH) patients who underwent wrist stimulation of the median nerve to record somatosensory evoked potentials (SSEPs). Patients completed the Migraine Disability Assessment (MIDAS) questionnaire, the most commonly used questionnaire to assess 3-months migraine-related disability, the Headache Impact Test (HIT-6), which measures the negative impact over 1-month, and the 12-item Allodynia Symptom Checklist (ASC-12). Patients also self-rated their headache-related disability on a scale from 0 to 3. We investigated the N20-P25 amplitude and its habituation, as well as high frequency oscillations (HFO) that most directly reflect thalamocortical (early HFO) and primary cortical (late HFO) activation.

Results: In patients with MOH, the values of self-rated disability ($r = 0.560$, $p = 0.01$), the ASC-12 scale ($r = 0.531$, $p = 0.01$), the amplitude of cortical HFOs ($r = 0.466$, $p = 0.03$), and the habituation deficit of SSEPs ($r = 0.588$, $p = 0.005$) are directly proportional to the HIT-6. There was no correlation between MIDAS scale values and the other clinical and electrophysiological variables evaluated.

Discussion: Our findings indicate that both primary cortical oscillatory activity and habituation deficit of SSEPs are measurable indicators of 1-month headache-related disability. In addition, allodynia and subjective perception of the disease are well encoded by the neurophysiology and HIT-6 combination.

Other secondary headache disorders

IHC23-DP-025

Phenotyping orthostatic headache in spontaneous intracranial hypotension.

Dwij Mehta, Sanjay Cheema, Sophie Glover, Ayman Qureshi, Indran Davagnanam, Salwa Kamourieh and Manjit Matharu

University College London (UCL) Queen Square Institute of Neurology and The National Hospital for Neurology and Neurosurgery, London, United Kingdom

Objectives: To conduct a detailed clinical phenotyping study of orthostatic headaches in patients with spontaneous intracranial hypotension (SIH) as part of the overall objective to describe a working definition for what constitutes an orthostatic headache.

Methods: Structured clinical review of consecutive patients with SIH confirmed on magnetic resonance imaging (MRI) referred to a specialist Headache clinic. The 75th centile values for baseline severity lying flat (0–10 scale), time to onset/exacerbation of headache on becoming upright, and time to baseline severity on lying flat were documented. Non-headache symptoms recognised in SIH were also systematically recorded.

Results: Hundred and two patients were recruited. An orthostatic headache was noted in 68% of the cohort at time of first review. The 75th centile values for baseline severity lying flat, time to onset/exacerbation of headache on becoming upright, and time to baseline severity upon recumbency were $\leq$2.5, $\leq$90 minutes, and $\leq$30 minutes, respectively. At least one audiovestibular symptom was present in in 61.2%, whilst at least one migrainous feature was observed in 78.6%.

Conclusions: Typical orthostatic headaches associated with SIH have a baseline severity when lying flat of $\leq$2.5 (0–10 scale), an onset/exacerbation in severity on becoming upright within 90 minutes, and offset to baseline severity on lying flat of within 30 minutes. Both audiovestibular and migrainous features are commonly present in this cohort of patients.

Disclosure of Interest: None Declared

Headache pathophysiology – Basic science

IHC23-DP-026

CGRP-induced relaxation of human coronary arteries is mediated via G protein $\beta\gamma$-subunit activation instead of second messenger cAMP

Tessa de Vries[1], Antoon van den Bogaerdt[2], A H Jan Danser[1] and Antoinette MaassenVanDenBrink[1]

[1]*Division of Vascular Medicine and Pharmacology, Department of Internal Medicine, Erasmus University Medical Center, Rotterdam, Netherlands*
[2]*ETB-BISLIFE, Heart Valve Department, Beverwijk, Netherlands*

Objective: Calcitonin gene-related peptide (CGRP) is a potent vasodilator and both CGRP and its receptor are a target for novel anti-migraine medication. Levels of the second messenger cAMP increase after activation of the CGRP receptor, and the subsequent relaxation of arteries is assumed to be mediated via cAMP. However, previous results showed that inhibition of protein kinase A (PKA), adenylate cyclase or guanylate cyclase does not have an effect on CGRP-induced relaxation [1]. Here, we further investigate the intracellular signaling following CGRP receptor activation resulting in relaxation of arteries.

Methods: Human coronary arteries were isolated from 23 heart valve donors (14 female, 9 male, age 53 ± 3) and mounted in a myograph system. Concentration-response curves to human αCGRP (10 pM–1 μM) were constructed after precontraction with 30 mM KCl. Vessel segments were incubated with or without additional inhibitors of adenylate cyclase (MDL-12330A), PKA (H89), exchange protein directly activated by cAMP (EPAC; ESI-09), PKG (KT5823), different potassium channels (apamin + TRAM, iberiotoxin, glibenclamide), $G\alpha_q$ subunit (YM254890) or the Gβγ-subunit (gallein). Moreover, intracellular cAMP levels were measured in the presence or absence of adenylate cyclase inhibitors SQ22536 and DDA.
Results: Inhibitors of adenylate cyclase, PKA, PKG, EPAC, potassium channels or $G\alpha_q$ did not affect the relaxation to CGRP, while adenylate cyclase inhibitors SQ22536 and DDA could effectively reduce the rise in cAMP after stimulation. The Gβγ-subunit inhibitor gallein did dose-dependently inhibit the relaxation to CGRP in human coronary arteries.
Conclusion: While CGRP signaling is generally assumed to act via cAMP, the CGRP-induced vasodilation in human coronary arteries could not be inhibited by targeting this intracellular signaling pathway at different levels. Instead, CGRP-induced vasodilation involves the activation of Gβγ-subunits. Future research should further identify the exact signaling pathway of CGRP resulting in relaxation of arteries. Possibly, the downstream signaling pathway of CGRP could be targeted to enhance the anti-migraine effect of medication, while limiting cardiovascular side effects.

Reference

1. De Vries, T., Labruijere, S., Van den Bogaerdt, A., Danser, A.H.J., MaassenVanDenBrink A. Intracellular pathways of calcitonin gene-related peptide-induced relaxation of human coronary arteries. International Headache Congress 8–12 September 2021. Cephalalgia, 41(1S) 59; P060.

Headache pathophysiology – Imaging and neurophysiology

IHC23-DP-027

Characterisation of thalamocortical responses to sensory and nociceptive stimuli in a mouse model of migraine

Hui Zhou Chen[1], Kirk Johnson[2] and Philip Holland[1]

[1]*King's College London, London, United Kingdom*
[2]*Eli Lilly, Indianapolis, USA*

Objective: Migraine is a disorder of sensory processing, characterised by throbbing head pain and often accompanied by multi-modal sensory symptoms, which point to a role of the thalamus. Structural and functional imaging has identified aberrant activation in the sensory thalamocortical circuits of migraine patients, however, clinical data are contradicting. Preclinical models allow for invasive investigation of the neurophysiology of these complex circuits across the migraine cycle, allowing us to identify underlying mechanisms and central targets for migraine treatment. Herein, we aimed to explore the role of thalamocortical circuits in a chronic mouse model to identify potential underlying neurophysiological signatures of disease chronification.
Methods: We used a lightweight wireless system (TaiNi) to record local field potentials in the mouse thalamic first-order somatosensory ventroposteromedial (VPM) nucleus and primary visual cortex (V1) bilaterally. Samples were acquired at 19.5KHz and lowpass filtered at 200Hz, and this wireless system allowed for freely moving, awake recordings. A chronic migraine model was established by injecting 10 mg/kg i.p. nitroglycerin on alternate days for nine days, and was confirmed with paw withdrawal thresholds using Von Frey filaments. The animals underwent a series of sensory and nociceptive tests to evoke response potentials at baseline, in the middle of the chronic injections (days 4–5) and two days after the last injection (day 11). The sensory tests involved two protocols with 60 trials of a 1 second presentation of high-intensity light (250Lx) interleaved with either of two levels of background light: dark (0Lx) or dim (20Lx). Auditory evoked potentials were also explored by delivering a 20ms tone every 10 seconds over 60 trials. In order to investigate nociception, we presented laser pulses to the hind paws at randomised intensities and evaluated behavioural responses to these stimuli.
Results: Paw withdrawal thresholds were significantly lowered after chronic nitroglycerin injections, confirming the establishment of mechanical hypersensitivity. Visual evoked potentials revealed a decrease in the negative N1 peak amplitude in V1 after chronification, potentially reflecting changes in visual thalamus connectivity to V1, whereas no changes were observed in the somatosensory VPM thalamus. Auditory responses were characterised by an altered waveform and reduced overall response magnitude in V1 after chronification, which may indicate dysfunctional cortico-cortical projections from auditory processing structures. On the other hand, there was a marked increase in peak-to-peak magnitude in the VPM, possibly via similar higher order pathways impinging into the somatosensory first-order thalamic nucleus. Finally, laser-evoked potentials showed a significant increase in V1 and VPM response magnitude after two NTG injections (day 4), but only when the moderate laser intensity (1.5J) was used, likely as a consequence of NTG-induced central sensitisation of the trigeminovascular system.

Conclusion: Here we demonstrate neurophysiological changes in thalamocortical structures in response to uni- and cross-modal stimuli in a mouse model of migraine. Such changes are dependent on stimulation parameters and reveal altered central mechanisms of migraine occurring during and after chronification. These data support the hypothesis of thalamocortical dysfunction in migraine and further studies will dissect the precise thalamocortical mechanisms underlying the diverse symptomatology in migraine.
Disclosure of Interest: None Declared

Other

IHC23-DP-028

Development of a branching logic questionnaire and a Computer Based Assessment Tool (COMBAT) for Android based smartphones for the diagnosis of primary headache disorders using International classification of Headache Disorders third version (ICHD3)

Vaibhav Deorari[1], Debashish Chowdhury[1], Kolin Paul[2], Pritesh Srivastava[2] and Ashish Duggal[1]

[1]*Department of Neurology, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research (G.I.P.M.E.R), New Delhi, India*
[2]*Department of Computer Science and Engineering, Indian Institute of Technology, New Delhi, India*

Objective: To develop a branching logic questionnaire and a computer-based assessment tool for Android based smartphones for the diagnosis of primary headache disorders using International Classification of Headache Disorders third version (ICHD3) and to test validity of constructed tool for English and Hindi users.
Methods: The development of COMBAT was done in four phases. In phase 1, an assessment of the core diagnostic features of primary headaches was done using ICHD3 criteria and a review of case records from our headache clinic. It was followed by the development of the questionnaire and the branching-logic algorithm in phase 2. COMBAT was created as a mobile application for the Android platform. In phases 3 and 4, validation of the tool was done using different sets of users against the diagnosis provided by two headache experts (gold standard). Initially, the English version was created followed by a Hindi version with a back-to-back translation. The basic architecture of COMBAT is shown in Table 1.
Results: In phase 1, 250 case records were analysed for core diagnostic features of primary headaches. We created 15 versions of the COMBAT and improved upon its features with each version and finally included 143 questions. 385 patients each were recruited for analysis in phase 3 and 4. In phase 3, the sensitivity, specificity, and accuracy for diagnosis of migraine by COMBAT was 96.79%, 82.19%, and 94.03% respectively; for tension-type headaches was 75%, 98.3%, and 96.36%, respectively; for trigeminal autonomic cephalalgias headaches was 90.9%, 100%, and 99.48%, respectively; for "other primary headaches" was 75%, 98.6%, and 97.9%, respectively. In phase 4, sensitivity, specificity, and accuracy for diagnosis of migraine headache was 95.54%, 89.8%, and 94.8%, respectively; for tension-type headaches as tension-type headaches was 84%, 98.06%, and 97.14%, respectively; for trigeminal autonomic cephalalgias headaches was 83.3%, 99.46%, and 98.7%, respectively; for "Other primary headaches" was 50%, 98.69%, and 98.44%, respectively. Only 4 patients each remained unclassified during phase 3 and 4. The mean test duration for the application of COMBAT was 10.6 (standard deviation-2.85) minutes. In addition to the diagnosis of primary headaches, COMBAT could diagnose episodic from chronic headaches, medication overuse headaches and possible secondary headaches.
Conclusion: We created "COMBAT", a computer based mobile application tool which demonstrated a high degree of accuracy, sensitivity, and specificity in recognizing various primary headache disorders, distinguishing chronic daily from episodic headaches and primary from secondary headaches. COMBAT is the first digital tool for the diagnosis of primary headache disorders that has been made in India.

Table 1. Basic architecture of the branching logic used in COMBAT

Levels	Basis of segregation	Outputs						
Level 1	Segregation based on frequency	Episodic or Chronic daily headaches	Chronic daily headaches or Episodic headaches under transformation	No Headache				
Level 2	Segregation based on etiology	Primary, secondary or Possible secondary headaches	Primary, Secondary or Possible secondary thunderclap headaches					
Level 3a	Segregation based on Type 4 - other primary headaches	Other Primary headaches	Possible 'other primary headaches'					
Level 3b	Segregation of Episodic headaches based on clinical features	Episodic migraine or Probable episodic migraine	Episodic TTH or Probable episodic TTH	Episodic cluster headache	Episodic paroxysmal hemicrania	Episodic SUNA/ SUNCT	Status migrainosus	
Level 3c	Segregation of Chronic headaches based on clinical features	Chronic migraine or Probable chronic migraine	Chronic TTH or Probable chronic TTH	Chronic cluster headache	Chronic paroxysmal hemicrania	Chronic SUNA/ SUNCT	New Daily persistent headaches	Hemicrania continua

Abbrv. SUNA-Short-lasting unilateral neuralgiform headache with autonomic symptoms;SUNCT- Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT);TTH - Tension type headache

Disclosure of Interest: None Declared

Headache and gender

IHC23-DP-029

Appeals about migraines in the region with a sharply continental climate

Kuanova Larissa, Tuimebayeva Aida and Zhulamanova Gulzhan

UMC, Astana, Kazakhstan

Goal: To study the influence of meteorological conditions on the frequency of migraine headaches in a large metropolis of Kazakhstan with a sharply continental climate.
Methods: The research population consisted of patients who applied for outpatient admission with migraine headaches to Astana polyclinics for the period March 2021 to March 2022. A total of 94 patients were included in the study, including 25 (26.6%) men and 69 (73.4%) women. The average age was 38.4 ± 11.6 years. There were 31 smoking patients (33%). Among these patients, 6 (6.4%) had a history of stroke, arterial hypertension was in 15 (16%), diabetes mellitus in 30 (29.8%). Among the patients there were 71 (75.5%) migraines without aura, 13 (13.8%) migraines with aura, 10 (10.6%) chronic migraines.
The climate of Astana is sharply continental with arid summers and cold, snowy winters. The average annual temperature is 3.5°C. The average annual precipitation is 318 mm. Astana (51.18°C 71.45°C, 358 m above sea level) is the second coldest capital in the world (after Ulaanbaatar). Summers here are warm and arid, and very windy in any season. Dust storms are possible in summer. The wind is caused by the pressure difference in the atmosphere. All pressure differences between different points of the earth's surface are directly or indirectly related to temperature differences. The greater the pressure difference between two regions, the faster the air moves between them. Therefore, changes in wind speed and direction are mainly explained by changes in temperature.
Patients kept a headache diary for a year. We conducted a prospective cohort study on diary entries. We analyzed a typical synoptic weather situation with a high wind speed (more than 10–12 m/s) and a large difference between night and day temperature (more than 13–19°C). The correlation between the frequency of headache obtained from headache diaries for 1 year and changes in the minimum and maximum daily temperature for 2 days before and 2 days after the onset of headache was evaluated. Daily and monthly data about The data were obtained through the home page of the meteorological department. To assess the relationship between the weather situation of the occurrence and persistence of migraine pain, we conducted a one-dimensional step-by-step multidimensional regression analysis of Coke.

The results obtained: The daily temperature difference was positively associated with the onset of migraine pains. The frequency of migraines increased when the difference between the minimum and maximum daily temperature from the day when the headache occurred was more than 13°C. An increase in daily temperature fluctuations for every 7°C was associated with an increase of 0.036 ([95% CI: 0.003, 0.045, $p < 0.05$) in the frequency of migraine pain. This dependence was found in 59 (62.8%). It decreased when the changes in the minimum and maximum daily temperature from the day when the headache occurred were less than 7°C. Diurnal temperature fluctuations showed a large statistical relationship with the onset of migraine pain in female patients, but did not reveal a statistical relationship in male patients. With an increase in daily temperature fluctuations by 7°C, we observed a significant increase in the incidence of migraine pain by 0.053 ([95% CI: 0.016, 0.062]; $p < 0.01$) in women compared with 0.005 ([95% CI: –0.017, 0.035]; $p > 0.05$) in men.
The relationship between meteorological variables and the onset of migraine pain varies regardless of the type of migraine.
Patients reported more migraine attacks induced by strong winds. The analysis of a subgroup of patients with "windy" migraine showed a significant increase in the frequency of migraine attacks in winter compared to summer ($p = 0.06$). Mean, minimum, maximum barometric pressure and daily fluctuations in changes in minimum and maximum daily temperature also showed a large statistical relationship with the onset of migraine pain in female patients.
Conclusion: A change in the minimum and maximum daily temperature may be one of the factors aggravating migraine headaches. We found that short-term exposure to higher daily fluctuations in temperature and barometric pressure, as well as stronger wind in the cold season, was associated with an increase in cases of migraine pain. When analyzing subgroups, the associations were more obvious in women, but did not reach statistical significance in male patients.
Disclosure of Interest: None Declared

Genetics and biomarkers of headache disorders

IHC23-DP-030

Causal relationship between COVID-19 and migraine: a Mendelian randomization study

Zhonghua Xiong, Dong Qiu, Wei Wang, Yanliang Mei, Ziyu Yuan, Peng Zhang and Yonggang Wang

Headache Center, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Objective: While observational studies have found a correlation between COVID-19 and migraine, the causal relationship remains unclear. Our study aims to fill this gap by utilizing the two-sample Mendelian randomization (MR) method to assess whether COVID-19 has a causal effect on migraine.

Methods: We identified COVID-19 genetic instrumental variables (IVs) using a largest genome-wide association study (GWAS) consisting of 32,494 cases and 1,316,207 controls with European ancestry. These IVs were then used to evaluate the previously reported GWAS results for migraine, which included 179,648 individuals also of European ancestry. To assess pleiotropy and heterogeneity in the MR analysis, we employed several statistical methods including MR-Egger-intercept, MR-PRESSO, MR-Egger, and inverse variance weighted (IVW) in Cochran's Q-test. Additionally, we used MR-egger, weighted median, IVW, simple mode and weighted mode for MR analysis. The effect of single nucleotide polymorphisms (SNPs) on SNP bias was also test

Results: Our analysis suggests that there was no significant pleiotropy or heterogeneity among all selected COVID-19 genetic instruments in the migraine GWAS. Our analysis revealed a positive correlation between genetically increased COVID-19 and migraine risk in European ancestries. Specifically, we observed an increasing trend in migraine risk as COVID-19 genetically increased, as determined by MR-egger (Beta = 0.178, p = 0.703; OR = 1.195), simple mode (Beta = 0.393, p = 0.153; OR = 1.481), weighted mode (Beta = 0.258, p = 0.302; OR = 1.295), and weighted median (Beta = 0.281, p = 0.099; OR = 1.325). This trend was further supported by IVW (Beta = 0.298, p = 0.039; OR = 1.348).

Conclusion: Our findings suggested a putative causal link between genetically increased COVID-19 and an increased risk of migraine in European ancestries.

The causal association of COVID-19 with migraine.

Method	nsnp	β	SE	p Value	OR	OR_lci95	OR_uci95
MR-Egger	4	0.178	0.406	0.703	1.195	0.539	2.650
Weighted median	4	0.281	0.170	0.099	1.325	0.948	1.850
IVW	4	0.298	0.145	0.039	1.348	1.015	1.790
Simple mode	4	0.393	0.207	0.153	1.481	0.988	2.221
Weighted mode	4	0.258	0.208	0.302	1.295	0.861	1.945

Note: $p < 0.05$ represents the causal association of the increased COVID-19 with migraine. Abbreviations: β, the regression coefficient based on COVID-19 raising effect allele; COVID-19, coronavirus disease 2019; IVW, inverse variance weighted; MR, Mendelian randomization; nsnp, number of single-nucleotide polymorphism; OR, odds ratio; OR_lci95, lower limit of 95% confidence interval for OR; OR_uci95, upper limit of 95% confidence interval for OR; SE, standard error.

Disclosure of Interest: None Declared

Headache and gender

IHC23-DP-031

Characterization of Menstrual Migraine and Proposed Diagnostic Criteria: A Population-Based Study

Mona Ameri Chalmer

Rigshospitalet, Glostrup, Denmark

Objective: Migraine is the number one cause of years lived with disability in females aged 15–49 years (Steiner, 2020; Vos, 2019), and overall females have more severe disease, resulting in a much higher migraine disease burden than indicated by prevalence alone (Chalmer, 2023). This difference between sexes might be partly explained by menstrual migraine (MM), however, to better understand the impact hereof, there is a need for better recognition and more extensive research into MM in the general population. The current diagnostic criteria for MM have critical issues, and a revision of the criteria is warranted to move the field forward. Increased understanding of MM is crucial for improving clinical care, diagnosis, and therapy for MM. The objective of this population-based study was to assess the clinical characteristics of MM, including severity and treatment response, and to propose new diagnostic criteria for pure MM and menstrually related migraine.

Methods: This is a population-based, case-control study of 12,618 Danish individuals with migraine. All individuals completed a 105-item validated diagnostic migraine questionnaire, sent via the Danish electronic mailing system (e-Boks) between May 2020 and August 2020, allowing

diagnosis of pure MM and menstrually-related migraine by the International Classification of Headache Disorders third edition (ICHD-3) criteria. Clinical features of migraine using the ICHD-3. Simulation was based on number of migraine attacks during three menstrual cycles (3x28 days), and simulation analyses were performed using 100,000 permutations of random migraine attacks in migraine patients.

Results: Among females with migraine, the prevalence of MM was 16.6% (1532 females). The mean (SD) age of females with MM was 38.7 years (8.67) and 37.0 years (9.17) for females with non-MM, 410 (25.6%) fulfilled ICHD-3 pure MM criteria, 1,037 (67.7%) fulfilled ICHD-3 defined menstrually-related migraine, and 152 (9.9%) fulfilled rare pure MM. MM was associated with a higher frequency of migraine accompanying symptoms (odds ratio [OR],1.98; 95%CI, 1.71–2.29), more frequent (OR, 7.21; 95% CI, 5.77–9.03) and more severe migraine attacks (OR,1.17; 95%CI,1.13–1.21), lower frequency of non-migraine headache (OR, 0.31: 95%CI, 0.18–0.49), an overall greater response to treatment with triptans (OR, 1.66; 95%CI, 1.24–2.24), better improvement of migraine attacks during late pregnancy (OR, 5.10; 95%CI, 2.17–14.00), and faster reappearance postpartum (OR, 3.19: 95%CI, 2.40–4.25). Hormonal contraceptive related MM was associated with a higher prevalence of migraine without aura than migraine related to spontaneous menstruation (OR, 1.82; 95%CI, 1.62–2.06). Otherwise, no differences between hormonal and spontaneous menstrual migraine were observed. The risk of random diagnostic misclassification of ICHD-3 menstrually-related migraine diagnosis in females with high frequency episodic migraine was 43%. This risk was markedly reduced to 3% when applying the proposed criteria for menstrually-related migraine.

Conclusion: In this case-control study of 12,618 Danish individuals with migraine, we found that pure MM and menstrually-related migraine were important diagnostic entities, with clinical characteristics that were quantitively different from non-menstrual migraine. We provided detailed descriptive data and suggested improved diagnostic criteria (Boxes 1 and 2).

Box 1: Proposed diagnostic appendix criteria for A1.1 Pure menstrual migraine

1. Attacks in menstruating females fulfilling the diagnostic criteria for 1.1 Migraine without aura and/or 1.2 Migraine with aura
2. Attacks occur exclusively in association with menstruation, beginning on day 1 +/–2 (i.e., days –2 to +3) of menstruation and at no other times of the cycle[A,B,]

Footnote:

[A]Attacks during at least three menstruations are reported.

[B]If after a menstrual migraine attack the patient is headache free for at least 24 hours, spontaneously or due to treatment, and migraine reoccurs within the –2 to +3-day menstrual interval, it is regarded as separate menstrual attacks.

Box 2: Proposed diagnostic appendix criteria for A2.1 Menstrually-related migraine:

1. Attacks in menstruating females fulfilling the diagnostic criteria for 1.1 Migraine without aura and/or 1.2 Migraine with aura
2. At least half of all migraine attacks begin on day 1 +/–2 (i.e., days –2 to +3) of menstruation,[A, B]

Footnote:

[A]Attacks during at least three menstruations are reported.

[B]If after a menstrual migraine attack the patient is headache free for at least 24 hours, spontaneously or due to treatment, and migraine reoccurs within the –2 to +3-day menstrual interval, it is regarded as separate menstrual attacks.

Disclosure of Interest: None Declared

Headache pathophysiology – Basic science

IHC23-DP-032

Potential Paracrine Interactions between CGRP and the AMY_1 Receptor in the Parabrachial Nucleus and Amygdala of Rodents

Lewis M Forrester[1], Michael L Garelja[1], Lara K Dalldorf[1], Angelina M Dawson[1], Annie J Leen[1], Tayla A Rees[2] and Debbie L Hay[1,3]

[1]*University of Otago, Dunedin, New Zealand*
[2]*The University of Auckland, Auckland, New Zealand*
[3]*Maurice Wilkins Centre for Molecular Biodiscovery, Auckland, New Zealand*

Objectives: Migraine is a prevalent neurological disease characterized by severe head pain, with complex hormonal and neurochemical components. Calcitonin gene-related peptide (CGRP) is one key player in the pathophysiology of migraine. CGRP-blocking drugs are efficacious at preventing or alleviating migraine symptoms. These CGRP-based migraine therapeutics are not, however, effective in all patients, indicating the need for further research. CGRP is known to act in migraine-relevant regions of the brain and has two receptors. The canonical CGRP receptor is comprised of calcitonin receptor-like receptor (CLR) and receptor activity-modifying protein 1 (RAMP1) and has been the target of several migraine drug development programs. CGRP can also act through the amylin 1 (AMY_1) receptor, comprising the calcitonin receptor (CTR) and RAMP1. The relative contribution of each receptor to CGRP biology is unknown. Here, we aimed to investigate the distribution of the AMY_1 receptor subunit, CTR, relative to CGRP, in selected migraine-relevant regions of the brain.

Methods: Tissues were collected from adult male and female Sprague-Dawley rats and C57BL/6J mice. The brains were removed, fixed, cryoprotected and sectioned at 10 μM. Sections were collected through the spinal trigeminal nucleus/tract (Sp5/sp5), parabrachial nucleus (PBN), locus coeruleus (LC) and amygdala (including the lateral (LA), basolateral (BLA), central (CeA) and medial (MeA) nuclei). Antibodies were selected following prior validation for specificity and cross-reactivity. Fluorescent immunohistochemistry was performed on sections using antibodies against CGRP and CTR, and counterstained with DAPI (cell nuclei) and Neurotrace (Nissl). Fluorescence was visualized using confocal microscopy on an Opera PHENIX High Content Imager. Images were analyzed using SignalsImageArtist and ImageJ (FIJI).
Results: CGRP and/or CTR like-immunoreactivity (IR) were detected in each region. In the Sp5/sp5, strong CGRP like-IR, but only sporadic CTR like-IR, were detected. Conversely, in the LC, strong CTR like-IR, but minimal CGRP like-IR, were detected. In the PBN, both CGRP and CTR like-IR were detected, often in close proximity. Likewise, in nuclei of the amygdala, both CGRP and CTR like-IR were detected in close proximity. Within each region investigated, CGRP like-IR was detected predominantly in fibers, whereas CTR like-IR was detected both in fibers and cell bodies. The data were broadly consistent between rats and mice, and male and female.
Conclusions: The relative absence of CTR as compared to CGRP in some regions suggest that CGRP signals primarily through the canonical CGRP receptor in those locations. However, the close proximity of CGRP and CTR in the PBN and nuclei of the amygdala suggest that CTR could be responsible for some paracrine CGRP signaling in these regions, likely as part of the AMY_1 receptor. In locations where CTR, but not CGRP, is present, other ligands could be involved. These data suggest that the AMY_1 receptor could produce some CGRP signaling in the brain and be relevant to migraine and beyond.
Disclosure of Interest: DLH has received research support from Living Cell Technologies and AbbVie, and has acted as an advisor, speaker or consultant for Amgen, Merck, Teva and Eli Lilly.

Headache pathophysiology – Basic science

IHC23-DP-033

Human trigeminal ganglia possess oxytocin receptors on CGRP positive neurons, the expression of which is dramatically increased by inflammation

David Yeomans[1], Vimala Bharadwaj[1], Michael Klukinov[1] and David Hsu[2]

[1]*Stanford University, Stanford, CA, USA*
[2]*Tonix Pharmaceuticals, Chatham, NJ, USA*

Objective: We have shown that oxytocin receptors on trigeminal neurons can inhibit the excitability of those neurons which could provide the basis for both analgesia as well as decreasing the likelihood of migraine triggering in migraineurs and other patients with craniofacial pain states. Critically, inflammation appears to play a critical role in this phenomenon in that it can drive a rapid upregulation of oxytocin receptors. Thus, inflammatory state, such as that accompanying chronic migraine likely plays a key role in oxytocin analgesia in this pain state. However, to date, the impact of inflammation on oxytocin receptor activity has not been examined in humans or human tissue. The purpose of this study was to examine, in vitro, the roll of inflammation in the expression of oxytocin receptors in human trigeminal neurons, particularly those that co-express CGRP, a key peptide in the pathogenesis of migraine as well as the impact of inflammation on activation of these neurons as indicated by expression of early immediate genes.
Methods: Human trigeminal ganglia (TG) were provided by Anabios (San Diego). Each TG of a pair from a given donor was transected and one half of one TG placed in 4% paraformaldehyde for immunohistochemistry; the other half quick frozen for quantitative immunoassay. The second TG of the pair is transected and both halves were injected with 10 ug/mL lipopolysaccharide (LPS) in artificial interstitial fluid (aIF) to induced in vitro inflammation and placed in a rocking water bath in aIF with LPS at 32°C, bubbling with carbogen. After 4 hours, one half of the second TG is immersion fixed in 4% paraformaldehyde overnight for immunohistochemistry. The other half quick frozen for quantitative immunoassay. Both fixed TG tissues were cryoprotected by immersion in 30% sucrose in aIF. Fixed tissue was cryosectioned (20 uM) and slide mounted for immunohistochemistry. Slides were incubated in primary antibodies for oxytocin receptors, CGRP, and the immediate early gene products c-FOS and p-ERK. Slides were then incubated with appropriate secondary fluorescent antibodies, coverslipped and examined using a laser confocal microscope which allowed semi-quantification of antigens.

Results: Numerous, small diameter human TG cell bodies were observed to be immunopositive for oxytocin receptors with a strong level of co-expression with CGRP. In addition, LPS treatment both dramatically increased expression of both oxytocin receptors and CGRP and induced expression of both c-FOS and p-ERK in oxytocin receptor expressing neurons.
Conclusions: These results are the first to demonstrate expression of oxytocin receptors on human trigeminal neurons, that these mostly co-express CGRP and that in vitro inflammation drives upregulation of both OTR and CGRP as well as activation of these cells as demonstrated by the presence of immediate early gene products in LPS treated and oxytocin receptor expressing TG neurons.
Disclosure of Interest: DC Yeomans is a consultant for Tonix Pharmaceuticals, which provided some funding for this work David Hsu is an employee of Tonix Pharmaceuticals

Migraine acute therapy

IHC23-DP-034

Targeting trigeminal α6GABA$_A$ receptors as a novel therapy for migraine

Lih-Chu Chiou[1,2], Shao-Kai Chou[1], Hung-Ruei Tzeng[1], James Cook[3], Marko Mihovilovic[4] and Werner Seighart[5]

[1]*Grad Inst of Pharmacol, Coll Medicine, National Taiwan University, Taipei, Taiwan*
[2]*Grad Inst of Brain and Mind Sci, Coll Med, National Taiwan Univerrsity, Tapei, Taiwan*
[3]*Dept of Chem and Biochem, Univ of Wisconsin-Milwaukee, Milwaukee, USA*
[4]*Inst Appl Synth Chem, TU Wien, Vienna, Austria*
[5]*Ctr for Brain Res, Dept of Mol Neurosci, Med Univ Vienna, Vienna, Austria*

Objective: Migraine treatment remains an unmet medical need despite the recent emergence of calcitonin gene-related peptide antagonists/antibodies. We have previously shown that the α6 subunit-containing GABA$_A$ receptors (α6GABA$_A$Rs) are enriched in trigeminal ganglia (TG),[1,2] a hub of the trigeminovascular system (TGVS), which is involved in migraine pathogenesis. Using an α6GABA$_A$R-selective positive allosteric modulator (PAM), pyrazoloquinolinone (PQ) Compound 6, and α6GABA$_A$R-selective antagonist, furosemide, we also showed an unprecedented role of TG α6GABA$_A$Rs in migraine induction. Our preclinical studies further suggested the α6GABA$_A$R-selective PAM is a potential novel therapy for migraine in two animal models, intracisternal capsaicin-induced TGVS activation in rats[1] and intermittently repeated nitroglycerin (NTG)-induced elevation of mouse grimaces,[2] a spontaneous cephalic pain indicator.
Methods: To further optimize druggable and patentable candidates, we developed Compound 6's analog, LAU 463, and their respective deuterated derivatives. Here, we evaluated anti-migraine efficacies and action durations of these PQs in the NTG mode, where NTG (10 mg/kg, i.p.) was injected once on Days 1, 3, 5, 7 and 9. Topiramate, an anti-migraine agent, was also examined as a positive control. Instead of grimace assessment, we measured von Frey filament-induced mechanical allodynia via decreased paw withdrawal thresholds (PWT) in ICR mice (male, 7–9 weeks), representing extracephalic evoked pain responses due to central sensitization.
Results: Repeated NTG injections in mice induced significant basal allodynia from Day 3, evidenced by the reduced PWT as compared to Day 1. Basal allodynia lasted for 9 days, gradually declined, and subsided on Day 21. NTG also induced acute allodynia, assessed by the reduction of PWT 60 min after NTG injection on Day 9. To compare action durations of PQs, they were administered 0, 30, 60, and 120 min before NTG injection on Day 9. All PQs (10 mg/kg, i.p.) significantly attenuated acute allodynia. The antiallodynic effect of Compound 6 peaked within 90 min, declined gradually, and subsided within 3 hours, while its deuterated derivative, DK-I-56-1, produced a comparable but long-lasting (>3hr) antiallodynic effect. Effects of LAU463 and DK-I-58-1 peaked within 1 hour but declined quickly, consistent with the finding of their shorter half-lives than Compound 6 in the microsomal enzyme assay.3 Topiramate (30 mg/kg, i.p.) reduced NTG-induced acute allodynia on Day 9 and also attenuated basal allodynia when administered daily. The antiallodynic effect of DK-I-56-1, but not topiramate, was prevented by furosemide (20 mg/kg, i.p.), a blood-brain barrier-impermeable α6GABA$_A$R-selective antagonist, suggesting α6GABAARs in the periphery, especially in TG, are PQs" site of action.
Conclusion: These results further support that trigeminal α6GABA$_A$Rs are a novel therapeutic target for migraine and α6GABA$_A$R-selective PAMs are a potential abortive pharmacotherapy for migraine, including central sensitization-induced extra-cephalic allodynia. Here, a single injection of DK-I-56-1, a PQ with a satisfied pharmacokinetic profile3 devoid of motor impairment and addictive potential,[2] can produce an antiallodynic effect lasting for more than 3 hours, suggesting its potential for future translational studies.
Disclosure of Interest: None Declared

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Cluster headache and other trigeminal autonomic cephalalgias

IHC23-DP-035

ATP-Sensitive Potassium Channel Activation Induces Cluster Headache Attack: A Randomized Controlled Trial.

Haidar Al-Khazali and Christina I Deligianni

Department of Neurology, Danish Headache Center, Glostrup, Denmark

Objective: To investigate whether levcromakalim, an opener of ATP-sensitive potassium channels (KATP), could induce cluster headache attacks.
Methods: A randomized, double-blind, placebo-controlled, crossover trial was conducted in 41 participants with cluster headache. Participants were divided into three groups: 10 with episodic cluster headache in bouts, 15 with remission phase episodic cluster headache, and 17 with chronic cluster headache. Each participant received a 20-minute infusion of levcromakalim or placebo (isotonic saline) on two experimental days, with a minimum washout period of 72 hours between infusions. The primary endpoint was the difference in the incidence of cluster headache attacks during the observational period (0–90 minutes) between levcromakalim and placebo.
Results: Levcromakalim induced cluster headache attacks in 6 out of 10 participants with episodic cluster headache in bouts (60%) compared to 1 out of 10 in the placebo group (10%) ($p = 0.037$). In the remission phase episodic cluster headache, 1 out of 15 participants reported cluster headache attack after levcromakalim, compared to none in the placebo group ($p = 0.500$). In participants with chronic cluster headache, levcromakalim induced cluster headache attacks in 5 out of 17 participants after levcromakalim (29%) compared with none after placebo ($p = 0.037$).
Conclusion: Activation of ATP-sensitive potassium channels is involved in episodic cluster headache in bouts and chronic cluster headache, but not in remission phase episodic cluster headache. These findings support the potential use of KATP channel blockers for cluster headache management and provide a basis for further research in this area.

Other secondary headache disorders

IHC23-DP-036

Raised intracranial pressure alters cortical spreading depression, induces neurovascular uncoupling and reduces trigeminal sensitivity thresholds which is rescued by GLP-1R agonist exenatide.

Olivia Grech[1], Eloisa Rubio-Beltran[2], Emily Stanyer[2,3], Alejandro Labastida-Ramirez[2], Philip Holland[2] and Alexandra Sinclair[1]

[1]*Translational Brain Science, Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom*
[2]*Headache Group, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[3]*Sleep and Circadian Neuroscience Institute, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom*

Objective: Raised intracranial pressure (ICP) is a feature of numerous secondary headaches including idiopathic intracranial hypertension (IIH), traumatic brain injury and stroke. The pathological mechanisms underlying headache are unknown, and targeted therapies are lacking. In IIH, ICP can predict headache morbidity, therefore reducing ICP may alter pathways which contribute towards headache. The glucagon-like peptide-1 (GLP-1) receptor agonist Exenatide has demonstrated the ability to reduce ICP and monthly headache days in IIH patients. The kaolin-induced rat model of raised ICP was used to investigate headache mechanisms including cortical spreading depression (CSD), neurovascular changes and sensitization of the trigeminovascular system. This study also investigated the impact of reducing ICP on headache pathology following exenatide treatment.
Methods: Kaolin (or equal volume saline as control) was injected into the cisterna magna of male Sprague-Drawley rats to block CSF drainage and increase ICP. ICP measurements were conducted using an ICP catheter under anesthesia. von Frey filaments were used to assess changes in periorbital and hind paw mechanical thresholds 7 days post kaolin/saline injection using the Up-Down method. Responses to KCL-induced CSD were also assessed 7 days after kaolin/saline injection. Changes in direct current shift [DC] and cerebral blood flow (CBF) were measured over 1 hour. The mean resulting % change in CBF, depolarisation duration and repolarization duration during CSD responses were calculated. von Frey and CSD measurements were repeated in a separate cohort of kaolin animals injected daily for 6 days with exenatide (20 ug/kg) or equal volume vehicle.

Results: ICP was significantly higher in kaolin versus saline animals (saline mean (SD) ICP = 5.457 mmHg (1.215) n = 6, kaolin = 17.722 mmHg (10.124) n = 8, p = 0.0012). 7 days after injection, periorbital and hind paw thresholds were significantly decreased in kaolin animals (periorbital; saline = 6.43g (1.88) n = 10, kaolin = 2.35 g (1.91) n = 12, p = 0.0003, hind paw; saline = 5.16 g (1.40), kaolin = 3.34 (2.21), p = 0.0008).

CSD responses were drastically different between saline and kaolin animals. Depolarisation duration was significantly longer in kaolin animals (saline = 62.18s (42.13) n = 9 vs kaolin = 126.72s (76.12) n = 11, p = 0.0381). % change in CBF was also significantly lower in kaolin (saline 217.65% (37.70) n = 8, kaolin = 85.55% (30.84) n = 9, <0.0001).

In kaolin animals, daily injection of exenatide significantly reduced ICP compared to vehicle (vehicle = 18.27mmHg (6.67) n = 16, exenatide = 9.74 mmHg (6.09) n = 19, p = 0.0001). Exenatide also rescued periorbital and hind paw sensitivity in kaolin animals (periorbital; vehicle = 4.67g (2.81), kaolin = 5.65 g (2.08) p = 0.0010, hind paw; vehicle = 2.53 g (1.24), kaolin = 6.78 g (1.20), n = 12 p < 0.000001). Exenatide also improved CSD responses, significantly reducing repolarization duration (vehicle = 986.25s (691.82) n = 6, kaolin = 257.55s (194.56) n = 7 p = 0.0023). % CBF change did show a trend towards improvement in the exenatide group (vehicle = 70.62% (47.75) n = 6, exenatide = 138.50% (116.80) n = 7, p = 0.2343). These alterations were independent of weight loss as there were no significant difference in weight between exenatide and vehicle cohorts.

Conclusion: This study demonstrated that kaolin increased ICP in rats, and led to altered trigeminal sensitivity thresholds, neurovascular uncoupling and altered CSD responses. These data suggest there may be shared pathophysiology between migraine and headache attributed to raised ICP. Reducing ICP with exenatide, a drug showing therapeutic promise in IIH, also demonstrates improvement in headache mechanisms. Therefore, ICP may be directly related to headache pathophysiology and reducing this with exenatide may provide a targeted therapeutic for headaches with raised ICP.

Disclosure of Interest: OG reports scientific consultancy fees from Invex therapeutics (2020). AJS reports personal fees from Invex therapeutics in her role as Director with stock holdings, during the conduct of the study (since 28.06.2019); other from Allergan, Novartis, Cheisi and Amgen outside the submitted work.

Headache pathophysiology – Basic science

IHC23-DP-037

Peripheral calcitonin gene-related peptide induces brain-wide resting state functional connectivity changes in mice

Yassine Filali[1], Zeru Peterson[1], Jayme Waite[2], Brandon Rea[1], Rainbo Hultman[3], Thomas Nickl-Jockschat[1] and Levi Sowers[1,4]

[1]*University of Iowa, Iowa City, USA*
[2]*VA Center for the Prevention and Treatment of Visual Loss, Iowa City, USA*
[3]*Unviersity of Iowa, Iowa City, USA*
[4]*VA Center For the Prevention and Treatment of Visual Loss, Iowa City, USA*

Background: Migraine is associated with disabling sensory abnormalities, is one of the most common neurological disorders and remains undertreated in 50% of patients. One reason treatments fall short is our lack of understanding of the neuroanatomic contributors to migraine pathophysiology. Human functional imaging studies have identified neural networks associated with migraine, but which networks are relevant for migraine behavior remains unknown. Small-animal imaging studies can address this gap by probing functional networks linked to migraine; in particular, central brain regions critical for multisensory integration like the cerebellum, are novel targets for understanding migraine pathophysiology and to understand how they affect migraine-like behavior. We hypothesized that peripheral CGRP injection would induce functional changes in brain-wide blood oxygen level-dependent (BOLD) resting-state functional magnetic resonance imaging (rs-fMRI) response.

Methods: Male and female C57BL/6J mice underwent a baseline rs-fMRI sequence to collect anatomical images and 15 minutes of BOLD activity recording for a "baseline state" measurement. Mice were anesthetized with ~1.5% isoflurane during entire recording. Following baseline recordings, mice were injected with 0.1 mg/kg CGRP and placed back into the MRI machine for the treatment resting state recordings 30 minutes post injection. This was followed by brain-wide hierarchical clustering analysis to determine changes in resting state connectivity between baseline and CGRP. Seed based approaches focused on brain areas associated with pain and sensory processing were used to determine connectivity changes between regions of interest. We also used awake behaving electrophysiological studies to confirm changes in activity in two regions identified by hierarchal clustering analysis.

Results: Preliminary results identified brain-wide changes in clustering of brain networks post-treatment. These include significant increases in connectivity between somatosensory and visual cortices and changes in other

pain sensory networks including the deep cerebellar nuclei and insula. Preliminary electrophysiology data in the somatosensory and visual cortices confirm activity increases in awake behaving mice.

Conclusion: These data provide a possible mechanism for CGRP-induced migraine-like sensory hypersensitivity in mice including touch hypersensitivity and photophobia. Future studies will begin to understand how other clinically validated migraine triggers that cause similar phenotypes in mice contribute to functional connectivity in the brain.

Migraine preventive therapy

IHC23-DP-038

Long-term safety and effectiveness of eptinezumab in patients with prior preventive migraine treatment failures

Messoud Ashina[1,2], Stewart J. Tepper[3], Astrid Gendolla[4], Bjorn Sperling[5], Anders Ettrup[5], Mette Krog Josiassen[5] and Amaal J. Starling[6]

[1]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark*
[2]*Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*
[3]*New England Institute for Neurology and Headache, Stamford, USA*
[4]*Praxis Gendolla, Essen, Germany*
[5]*H. Lundbeck A/S, Copenhagen, Denmark*
[6]*Mayo Clinic Arizona, Scottsdale, USA*

Objective: DELIVER (NCT04418765) evaluated the safety and efficacy of eptinezumab for migraine prevention in patients with prior preventive migraine treatment failures. Here, we report results of the 48-week dose-blinded extension period.

Methods: Eptinezumab 100mg and 300mg were evaluated vs placebo (pbo) (infusions every 12 weeks) in adults with migraine and 2–4 prior preventive failures. Patients randomized to pbo during the initial treatment period were randomized to eptinezumab 100mg or 300mg in the extension period; patients initially randomized to eptinezumab continued their assigned dose. Efficacy measures included change from baseline in number of monthly migraine days (MMDs), $\geq$50% and $\geq$75% reduction from baseline in MMDs, change from baseline in the 6-item Headache Impact Test (HIT-6), migraine severity, and acute headache medication (AHM) use.

Results: After the pbo-controlled period (Weeks 1–24), 782/865 patients (90.4%) completed the 48-week extension. Patients switching from pbo experienced a steep decrease in MMDs over Weeks 25–28 (pbo-to-100mg, –5.8 days; pbo-to-300mg, –7.2 days) compared with the pbo-controlled baseline. All treatment arms had sustained reductions from baseline in MMDs over Weeks 61–72, with $>$60% of patients experiencing $\geq$50% MMD reductions and $>$30% of patients experiencing $\geq$75% reductions. Patients switched from pbo to eptinezumab had reductions in HIT-6 scores, migraine severity, and AHM use after the first eptinezumab dose. No new safety signals were identified.

Conclusion: In DELIVER, the long-term effectiveness and safety of eptinezumab was demonstrated by high completion rates, sustained MMD reductions, and reductions in migraine severity. Similar improvements were observed in patients switched from pbo to eptinezumab in the extension period and in those continuing treatment for up to 18 months.

Headache pathophysiology – Imaging and neurophysiology

IHC23-DP-039

Cortical thickness of facial somatosensory area is associated with the treatment response to flunarizine in patients with chronic migraine

Kuan-Lin Lai[1,2,3], Yi-Ting Hsiao[3] and Shuu-Jiun Wang[1,2,3]

[1]*Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*School of Medicine, National Yang Ming Chiao Tung Univeristy, Taipai, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*

Objective: Chronic migraine (CM) accounts for approximately 2% of the general population, and is associated with a greater use of healthcare resources as compared to episodic migraine. Preventive medication is recommended for all patients with CM in order to relieve the disease burden and avoid overuse of acute medication. Nevertheless, the response to prevention is unpredictable, and a three-month treatment period is usually suggested to determine the responsiveness. Such practice, however, may prolong patients" suffering. It is of great importance to find ways to early detect those who may not respond to some specific kind of preventive medication, so that these patients may be placed with other therapeutic options. Previous study using neuroimage biomarkers (e.g cortical thickness) has demonstrated the feasibility to predict the responsiveness in patient with CM to the treatment of botulinum toxin. Whether the responsiveness to flunarizine, another wildly used and important preventive medication for CM especially in Asian and

European countries, can be predicted by using neuroimage biomarker deserves further evaluation. In the study, we aim to correlate the responsiveness to flunarizine in patients with CM and their baseline neuroimage features (cortical thickness) derived from magnetic resonance image (MRI) prior to prevention, and test if it can be used to predict the responsiveness.

Methods: Patients with CM were recruited from the Department of Neurology of Taipei Veterans General Hospital. At their first visit, all potential participants completed a structured headache questionnaire consisting of headache profiles and assessment of disease severity. After the initial visit, eligible patients who met the ICHD3 criteria for CM were asked to keep headache diaries during a prospective baseline period for 4 weeks (M0). Subjects with $\geq$15 monthly headache days (MHD) and $\geq$8 monthly migraine days (MMD) within this period then entered a preventive treatment course for 12 weeks (M1-M3) with flunarizine (5 mg, twice daily). Before prevention, all patients underwent their MRI scan, consisting of a high-resolution structure (T1) image, among others. Throughout the study period, patients were instructed to maintain the headache diary, which was used to calculate the number of MHD as the outcome measure. The mean percent change in the MHD reduction between the baseline period and the 12 weeks of prevention were used to correlate with neuroimage biomarkers. Responders (R) denote those with a $\geq$30% reduction in MHD across M1-M3 as compared to that of M0, while non-responders (NR) are those without.

Results: Sixty-Seven patients with CM, aged 38.1 $\pm$ 11.2 years (mean $\pm$ standard deviation), were recruited (M:F = 5:62). The MHD at baseline was 21.6 $\pm$ 5.8 days, while MMD was 11.2 $\pm$ 6.9 days. The disease duration was 18.9 $\pm$ 11.1 years. After a 12-week preventive treatment with flunarizine, 44 had a $\geq$30% reduction in MHD throughout M1-M3 (R), while 23 did not (NR). Overall, the extend of reduction in MHD throughout M1-M3 was positively correlated with the cortical thickness in bilateral facial somatosensory areas ($p < 0.05$, family-wise error corrected). Moreover, using a mean value of 1.94 mm within these areas derived from a control subject cohort, the sensitivity and specificity for differentiating R from NR were 81.6% and 55.2%, respectively, with an accuracy of 70.1%. Patients with CM who had an average cortical thickness $\geq$1.94 mm prior to prevention, compared to those without, had an odd's ratio of 5.5 for $\geq$30% reduction in MHD throughout a 12-week prevention with flunarizine ($p = 0.002$).

Conclusion: In this prospective study, we demonstrated that in patients with CM, baseline cortical thickness in bilateral facial somatosensory areas is associated with clinical outcome to flunarizine prevention. Those with a relatively thicker cortical thickness (above the mean value of control subjects) had a better chance to benefit from flunarizine. Such observation is in accordance with the idea that chronic pain may damage the brain, and a preserved brain morphometry may be associated with a better clinical outcome. Nevertheless, this study is limited by small case number. Further large-scale study is warranted to verify such important issue.

Disclosure of Interest: None Declared

Migraine preventive therapy

IHC23-DP-040

Long-term reductions in acute headache medication use after eptinezumab treatment in patients with prior preventive treatment failures

Anna Gryglas-Dworak[1], Jack Schim[2], Anders Ettrup[3], Line Pickering Boserup[3], Mette Krog Josiassen[3], Kristina Ranc[3], Bjorn Sperling[3] and Messoud Ashina[4,5]

[1]*MIGRE Polish Migraine Center, Wroclaw, Poland*
[2]*Neurology Center of Southern California, Carlsbad, USA*
[3]*H. Lundbeck A/S, Copenhagen, Denmark*
[4]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital–Rigshospitalet, Copenhagen, Denmark*
[5]*Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*

Objective: To evaluate long-term reductions in acute headache medication (AHM) use with eptinezumab vs placebo (pbo) in patients with prior preventive migraine treatment failures, including those with medication overuse (MO).

Methods: DELIVER (NCT04418765) randomized adults with migraine and 2–4 prior preventive failures to eptinezumab 100mg, 300mg, or pbo infusion every 12 weeks; patients initially given pbo received eptinezumab 100mg or 300mg in the extension period. MO was defined according to ICHD-3 criteria and baseline diary reports. Post hoc analysis included change from baseline in AHM days/month of use (ergotamines, triptans, simple or combination analgesics, opioids; total and class-specific use) in the MO subgroup.

Results: Of 890 patients in the full analysis set (FAS), 438/890 (49.2%) had MO at baseline. Eptinezumab resulted in greater reductions than pbo in total AHM days/month of use during Weeks 1–24 (FAS and MO; $p < 0.0001$ all comparisons), with triptans showing the largest reduction among AHM classes. Patients switching from pbo to eptinezumab experienced reductions similar to that of initial eptinezumab treatment: FAS changes over Weeks 1–4 were –4.6 (100 mg) and –4.8 (300mg) and over Weeks 25–28 were –4.8 (pbo-to-100 mg) and –5.5 (pbo-to-300 mg); MO subgroup changes over Weeks 1–4 were –6.5 and –6.6 and over Weeks 25–28 were –7.1 and

–8.0, respectively. All treatment arms sustained or further reduced AHM use across 18 months of treatment (Weeks 69–72 range: FAS, –4.7 to –5.7; MO, –7.0 to –7.9).
Conclusions: Eptinezumab reduced total AHM use more than pbo in patients with prior preventive failures as well as in patients with MO; largest reductions were observed for triptans. Robust reductions in AHM use after eptinezumab were sustained or further reduced with up to 18 months of treatment.

Headache pathophysiology – Basic science

IHC23-DP-041

Atogepant – an orally-administered CGRP antagonist – prevents activation of high-threshold and attenuates activation of wide dynamic range dura-sensitive neurons in the spinal trigeminal nucleus

Agustine Melo-Carrillo[1,2], Andrew Strassman[3,4], Ron Briode[5], Aubrey Adams[5], Brett Dabruzzo[6], Mitchell Brin[5,7] and Rami Burstein[1,4]

[1]*Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center., Boston, USA*
[2]*Harvard Medical School, Boston, Boston, USA*
[3]*Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, USA*
[4]*Harvard Medical School, Boston, USA*
[5]*Abbvie, Irvine, USA*
[6]*Abbvie, Madison, USA*
[7]*University of California, Irvine, Irvine, USA*

Objective: This study investigated mechanism of action of atogepant, a small-molecule CGRP receptor antagonist or gepant, recently approved for preventive treatment of migraine, by assessing its effect on activation and sensitization of central high-threshold (HT) and wide dynamic range (WDR) dura-sensitive neurons by cortical spreading depression (CSD).
Methods: In anesthetized male rats, single-unit recordings were used to assess effects of atogepant (5mg/kg) vs vehicle on activation and sensitization of HT and WDR dura-sensitive neurons by CSD.
Results: In vehicle-treated rats, CSD induced activation in 8/10 (80%) HT and 7/10 (70%) WDR neurons. In atogepant treated rats, CSD induced activation in 1/10 (10%) HT and 5/10 (50%) WDR neurons (Fisher exact HT: $p = 0.005$; WDR: $p = 0.64$). In HT neurons, the firing rate increased significantly at 1 and 2 hrs after CSD in untreated rats [baseline: 3.9 [0–14.4] (median [IQR]), 1hr: 8.5 [0.25–23.3], 2hr: 14.6 [5.1–20.2] $p = 0.01$], whereas in the treated rats it was reduced significantly [baseline: 3.2 [0.5–9.0] (median [IQR]), 1hr: 1.9 [0.1–6.7], 2hr: 2.0 [0–7.3] $p = 0.02$]. In contrast, in WDR neurons, the firing rate increased significantly at 1 and 2 hrs after CSD in untreated rats [baseline: 1.8 [0–5.2] (median [IQR]), 1hr: 3.7 [0–18.5], 2hr: 3.1 [0–7.7] $p = 0.02$], whereas in the treated rats it remained unchanged [baseline: 4.1 [0.1–9.5] (median [IQR]), 1hr: 2.3 [0.6–7.5], 2hr: 5.4 [1.1–7.5] $p = 0.44$]. Atogepant prevented CSD induced mechanical sensitization in the dura in HT (control: 18.3 to 22.5 (median) $p = 0.03$ atogepant: 18.7 to 15.8, $p = 0.54$) and to a lesser extent in the WDR neurons (control: 9 to 17.3 (median) $p = 0.03$ atogepant: 10.9 to 16.8, $p = 0.84$).
Conclusion: Atogepant prevented CSD-induced activation and dural sensitization of HT neurons While atogepant did not significantly reduce CSD-induced activation or sensitization of WDR neurons, it did suppress any increased activation and sensitization compared to controls. These findings align with previous studies that evaluated atogepant's effect on CSD induced activation of Ad and C-fibers.
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Migraine preventive therapy

IHC23-DP-042

Atogepant for the Preventive Treatment of Migraine Among Participants With Episodic Migraine With Prior Treatment Failure: Results From the ELEVATE Trial

Patricia Pozo-Rosich[1], Krisztian Nagy[2], Cristina Tassorelli[3], Michel Lanteri-Minet[4], Sara Sacco[5], Tomáš Nežádal[6], Michelle Finnegan[7], Hua Guo[7], Rosa De Abreu Ferreira[8] and Joel M. Trugman[7]

[1]*Vall d"Hebron University Hospital, Barcelona, Spain; Universitat Autonoma de Barcelona, Barcelona, Spain*
[2]*AbbVie, Budapest, Hungary*
[3]*Headache Science & Neurorehabilitation Centre, C. Mondino Foundation and University of Pavia, Pavia, Italy*
[4]*Pain Department and FHU InovPain, CHU Nice and Côte d"Azur University, Nice, France*
[5]*Director, Carolinas Headache Clinic, Matthews, NC, USA*
[6]*Neurology Department, Military University Hospital, First Faculty of Medicine, Charles University, Prague, Czech Republic*
[7]*AbbVie, Madison, NJ, USA*
[8]*AbbVie, North Chicago, UL, USA*

Objective: Atogepant, an oral calcitonin gene-related peptide receptor antagonist, is approved in the United States for the preventive treatment of migraine in adults, and in Puerto Rico, Canada, and Israel for the preventive

treatment of episodic migraine in adults. The ELEVATE trial evaluated the efficacy, safety, and tolerability of atogepant 60 mg once daily (QD) for the preventive treatment of episodic migraine (EM) in participants who were previously failed by 2–4 classes of oral preventive medications.

Methods: ELEVATE was a randomized, double-blind, placebo-controlled trial conducted in Europe and North America. Adults (aged 18–80 years) who previously failed 2–4 classes of conventional oral medications for migraine prevention and reported 4–14 monthly migraine days (MMDs) during the 28-day screening period were randomized to treatment with atogepant 60 mg QD or placebo. The primary endpoint was the change from baseline in mean MMDs across 12 weeks. Secondary endpoints included achievement of ≥50% reduction in MMDs, change from baseline in Headache Impact Test-6 (HIT-6) total score at week 12, and change from baseline in Migraine-Specific Quality of Life questionnaire version 2.1 Role Function–Restrictive (MSQ v2.1 RFR) domain score at week 12. This analysis was conducted in the off-treatment hypothetical estimand (OTHE) population.

Results: A total of 309 participants were included in the OTHE population (placebo: n = 155; atogepant 60 mg QD: n = 154). Of these participants, 56.0% failed 2 classes of oral migraine preventive medications and 44.0% failed ≥3 classes. A significantly greater decrease in MMDs (mean [standard error]) across the 12-week treatment period was observed with atogepant 60 mg QD (−4.20 [0.39]) vs placebo (−1.85 [0.39]; $P < 0.0001$). Secondary endpoints of achievement of ≥50% reduction in MMDs, reduction in HIT-6 and improvement in MSQ v2.1 RFR scores also showed a statistically significant treatment effect for atogepant vs placebo (**Table**). The most commonly (≥5%) reported treatment-emergent adverse events (atogepant vs placebo, respectively) included constipation (10.3% vs 2.5%), COVID-19 (8.3% vs 9.6%), nausea (7.1% vs 3.2%), and nasopharyngitis (5.1% vs 7.6%).

Conclusion: Atogepant 60 mg QD was efficacious, safe, and well-tolerated for the preventive treatment of EM in participants who were previously failed by 2–4 classes of oral preventive migraine medications.

Disclosure of Interest: This study was supported by AbbVie. Patricia Pozo-Rosich, MD, PhD, has received, in the last 3 years, personal fees for advisory boards and speaker panels from AbbVie, Amgen, Chiesi, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva and for serving on a scientific advisory or data safety monitoring board for Lilly Foundation Spain. She is the principal investigator for clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva. Her group has received grants from AbbVie, ERA-Net NEURON, European Commission, Instituto Carlos III, Novartis, and Teva. She serves as an associate editor for Cephalalgia, Headache, Neurologia, and Revista de Neurología. Cristina Tassorelli, MD, PhD, has participated in advisory boards for AbbVie, Dompé, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva. She has lectured at symposia sponsored by AbbVie, Eli Lilly, Novartis, and Teva. She is principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva. She has received research grants from the European Commission, the Italian Ministry of Health, the Migraine Research Foundation, and the Italian Multiple Sclerosis Foundation. She serves as an associate editor for Cephalalgia and The Journal of Headache and Pain. Michel Lanteri-Minet, MD, reports personal fees for advisory boards, speaker panels, or investigation studies from Allergan, Amgen, Biosavia, Boston Scientific, Eli Lilly, Grünenthal, Ipsen, Lundbeck, Medtronic, Novartis, Pfizer, Reckitt Benckiser, St. Jude, Sanofi-Aventis, Sun Pharma,

Table. Summary of Key Secondary Efficacy Endpoints (OTHE Population)

	Placebo (n = 155)	Atogepant 60 mg QD (n = 154)
Achievement of ≥50% reduction in MMDs across the 12-week treatment period, n (%)	28 (18.1)	78 (50.6)
Atogepant vs placebo odds ratio (95% CI)		4.82 (2.85, 8.14)
Adjusted P value		<0.0001
Change from baseline in HIT-6 total score at week 12, LS mean (SE)	−4.14 (0.795)	−10.56 (0.804)
Atogepant vs placebo LSMD (95% CI)		−6.42 (−8.22, −4.63)
Adjusted P value		<0.0001
Change from baseline in MSQ v2.1 RFR domain score at week 12, LS mean (SE)	15.38 (2.047)	33.26 (2.065)
Atogepant vs placebo LSMD (95% CI)		17.88 (13.34, 22.42)
Adjusted P value		<0.0001

HIT-6, Headache Impact Test-6; LS, least-squares; LSMD, least-squares mean difference; MSQ v2.1 RFR, Migraine-Specific Quality of Life questionnaire version 2.1 Role Function–Restrictive; OTHE, off-treatment hypothetical estimand.

Teva, UPSA, and Zambon. He has received research grants from the French Ministry of Health, the French Pain Society, The APICIL Foundation, and the Migraine Research Foundation. He served as an associate editor for The Journal of Headache and Pain. Sara Sacco, MD, has participated in advisory boards and/or is a speaker for Allergan (now AbbVie), Amgen, BDSI, Biohaven, Eli Lilly, Impel Neuropharma, and Teva. Tomáš Nežádal, MD, has received consulting fees, speaking fees, and travel grants from Eli Lilly, Glenmark, Lundbeck, Novartis, Pfizer, St. Jude Medical, Teva, and UCB. He also has served on advisory boards or as a principal investigator in clinical trials for AbbVie, Amgen, Eli Lilly, Lundbeck, Neurocrine, Novartis, Teva, and UCB. Joel M. Trugman, MD, Krisztian Nagy, MD, Hua Guo, PhD, and Pranav Gandhi, PhD, are employees of AbbVie and may hold AbbVie stock. Michelle Finnegan, MPH, was an employee of AbbVie at the time of the study and may hold AbbVie stock.

Headache epidemiology, outcomes and burden

IHC23-DP-043

A Multi-country Comparison of Migraine-Related Stigma in People Living With Migraine: Results From the CaMEO-International Study

Robert E. Shapiro[1], Dawn C. Buse[2], Elizabeth Seng[2], Richard B. Lipton[2], Kristina Fanning[3], Brett Dabruzzo[4], Michael Seminerio[5] and William Young[6]

[1]*The Larner College of Medicine, University of Vermont, Burlington, VT, USA*
[2]*Albert Einstein College of Medicine, Bronx, NY, USA*
[3]*MIST Research, Wilmington, NC, USA*
[4]*AbbVie, Madison, NJ, USA*
[5]*AbbVie, Irvine, CA, USA*
[6]*Thomas Jefferson University, Philadelphia, PA, USA*

Objective: To measure migraine-related stigma among people living with migraine across multiple countries.
Methods: The Chronic Migraine Epidemiology and Outcomes – International (CaMEO-I) Study was a cross-sectional, web-based survey conducted in 2021–2022 in Canada, France, Germany, Japan, the United Kingdom (UK), and the United States (US). Respondents meeting modified *International Classification of Headache Disorders*, 3rd edition, criteria for migraine were identified via a validated diagnostic questionnaire. In this analysis, using the Stigma Questionnaire for Migraine (SQM), 9 items related to migraine-related stigma were assessed with responses ranging from "never" (1) to "very often" (5). Responses of "does not apply to me" were scored as 0 and were not included. Items were summed and rescaled to have a range of 0 to 100. Quartile scores were calculated: 1st quartile: $\leq$8.33, 2nd quartile: 8.34–25.00, 3rd quartile: 25.01–47.22, and 4th quartile: $>$47.22. An overall chi-square test and paired country chi-square tests were used to evaluate differences in SQM quartiles across the 6 countries.
Results: This analysis included 14,492 respondents with migraine (5.4%–9.5% respondents across the 6 countries had $\geq$15 monthly headache days). The median (interquartile range) SQM scores in the 1st, 2nd, 3rd, and 4th SQM quartiles were 2.8 (5.6), 16.7 (8.3), 36.1 (11.1), and 61.1 (18.7), respectively. The overall median stigma scores were highest among respondents with 15 or more monthly headache days. The proportion of people with migraine reporting stigma occurring "more than sometimes" varied by SQM items and countries. Among all respondents (all countries), 31.5% felt that others viewed their migraine or severe headache attacks with a lack of understanding of the pain and impact often or very often, 17.5% reported feeling that others viewed their migraine or severe headache attacks as if they were their own fault often or very often, and 15.9% reported feeling that others viewed their migraine or severe headache attacks as a way to get out of work, activities, or other commitments often or very often. Additionally, 15.5%, 13.1%, and 11.8% of all respondents reported feeling criticized or thought less of by someone in their family, their co-workers, or their boss/supervisor often or very often, respectively, because of their migraine or severe headaches. Finally, 16.5% of all respondents reported that they thought less of themselves, felt ashamed, and/or felt guilty because of their migraine or severe headaches often or very often. Overall, the proportion of people with stigma was lowest in France and highest in the UK based on the percentages of respondents in the highest (4th) quartile of SQM responses (11.7% and 28.2%, respectively). The difference among countries in the overall distribution of SQM scores was statistically significant (chi-squared = 750.023, $P < 0.001$; **Table**). Paired post hoc comparisons with the US revealed that the distribution of SQM scores did not differ between the US and Canada, Germany, and the UK. People in the US felt greater migraine-related stigma compared with France and Japan (chi-squared = 287.5 and 167.5 respectively, $P < 0.001$).
Conclusion: To our knowledge, this is the first study to measure migraine-related stigma across multiple countries. People living with migraine commonly experience some form of stigma, and respondents most commonly reported feeling that others viewed their migraine attacks with a lack of understanding. Further research is needed to explore country-specific differences in culture, workplace norms, economics, accommodations, or comorbidities that may add insights into the stigma findings observed in this analysis.
Disclosure of Interest: Allergan (prior to its acquisition by AbbVie) Disclosures: Robert Shapiro, MD, PhD, has

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Table Stigma Questionnaire for Migraine (SQM) Across 6 Countries

	US (N = 2404)	Canada (N = 2382)	Germany (N = 2397)	France (N = 2464)	UK (N = 2436)	Japan (N = 2409)	Total (14,492)
1st Quartile: Least stigma	27.3%	28.7%	24.1%	43.2%	27.2%	16.2%	27.8%
2nd Quartile	19.6%	20.6%	21.5%	26.1%	20.9%	27.8%	22.8%
3rd Quartile	25.9%	25.5%	28.7%	19.0%	23.7%	35.9%	26.4%
4th Quartile: Most stigma	27.2%	25.2%	25.7%	11.7%	28.2%	20.0%	23.0%
Chi^2 (vs US)	NA	3.4	11.2	287.5	3.9	167.5	750.0[a]
P value (vs US)	NA	0.330	0.011	<0.001	0.278	<0.001	<0.001[a]
Mean (SD) SQM score	32.1 (26.2)	30.4 (25.2)	31.4 (23.7)	20.0 (20.3)	32.2 (26.1)	31.4 (20.9)	29.6 (24.2)
Median (IQR) SQM score	28.1 (41.7)	27.8 (41.7)	29.2 (38.9)	13.9 (27.8)	27.8 (41.7)	29.2 (30.4)	25.0 (38.9)

[a]Chi^2 test among all 6 countries.

IQR, interquartile range; NA, not applicable; SD, standard deviation.

received financial and/or authorship compensation for research consulting from AbbVie, Eli Lilly, Lundbeck, and Theranica. Dawn C. Buse, PhD, has received grant support and honoraria from AbbVie, Amgen, Biohaven, Eli Lilly and Company, Collegium, Lundbeck, and Teva and for work on the editorial board of Current Pain and Headache Reports. Elizabeth Seng, PhD, has consulted for Click Therapeutics and GlaxoSmithKline and has served on an advisory board for AbbVie and Theranica. Richard B. Lipton, MD, has received research support from the National Headache Foundation, the National Institutes of Health, and the US Food and Drug Administration. He serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee. William Young, MD, has nothing to disclose. Kristina Fanning, PhD, is managing director of MIST Research which has received research funding from AbbVie, Allay Lamp, GlaxoSmithKline, Juva Health, and NYC Langone Health via grants to the National Headache Foundation. Brett Dabruzzo, PharmD, and Michael Seminerio, PhD, are employees of AbbVie and may hold AbbVie stock.

Headache pathophysiology – Basic science

IHC23-DP-044

Circadian properties of the mouse trigeminal ganglion and a chronic headache model

Chorong Han, Ji Ye Lim, Sun Young Kim, Celia Tran, Kaori Ono, Eunju Kim, Zheng Chen, Seung-Hee Yoo and Mark Burish

UTHealth Houston, Houston, USA

Objective: Several headache disorders, including migraine and cluster headache, are known to display distinct circadian rhythms and involve the trigeminovascular system. However, the circadian basis underlying rhythmic pain responses in headache pain disorders remains poorly understood. We aimed to elucidate the circadian regulation of pain responses in the trigeminovascular system.

Methods: We examined the circadian rhythm of trigeminal ganglia (TG) ex vivo cultures using Period2::LucSV reporter mice and investigated single-cell bioluminescence rhythms of TG neurons. We also performed immunohistochemistry to determine core clock protein expression in TG. Next, we examined pain behavior in Period1/Period2 double knockout mice using the chronic nitroglycerin (NTG) mouse model. Finally, we performed RNA sequencing of the TG (obtained every 4 hours for 24 hours) in both vehicle- and NTG-treated mice. Genes identified from RNA sequencing were cross-referenced with genes targeted by medications used to treat migraine, cluster headache, and trigeminal neuralgia.

Results: We discovered strong circadian rhythms in TG ex vivo and single-cell cultures, and TG staining revealed core circadian genes in both neurons and glia. In the chronic NTG mouse model we demonstrated diurnal rhythms of pain sensitivity which were abolished in arrhythmic mice lacking the core clock genes Period1 and Period2. TG RNA-sequencing analysis revealed a

robust circadian transcriptome where 466 genes (2.7% of the total expressed genes in the TG) display circadian oscillation in the control group, including core clock genes and clock-regulated pain neurotransmitters. Whereas core clock gene oscillation remained largely intact in the NTG group, we observed a profound reprogramming of the global circadian transcriptomic landscape: 71% of circadian genes in the control group lost rhythm, and 584 de novo circadian genes (composing 81% of NTG rhythmically expressed genes) were induced by NTG. Finally, pharmacogenetic analysis of medications used to treat migraine, cluster headache, and trigeminal neuralgia identified 10 genes in our TG circadian transcriptome encoding target proteins of current medications used for migraine, cluster headache, and/or trigeminal neuralgia medications.

Conclusions: Our study unveils a robust circadian clock in the TG and illustrates a highly dynamic circadian transcriptome in response to headache pain and headache medications. Our results support a fundamental role of the clock in pain pathophysiology and may ultimately lead to innovative strategies targeting the circadian machinery to ameliorate headache pain.

Disclosure of Interest: Mark J Burish was an unpaid medical advisor for Praxis Precision Medicines (in lieu of compensation a fee was paid to the University of Texas Health Science Center at Houston) and was an unpaid consultant for Beckley Psytech limited (in lieu of compensation a donation was made to the Will Erwin Headache Research Foundation). It should be noted, however, that Dr. Burish is employed by the University of Texas Health Science Center at Houston and receives research funding from the Will Erwin Headache Research Foundation. He is an unpaid member of the medical advisory board of Clusterbusters, and is a site investigator for a cluster headache clinical trial funded by Lundbeck. He was paid to take surveys for Doximity. Other authors: no disclosures of interest.

Headache epidemiology, outcomes and burden

IHC23-IND-001

Characterizing Barriers to Care in Migraine: Multicountry Results From the Chronic Migraine Epidemiology and Outcomes – International Study

Michel Lanteri-Minet[1], Elizabeth Leroux[2], Zaza Katsarava[3,4], Richard B. Lipton[5], Fumihiko Sakai[6], Manjit Matharu[7], Kristina Fanning[8], Katherine Sommer[9], Michael Seminerio[10] and Dawn C. Buse[5]

[1]*Pain Department and FHU InovPain, CHU Nice and Côte Azur University, Nice, France*
[2]*Brunswick Medical Center, Montreal, Canada*
[3]*Evangelical Hospital Unna, Unna, Germany*
[4]*University of Duisburg-Essen, Duisburg, Germany*
[5]*Albert Einstein College of Medicine, Bronx, USA*
[6]*Saitama International Headache Center, Chuo-ku, Saitama City, Japan*
[7]*Institute of Neurology, London, United Kingdom*
[8]*MIST Research, Wilmington, USA*
[9]*AbbVie, Irvine, USA*
[10]*AbbVie, North Chicago, USA*

Objective: This analysis of the Chronic Migraine Epidemiology and Outcomes – International (CaMEO-I) study assessed rates of traversing barriers to good medical outcomes in people with migraine.

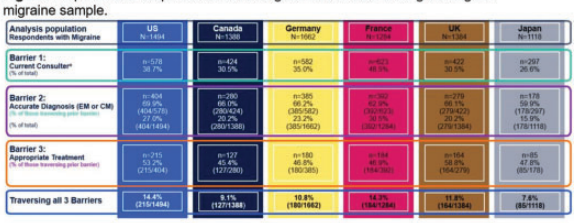
Methods: CaMEO-I was a cross-sectional, Web-based survey conducted in 2021 that identified individuals in Canada, France, Germany, Japan, UK, and US who met modified criteria for migraine consistent with the International Classification of Headache Disorders, 3rd edition. Respondents with a Migraine Disability Assessment (MIDAS) grade of $\geq$2 were judged to need medical care and included. Minimally effective treatment required participants were currently consulting a health care professional for headache, reported an accurate diagnosis, and reported use of minimally appropriate pharmacologic treatment. Accurate diagnosis was defined as respondents with episodic migraine who reported receiving a diagnosis of migraine or menstrual migraine and respondents with chronic migraine who reported receiving a diagnosis of chronic or transformed migraine. Minimally appropriate treatment was evaluated based on whether respondents received appropriate prescription acute and preventive treatments for migraine. Chi-square tests determined whether an overall difference across the countries existed in the proportions of respondents who traversed each barrier.

Results: Of 14,492 respondents with migraine, 8330 were eligible for this analysis (Canada: 1388; France: 1284; Germany: 1662; Japan: 1118; UK: 1384; US: 1494). Current headache consultation was reported by 26.6% (Japan) to 48.5% (France) of respondents (Figure); based on the chi-square test, an overall difference was detected across all 6 countries ($P < 0.001$). Among consulters, 59.9% (Japan) to 69.9% (US) of respondents reported receiving a diagnosis of chronic or episodic migraine; proportions differed between the US and each of the other 5 non-US countries ($P < 0.050$). Among diagnosed consulters, 45.4% (Canada) to 58.8% (UK) of respondents reported receiving minimally appropriate pharmacologic treatment, with an overall significant difference among countries ($P = 0.007$). All 3 barriers were traversed by 7.6% (Japan) to 14.4% (US) of respondents, with differences among countries ($P < 0.001$).

Conclusions: Results demonstrate that <15% of people with migraine in need of medical care traverse all 3

barriers to care. Assessing barriers to care based on the specific treatment guidelines in each country is an area of potential future analysis.

Figure. Proportions of respondents traversing barriers to care among the eligible migraine sample.



*Current consulters included respondents within the migraine population who had their migraine managed by a healthcare provider other than emergency department or urgent care providers.

Disclosure of Interest: Michel Lanteri-Minet, MD, reports personal fees for advisory boards, speaker panels, or investigation studies from Allergan, Amgen, Astellas, ATI, BMS, Boehringer, Boston Scientific, CoLucid, Convergence, GlaxoSmithKline, Grunenthal, IPSEN, Lilly, Lundbeck, Medtronic, Menarini, MSD, Novartis, Pfizer, Reckitt Benckiser, Saint-Jude, Salvia BioElectronics, Sanofi-Aventis, Teva, UCB, UPSA, and Zambon. Elizabeth Leroux, MD, has received speaker fees and consulting fees from Allergan, Eli Lilly, and Teva Neuroscience; consulting fees from Aralez Pharmaceuticals, McKesson Canada, and Medscape; speaking fees, consulting, and reimbursement for travel from Novartis; and reimbursement for travel from IHS-GPAC. Zaza Katsarava, MD, has been a speaker and/or consultant and/or received research support from Allergan, Amgen/Novartis, Eli Lilly, Merck, and Teva. Richard B. Lipton, MD, has received research support from the National Headache Foundation, the National Institutes of Health, and the US Food and Drug Administration. He serves as consultant, advisory board member, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Pfizer, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009) and Informa. He holds stock/options in Biohaven and Manistee. Fumihiko Sakai, MD, is a consultant, speaker, or scientific advisor for Amgen, Eisai, Eli Lilly, Otsuka, and Teva. Manjit Matharu, MD, serves on the advisory board for Abbott, Allergan, Eli Lilly, Medtronic, Novartis, and Teva and has received payment for the development of educational presentations from Allergan, electroCore, Eli Lilly, Novartis, and Teva. Kristina Fanning, PhD, is Managing Director of MIST Research, which has received research funding from AbbVie, Allay Lamp, GlaxoSmithKline, Juva Health, and NYC Langone Health via grants to the National Headache Foundation. Katherine Sommer, PhD, and Michael Seminerio, PhD, are employees of AbbVie and may hold AbbVie stock. Dawn C. Buse, PhD, has received grant support and honoraria from AbbVie, Amgen, Biohaven, Collegium, Eli Lilly, Lundbeck, and Teva and for work on the editorial board of Current Pain and Headache Reports.

Headache epidemiology, outcomes and burden

IHC23-IND-002

Subjective Cognitive Impairment During Migraine or Severe Headaches: Multi-Country Results From the CaMEO-International Study

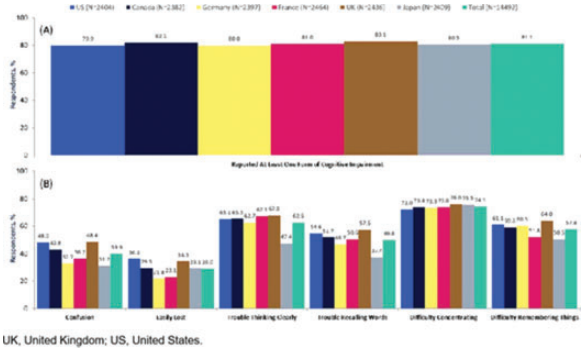
Richard B. Lipton[1], Kristina Fanning[2], Sait Ashina[3], Elizabeth Seng[2], Manjit Matharu[4], Brett Dabruzzo[5], Katherine Sommer[6], Michael Seminerio[7] and Dawn C. Buse[1]

[1]*Albert Einstein College of Medicine, Bronx, USA*
[2]*MIST Research, Wilmington, USA*
[3]*Department of Neurology and Department of Anesthesia, Critical Care and Pain Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, USA*
[4]*Institute of Neurology, London, United Kingdom*
[5]*AbbVie, Madison, USA*
[6]*AbbVie, Irvine, USA*
[7]*AbbVie, North Chicago, USA*

Objective: The objective of this analysis is to describe subjective cognitive impairment during migraine attacks or severe headaches in people with migraine.
Methods: Chronic Migraine Epidemiology and Outcomes – International (CaMEO-I) was a cross-sectional, web-based survey conducted in 2021 in Canada, France, Germany, Japan, the UK, and the US. A validated questionnaire identified respondents with migraine, based on modified International Classification of Headache Disorders, 3rd edition criteria. Using the subjective Migraine Cognitive Impairment Questionnaire, 6 questions related to the frequency of subjective cognitive impairment during migraine attacks or severe headaches were assessed. Responses ranged from "never" (0), "rarely" (1), "less than half the time" (2), to "half the time or more" (3). Items were summed and rescaled to have a range of 0 to 100. Using the pooled sample (N = 14,492), quartile scores were calculated to represent ordered categories of subjective cognitive impairment: 1st quartile: $\leq$33.33, 2nd quartile: 33.33–55.56, 3rd quartile: 55.57–72.22, and 4th quartile: $>$72.22.
Results: The proportion of people with migraine reporting subjective cognitive impairment occurring "more than rarely" varied by type of cognitive impairment and among countries. In total, 11,752 of 14,492 (81.1%) individuals reported at least one form of cognitive impairment more than rarely (Figure 1A). The proportion of people with migraine with particular types of cognitive

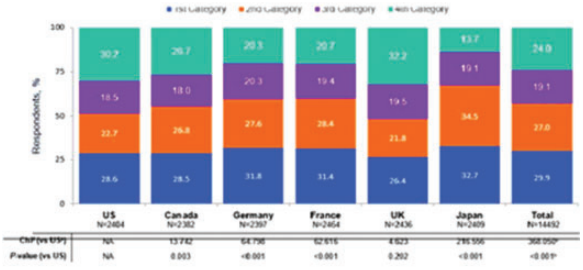
impairment averaged across the countries studied was 74.1% for difficulty concentrating, 62.6% for trouble thinking clearly, 57.8% for difficulty remembering things, 49.8% for trouble recalling words, 39.9% for confusion, and 29.0% for getting easily lost (Figure 1B). Overall, the proportion of people with subjective cognitive impairment during migraine attacks was lowest in Japan and highest in the UK based on the percentage of respondents in the highest (4th) category of cognitive complaints (13.7% and 32.2%, respectively; Figure 2). The difference among countries in the overall distribution of cognitive impairment was statistically significant (Chi-squared = 368.1, $P < 0.001$). People in the US had greater cognitive impairment compared with all the other countries besides the UK (all $P < 0.01$; Figure 2).

Conclusions: Among people with migraine, subjective cognitive impairment during migraine attacks was common across all 6 countries.



UK, United Kingdom; US, United States.

Figure 2. Subjective Cognitive Impairment Across Countries



a Chi-square test among all 6 countries was $P<0.001$; therefore, pairwise post hoc tests vs US were run.
b Chi-square test among all 6 countries.
IQR, interquartile range; SD, standard deviation; UK, United Kingdom; US, United States.

Disclosure of Interest: Richard B. Lipton, MD, has received research support from the National Institutes of Health, the FDA, and the National Headache Foundation. He serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee. Kristina Fanning, PhD, is Managing Director of MIST Research which has received research funding from AbbVie, Allay Lamp, GlaxoSmithKline, Juva Health, and NYC Langone Health via grants to the National Headache Foundation. Sait Ashina, MD, has received honoraria for consulting from AbbVie/Allergan, Amgen, Biohaven, Eli Lilly, Impel NeuroPharma, Lundbeck, Novartis, Percept, Satsuma, Supernus, Teva, and Theranica. Elizabeth Seng has consulted for Click Therapeutics and GlaxoSmithKline and has served on an advisory board for AbbVie and for Theranica. Manjit Matharu, MD, serves on the advisory board for Abbott, Allergan, Eli Lilly, Medtronic, Novartis, and Teva, and has received payment for the development of educational presentations from Allergan, electroCore, Eli Lilly, Novartis, and Teva. Dawn C. Buse, PhD, has received grant support and honoraria from AbbVie, Amgen, Biohaven, Eli Lilly and Company, Collegium, Lundbeck, and Teva and for work on the editorial board of Current Pain and Headache Reports. Brett Dabruzzo, PharmD; Katherine Sommer, PhD; and Michael Seminerio, PhD, are employees of AbbVie and may hold AbbVie stock.

Headache epidemiology, outcomes and burden

IHC23-IND-003

Disability in Migraine: Multicountry Results From the CaMEO-International Study

Zaza Katsarava[1], Dawn C. Buse[2], Elizabeth Leroux[3], Michel Lanteri-Minet[4], Fumihiko Sakai[5], Manjit Matharu[6], Katherine Sommer[7], Michael Seminerio[8], Kristina Fanning[9] and Richard B. Lipton[2]

[1]*Evangelical Hospital Unna, Unna, Germany*
[2]*Albert Einstein College of Medicine, Bronx, USA*
[3]*Brunswick Medical Center, Montreal, Canada*
[4]*CHU Nice and Côte Azur University, Nice, France*
[5]*Saitama International Headache Center, Chuo-ku, Saitama City, Japan*
[6]*Institute of Neurology, London, United Kingdom*
[7]*AbbVie, Irvine, USA*
[8]*AbbVie, North Chicago, USA*
[9]*MIST Research, Wilmington, USA*

Objective: To describe disability among individuals with migraine. Although individual studies evaluating headache burden are available from many countries, few studies have been conducted across multiple countries using the same methodology.

Methods: Chronic Migraine Epidemiology and Outcomes-International (CaMEO-I) was a cross-sectional, web-based survey conducted in 2021–2022 in Canada, France, Germany, Japan, the United Kingdom, and the United States.

The American Migraine Study/American Migraine Prevalence and Prevention Study diagnostic questionnaire identified respondents with migraine based on modified International Classification of Headache Disorders, 3rd edition, criteria. This analysis evaluated migraine burden using the Migraine-Specific Quality of Life Questionnaire (MSQ) and the Work Productivity and Activity Impairment Questionnaire (WPAI). The MSQ is a 14-item questionnaire that measures the effect of migraine on daily functioning across 3 domains, with higher scores corresponding to better quality of life. The WPAI evaluates the impact of migraine on work productivity and regular activities.

Results: This analysis included 14,492 respondents with migraine (~2400 from each country). Mean (SD) MSQ scores ranged from 57.7 (23.4) in Canada to 63.3 (21.1) in France for the role function restrictive domain, 67.6 (22.9) in Germany to 77.3 (22.7) in Japan for the role function preventive domain, and 63.9 (29.1) in the US to 69.2 (24.8) in France for the emotional function domain. Based on the WPAI, the mean (SD) percentage of work missed (absenteeism) ranged from 4.3% (16.2) in France to 9.0% (21.7) in Germany, percentage of work impaired (presenteeism) ranged from 31.2% (28.0) in France to 47.8% (28.6) in Japan, percentage of overall work impaired ranged from 33.5% (30.3) in France to 49.4% (29.4) in Japan, and percentage of activity impaired ranged from 39.3% (30.2) in France to 50.7% (28.4) in Japan.

Conclusions: For every country surveyed, migraine is associated with substantial burden, including poor quality of life and work/activity impairment.

Disclosure of Interest: Zaza Katsarava, MD, has been a speaker and/or consultant and/or has received research support from Allergan, Amgen/Novartis, Eli Lilly, Merck, and Teva. Dawn C. Buse, PhD, has received grant support and honoraria from AbbVie, Amgen, Biohaven, Collegium, Eli Lilly, Lundbeck, and Teva and for work on the editorial board of Current Pain and Headache Reports. Elizabeth Leroux, MD, has received speaker fees and consulting fees from Allergan, Eli Lilly, and Teva Neuroscience; consulting fees from Aralez Pharmaceuticals, McKesson Canada, and Medscape; speaking fees, consulting fees, and reimbursement for travel from Novartis; and reimbursement for travel from IHS-GPAC. Michel Lanteri-Minet, MD, reports personal fees for advisory boards, speaker panels, or investigation studies from Allergan, Amgen, Astellas, ATI, BMS, Boehringer, Boston Scientific, CoLucid, Convergence, GlaxoSmithKline, Grunenthal, IPSEN, Lilly, Lundbeck, Medtronic, Menarini, MSD, Novartis, Pfizer, Reckitt Benckiser, Saint-Jude, Salvia BioElectronics, Sanofi-Aventis, Teva, UCB, UPSA, and Zambon. Fumihiko Sakai, MD, is a consultant, speaker, or scientific advisor for Amgen, Eisai, Eli Lilly, Otsuka, and Teva. Manjit Matharu, MD, serves on the advisory board for Abbott, Allergan, Eli Lilly, Medtronic, Novartis, and Teva and has received payment for the development of educational presentations from Allergan, electroCore, Eli Lilly, Novartis, and Teva. Katherine Sommer, PhD, and Michael J. Seminerio, PhD, are employees of AbbVie and may hold AbbVie stock. Kristina Fanning, PhD, is Managing Director of MIST Research, which has received research funding from AbbVie, Allay Lamp, NYC Langone Health, Juva Health, and GlaxoSmithKline via grants to the National Headache Foundation. Richard B. Lipton, MD, has received research support from the National Headache Foundation, the National Institutes of Health, and the US Food and Drug Administration. He serves as consultant, advisory board member, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Pfizer, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee.

Headache epidemiology, outcomes and burden

IHC23-IND-004

Efficacy of OnabotulinumtoxinA Among Diverse Racial/Ethnic Groups: Post hoc Analysis of the Phase 4 COMPEL Trial

Andrew Blumenfeld[1], Larry Charleston IV[2], Katherine Sommer[3] and Hope L. O"Brien[4]

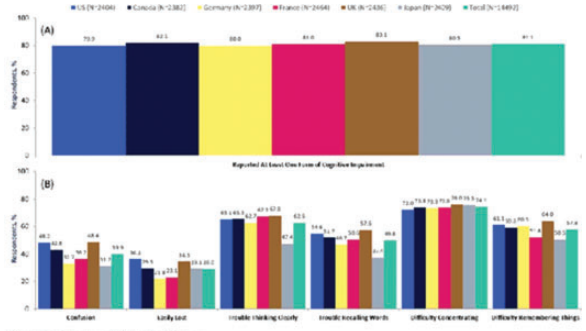
[1]*The Los Angeles Headache Center, Los Angeles, USA*
[2]*Department of Neurology and Ophthalmology, Michigan State University College of Human Medicine, East Lansing, USA*
[3]*AbbVie, Irvine, USA*
[4]*Headache Center of Hope, University of Cincinnati College of Medicine, Cincinnati, USA*

Objective: This study analyzed efficacy of migraine-preventive medications among different racial/ethnic groups.

Methods: Single-arm, open-label COMPEL study (NCT01516892) enrolled adults with chronic migraine (CM) receiving onabotulinumtoxinA (onabotA) 155U every 12 weeks (9 treatments over 108 weeks). Patients who were Asian, African American, or Pacific Islander/Alaska Native (pooled) were included in analysis. Non-Hispanic Whites (NHW) were used as comparison group. Baseline demographics and change in number of monthly headache days (MHDs) at each visit than with baseline, change from baseline in 6-item Headache Impact Test (HIT-6) total score, change from baseline in Migraine Disability Assessment (MIDAS) score, and change from baseline in Migraine-Specific Quality-of-Life Questionnaire (MSQ) v2.1 score were evaluated. Two-sided paired t-test was conducted to calculate P-value for change from baseline.

Results: At baseline, the intent-to-treat analysis population included a total of 715 patients (n = 581 NHW; n = 89 Asian; n = 41 African American; n = 4 Pacific Islander/Alaska Native); 373 patients competed the 108-week study, (n = 288 NHW; n = 60 Asian; n = 21 African American; n = 4 Pacific Islander/Alaska Native). Demographic and baseline characteristics showed the Asian population had a higher proportion of males, lower body mass index, and a later age of migraine onset than the NHW and African American populations and the African American population had earlier onset of migraine than the Asian population and a higher incidence of sleep disorders and head trauma than the NHW and Asian populations. After treatment with 155U of onabotA every 12 weeks, all racial/ethnic groups demonstrated significant reductions in MHDs at all time points (all, $P < 0.0001$; Table). All racial/ethnic groups demonstrated similar proportions of participants who achieved ≥50% reduction in MHDs from baseline at all time points (Figure). Each racial/ethnic group demonstrated significant reductions in HIT-6 ($P < 0.01$), MIDAS ($P < 0.05$), and MSQ 2.1 ($P < 0.05$) Role Function Restrictive scores at all time points. Treatment with onabotA was safe and effective based on mean reductions in MHDs and proportion of ≥50% responders across various racial/ethnic groups. Most common adverse events (>2% across all groups) were neck pain, eyelid ptosis, musculoskeletal stiffness, and injection site pain.

Conclusions: OnabotA was safe and effective for preventive treatment of CM among diverse racial/ethnic groups.



UK, United Kingdom; US, United States.

Table 1: Baseline migraine burden of patients before switching to or initiating Galcanezumab, other CGRP mAbs, TOMP, or botulinum toxin A/B[a]

Baseline Migraine burden, mean (SD)	Overall (n=2573)	Galcanezumab (N=953)	Other CGRP mAbs[a] (n=297)	TOMP[b] (n=1189)	Botulinum Toxin A/B (n=84)
MIDAS summary score	46.1 (45.2)	52.7 (48.8)	48.0 (42.8)	38.6 (39.3)	78.7 (60.4)
MSQ v2.1 Restrictive score	46.5 (21.3)	42.5 (20.6)	46.4 (19.9)	50.5 (21.3)	30.2 (21.5)
MSQ v2.1 Preventive score	63.2 (22.6)	60.1 (22.5)	62.9 (22.1)	66.3 (21.9)	49.3 (27.8)
MSQ v2.1 Emotional function score	53.9 (28.3)	48.9 (28.5)	52.6 (28.0)	58.9 (27.1)	40.2 (29.2)
PGI-S score	4.3 (1.3)	4.5 (1.2)	4.3 (1.2)	4.0 (1.3)	4.7 (1.4)
WPAI – Presenteeism score	50.1 (26.1)	51.0 (25.3)	50.8 (26.8)	49.3 (26.8)	55.3 (19.5)
WPAI – Absenteeism score	10.9 (20.4)	13.5 (21.4)	12.6 (23.6)	8.2 (17.1)	27.0 (36.1)
WPAI – Work productivity loss score	53.4 (27.0)	55.0 (26.7)	54.7 (27.2)	52.0 (27.5)	59.9 (19.8)
WPAI – Activity impairment score	55.3 (25.4)	56.7 (25.1)	54.9 (24.3)	54.1 (25.7)	67.3 (24.1)

[a]Other CGRP mAbs included Eremumab, Fremanezumab, Eptinezumab. [b]TOMPs included beta blockers, anticonvulsants, tricyclic antidepressants, calcium channel blockers, and angiotensin II receptor antagonists.
[a] Data for locally approved treatments are not shown because of the small sample size.
Abbreviations: CGRP: Calcitonin Gene-Related Peptide; mAb: Monoclonal antibodies; MIDAS: Migraine Disability Assessment; MSQ: Migraine-specific Quality of Life Questionnaire; TOMP: Traditional Oral Migraine Preventive Medications; PGI-S: Patient Global Impression of Severity; SD: Standard Deviation; WPAI: Work Productivity and Activity Impairment.

Disclosure of Interest: Andrew Blumenfeld, MD, within the past 12 months, has served on advisory boards for, consulted for, and/or been a speaker or contributing author for Allergan/AbbVie, Aeon, Alder, Amgen, Axsome, Biohaven, Impel, Lundbeck, Revance, BDSI, Eli Lilly, Novartis, Teva, Theranica, and Zoscano. He has received grant support from AbbVie and Amgen. Larry Charleston IV, MD, MSc, within the past 24 months, has received personal compensation for serving as a consultant for Allergan/AbbVie, Amneal, Biohaven, Haleon, LinPharma, Satsuma and Teva; was on the advisory panel for Ctrl M Health (stock); received grant/research support from the Disparities in Headache Advisory Council and Amgen. He has received CME honoraria from American Headache Society, American Academy of Neurology, BrainWeekend, NeurologyWeek, and Migraine360 CME Program. He receives a salary as faculty from Michigan State University College of Human Medicine and Thomas Jefferson University. He is a non-compensated associate editor for Headache: The Journal of Head and Face Pain and serves as a non-compensated Board Member-at-Large for the Clinical Neurological Society of America. Katherine Sommer, PhD, is an employee of AbbVie and may hold AbbVie stock. Hope L. O''Brien, MD, MBA, within the past 12 months, has served on advisory boards for, consulted for, and/or been speaker for AbbVie, Eli Lilly, Biohaven, BDSI, Amgen, Guidepoint, Gather-ed, and Medscape. She has served as a non-compensated author for Pfizer. She has received research support to the institution from AbbVie and Eli Lilly along with editorial royalties for UpToDate. She is a member of the American Headache Society, a board member of 1N9 and Ms. Medicine, and serves on committees of the American Academy of Neurology.

Migraine acute therapy

IHC23-IND-005

A Tri-Specific VHH Molecule for the Treatment and Prevention of Episodic Migraines

Ming Huang[1], Cathay Zhan[1], Yi Luo[1], Ziyang Shen[1], Iris Huang[2], Kaiming Liu[3], Yin Zhu[1], Ruyi Mei[4], Xiaoning Liu[4], Gang Lin[4] and Ji Jing[4]

[1]*Biyopharma, Hangzhou, China*
[2]*University of Chicago, Chicago, USA*
[3]*Zhejiang University, Hangzhou, China*
[4]*Zhejiang Cancer Hospital, Institute of Basic Medicine and Cancer (IBMC), Chinese Academy of Sciences, Hangzhou, China*

Objective: Migraines rank sixth among the most disabling diseases, affecting 1.2 billion people around the world. Despite the availability of many medicines, most migraineurs cannot benefit from them.

CGRP antagonists have gained momentum in recent years due to their on-target mechanisms for treating migraines and acceptable side effect profiles. However, CGRP antagonists are not without weaknesses. Small molecules have a limited response rate (about 10%), can cause side effects such as nausea and vomiting that overlap with migraine symptoms, have drug-drug interaction issues, and a short half-life. Meanwhile, large molecules are too expensive for many chronic patients, who must use these medications for many years. Therefore, unmet medical needs exist for an inexpensive CGRP antagonist that can bridge the gap between small and large molecules.

The objective of this study is to develop an inexpensive CGRP antagonist that acts quickly, lasts for a reasonably long time, and is more accessible to migraine patients.

Methods: Single-domain antibodies (VHHs) were chosen due to their small size, stability, and high target specificity. Anti-CGRP receptor VHH and anti-HSA VHH were obtained from llamas that were immunized. Screening, binding, and cell-based functional assays were used to select candidates. Binning and ExchaBody™ screening were used to identify synergistic VHH pairs to create tri-valent molecules.

Results: Eight llamas were immunized with five antigens, including CGRP and the CGRP receptor. After 2 to 3 rounds of panning from 5 phage libraries, 665 positive clones were sequenced, and 20 unique VHHs were identified. Using ExchaBody™ technology, we found two anti-CGRP receptor VHHs that, when linked together, showed much better inhibitory effects in the cAMP assay. To increase the half-life, we fused it with a third VHH that binds human and mouse albumin with similar affinity. After VHH humanization and linker optimization, we obtained a tri-valent molecule (BY002) that has sub-nanomolar affinity, excellent selectivity and superior cellular IC50, approximately five times better than Erenumab, a mAb approved for migraine prevention in 2018.

BY002 is stable for at least 28 days in PBS at 40°C and 4 hours in fresh rat serum at 37°C. When subcutaneously injected into rats, BY002 enters the circulation much faster than a mAb, reaching therapeutic concentration in less than 5 minutes. Additionally, it stays detectable for 30 days after injection.

Conclusion: BY002 is a promising candidate for treating and preventing episodic migraines. It is 42 kD in size, enters the circulation quickly, and stays in the blood for weeks. It can be produced inexpensively using yeast, making it a potentially more accessible and effective treatment option for migraine sufferers.

Migraine acute therapy

IHC23-IND-006

The Impact of Ubrogepant on the Use of Other Migraine Acute Treatments, Opioid Discontinuation, and Medication Overuse: Results From a Pre-Post Opioid Subcohort Analysis

Jessica Ailani[1], Krutika Parikh[2], Sarah Ayton[3], Molly Duan[2], Pranav Gandhi[4], Kandavadivu Umashankar[5], Lauren Wilson[3] and Richard B. Lipton[6]

[1]*MedStar Georgetown University Hospital, Washington, DC, USA*
[2]*AbbVie, North Chicago, USA*
[3]*Genesis Research, Hoboken, USA*
[4]*AbbVie, Madison, USA*
[5]*AbbVie, Irvine, USA*
[6]*Albert Einstein College of Medicine, Bronx, USA*

Objective: This study evaluated baseline characteristics, acute medication fills, opioid discontinuation, and medication overuse headache in new ubrogepant (ubro) patients with prior migraine-related opioid fills.

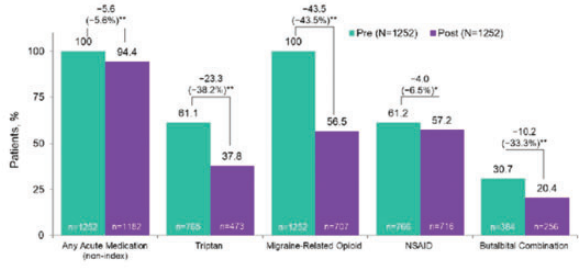
Methods: This study evaluated MarketScan data from 1/2019 to 3/2022. Patients who were ≥18 years of age and had ≥1 claim for ubro after January 1, 2020, ≥1 refill claim for ubro in post-index period, and ≥1 claim for opioid medication for migraine-related use in the pre-index period were included. First fill date for ubro was considered the index date. Patient characteristics, acute medication fills, discontinuation of prior migraine-related opioid medications, acute medication overuse (AMO), and medication overuse headache (MOH) were assessed.

Results: Of 31,516 patients who filled ≥1 prescription for ubro after January 1, 2020, 1607 filled ≥1 prescription for a migraine-related opioid during pre-index period. Of those patients, 1252 filled an additional prescription of

ubro during the 12-month post-index period and were eligible for inclusion. Mean age was 47.8 years, 99.0% of patients were commercially insured, and 54.8% had an exclusive provider organization/preferred provider organization plan. Reductions were observed in the proportion of patients with non-index acute medication fills across all categories after initiating ubro (Figure 1). A 5.6% reduction in patients with any acute medication fill (non-index) was observed after initiating ubro ($P < 0.001$). Highest reductions were seen in migraine-related opioid medication fills (43.5%; $P < 0.001$), followed by triptan fills (38.2%; $P < 0.001$) and butalbital combination medication fills (33.3%; $P < 0.001$). A 12.6% reduction in number of claims for acute medication fills (non-index) was observed following initiation of ubro ($P < 0.001$). Highest reductions in number of claims were in fills of triptans (36.4%; $P < 0.001$), then migraine-related opioid medications (21.2%; $P < 0.001$) and butalbital combination medications (19.2%; $P < 0.001$). Discontinuation rate for migraine-related opioid medications was 66.9% ($n = 838$) in post-index period, including a total of 545 patients (43.5%) who had complete discontinuation of migraine-related opioid medications after initiating ubro. For AMO/MOH, a 19.3% reduction was observed following the initiation of ubro (Figure 2).

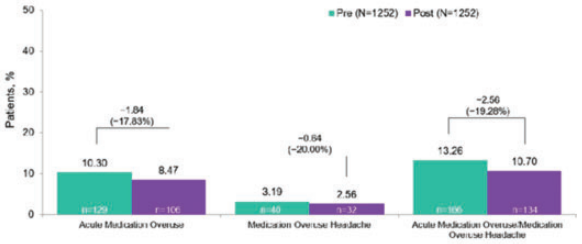
Conclusions: Total of 67% of patients discontinued migraine-related opioid medications, including 44% with complete discontinuation post-ubro initiation.

Figure 1. Proportion of Patients With Acute Medication Fills Other Than Ubrogepant Before and After Initiation of Ubrogepant



*P<0.05. **P<0.001.
XX (%) = Difference (% change).
Migraine-related opioid use indicated a migraine (ICD-10: G43.XXX) diagnosis in the 15-day window prior to (and including) the prescription fill date.
Non-index acute medications included acetaminophen, almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan, dihydroergotamine, ergotamine, amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, metharbital, pentobarbital, phenobarbital, secobarbital, talbutal, barbital, codeine, hydrocodone, meperidine, morphine, oxycodone, propoxyphene, tramadol, aspirin, bromfenac, celecoxib, diclofenac, diflunisal, esomeprazole, etodolac, famotidine, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin, lasmiditan, and rimegepant.
Opioid use included acetaminophen/tramadol, oxymorphone, levorphanol, buprenorphine/naloxone, meperidine, morphine, oxycodone, codeine, methadone, hydromorphone, butorphanol, and tapentadol.

Figure 2. Proportion of Patients With Acute Medication Overuse and/or Medication Overuse Headache Before and After Initiation of Ubrogepant



*P<0.05. **P<0.001.
XX (%) = Difference (% change).
Medication overuse headache was defined using an ICD-10-CM diagnosis code of G44.40.
For acute medication overuse, patients needed to meet the following criteria for each prescription over a 6-month window: mean cumulative days of therapy ≥10 d/mo across all prescriptions for triptans, opioids, ergotamines, or combination analgesics, alone or in combination, and mean cumulative days of therapy ≥15 d/mo across all prescriptions for other simple analgesics alone or in combination.

Disclosure of Interest: Jessica Ailani, MD, has served as a consultant for AbbVie, Aeon, Amgen, Biohaven, Eli Lilly, GlaxoSmithKline, Impel, Lundbeck, Miravo, Nesos, Neurolief, Pfizer, Satsuma, Teva, and Theranica; received stock options from CtrlM; provided editorial services to Current Pain and Headache Reports, SELF, and Medscape; and received clinical trial support from AbbVie, Biohaven, Eli Lilly, Satsuma, and Zosano. Sarah Ayton and Lauren Wilson are employees of Genesis Research, which provides consulting services to AbbVie. Krutika Parikh, PhD; Pranav Gandhi, PhD; Molly Duan, and Kandavadivu Umashankar are employees of AbbVie and may hold AbbVie stock. Richard B. Lipton, MD, has received research support from the National Institutes of Health, the FDA, and the National Headache Foundation. He serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee.

Migraine acute therapy

IHC23-IND-007

Ubrogepant for the Acute Treatment of Migraine When Administered During the Prodrome (Premonitory Phase): Results From a Phase 3, Randomized, Double-blind, Placebo-Controlled, Crossover Study

David W. Dodick[1], Peter J. Goadsby[2,3], Todd J. Schwedt[1], Richard B. Lipton[4], Chengcheng Liu[5], Kaifeng Lu[5], Sung Yun Yu[5], Lawrence Severt[5], Michelle Finnegan[5] and Joel M. Trugman[5]

[1]*Mayo Clinic, Phoenix, USA*
[2]*King's College London, London, United Kingdom*
[3]*University of California, Los Angeles, USA*
[4]*Albert Einstein College of Medicine, Bronx, USA*
[5]*AbbVie, Madison, USA*

Objective: Ubrogepant is a calcitonin gene-related peptide (CGRP) receptor antagonist approved for the acute treatment of migraine. The prodrome is the earliest phase of the migraine attack and is characterized by symptoms other than aura, which precede onset of headache. This study examined the potential of ubrogepant, when administered during the prodrome, to prevent or attenuate headache and disability to evaluate the efficacy, safety, and tolerability of ubrogepant 100 mg when administered during the prodrome (premonitory phase) of a migraine attack.

Methods: PRODROME (NCT04492020) was a multicenter, randomized, double-blind, placebo-controlled, crossover trial. Eligible participants treated 2 "qualifying prodrome events," defined as a migraine attack with prodromal symptoms in which the participant was confident a headache would follow within 1–6 hours. The primary endpoint was absence of moderate/severe intensity headache within 24 hours post-dose. Secondary endpoints were absence of moderate/severe intensity headache within 48 hours, ability to function normally over 24 hours, and absence of a headache of any intensity within 24 hours post-dose.

Results: The safety population included 480 participants and the modified intent-to-treat population included 477 participants. The absence of moderate/severe intensity headache within 24 hours was achieved following 45.5% of ubrogepant-treated qualifying prodrome events vs 28.6% of placebo-treated events ($P < 0.0001$). Absence of moderate/severe intensity headache within 48 hours (40.7% vs 24.6%; $P < 0.0001$), ability to function normally over 24 hours (OR = 1.66; $P < 0.0001$), and absence of headache of any intensity within 24 hours (23.7% vs 13.9%; $P < 0.0001$) were achieved at significantly greater rates following ubrogepant-treated events vs placebo. Ubrogepant was well-tolerated with no new safety signals observed when administered during the prodrome.

Conclusions: Treatment with ubrogepant 100 mg during the prodrome prevented the development of moderate/severe headache for 24 and 48 hours post-dose and headache of any intensity within 24 hours and reduced functional disability compared with treatment with placebo.

Disclosure of Interest: David W. Dodick, MD, reports the following conflicts: Consulting: Amgen, Atria, CapiThera Ltd., Cerecin, Ceruvia Lifesciences LLC, CoolTech, Ctrl M, Allergan, AbbVie, Biohaven, GlaxoSmithKline, Lundbeck, Eli Lilly, Novartis, Impel, Satsuma, Theranica, WL Gore, Genentech, Nocira, Perfood, Praxis, AYYA Biosciences, Revance, Pfizer. Honoraria: American Academy of Neurology, Headache Cooperative of the Pacific, Canadian Headache Society, MF Med Ed Research, Biopharm Communications, CEA Group Holding Company (Clinical Education Alliance LLC), Teva (speaking), Amgen (speaking), Eli Lilly (speaking), Lundbeck (speaking), Pfizer (speaking), Vector Psychometric Group, Clinical Care Solutions, CME Outfitters, Curry Rockefeller Group, DeepBench, Global Access Meetings, KLJ Associates, Academy for Continued Healthcare Learning, Majallin LLC, Medlogix Communications, Medica Communications LLC, MJH Lifesciences, Miller Medical Communications, WebMD Health/Medscape, Wolters Kluwer, Oxford University Press, Cambridge University Press. Non-profit board membership: American Brain Foundation, American Migraine Foundation, ONE Neurology, Precon Health Foundation, International Headache Society Global Patient Advocacy Coalition, Atria Health Collaborative, Arizona Brain Injury Alliance, Domestic Violence HOPE Foundation/Panfila. Research support: Department of Defense, National Institutes of Health, Henry Jackson Foundation, Sperling Foundation, American Migraine Foundation, Henry Jackson Foundation, Patient Centered Outcomes Research Institute (PCORI). Stock options/shareholder/patents/board of directors: Ctrl M (options), Aural analytics (options), Axon Therapeutics, ExSano (options), Palion (options), Man and Science, Healint (options), Theranica (options), Second Opinion/Mobile Health (options), Epien (options/board), Nocira (options), Matterhorn (shares/board), Ontologics (shares/board), King-Devick Technologies (options/board), Precon Health (options/board), AYYA Biosciences (options), Axon Therapeutics (options/board), Cephalgia Group (options/board), Atria Health (options/employee). Patent 17189376.1–1466:vTitle: Onabotulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (Non-royalty bearing). Patent application submitted: Synaquell® (Precon Health). Peter J. Goadsby, MD, PhD, DSc, reports, over the last 36 months, a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly and Company, Epalex,

GlaxoSmithKline, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer, and for medicolegal advice in headache, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee. Todd J. Schwedt, MD, serves on the Board of Directors for the American Headache Society and the American Migraine Foundation. Within the prior 36 months, he has received research support from the American Migraine Foundation, Amgen, Henry Jackson Foundation, Mayo Clinic, National Institutes of Health, Patient-Centered Outcomes Research Institute, SPARK Neuro, and US Department of Defense. Within the prior 36 months, he has received personal compensation for serving as a consultant or advisory board member for AbbVie, Allergan, Axsome, BioDelivery Science, Biohaven, Click Therapeutics, Collegium, Eli Lilly, Equinox, Ipsen, Linpharma, Lundbeck, Novartis, Satsuma, Theranica, and Tonix Pharma. He holds stock options in Aural Analytics and Nocira. He has received royalties from UpToDate. Richard B. Lipton, MD, has received research support from the National Institutes of Health, the FDA, and the National Headache Foundation. He serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee. Chengcheng Liu, PhD, and Joel M. Trugman, MD, are employees of AbbVie and may hold AbbVie stock. Kaifeng Lu; Sung Yun Yu, BA; Michelle Finnegan, MPH; and Lawrence Severt, MD, PhD, were employees of AbbVie at the time of the study and may hold AbbVie stock.

Migraine preventive therapy

IHC23-IND-008

A Bi-Functional Fusion Protein for the Prevention of Refractory Migraine

Ming Huang[1], Iris Huang[2], Yilong Shen[3], Cathay zhan[1], Yi Luo[1], Kaiming Liu[4], Ruyi Mei[5], Xiaoning Liu[5], Gang Lin[5] and Ji Jing[5]

[1]*Biyopharma, Hangzhou, China*
[2]*University of Chicago, Chicago, USA*
[3]*UCLA, Los Angeles, USA*
[4]*Zhejiang University, Hangzhou, China*
[5]*Zhejiang Cancer Hospital, Institute of Basic Medicine and Cancer (IBMC), Chinese Academy of Sciences, Hangzhou, China*

Objective: Chronic migraines affect about 1.5–2% of the global population and are disabling. Despite the development of many preventive treatments, response rates are less than 25%, even with emerging anti-CGRP or anti-CGRP receptor monoclonal antibodies (mAbs). Multiple neuropeptides contributing to migraines are among the main focuses. In this study, we aimed to develop a bispecific fusion protein that can block the signaling of multiple neuropeptides, preventing them from reaching sites of action. This molecule would be an ideal candidate for patients who do not respond to anti-CGRP treatment.
Methods: The fusion protein (BY003) is composed of a single-domain VHH obtained from immunizing llamas with CGRP receptors and a protein that binds neuropeptides. The two functional modules were linked with an ADCC-knockdown human IgG1 Fc, with the the anti-CGRPr VHH located on the N-terminal and the soluble protein on the C-terminal. The affinity of BY003 for targets was determined using ELISA. The inhibition of cAMP production was evaluated using CHO cells overexpressing CGRP. BY003 was also assessed in neuropeptide-challenged rats for its ability to suppress ligand-induced cAMP production.
Results: ELISA shows that BY003 binds specifically to human CGRP receptors with an affinity of 15 pM without binding to rat CGRP or human Amylin-1 receptors. When tested in a cell-based system, BY003 is slightly more potent than Erenumab in inhibiting cAMP production. In in vivo rat studies, BY003 is also shown to significantly block ligand-induced cAMP production. BY003 is stable in PBS for at least 28 days at 42°C and in rat serum for 4 hours at 37°C. PK studies in rats show that BY003 has a half-life that is comparable to a mAb.
Conclusion: We generated the first bi-functional VHH fusion protein that targets multiple neuropeptide pathways. BY003 has high potency on the CGRP receptor with a cellular IC50 of 0.45 nM. BY003 also binds other neuropeptides in vitro and in vivo, resulting in reduced

cAMP production. As a dual function inhibitor, BY003 has the potential to be a preventive medicine for refractory migraine patients.

Migraine preventive therapy

IHC23-IND-009

A Randomized, Double-Blind, Placebo-Controlled Study of Fremanezumab for the Preventive Treatment of Migraine in Chinese Adults: Study Protocol

Xiaoping Ning[1], Steve Barash[1], Zipora Roth-Ben Arie[2], Verena Ramirez Campos[1], Lynda J. Krasenbaum[1] and Andrew H. Ahn[1]

[1]*Teva Branded Pharmaceutical Products R&D, Inc., West Chester, USA*
[2]*Teva Pharmaceuticals Industries Ltd., Petah Tikva, Israel*

Objective: Clinical care guidelines in China state that migraine preventive treatment should be used when the patient's quality of life is seriously impaired, migraine frequency is >2 times per month, or when acute treatment is ineffective or not tolerated. However, there is a need for safe and effective medications in China. Fremanezumab, a humanized monoclonal antibody that selectively targets the calcitonin gene-related peptide pathway, is approved for the preventive treatment of migraine in adults in the United States and Europe. This study aims to demonstrate the efficacy and safety of monthly and quarterly doses of fremanezumab in adult Chinese patients with migraine.
Methods: This efficacy study with an overall duration of 9 months consists of a 4-week baseline period, 12-week double-blind period (DBP), 12-week open-label extension (OLE), and 3-month follow-up. Eligible patients are 18–70 years of age, have a diagnosis of migraine with onset at ≤50 years of age, and a ≥12-month history of migraine prior to screening. In the DBP, patients are randomized to receive monthly (225 mg) or quarterly (675 mg) fremanezumab or matched monthly placebo. During the OLE, all patients will receive monthly fremanezumab treatment. The primary endpoint is the mean change from baseline in average number of monthly migraine days (MMD) during the DBP. Secondary endpoints include mean change from baseline in the frequency of acute headache medication use, the average monthly number of days with headaches of at least moderate severity, and the proportion of patients achieving ≥50% reduction in MMD. Safety and tolerability will be assessed through the reporting of adverse events, including study discontinuations.
Results: The study is currently recruiting patients to 16 study sites across China and has a targeted sample size of 372 patients.
Conclusion: Through the assessment of a range of efficacy and safety outcomes, this study will provide valuable evidence for the use of fremanezumab in adult Chinese patients with migraine.

Migraine preventive therapy

IHC23-IND-010

Adherence and Persistence to Galcanezumab Versus Standard of Care Preventive Migraine Medications over 24 Months Follow-Up in Adults with Migraine

Oralee Varnado[1], Michelle Vu[2], Lars Viktrup[1], Helen Trenz[2], Margaret Hoyt[1], Erin Buysman[2], Feng Cao[2], Gayle Allenback[2] and Gilwan Kim[1]

[1]*Eli Lilly and Company, Indianapolis, USA*
[2]*Optum life sciences, Eden Prairie, USA*

Objective: This study compared the adherence and persistence to galcanezumab (GMB) versus standard of care (SOC) preventive migraine treatments over 24 months (mo) in adults with migraine.
Methods: This retrospective cohort study was conducted using Optum's de-identified Market Clarity Data. Patients included were ≥18 years with ≥1 claim for a newly initiated GMB or SOC preventive migraine therapy from September 2018 – March 2020 (first claim = index date) and continuous health plan enrollment in the 12-mo baseline and 24-mo follow-up periods. Adherence was measured as proportion of days covered (PDC) and medication possession ratio (MPR). Those patients with PDC or MPR ≥ 0.80 were considered adherent to index medication. Persistence was defined as continuous therapy from baseline until the end of the follow-up period, allowing for gaps of <60 days. Comparison between the groups was performed using two-sample t-tests (continuous measures) and Pearson chi-square test (binary measures). All data were presented descriptively with a significance level $p < .001$.
Results: This study included 2,363 patients in the GMB cohort and 61,576 in the SOC. Patient baseline characteristics are presented in Table 1. PDC [mean (SD)] was significantly higher in the GMB cohort vs. the SOC cohort [0.48 (0.33) vs. 0.35 (0.33), $p < .001$]. A greater proportion of patients in the GMB cohort achieved PDC ≥ 0.80 compared to the SOC cohort (26.6% vs. 17.4%, $p < .001$). Similarly, relative to the SOC cohort, the GMB cohort had a higher MPR [mean (SD)] [0.82 (0.21) vs. 0.74 (0.29), $p < .001$] and a greater proportion of patients achieving MPR ≥ 0.80 (67.6% vs. 55.8%, $p < .001$). Percentage of patients persistent at the end of follow-up period was higher in the GMB cohort vs. the SOC cohort

(19.8% vs. 12.7%, $p < .001$). Mean (SD) days of persistence were higher in the GMB cohort than in the SOC cohort [322.2 (263.4) vs. 215.1 (244.5), $p < .001$].

Conclusion: Patients in GMB group were more adherent and persistent to treatment than those on SOC preventive migraine medications over 24-mo follow-up.

Table 1. Patient baseline characteristics

Demographics	GMB (N = 2,363)	SOC (N = 61,576)
Age in years, mean (SD)	44.5 (12.0)	43.3 (13.9)
Female, %	87.1	81.9
Chronic migraine (%)	44.8	20.1
Geographic region (%)		
Northeast	17.0	17.4
Midwest	34.5	41.6
South	35.4	27.0
West	8.0	8.6
Other/Unknown	5.0	5.4
Baseline migraine medications		
Any Preventive (%)[1]	18.7	6.2
Count of unique preventive drug classes		
0	81.3	93.8
1	14.8	5.4
2	3.1	0.7
3+	0.7	0.1
Any Acute (%)[2]	86.0	72.2
Count of unique acute drug classes		
0	14.0	27.8
1	25.9	27.6
2	25.3	22.5
3+	34.7	22.1

GMB = Galcanezumab; SD = Standard deviation; SOC = Standard of Care.

[1]Preventive migraine medication classes include CGRP antagonists (Mab), CGRP antagonists (GePant), beta blockers, anticonvulsants, tricyclic antidepressants, calcium-channel blockers, angiotensin II receptor antagonists, and onabotulinumtoxinA.

[2]Acute migraine medication classes include CGRP antagonists approved for acute treatment, serotonin 5-HTF receptor agonists, triptans, ergotamine, nonsteroidal anti-inflammatory drugs, acetaminophen and combinations, butalbital-containing combinations, antiemetics, isometheptene-containing compounds, and short-acting opioid.

Disclosure of Interest: Oralee Varnado, Lars Viktrup, Margaret Hoyt, and Gilwan Kim are employees and stockholders of Eli Lilly and Company. Michelle Vu, Helen Trenz, Erin Buysman, and Feng Cao are employees and stockholders of Optum life sciences. Gayle Allenback is an employee of Optum life sciences. This study was funded by Eli Lilly and Company. Optum life sciences received funding from Eli Lilly for this study.

Migraine preventive therapy

IHC23-IND-011

Discontinuation, Restart and Switching Patterns of Galcanezumab versus Standard of Care Preventive Migraine Medications over 24 Months Follow-Up in Adults with Migraine

Oralee Varnado[1], Michelle Vu[2], Lars Viktrup[1], Helen Trenz[2], Margaret Hoyt[1], Erin Buysman[2], Feng Cao[2], Gayle Allenback[2] and Gilwan Kim[1]

[1]*Eli Lilly and Company, Indianapolis, USA*
[2]*Optum life sciences, Eden Prairie, USA*

Objective: To compare discontinuation and switching patterns of patients initiating galcanezumab (GMB) versus standard of care (SOC) preventive migraine treatments, such as anticonvulsants, beta-blockers, antidepressants, or onabotulinumtoxinA, over 24 months using administrative claims data.

Methods: This retrospective cohort study utilized Optum's de-identified Market Clarity Data. The study included adults diagnosed with migraine, with ≥1 claim for GMB or a SOC preventive migraine therapy (01 Sep 2018 – 31 Mar 2020), continuous database enrollment for 12 months before (baseline period) and 24 months after (follow-up period) index date (date of first claim). Patients were grouped into GMB and SOC groups based on the claim on index date. Restart was defined as initiation of index medication following discontinuation (based on a 60-day gap) over the follow-up period. Switching was defined as initiation of a non-index preventive migraine treatment after index drug discontinuation. Descriptive analyses were conducted on all study measures.

Results: The GMB and SOC groups comprised of 2,363 and 61,576 patients, respectively. At index, patients had a mean (SD) age of 44.4 (12.0) and 43.3 (13.9) years with 87.1% and 81.9% females and 44.8% and 20.1% with chronic migraine in the GMB and SOC groups, respectively. Over 24 months follow-up, a lesser proportion of GMB initiators discontinued index therapy and were treated for a longer period compared with SOC initiators (**Table 1**). Among those who discontinued, a lesser proportion of patients restarted their index drug and a greater proportion of patients switched to a non-index drug in the GMB group compared with SOC group.

Conclusion: Fewer GMB initiators discontinued therapy; however, of those who discontinued, a greater proportion of GMB initiators switched to a non-index therapy compared with SOC initiators. A limitation of the current study is that it compares a single drug with a drug class. Future studies including patient surveys are necessary to understand reasons for discontinuing and switching migraine preventive therapies.

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Table 1. Treatment patterns during 24-month follow-up

Treatment Patterns	GMB (N = 2,363)	SOC (N = 61,576)	p-value
Patients who discontinued index drug, n (%)	1,834 (77.6)	52,853 (85.8)	<0.001
Days from index date to discontinuation, mean (SD)	221.6 (188.1)	140.0 (155.4)	<0.001
Among patients who discontinued index drug, 60-day gap	**n = 1,834**	**n = 52,853**	
Patients who restarted index drug, n (%)	513 (28.0)	16,711 (31.6)	<0.001
Days from discontinuation date to first restart, mean (SD)	162.5 (125.2)	196.6 (147.6)	<0.001
Patients who switched to non-index preventive migraine treatment, n (%)	761 (41.5)	14,440 (27.3)	<0.001
Days from index date to first switch, mean (SD)	355.5 (195.1)	320.7 (198.2)	<0.001

Note: Two-sample t-test was used for continuous measures. Pearson chi-square test was used for binary measures.
Abbreviations: GMB, galcanezumab; N = number of patients in the overall population; n = number of patients in the specified category; SD, Standard Deviation; SOC, Standard of care.

Disclosure of Interest: Oralee Varnado, Lars Viktrup, Margaret Hoyt, Gilwan Kim are employees and stockholders of Eli Lilly and Company. Michelle Vu, Helen Trenz, Erin Buysman, and Feng Cao are employees and stockholders of Optum life sciences. Gayle Allenback is an employee of Optum life sciences. This study was funded by Eli Lilly and Company. Optum life sciences received funding from Eli Lilly and Company for this study.

Migraine preventive therapy

IHC23-IND-012

Improvement in Patient-Reported Outcomes When Ubrogepant Is Administered During the Migraine Prodrome (Premonitory Phase): Results From the PRODROME Trial

Richard B. Lipton[1], Andrea Harriott[2], Julia Ma[3], Jonathan H. Smith[4], Lawrence Severt[3], Jonathan Stokes[3], Pranav Gandhi[3], Krutika Parikh[5], Joel M. Trugman[3] and David W. Dodick[6]

[1]*Albert Einstein College of Medicine, Bronx, USA*
[2]*Massachusetts General Hospital, Boston, USA*
[3]*AbbVie, Madison, USA*
[4]*AbbVie, Irvine, USA*
[5]*AbbVie, North Chicago, USA*
[6]*Mayo Clinic, Phoenix, USA*

Objective: Ubrogepant is a calcitonin gene-related peptide (CGRP) receptor antagonist approved for the acute treatment of migraine. The PRODROME (NCT04492020) trial demonstrated that treatment during the prodrome prevents the onset of moderate or severe headache and reduces functional disability. Here we examine the benefits of treatment during the prodrome on patient-reported outcomes to characterize the improvement in patient-reported outcomes when ubrogepant is administered during the migraine prodrome (premonitory phase).

Methods: This was a multicenter, randomized, double-blind, placebo-controlled, crossover trial that enrolled adults who experienced 2–8 migraine attacks per month with moderate to severe headache. Eligible participants treated 2 "qualifying prodrome events," defined as a migraine attack with prodromal symptoms in which the participant was confident a headache would follow within 1–6 hours. Participants were randomized to treatment Sequence A (placebo then ubrogepant 100 mg) or Sequence B (ubrogepant 100 mg then placebo). This analysis evaluated the ability to function normally over 48 hours, activity limitation over 24 hours, and satisfaction with study medication at 8 and 24 hours.

Results: Following treatment of qualifying prodrome events, higher rates of ability to function normally over 24 hours were observed following treatment with ubrogepant 100 mg compared with placebo ($P < 0.0001$). Ubrogepant treatment was associated with a higher rate of ability to function normally as early as 2 hours post-dose compared with placebo (37.0% vs 26.1%; nominal $P = 0.0001$). Ubrogepant-treated events also demonstrated higher rates of little or no activity limitations over 24 hours post-dose (65.4% vs 47.8%; nominal $P < 0.0001$). At 24 hours post-dose, rates of being "satisfied" or "extremely satisfied" were higher for ubrogepant than placebo (65.6% vs 45.0%; nominal $P < 0.0001$).

Conclusions: Ubrogepant 100 mg administered during the prodrome was associated with significantly greater ability to function normally, greater satisfaction with study medication, and reductions in activity limitation compared with placebo.

Disclosure of Interest: Richard B. Lipton, MD, has received research support from the National Institutes of Health, the FDA, and the National Headache Foundation. He serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee. Andrea

Harriott, MD, has received personal compensation for serving as an officer or member of the Board of Directors for Headache Cooperative of New England. The institution of Dr. Harriott has received research support from electroCore. Dr. Harriott has a non-compensated relationship as an Author with AbbVie that is relevant to AAN interests or activities. Julia Ma; Jonathan H. Smith, MD; Jonathan Stokes, MBA; Pranav Gandhi, PhD; Krutika Parikh, PhD; and Joel M. Trugman, MD, are employees of AbbVie and may hold AbbVie stock. Lawrence Severt, MD, PhD, is a former employee of AbbVie and may hold AbbVie stock. David W. Dodick, MD, reports the following conflicts: Consulting: Amgen, Atria, CapiThera Ltd., Cerecin, Ceruvia Lifesciences LLC, CoolTech, Ctrl M, Allergan, AbbVie, Biohaven, GlaxoSmithKline, Lundbeck, Eli Lilly, Novartis, Impel, Satsuma, Theranica, WL Gore, Genentech, Nocira, Perfood, Praxis, AYYA Biosciences, Revance, Pfizer. Honoraria: American Academy of Neurology, Headache Cooperative of the Pacific, Canadian Headache Society, MF Med Ed Research, Biopharm Communications, CEA Group Holding Company (Clinical Education Alliance LLC), Teva (speaking), Amgen (speaking), Eli Lilly (speaking), Lundbeck (speaking), Pfizer (speaking), Vector Psychometric Group, Clinical Care Solutions, CME Outfitters, Curry Rockefeller Group, DeepBench, Global Access Meetings, KLJ Associates, Academy for Continued Healthcare Learning, Majallin LLC, Medlogix Communications, Medica Communications LLC, MJH Lifesciences, Miller Medical Communications, WebMD Health/Medscape, Wolters Kluwer, Oxford University Press, Cambridge University Press. Non-profit board membership: American Brain Foundation, American Migraine Foundation, ONE Neurology, Precon Health Foundation, International Headache Society Global Patient Advocacy Coalition, Atria Health Collaborative, Arizona Brain Injury Alliance, Domestic Violence HOPE Foundation/Panfila. Research support: Department of Defense, National Institutes of Health, Henry Jackson Foundation, Sperling Foundation, American Migraine Foundation, Patient Centered Outcomes Research Institute (PCORI). Stock options/shareholder/patents/board of directors: Ctrl M (options), Aural Analytics (options), ExSano (options), Palion (options), Man and Science, Healint (options), Theranica (options), Second Opinion/Mobile Health (options), Epien (options/board), Nocira (options), Matterhorn (shares/board), Ontologics (shares/board), King-Devick Technologies (options/board), Precon Health (options/board), AYYA Biosciences (options), Axon Therapeutics (options/board), Cephalgia Group (options/board), Atria Health (options/employee). Patent 17189376.1–1466:vTitle: Onabotulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (Non-royalty bearing). Patent application submitted: Synaquell® (Precon Health).

Migraine preventive therapy

IHC23-IND-013

The burden of migraine: 3-month findings from the TRIUMPH (Preventive TReatment of mIgraine: oUtcoMes for Patients in Real-world Healthcare Systems) Study

Cristina Tassorelli[1,2], Manjit Matharu[3], Shivang Joshi[4], Sait Ashina[5], Rebecca L. Robinson[6], Diego Novick[6], Carlos Vallarino[6], Lars Viktrup[6] and Maurice Vincent[6]

[1]*Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy*
[2]*Headache Science and Neurorehabilitation Centre, IRCCS Mondino Foundation, Pavia, Italy*
[3]*Headache and Facial Pain Group, UCL Queen Square Institute of Neurology and National Hospital for Neurology and Neurosurgery, London, United Kingdom*
[4]*Community Neuroscience Services, Westborough, MA, USA*
[5]*Comprehensive Headache Center, Department of Neurology and Anesthesia, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA*
[6]*Eli Lilly and Company, Indianapolis, IN, USA*

Objective: Migraine has a considerable impact on quality of life (QoL), work, and social relationships. TRIUMPH is a 2-year study conducted to assess outcomes of migraine preventive treatments in real-world clinical practice. The current analysis describes the changes in migraine burden in the Galcanezumab group and other medication classes [other Calcitonin Gene-Related Peptide monoclonal antibodies (CGRP mAbs), traditional oral migraine preventive medications (TOMP), or botulinum toxin A/B] 3 months after the patients initiated/switched to a new preventive migraine treatment.
Methods: This ongoing, prospective, observational study enrolled patients ($\geq$18 years) from February 2020 to August 2022, with ICHD-3 diagnosis of migraine (episodic or chronic), who switched or initiated preventive treatment. Self-administered questionnaires including the Migraine disability Assessment Test (MIDAS), Migraine-Specific Quality of life questionnaire (MSQ), version 2.1, Patient Global Impression of Severity (PGI-S), Work Productivity and Activity Impairment Questionnaire (WPAI) were used. This interim, preliminary analysis was descriptive in nature and categorical variables were summarized using proportions, until increased sample sizes allow weighted statistical analysis. Continuous variables were summarized using means with standard deviations (SD) at baseline and 3 months, as well as mean change from baseline.
Results: A total of 2573 patients (mean age [SD], 42.7 [13.5] years, 85.2% females) with migraine from the United States (51.4%), Germany (15.4%), Japan (18.4%),

Italy (7.6%), United Arab Emirates (2.8%), United Kingdom (2.4%) and Spain (2.0%) were included. The proportion of patients who initiated/switched to Galcanezumab was 37.0%, TOMP: 46.2%, other CGRP mAbs: 11.5%, botulinum toxin A/B: 3.3%, or other locally approved medications: 1.9%. At baseline, patients had a mean (SD) of 13.2 (7.2) monthly migraine headache days. Overall, 67.9% of patients had chronic migraine, and 41.1% had migraine with aura (visual: 35.8%; sensory: 18.3%). At baseline, the Galcanezumab group tended to have worse scores than TOMP, better than botulinum toxin, and similar to other CGRP mAbs across all measures of migraine burden. At 3 months from baseline, Galcanezumab group had the largest mean (SD) change in MIDAS score (–21.2 [45.7]) and WPAI domains of presenteeism (–22.4 [29.1]), work productivity (–24.2 [30.7]), and activity impairment (–23.1 [30.7]). For the MSQ v2.1 domain scores, the Galcanezumab group reported improvement in restrictive [19.6 (24.3)], preventive [15.9 (21.0)], and emotional function scores [22.1 (27.8)]. Mean (SD) change in PGI-S scores at 3 months from baseline were similar across the treatment groups (Galcanezumab: –0.4 [1.3], other CGRP mAbs: –0.4 [1.2], OTPM: –0.5 [1.3], botulinum toxin A/B: –0.4 [1.3], other locally approved treatments –0.5 [1.3]).

Conclusion: Although all patients presented high but different levels of migraine burden at baseline, those initiating Galcanezumab treatment tended to present greater numerical improvement from baseline for the majority of scales than the other drug classes. However, further substantiation of these findings depends on weighted statistical analyses of patient reported outcomes scheduled for subsequent timepoints with increased sample size.

Table 1: Baseline migraine burden of patients before switching to or initiating Galcanezumab, other CGRP mAbs, TOMP, or botulinum toxin A/B[#]

Baseline Migraine burden, mean (SD)	Overall (n=2573)	Galcanezumab (N=953)	Other CGRP mAbs[a] (n=297)	TOMP[b] (n=1189)	Botulinum Toxin A/B (n=84)
MIDAS summary score	46.1 (45.2)	52.7 (48.8)	48.0 (42.8)	38.6 (39.3)	78.7 (60.4)
MSQ v2.1 Restrictive score	46.5 (21.3)	42.5 (20.6)	46.4 (19.9)	50.5 (21.3)	30.2 (21.5)
MSQ v2.1 Preventive score	63.2 (22.6)	60.1 (22.5)	62.9 (22.1)	66.3 (21.9)	49.3 (27.8)
MSQ v2.1 Emotional function score	53.9 (28.3)	48.9 (28.5)	52.6 (28.0)	58.9 (27.1)	40.2 (29.2)
PGI-S score	4.3 (1.3)	4.5 (1.2)	4.3 (1.2)	4.0 (1.3)	4.7 (1.4)
WPAI – Presenteeism score	50.1 (26.1)	51.0 (25.3)	50.8 (26.8)	49.3 (26.8)	55.3 (19.5)
WPAI – Absenteeism score	10.9 (20.4)	13.5 (21.4)	12.6 (23.6)	8.2 (17.1)	27.0 (36.1)
WPAI – Work productivity loss score	53.4 (27.0)	55.0 (26.7)	54.7 (27.2)	52.0 (27.5)	59.9 (19.8)
WPAI – Activity impairment score	55.3 (25.4)	56.7 (25.1)	54.9 (24.3)	54.1 (25.7)	67.3 (24.1)

[a]Other CGRP mAbs included Eremumab, Fremanezumab, Eptinezumab. [b]TOMPs included beta blockers, anticonvulsants, tricyclic antidepressants, calcium channel blockers, and angiotensin II receptor antagonists.
[#] Data for locally approved treatments are not shown because of the small sample size.
Abbreviations: CGRP: Calcitonin Gene-Related Peptide; mAb: Monoclonal antibodies; MIDAS: Migraine Disability Assessment; MSQ: Migraine-specific Quality of Life Questionnaire; TOMP: Traditional Oral Migraine Preventive Medications; PGI-S: Patient Global Impression of Severity; SD: Standard Deviation; WPAI: Work Productivity and Activity Impairment.

Disclosure of Interest: CT is employed by the University of Pavia and is affiliated with Neurological Institute C Mondino Foundation Society, she holds a leadership/board position and is a co-sponsor at "Headache research Priorities" in collaboration with AHS, serves as a member of Italia Medical Association, Italian Society of Neurology, Italian Headache Society (SISC), Fellow of EAN and the Board of the Italian Full Professors of Neurology. She reports scientific consultant fees from Allergan/Abbvie, Lilly, Novartis, Lundbeck, Pfizer, Biohaven, Teva, WebMD, and research support from Allergan/Abbvie (to institution). She serves on the advisory board at Allergan/Abbvie, Dompé, Lilly, Novartis, Lundbeck, Biohaven, Teva and WebMD and the editorial board at Journal of Headache and Pain and Cephalalgia. Clinical trials involvement: Allergan/Abbvie, Amgen, Lilly, Novartis, Lundbeck, Teva (all payments made to institution). MM has received grants or contracts from Abbott and Medtronics, received consulting fees from Allergan, Eli Lilly, Novartis, and TEVA and has received payment or honoraria for lectures, presentations, speakers" bureaus, manuscript writing or educational events from Allergan, Salvia, Eli Lilly, Novartis and Teva. SJ has no conflicts to report. SA reports consulting, teaching, honoraria: Allergan, Amgen, Biohaven Pharmaceuticals, Eli Lilly and Company, Impel NeuroPharma, Novartis, Satsuma, Supernus, Percept, and Theranica. RLR, DN, CV, LV and MV are employees of Eli Lilly and Company and may own Lilly stock.

Migraine preventive therapy

IHC23-IND-014

UNITE: Efficacy and Impact of Fremanezumab in Patients with Migraine and Major Depressive Disorder

Verena Ramirez Campos[1], Richard B. Lipton[2], Lynda J. Krasenbaum[1], Xiaoping Ning[1], Piero Barbanti[3], Zipora Roth-Ben Arie[4], Maja Galic[5], Lex Denysenko[6,7], Michael Marmura[8], Peter McAllister[9] and Dimos Mitsikostas[10]

[1]*Teva Branded Pharmaceutical Products R&D, Inc., West Chester, USA*
[2]*Departments of Neurology, Psychiatry & Behavioral Sciences, Albert Einstein College of Medicine, New York, USA*
[3]*Headache & Pain Unit, IRCCS San Raffaele, San Raffaele University, Rome, Italy*
[4]*Teva Pharmaceuticals Industries Ltd., Petah Tikva, Israel*
[5]*TEVA-PHARMA, Produtos Farmacêuticos, Lda., Porto Salvo, Portugal*
[6]*Jefferson Headache Center, Departments of Neurology, Thomas Jefferson University Hospital, Philadelphia, USA*
[7]*Department of Psychiatry & Human Behavior, Thomas Jefferson University Hospital, Philadelphia, USA*
[8]*Jefferson Headache Center, Department of Neurology, Thomas Jefferson University Hospital, Philadelphia, USA*
[9]*New England Institute for Neurology & Headache, Stamford, USA*
[10]*Department of First Neurology, Aeginition Hospital, National and Kapodistrian University of Athens, Athens, Greece*

Objective: To evaluate the efficacy and impact of fremanezumab in patients with migraine and major depressive disorder (MDD).
Methods: A 12-week randomized (1:1), Phase 4 study with a 12-week open-label extension (OLE). Patients (12 months MDD [DSM-V, PHQ-9 score ≥10]) received monthly fremanezumab (225 mg) or matched placebo (PBO) for 12 weeks. OLE patients received quarterly fremanezumab (675 mg). Primary endpoint: mean change (baseline [BL]) to Week 12) in average number of monthly migraine days (MMD). Secondary endpoints: mean change from BL in symptoms of depression (HAMD-17, PHQ-9), disability (HIT-6, CGI-S), patients achieving ≥50% MMD reduction (BL to Week 12).
Results: 330/353 patients (fremanezumab, n = 164; PBO, n = 166) completed the 12-week period. Fremanezumab showed statistically significant reductions in MMD and depression scores (**Table**). Results were maintained through the OLE. Safety was consistent with pivotal fremanezumab RCTs, with AEs reported in 40% (fremanezumab) vs 27% (PBO) patients.
Conclusion: In these patients, fremanezumab showed a reduction in MMDs and depression scores that were maintained in the OLE. Fremanezumab may reduce the burden of these comorbid diseases and improve quality of life.
Disclosure of Interest: R.L. has received research support from the NIH, FDA, Alzheimer's Association, National Headache Foundation, Marx Foundation, Allergan/Abbvie, Amgen, Eli Lilly, and Electrocore; personal fees as a consultant or advisor from Allergan/Abbvie, Amgen, Biohaven, Dr. Reddy's, GlaxoSmithKline, Grifols, Impel, Novartis, Eli Lilly, Lundbeck, Pfizer, and Teva Pharmaceuticals; and holds stock or options in Biohaven and Manistee; P.B has received travel grants, honoraria for advisory boards, speaker panels or clinical investigation studies from Alder, Allergan, Angelini, Assosalute, Bayer, ElectroCore, Eli-Lilly, GSK, Lundbeck, 1MED, MSD, New Penta, Noema Pharma, Pfizer, Novartis, Stx-Med, Teva, Visufarma, and Zambon; M.M has received compensation for consultation from Lumbeck, Axsome, Upsher-Smith, Theranica, and Satsuma; has participated in speaker bureaus for Eli Lilly and Amgen; and has received institutional support for serving as principal investigator from Teva and AbbVie; D.M has received consulting fees, speaking fees, and travel grants from Allergan, Amgen, Bayer, Biogen, Cefaly, ElectroCore, Eli Lilly, Genesis Pharma, Merck Serono, Merz, Mylan, Novartis, Roche, Sanofi Genzyme, Specifar, and Teva Pharmaceuticals; is serving as associate Editor for the Journal of Headache and Pain, President of the Hellenic Headache Society and Co-Chair of the Headache Scientific Panel at the European Academy of Neurology; and has served as principal investigator for Phase 3 and 4 trials for Amgen, Biogen, Genesis Pharma, Eli Lilly, ElectroCore, Lundbeck, Novartis, and Teva Pharmaceuticals; P.A. has received consulting fees from Revance, AbbVie, Lundbeck, Theranica, and Upsher-Smith; has participated in speaker bureaus for Lundbeck, Impel, Abbvie, and Pfizer, and has received research support from Revance, Lundbeck, Abbvie, Amgen, and Pfizer; V.R.C, Z.R-BA, L.J.K, X.N, and M.G are employees of Teva Pharmaceuticals; L.D. has no disclosures to declare.

Migraine preventive therapy

IHC23-IND-015

Time-course Analysis of Remote Electrical Neuromodulation (REN) for Migraine Prevention

Andrew Blumenfeld[1], Liron Rabany[2], Alon Ironi[2], Alit Stark-Inbar[2], Dagan Harris[2], Andrea Harriott[3] and Rashmi Halker Singh[4]

[1]*The Los Angeles Headache Center, Los Angeles, CA, USA*
[2]*Theranica Bio-Electronics, Netanya, Israel*
[3]*Massachusetts General Hospital, Boston, MA, USA*
[4]*Mayo Clinic, Scottsdale, AZ, USA*

Background: Remote electrical neuromodulation (REN) is a migraine treatment that stimulates upper arm peripheral nerves to induce conditioned pain modulation (CPM) – an endogenous analgesic mechanism.

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Table. Primary and Secondary Endpoints

	Week 8			Week 12		
	Fremanezumab	PBO	P value	Fremanezumab	PBO	P value
Mean change from BL						
MMD	–	–	–	–5.1	–2.9	<0.0001
HAMD-17	–6.0	–4.6	0.0205	–6.7	–5.4	0.0228
PHQ-9	–7.1	–5.8	0.0283	–7.8	–6.3	0.0108
HIT-6	–	–	–	–8.8	–5.2	≤0.0001
CGI-S	–1.0	–0.6	0.0006	–1.1	–0.8	0.003
≥50% MMD reduction (% patients)	–	–	–	33	13	<0.0001

REN is indicated for acute and/or preventive treatment of migraine with or without aura in patients 12 years of age or older. It is a prescribed, self-administered device for use in the home environment. It can be used every other day for preventive treatment, and/or at the onset of migraine headache or aura for acute treatment. In a recent prospective, randomized, double-blind, placebo-controlled trial, REN was shown to be safe and effective for the prevention of migraine. The current analysis assessed the temporal patterns of response to REN treatment, used every other day over two months, for the prevention of migraine.

Methods: The current post-hoc analysis was conducted on data from a prospective, double-blind, placebo-controlled multi-center randomized clinical trial, which assessed the efficacy of REN treatment, applied every other day, for the prevention of migraine (NCT04828707). Participants were men and women aged 18–75. Following 4 weeks of baseline, patients were randomly assigned to receive either a REN device (Nerivio), or a placebo device. Participants were instructed to use the device every other day for eight weeks, and to report their migraine attacks daily via a designated smartphone app. The mean number of monthly migraine days (MMD) per group was calculated in two-week intervals (using a sliding window of four weeks). A repeated measures ANOVA was used, with group as the independent variable, and time as the dependent variable. Sub-analyses of change from baseline in MMD in the episodic and chronic sub-samples were also performed. The analyzed dataset included 179 participants (active group $N = 95$, placebo group $N = 84$).

Results: The differences between the active and placebo groups demonstrated statistical significance as early as the first tested timepoint of 2-weeks of treatment (active:1.67 MMD $\pm$ SE of 0.23 days; placebo: 0.83 ± 0.24 MMD), resulting in a therapeutic gain of 0.84 monthly migraine days, $p = 0.036$. The differences between the groups further increased over time: 4-weeks therapeutic gain of 1.59 $p = 0.025$, 6-weeks therapeutic gain of 2.27 $p < 0.001$, and peak therapeutic gain of 2.68 $p < 0.001$ after 8-weeks.

Analyses of the chronic and episodic subsets indicate a similar trend in both sub-groups. The episodic sub-set displayed statistical significance starting at the first measured timepoint of two weeks ($p = 0.039$). The chronic sub-set's results became statistically significant at the 6-week timepoint ($p = 0.019$).

Conclusion: The results indicate a rapid and effective response to REN treatment applied every other day, at as early as two weeks from the beginning of the treatment, with increased efficacy over time.

Disclosure of Interest: Dr. Blumenfeld: Speaker bureau/advisory board – Abbvie, Allergan, Aeon, Biohaven, Lilly, Impel, Collagium, Amgen, Lundbeck, Theranica, Axsone, Revance. Dr. Rabany, Dr. Stark-Inbar, Dr. Harris and Mr. Ironi are Thranica employees. They receive a salary and hold stock options. Dr. Harrriott: Science Committee American Academy of Neurology, Board of Directors of the American Headache Society, Board of Directors American Migraine Foundation, Board of Directors Headache Cooperative of New England, Scientific Advisory Board for Theranica, Authorship agreement Abbvie, Received study drug for research from Praxis Inc. Dr. Halker Singh: Royalties- Oxford University Press, Editorial services- Current Neurology and Neuroscience Reports, Headache Journal

Migraine preventive therapy

IHC23-IND-016

Reduction in headache days with treatment is more important for migraine patients than if the treatment is administered subcutaneously or orally: Results from a Patient Preference Survey on calcitonin gene-related peptide (CGRP) antagonists

Chiara Whichello[1], Lars Viktrup[2], Oralee J. Varnado[2], Matt Quaife[1], Myrto Trapali[1] and Antje Tockhorn-Heidenreich[2]

[1]*Evidera, London, United Kingdom*
[2]*Eli Lilly and Company, Indianapolis, Indiana, USA*

Objectives: Novel therapies for the acute and preventive management of migraine act via antagonism of calcitonin gene-related peptide (CGRP). The monoclonal antibodies (mAbs) to CGRP or its receptor (galcanezumab, fremanezumab, erenumab) may be administered by monthly subcutaneous injection for the prevention of migraine. In comparison, small-molecule CGRP receptor antagonists (rimegepant and atogepant) are administered orally every other day or daily when used as preventive treatment. There are currently no head-to-head studies published that explore whether there are differences in clinical efficacy, safety or tolerability between the self-injectable CGRP mAbs or oral gepants. Patient preference studies can help determine the relative importance that patients place on different treatment characteristics. Here, we present a discrete choice experiment (DCE) that assessed the preferences of people with episodic migraine for the attributes of self-injectable CGRP mAbs and an oral gepant. A key advantage of DCEs is their ability to quantify trade-offs participants make, allowing an estimation of how much of an attribute a participant is willing to give up in order to get more or less of another attribute. DCEs can also be used to calculate the probability that a participant would prefer one treatment profile over another.

Methods: Individuals in the United States $\geq$18 years of age with episodic migraine were recruited to an on-line DCE survey. Participants were asked to choose their

preferred hypothetical treatment from alternatives with 5 attributes: administration (once monthly self-injection, orally disintegrating tablet every other day, and oral pill daily), chance of ≥50% reduction in monthly migraine headache days, time to onset, impact of migraine on daily activities (minimally, moderately, and extremely impaired, according to the Migraine-Specific Quality of Life Questionnaire – role function restriction subdomain), and reduction in the number of days with acute medication use. Participants indicated their preferred choice from among several scenarios with differing attributes and levels of attributes. The relative attribute importance (RAI) scores indicating how important an attribute is in comparison to the remaining attributes were calculated using a mixed logit model.

Results: A total of 601 participants (300 with clinical documentation of diagnosis) completed the DCE survey. Mean (standard deviation) age was 44.8 (13.0) years, and a majority (67.6%) were female. Approximately half (51.0%) experienced ≥8 migraine headache days per month. More than two-thirds of participants had previously used preventive treatments for migraine, and over half (53.2%) of the participants had experience with a ready-to-use syringe. More than one-half (57.8%) of the participants were "not at all" or "a little" afraid of injecting themselves with a medicine.

The attribute of a ≥50% reduction in the number of monthly migraine headache days, with an RAI score 36.3% (95% CI: 32.1%; 40.5%) was the most important driver of the participants" preferences for a migraine treatment., followed by the impact on daily activities (RAI: 24.4%; 95% CI: 20.0%; 28.8%), treatment onset (RAI: 19.5%; 95% CI: 16.3%; 22.6%), reduction in acute medication (RAI: 15.2%; 95% CI: 11.9%; 18.5%). Treatment administration was the least important driver of patient preferences (RAI: 4.6%; 95% CI: 0.7%; 8.5%).

These results indicate that participants felt that reducing the chance of having a migraine attack was 7.9 times more important than the way that treatment was administered (36.3%/4.6% = 7.9), and more important than treatment onset (19.5%) and reduction in acute medication use (15.2%). Participants also indicated that reducing the impact of migraine on daily activities (24.4%) was more important than time to onset (19.5%) and treatment administration (4.6%). Patients who were "not at all" or "a little" reluctant to self-inject had a significantly higher RAI for treatment administration (27% vs. 5%, $p < 0.001$) compared with the overall sample.

Conclusion: Patients with episodic migraine value the chance of achieving ≥50% reduction in monthly migraine headache days being most important, and the method of administration as the least important attributes when choosing between potential treatments. Other treatment aspects presented varying degrees of importance between these extremes. A patient-centered treatment strategy should consider the relative importance of treatment aspects to patients.

Disclosure of Interest: CW, MQ, and MT are employees of Evidera. AT-H, LV, and OJV are employees of Eli Lilly and Company and may own Lilly stock.

Migraine preventive therapy

IHC23-IND-017

Insights into migraine patient characteristics and treatment patterns: Interim baseline results from the TReatment of mIgraine: oUtcoMes for Patients in real-world Healthcare systems Europe (TRIUMPH [Europe]) study.

Niraj Patel[1], Diego Novick[1], Gina Kennedy[2], Georgia Martimianaki[1], Hugo Gabilondo[1] and Patricia Pozo-Rosich[3,4]

[1]*Eli Lilly and Company, Indianapolis, Indiana, USA*
[2]*South Tyneside and Sunderland NHS Foundation Trust, South Tyneside and Sunderland, United Kingdom*
[3]*Headache Unit, Neurology Department, Vall d"Hebron University Hospital, Barcelona, Spain*
[4]*Headache and Neurological Pain ResearchGroup, Vall d"Hebron Institute of Research (VHIR), Departament de Medicina, Universitat Autònoma de Barcelona, Barcelona, Spain*

Objectives: To describe baseline clinical characteristics of patients with migraine in routine clinical care who are switching or initiating pharmacological treatment for migraine prevention within TRIUMPH [Europe], with a focus on those initiating galcanezumab.

Methods: TRIUMPH is an ongoing, 24-month observational study investigating migraine prevention treatment in the United States, Japan, Europe (Germany, Italy, Spain, and United Kingdom [UK]) and United Arab Emirates. Eligible patients are ≥18 years old, have a migraine diagnosis and are switching or initiating pharmacological treatment for migraine prevention. Interim cross-sectional baseline clinical characteristics, current and historical migraine treatment patterns, and quality of life indicators were collected June 30, 2020 to August 26, 2022. Data are presented as percentages or mean ± standard deviation.

Results: TRIUMPH [Europe] enrolled 706 patients aged 41.2 ± 13.1 years, 85.4% were females. Patients initiated galcanezumab (n = 313), other calcitonin gene-related peptide monoclonal antibodies (n = 57), Traditional Oral Migraine Preventive (TOMP) medications (n = 292), botulinum toxin (n = 33) or other locally approved treatments (n = 11). Patients first experienced migraine symptoms 21.8 ± 14.0 years prior to enrolment and have been diagnosed for 12.1 ± 11.9 years. The number of monthly headache days and monthly migraine headache days was 14.7 ± 7.8 and 13.1 ± 6.9 days for all patients, respectively and 16.5 ± 8.0

and 15.0 ± 7.0 days for patients initiating galcanezumab. The number of monthly migraine headache days with acute medication use was 10.9 ± 6.6 days for the total cohort and 12.6 ± 7.0 days for those initiating galcanezumab.

Conclusion: At baseline, patients enrolled in TRIUMPH [Europe] initiating galcanezumab reported more headache days, migraine headache days and migraine headache days with acute medication use than the overall enrolled cohort.

Disclosure of Interest: NP, DN, GM, HG are full-time employees of Eli Lilly and Company. GK reports partnership agreement in progress to support a headache diary app, consulting fees from Pfizer, honoraria from Abbvie and Eli Lilly and Company, travel and meeting attendance support from TEVA, Electrocore, Abbvie and Eli Lilly and Company, and an unpaid board membership of BASH council. PPR reports honoraria as a consultant and participation in the last three years in advisory boards for AbbVie, Amgen, Biohaven, Eli Lilly, Lundbeck, Novartis, Pfizer and Teva Pharmaceuticals; institutional research support from AbbVie, AGAUR, EraNet NEURON, Instituto Investigación Carlos III, International Headache Society, Novartis, PERIS, RIS3CAT FEDER, and Teva Pharmaceuticals; being a principle investigator for over 50 clinical trials (phases II, III, and IV) for the preventive treatment of migraine and other headaches; education projects with AbbVie, Almirall, Chiesi, Eli Lilly, Lundbeck, Medlink, Medscape, Neurodiem, Novartis, Pfizer and Teva Pharmaceuticals; participation in the Scientific Advisory Board of Lilly Foundation Spain and Honorary Secretary of the International Headache Society; and being an associate editor for Cephalalgia, Headache, Neurologia and The Journal of Headache and Pain.

Big data

IHC23-PO-001

GPT3 Meets PubMed: A Novel Approach to Meta-Analysis Using a Large Language Model to Crowdsource Migraine Medication Reviews

Elyse Mackenzie, Roger Cheng and Pengfei Zhang

Rutgers University, New Brunswick, USA

Introduction: Sentiment analysis is a class of machine learning algorithm often used to quantify positive/negative experiences (such as user reviews) with products or services for strategic decision-making. Recently, Myszewski et al. successfully applied sentiment analysis to meta-analysis in a clinical setting by using a generative adversarial network (GAN). In this study, we attempt to use the large language model (LLM) GPT-3.5 (OpenAI Incorporated, via ChatGPT) to identify favorable migraine medications from clinical trial abstracts in PubMed as a pilot study.

Methods: This project was separated into three phases. In the first phase, we identified and acquired relevant article abstracts in PubMed through the MeSH search term "migraine disorders[mh]." Resulting clinical trial abstracts were then included for our study. We also created a list of FDA approved medications and biologics by extracting their generic names from their reference guide of approved medications (the "Orange Book" and "Purple Book") for use in the subsequent phase.

We inputted the text abstracts of each clinical trial into the application programming interface (API) for ChatGPT, with a specific prompt to 1) process and list all medications/biologics in the abstract, and 2) determine a positive, negative, or indifferent sentiment for each identified item. If a medication/biologic had a positive sentiment in the abstract, it received a score of 1; a negative sentiment received a score of −1, and an indifferent sentiment received a score of 0. We requested that ChatGPT structure its output for each abstract as sets of tuples in the format ("medication", sentiment").

Some ChatGPT output included non-drug words, or nonsensical words, such as portions of drug names or base components (i.e. "acid," "ether"). These were manually screened out using our FDA medication list.

During the final evaluation phase, each medication/biologic received a cumulative "score" where the totality of 1s, 0s, or −1s from phase two were added in sum.

Results: Data identification and acquisition was completed on January 8, 2023. A total of 2700 clinical trials were downloaded. ChatGPT API evaluation was completed on March 24th, 2023. While the majority of the ChatGPT output was in the requested tuples format, a minority of outputs were not, and therefore required separate processing to unify the output format.

Excluding non-sensical entries as described above, the ten most favorable medications described in clinical trials were sumatriptan, topiramate, rizatriptan, zolmitriptan, almotriptan, erenumab, naproxen, valproate, metoclopramide, and galcanezumab. The remainder of the top 30 medications are shown in Table 1.

Discussion/Conclusion: The majority of the medications identified with the method above are familiar to practicing headache medicine clinicians as evidence-based medications used for either abortive or preventive treatment of migraine. While traditional meta-analyses are time consuming, sentiment analysis may provide an economical alternative for real-time incorporation of primary literature into patient care. It also may aid in identification of novel approaches to problems and/or areas of study, such as evaluating treatments described in case reports. Some known limitations of ChatGPT translate directly into our study: 1) GPT3 outputs are of inconsistent format despite a consistent input prompt, which raises some questions about repeatability. 2) Misinformation and overconfidence are well-publicized weaknesses of GPT-3, and by the nature of the model, there is very limited rationale to explain these outputs. As these limitations are known

with reported efforts to be improved on in subsequent iterations, a comparison of our results to a GPT-4 implementation in the near future might better define these limitations. Future refined implementation of our algorithm may be used to support physician decision-making in medication management, saving time and resources for more nuanced analysis of the patient at hand.

Table 1: Sentiment analysis output for clinical trials

ChatGPT Clinical Trials Sentiment:	
Drug	**Output**
sumatriptan	244
topiramate	73
rizatriptan	66
zolmitriptan	57
almotriptan	44
erenumab	37
naproxen	37
valproate	31
metoclopramide	31
galcanezumab	30
frovatriptan	26
lasmiditan	23
eletriptan	23
onabotulinumtoxina	23
fremanezumab	21
eptinezumab	20
naratriptan	16
prochlorperazine	14
metoprolol	11
diclofenac	11
venlafaxine	10
ubrogepant	9
ketorolac	9
verapamil	8
nimodipine	8
ketoprofen	7
fluoxetine	7
bupivacaine	7
timolol	6
rimegepant	6

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IHC23-PO-002

Developing an Artificial Intelligence-Based Headache Diagnostic Model Based on Experiences Gained from Prevalence Surveys and Awareness-raising Activities

Masahito Katsuki[1,2], Yasuhiko Matsumori[3], Akihito Koh[1], Naomichi Wada[2], Tetsuya Goto[2] and Fuminori Yamagishi[1]

[1]*Itoigawa General Hospital, Itoigawa, Japan*
[2]*Suwa Red Cross Hospital, Suwa, Japan*
[3]*Sendai Headache Neurology Clinic, Sendai, Japan*

Introduction: We investigated the prevalence of medication-overuse headache. Then we succeeded in the large-scale headache awareness campaign in Itoigawa City. Through these experiences, it was found that the physician did not spend enough time interviewing the patient about the headache and could not properly diagnose the headaches. Also, many respondents were dissatisfied with the doctor's diagnosis and treatment and would not see the doctor. Therefore we identified the need for AI-based headache diagnostics and developed the AI model. AI diagnostic models can accurately diagnose headaches with only a medical questionnaire sheet, thereby reducing interview time by a doctor, avoiding misdiagnosis, and potentially simulating the experience of a visit to a specialist at any time from the comfort of one's home.
Methods: We developed an AI-based diagnostic model from a retrospective investigation of 6058 patients (4240 training and 1818 test dataset) diagnosed by a headache specialist. The ground truth was the diagnosis by the headache specialist.
Results: About the AI-based headache diagnosis model, the dataset included about 80% of the patients who had migraine, 13% tension-type headaches, 1% trigeminal autonomic cephalalgias, 1% other primary headaches, and 5% secondary headaches. The mean age was approximately 35 years, and 66% were women. The model's micro-average accuracy, sensitivity (recall), specificity, precision, and F values for the test dataset were 90.81%, 90.81%, 90.81%, 97.70%, and 90.81%, respectively.
Conclusions: We conducted the epidemiological survey and this campaign. We finally developed the AI-based headache diagnosis model, and it will solve the unmet need in clinical headache practice.
Disclosure of Interest: None Declared

IHC23-PO-003

Impact of primary headache on daily activities from real world data in Japan

Koichi Hirata[1], Hiromi Sano[2], Hiroyuki Kondo[3], Nobuyuki Koga[4] and Yoshiyuki Shibasaki[3]

[1]*Dokkyo Medical University, Tochigi, Japan*
[2]*Otsuka Pharmaceuticals Co., Ltd, Medical affairs, Osaka, Japan*
[3]*Otsuka Pharmaceuticals Co., Ltd, Medical affairs, Tokyo, Japan*
[4]*Otsuka Pharmaceuticals Co., Ltd, Medical affairs, Tokushima, Japan*

Objective: To understand primary headache, inducing factors, interference with daily life, and related issues according to type.
Methods: Study participants were members of the health insurance union (n = about 550,000), registered with the health promotion support application "kencom" provided by DeSC (n = about 200,000), and aged 19–74 years. A self-administered questionnaire survey was conducted using kencom® with 21,480 valid responses received. Only de-identified, previously generated information was used in this study. From the questionnaire results, we classified the headache as migraine, tension-type, and cluster according to the International Classification of Headache Disorders, 3rd edition .
Results: Survey results showed 691, 1441, and 21 participants experienced migraine, tension-type, and cluster headache, respectively. Regarding headache triggers, fatigue and stress were most commonly selected in migraine (47.3% and 44.4%, respectively) and tension-type headache (45.0% and 34.7%). Regarding menstruating females, approximately half of participants in all headache types indicated "menstruation" as a trigger factor. Regarding interference with daily life, "unable to concentrate on (or unable to make progress with) work or study", "unable or unmotivated to perform household chores", and "unmotivated to work or study" were ranked higher in all headache types. When "refraining from activities because of headache" was analyzed by sex, migraine and tension-type headache showed that "operation of PCs and smartphones" and "drinking alcohol" were ranked higher in both males and females; "shopping, cooking, laundry, and others" was higher in females. Work Productivity and Activity Impairment Questionnaire scores were lower for tension-type headache and higher for cluster headache compared to that of migraine.
Conclusion: This study revealed the characteristics and impact on daily life of primary headache according to headache type. When limiting to females, household chores were also included in Japan where females have a high rate of household chore burden. These study results have clinical value in the diagnosis and treatment of primary headache.
Disclosure of Interest: KH has an advisory role for Otsuka Pharmaceutical Co., Ltd. HS, HK, NK and YS are employees of Otsuka Pharmaceutical Co., Ltd.

IHC23-PO-004

Effect of body weight on the risk of migraine: a nationwide cohort study

Namoh KIM[1], Kyungdo Han[2] and Mi Ji Lee[1,3]

[1]*Department of Neurology, Seoul National University Hospital, Seoul, Korea, Republic of*
[2]*Department of Statistics and Actuarial Science, Soongsil University, Seoul, Korea, Republic of*
[3]*Seoul National University College of Medicine, Seoul, Korea, Republic of*

Background: While migraine is a genetically predisposed disorder, lifestyle factors and medical comorbidities can influence the development of migraine attacks. Obesity is recognized as a risk factor of migraine chronification in cross-sectional studies and 1-year longitudinal study. In this study, we aimed to investigate the effect of body weight on the incidence of migraine in young adults with long-term follow up.
Methods: Using a nationally representative database from the Korean National Health Insurance System, 6,891,400 individuals aged $\geq$20 and $<$40 years who underwent regular health checkups between 2009 and 2012 were followed up until the end of 2018. The body mass index (BMI) was stratified into 5 groups: underweight (BMI $<$ 18.5 kg/m^2), normal ($\geq$18.5 to $<$23 kg/m^2), overweight ($\geq$23 to $<$25 kg/m^2), stage 1 obesity ($\geq$25 to 30 kg/m^2), and stage 2 obesity ($\geq$ 30 kg/m^2). Obesity was defined as BMI $\geq$25, and abdominal obesity was classified based on waist circumference (WC) ($\geq$90 cm in men and $\geq$85 cm in women). The independent effect of BMI and obesity and its interaction with abdominal obesity on the risk of migraine incidence were expressed as hazard ratio (HR) and 95% confidence interval (CI) using a Cox proportional hazard regression model adjusted for age, sex, household income, hypertension, diabetes mellitus, dyslipidemia, smoking, alcohol assumption, and regular physical activity.
Results: A total of 6,106,560 individuals (61% men; 39% women) were included in the analysis. 61.0% patients were men. Compared to the normal BMI group as reference, the risk of migraine increased as BMI increased: adjusted HR 1.047 (95% CI 1.040, 1.055), 1.087 (95% CI 1.079, 1.094), and 1.121 (95% CI 1.106, 1.136) in overweight, stage 1 obesity, and stage 2 obesity groups. The bidirectional interaction between obesity and abdominal obesity

was present; obesity decreased the effect of abdominal obesity on the risk of migraine (p for interaction <0.0001) and the effect of obesity decreased under the presence of abdominal obesity (p for interaction <0.0001). Younger age (<30 years) (p for interaction = 0.0001), female sex (p for interaction = 0.0031), smoking (p for interaction <0.0001), alcohol consumption (p for interaction = 0.0001), and regular exercise (p for interaction = 0.0435) modified the effect of obesity on the risk of migraine.

Conclusion: Our study shows that overweight and obesity independently affect the early incidence of migraine in young adults with a possible dose-response relationship. Abdominal obesity, demographics, and lifestyle factors had an effect modification on the obesity-migraine relationship. Our study findings suggest modifiable risk factors in developing migraine attacks in young individuals.

IHC23-PO-005

Carbon monoxide poisoning is associated with increased risk of migraine: Nationwide population-based cohort study

Heewon Hwang[1], Solam Lee[2], Kyung Min Kim[3] and Yong Sung Cha[4,5]

[1]*Department of Neurology, Yonsei University Wonju College of Medicine, Wonju, Korea, Republic of*
[2]*Department of Dermatology, Yonsei University Wonju College of Medicine, Wonju, Korea, Republic of*
[3]*Department of Neurology, Epilepsy Research Institute, Yonsei University College of Medicine, Seoul, Korea, Republic of*
[4]*Department of Emergency Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea, Republic of*
[5]*Research Institute of Hyperbaric Medicine and Science, Yonsei University Wonju College of Medicine, Wonju, Korea, Republic of*

Introduction: Acute carbon monoxide (CO) poisoning may cause various neurological injury, including migraine. In Korea, the estimated incidence of migraine is 6.1%. Several cases reported in the literature that prolonged exposure to non-lethal concentrations of CO mimicked migraine-like attacks. Carbon monoxide may play an important role in the mechanisms of migraine and other headaches. However, the association between CO poisoning with developing risk of migraine have not been well studied. This study aimed to investigate the long-term risk of developing migraine in patients with CO poisoning

Method: This nationwide population-based cohort study was conducted by using the administrative database of the National Health Insurance Service (NHIS) of Korea from January 1, 2002 to December 31, 2021 or death. Patients with CO poisoning (≥18 years of age) with at least one visit documented with the International Statistical Classification of Diseases, 10th Revision code of T58 between 2002 and 2021 were included. For comparison purposes, patients were matched with controls without a T58 code for age, sex, insurance type, income level, and location of residence in a 1:1 ratio. Operational definitions of migraine were based on ICD-10 diagnostic code: migraine (G43). The baseline demographic characteristics of the study population were described as frequencies with percentages or means with standard deviations (SDs). Independent t-test and chi-square test were used to analyze differences of clinical characteristics between each group. Incidence rates for outcomes were calculated as the number of diseases per 10,000 person-years. Hazard ratios (HRs) and 95% confidence intervals (95% CI) for CO poisoning group compared to control group over the study period was analyzed through multivariate Cox proportional hazards regression analyses. For the accuracy of diagnoses, we only included patients who had visited outpatient clinics twice or more with the same diagnostic code. Patients diagnosed with headache related codes (G43, G44, and R51) before the index date were excluded. Control group was also sampled from population who were not diagnosed with any headache related codes (G43, G44, and R51).

Primary outcome of the study was the incidence of migraine with CO poisoning, and controls. Secondary outcome was incidence of migraine for patients with CO poisoning who had HBO2 therapy, confirmed through presence of NHIS procedural code of M0581–M0588 and M5861–M5868 at CO poisoning, to those who had not.

Results: In total, this study included 53,380 patients with CO poisoning and 53,380 age-, sex-, insurance type-, income level-, and residence location-matched controls. Both the patient and the control group included 44.2% of female subjects and had a mean age of 45.7 years. The overall risk of migraine was significantly higher in CO poisoning group (adjusted HR [aHR], 1.38; 95% confidence interval [CI], 1.28–1.48). The overall risk of migraine was significantly higher in patients with CO poisoning regardless of age, and presence or absence of HBO2 treatment.

Conclusions: In this nationwide cohort study, CO poisoning was associated with an increased overall risk of migraine. Relative risk for migraine was higher in the CO poisoning group irrespective of subgroups including age, and presence or absence of HBO2 treatment.

Disclosure of Interest: None Declared

IHC23-PO-006

An observational study of the relationship between climate and migraine onset using claims data and meteorological data

Koichi Hirata[1], Muneto Tatsumoto[1], Takeo Nakayama[2], Kentaro Yamato[3], Hiromi Sano[4] and Lyo Inuyama[3]

[1]*Dokkyo Medical University, Tochigi, Japan*
[2]*Kyoto University, Kyoto, Japan*
[3]*Otsuka Pharmaceuticals Co., Ltd, Medical affairs, Tokyo, Japan*
[4]*Otsuka Pharmaceuticals Co., Ltd, Medical affairs, Osaka, Japan*

Objective: This study aimed to investigate seasonal differences in the onset of migraine in Japan.
Methods: This study used healthcare claim data from health insurance societies retained by JMDC, Inc. and meteorological data from the Japan Weather Association. The data period was January 2018–December 2021. The enrollment period was January 1 to December 31, 2019. The study sample consisted of patients (18 years or older) with a diagnosis of migraine (ICD-10: G43), who had been prescribed triptans during a period of one year prior to each season in the enrollment period. Patients were categorized into four seasons (time points): winter (January to March), spring (April to June), summer (July to September), and autumn (October to December). Migraine onset was defined as ICD-10 code G43. The amount of triptans prescribed was compared to other seasons using spring (April to June) as the reference. Least-square mean differences by period were analyzed using a repeated measures linear mixed effects model with the following covariates: sex, age, acute migraine treatment, migraine prophylaxis, triptans prescribed up to one year prior to the first day of the season, comorbidities that can induce migraine, other comorbidities, and estimated age of menopause in women.
Results: There were 12,986 patients enrolled in the study (male: 25.9%, female: 74.1%). The mean age was 44.1 years. The amount of triptans prescribed in January to March (winter) was lower than that in spring (April to June) (parameter estimate: –0.121, $P < 0.001$).
Conclusion: The study results suggest that seasonal differences may affect the onset of migraine.
Disclosure of Interest: KH, MT and TN has an advisory role for Otsuka Pharmaceutical Co., Ltd. KY, HS and LI are employees of Otsuka Pharmaceutical Co., Ltd.

IHC23-PO-007

Metaphorical Use of Headache and Migraine in Media: A Cross-Sectional Study of 1.3 Million Articles in the Newsrooms of Major Publications

Pengfei Zhang[1], Advika Ventrapragada[2], Robert Shapiro[3] and Thien Phu Do[4]

[1]*Rutgers University, New Brunswick, USA*
[2]*University of Pittsburgh, Pittsburgh, USA*
[3]*University of Vermont Larner College of Medicine, Burlington, USA*
[4]*Danish Headache Center, Copenhagen, Denmark*

Objective: Stigmatization and trivialization of headache confront individuals with headache disorders, but the degree to which media may contribute is incompletely understood. The objective was to quantify the frequency of disparaging metaphorical use of the words "headache" and "migraine" in articles and summaries of major publications.
Methods: This cross-sectional study analyzed a data set of 1.3 million articles and summaries written by authors and editors in the newsrooms of 38 major publications. The use of the words "headache" or "migraine" in articles and summaries by major publications was rated by two authors (P.Z. and A.V.) as either "metaphorical" or "medical" based on their contextual application. Secondary outcomes were source of publication and time of publication.
Results: 6195 and 740 articles included the words "headache" or "migraine" respectively; 7100 sentences contained the word "headache" and 1652 sentences contained the word "migraine". Among a random sample of 1000 sentences with the word "headache", there was a metaphorical use in 492 (49.2% [95% CI, 46.1–52.3]) of sentences. Among a random sample of 1000 sentences with the word "migraine", there was a metaphorical use in 45 (4.5% [95% CI, 3.2–5.8]) of sentences. The five most prevalent sources were CNN, Fox News, New York Times, The Guardian, and The Washington Post. There was an overall increase in number of articles containing the words "headache" or "migraine" from database inception until analysis (1998 to 2017). There was a higher metaphorical use of "headache" in comparison to "migraine" ($p < 0.00001$).
Conclusions and Relevance: In this cross-sectional study, authors and editors in major publications applied a metaphorical use of "headache" about half of the time. The metaphorical use of "headache" is 11-fold greater than the metaphorical use of "migraine" in the same media sample. These depictions may contribute to trivialization of headache and stigmatization of individuals with headache disorders. Studies with individuals affected by headache disorders are needed to clarify potential influences.

Disclosure of Interest: Pengfei Zhang has received honorarium from Alder Biopharmaceuticals, Board Vitals, and Fieve Clinical Research. He collaborates with Headache Science Incorporated without receiving financial support. He has ownership interest in Cymbeline LLC. Advika Ventrapragada reports no conflicts of interest. Robert E. Shapiro has received compensation as a consultant for Eli Lilly, Lundbeck, and Theranica. Thien Phu Do reports no conflicts of interest.

IHC23-PO-008

Effects of five major classes of blood pressure lowering drugs and their combinations on headache: a systematic review and network meta-analysis of 402 randomised, double-blind clinical trials

Faraidoon Haghdoost[1], Abdul Salam[1], Rashmi Pant[2], Vidyasagar Kota[2], Rupasvi Dhurjati[2] and Anthony Rodgers[1]

[1]*The George Institute for Global Health, University of New South Wales (UNSW), Sydney, Australia*
[2]*The George Institute for Global Health, Hyderabad, India*

Objective: To evaluate the effects of five major classes of blood pressure (BP) lowering drugs – beta-blockers (BBs), angiotensin-converting-enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs) and diuretics – and their combinations compared to placebo on risk of headache.

Methods: We conducted a systematic review and network meta-analysis (NMA). We searched Cochrane Central Register of Controlled Trials until October 2018 for randomised controlled trials (RCTs), MEDLINE from 1946 to September 2017, and Epistemonikos until September 2017 for systematic reviews from which relevant RCTs were identified. Double-blind RCTs published in English, involving adults (age $\geq$18 years) and studied one or more of the five major classes of BP-lowering drugs, including BBs, ACEIs, ARBs, CCBs and diuretics or their combinations compared with placebo or with each other (active vs. active) were included. BP-lowering drugs had to be taken orally in fixed doses, and studies of duration 2 to 26 weeks were eligible. Screening of studies for inclusion and data extraction, were performed in duplicate by independent reviewers. Conflicts were resolved by discussing with a senior reviewer. The primary outcome was the number of participants with $\geq$1 headache event from randomisation to the end of the study in each trial. Risk ratio (RR) with 95% confidence interval (95% CI) were calculated for an NMA using the fixed-effect model. The relative effectiveness of drug class in reducing headache risk was presented in a table of P-scores, that assess the likelihood that one therapy is superior to another averaged over all competing treatments. Analyses were also conducted to assess whether larger reductions in systolic and diastolic BP (SBP and DBP) resulted in larger reductions in headache risk.

Results: Of the 31,890 records screened, 402 RCTs with 119,009 participants were found eligible and were included. Studies were published between 1973 and 2018, 78% had parallel design, 60% of participants were male, and the mean age was 55 years. All classes except for CCBs reduced headache risk compared to the placebo (Table 1). Based on the P-scores from NMA, BB reduced headache the most, followed by the combination of drugs from two classes. A 10 mmHg reduction in SBP and DBP were associated with 25% (95% CI 20%–30%, p = < 0.0001) and 23% (95% CI 15% to 31%, p = <0.0001) lower risk of headache, respectively.

Conclusion: BBs, followed by combinations, ACEIs, ARBs, and diuretics, were found most to least efficacious in reducing the risk of headache. CCBs did not reduce headache risk. Larger BP reductions confer larger reductions in headache risk.

Disclosure of Interest: None Declared

Abstract number: IHC23-PO-008

Table 1. Effects of five major classes of BP-lowering drugs and their combinations on the risk of headache.

Class	Ranking*	Number (%) of RCTs with at least one group of the respective class	Relative risk vs placebo (95% CI)	P-value
BB	1	99 (25%)	0.63 (0.54, 0.73)	0.0001
Combination	2	256 (65%)	0.68 (0.62, 0.75)	<0.0001
ACEI	3	157 (40%)	0.69 (0.60, 0.77)	<0.0001
ARB	4	131 (33%)	0.76 (0.69, 0.85)	<0.0001
Diuretics	5	124 (32%)	0.82 (0.73, 0.94)	0.0035
Placebo	6	322 (82%)	–	
CCB	7	266 (68%)	1.03 (0.94, 1.14)	0.508

*NMA ranking in terms of reducing headache risk based on P-score.

IHC23-PO-009

Simultaneous comparisons of 25 acute migraine medications based on 10 million users self-reported records from a smartphone application

Chia-Chun Chiang[1], Xuemin Fang[2], Zsolt Horvath[3], Francois Cadiou[3], Alexandre Urani[3], Weijie Poh[3], Hiroto Narimatsu[4], Yu Cheng[5] and David Dodick[6]

[1]*Mayo Clinic, Rochester, MN, USA*
[2]*Kanagawa University of Human Services, Kawasaki, Japan*
[3]*Healint Pte. Ltd, Singapore, Singapore*
[4]*Kanagawa Cancer Center Research Institute, Kanagawa, Japan*
[5]*University of Pittsburgh, Pittsburgh, USA*
[6]*Mayo Clinic, Scottsdale, USA*

Background: Many acute treatment options exist for migraine. However, large-scale, head-to-head comparisons of treatment effectiveness from real-world patient experience reports are lacking.

Methods: This is a cross-sectional analysis of 10,842,795 migraine attack records extracted from an e-diary smartphone application between June 30, 2014, and July 2, 2020. We analyzed 25 acute medications among seven classes-acetaminophen, NSAIDs, triptans, combination analgesics, ergots, anti-emetics, and opioids. Gepants and ditan were not included in this analysis. We employed a two-level nested logistic regression model to analyze the odds ratio (OR) of treatment effectiveness of each medication by adjusting concurrent medications and the covariance within the same user. Subgroup analyses were conducted for users in the United States (US), the United Kingdom (UK), and Canada (CAN).

Results: Our final analysis included 4,777,524 medication-outcome pairs from 3,119,517 migraine attacks among 278,006 users. Triptans (mean OR 4.8), ergots (mean OR 3.02), and anti-emetics (mean OR 2.67) were the top three classes of medications with the highest effectiveness, followed by opioids (mean OR 2.49), NSAIDs (other than ibuprofen, mean OR 1.94), combination analgesics (acetaminophen/acetylsalicylic acid/caffeine) (OR 1.69), others (OR 1.49), and acetaminophen (OR 0.83), using ibuprofen as the reference. Individual medications with the highest ORs were eletriptan (OR 6.1), zolmitriptan (OR 5.7), and sumatriptan (OR 5.2). The ORs of acetaminophen, NSAIDS, combination analgesics and opioids were mostly around or less than 1, suggesting similar or lower reported effectiveness compared to ibuprofen. The ORs for 24 medications, except that of acetylsalicylic acid, achieved statistical significance with $p < 0.0001$, and our nested logistic regression model achieved an area under the curve (AUC) of 0.849. Country-specific subgroup analyses revealed similar ORs of each medication and AUC (US 0.849, UK 0.864, and CAN 0.842), demonstrating the robustness of our analysis.

Conclusion: Using a big-data approach, we analyzed patient-generated real-time records of 10 million migraine attacks and conducted simultaneous head-to-head comparisons of 25 acute migraine medications. Our findings that triptans, ergots and anti-emetics are the most effective classes of medications align with the guideline recommendations and offer generalizable insights to complement clinical practice.

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IHC23-PO-010

Migraine and MRI Radiomics-Based Machine Learning Model for Periaqueductal Gray Matter Evaluation

Ismail Mese[1], Saime Fusun Mayda Domac[2], Rahsan Karaci[2] and Ceylan Altintas Taslicay[3]

[1]*Department of Radiology, Health Sciences University Address: Erenkoy Mental Health and Neurology Training and Research Hospital, Istanbul, Turkey*
[2]*Department of Neurology, Health Sciences University Address: Erenkoy Mental Health and Neurology Training and Research Hospital, Istanbul, Turkey*
[3]*Departmen of Radiology, MD Anderson Cancer Center, Houston, USA*

Objective: This study aimed to evaluate the diagnostic utility of a magnetic resonance imaging radiomics-based machine learning model in differentiating migraine patients, including its subtypes, from healthy subjects.
Methods: This retrospective study included 204 participants, with 102 migraine patients (81 episodic and 21 chronic) and 102 healthy subjects.A review of clinical and imaging data from migraine patients and healthy subjects was conducted, with the periaqueductal gray matter segmented and radiomics features extracted using 3DSlicer software. Various algorithm-based feature reduction methods were compared, and the optimal method was selected to identify the 10 most significant features for distinguishing between patients. Models utilizing various artificial intelligence algorithms were created to evaluate and compare their classification performance based on the selected features.
Results: The "gain" method demonstrated the best performance among feature reduction methods. The Random Forest algorithm showed the best classification performance for migraine patients, with an area-under-curve of 0.873, sensitivity of 82.4%, and specificity of 77.5%. The k-Nearest Neighbor algorithm correctly classified 74.1% of episodic migraine patients (AUC: 0.848, sensitivity: 74.1%, specificity: 78.4%). The Random Forest algorithm correctly classified 90.5% of chronic migraine patients (AUC: 0.983, sensitivity: 90.5%, specificity: 95.1%).
Conclusion: A radiomics-based machine learning model, utilizing standard magnetic resonance images obtained during the diagnosis and follow-up of migraine patients, shows promise in aiding migraine diagnosis and classification for clinical approach.
Disclosure of Interest: None Declared

IHC23-PO-011

The influence of reproductive factors on migraines in middle-aged premenopausal women: A nationwide population-based study in South Korea

Kyung Won Lee, Seonghoon Kim and Jeong Wook Park

Department of Neurology, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of

Objectives: Women can experience various reproductive events, such as pregnancy, childbirth, lactation, and contraception, which cause long-term changes in female hormones. In middle-aged women, the prevalence of migraine is high, and a clear gender difference is evident. This study investigated the effects of factors associated with past reproductive events on the prevalence of migraine in middle-aged premenopausal women.
Methods: The influence of reproductive factors on migraine in middle-aged women was investigated using the Korean National Health Insurance Service (KNHIS) and Korean Health Examination (KHE) databases. The reproductive factors of interest were parity, breastfeeding, and oral contraceptive (OC) use. The study included 949,704 middle-aged premenopausal women 40–60 years of age. The study population was divided into two groups based on novel diagnosis of migraine during the follow-up period (2009–2018).
Results: The risk of migraine tended to increase in the primiparous (hazard ratio, HR: 1.179; 95% confidence interval, CI: 1.137–1.221) and multiparous groups (HR: 1.181; 95% CI: 1.142–1.221) compared with the nulliparous group. The breastfeeding $\geq$12 months group (HR: 1.071; 95% CI: 1.052–1.091) showed significantly increased migraine risk compared with the non-breastfeeding group. All women in the OC groups ($<$1 year, HR: 1.048; 95% CI: 1.028–1.069 and $\geq$1 year, HR: 1.100; 95% CI: 1.067–1.134) showed a higher migraine risk than the non-OC group.
Conclusion: The results indicated that the experiences of childbirth, longer breastfeeding, and OC use may be associated with higher risk of migraine in middle-aged premenopausal women.

IHC23-PO-012

Machine-learning based drug-drug interaction prediction identifies acetylsalicylic acid as risk for cardiovascular events during migraine treatment

Kinga Gecse[1,2], Duc Anh Nguyen[3], Gabriella Juhasz[1,2], Hiroshi Mamitsuka[3,4] and Peter Petschner[1,3,5]

[1]*Department of Pharmacodynamics, Semmelweis University, Budapest, Hungary*
[2]*NAP3.0-SE Neuropsychopharmacology Research Group, Hungarian Brain Research Program, Semmelweis University, Budapest, Hungary*
[3]*Bioinformatics Center, Institute for Chemical Research, Kyoto University, Uji, Japan*
[4]*Department of Computer Science, Aalto University, Espoo, Finland*
[5]*Research Unit for Realization of Sustainable Society, Kyoto University, Uji, Japan*

Objective: Large population-based cohort studies demonstrated strong association between migraine and cardiovascular diseases. Thus, elevated risk of cardiovascular events as a consequence of migraine drug combinations can be a major concern during therapy. Machine-learning algorithms provide a new approach to identify these cardiovascular adverse events.
Methods: Two pharmacovigilance databases [FDA Adverse Event Reporting System (FAERS) and Japanese Adverse Drug Event Report (JADER)] were investigated to predict possible drug-drug interactions of migraine treatment drugs and associated adverse events. SPARSE, a state-of-the art machine learning model was used for the prediction. The top significant predictions were extracted for each dataset ($p \leq 10–4.60$), and drug-drug interactions associated with a cardiovascular adverse event were identified.
Results: We found 19 significant drug-drug interactions associated with cardiovascular adverse event based on FAERS, all of them related to acetylsalicylic acid. Using JADER, 51 drug-drug interactions associated with cardiovascular adverse events were identified, 30 related to acetylsalicylic acid, 11 to droperidol and 10 to verapamil. In general, the predicted cardiovascular adverse events were more severe in JADER than FAERS.
Conclusions: Acetylsalicylic acid is a widely used and affordable analgesic to treat acute migraine attacks. Based on the results, however, it also seems to be the most prevalent drug associated with cardiovascular adverse events. Clinicians are advised to assess cardiovascular risk profile of patients to reduce unwanted side-effects of acetylsalicylic acid, when combined with other migraine medications.
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IHC23-PO-013

Uncovering Potential Interictal Suppression of ERK Cascade and miR-21 in Migraine Patients: Insights from RNA-Seq Analysis

Sahel Kumar[1,2], Kinga Gecse[1,2], Daniel Baksa[1,2], Gyorgy Bagdy[1,2], Gabriella Juhasz[1,2] and Peter Petschner[1,2,3,4]

[1]*Department of Pharmacodynamics, Faculty of Pharmacy, Semmelweis University, Budapest, Hungary*
[2]*NAP-3.0-SE Neuropsychopharmacology Research Group, Hungarian Brain Research Program, Semmelweis University, Budapest, Hungary*
[3]*Bioinformatics Center, Institute for Chemical Research, Kyoto University, Uji, Kyoto, Japan*
[4]*Research Unit for Realization of Sustainable Society, Kyoto University, Gokasho, 611–0011, Uji, Kyoto, Japan*

Objective: Transcriptomic studies in migraine without aura (MO) pointed to targets in the disorder, few highlighted potential regulatory elements behind the changes in RNA levels. We performed analyses on a large, well-defined population with MO using a sensitive RNA sequencing with ISO standards and searched for potential, interictal regulatory factors in MO.
Methods: Our study included 22 individuals (17 female) with episodic MO in interictal phase and 30 healthy controls (16 female), aged 20–37 years. Participants did not take regular medications, except contraceptives or occasional headache medication. RNA-Sequencing was conducted on whole blood samples and migraineurs and controls were compared adjusting for age and sex. The R package fast Gene Set Enrichment Analysis (fGSEA) with MSigDB Micro RNA targets (MIRs) and Gene Ontology (GO) gene sets (C3 and C5, respectively) was used to identify altered pathways. Significant results after multiple hypothesis correction ($FDR < 0.05$) were screened for pathways related to regulatory elements relevant for the disorder.
Results: We found "MIR 21 5p" ($NES = -2.02$, $FDR = 1.15 \times 10^{-6}$), "MIR 21 3p" ($NES = -1.57$, $FDR = 0.009$) and the pathway "GOBP positive regulation of ERK1 and ERK2 cascade" ($NES = -1.56$, $FDR = 0.003$) to be significantly negatively enriched in MO patients compared to controls.

Conclusions: The study identified downregulated miR-21 and ERK1 and ERK2 cascade regulation pathways in MO compared to controls. ERK pathway has been shown to be upregulated following elevated miR-21 levels and, vice versa, a downregulation of the aforementioned pathway followed by a decreased expression of miR-21. Our findings suggest a potential interictal suppression of the ERK cascade by miR-21 downregulation in MO patients. Previously, ERKs inhibition has been linked to reduced proinflammatory mediators in cerebral arteries and miR-21 downregulation was also associated with suppressed inflammatory processes. Thus, suppression of the ERK cascade in episodic MO patients may diminish neuroinflammatory processes and may contribute to the headache-free phase.
All in all, our results demonstrate the potential role of a suppressed miR-21-regulated ERK cascade in the reduced neuroinflammatory state between migraine attacks.
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Disclosure of Interest: None Declared

IHC23-PO-014

The impact of migraine on healthcare resource use in Italy: results from the Italian Migraine Registry (I-GRAINE) prospective study

Giulia Fiorentini[1,2], Cinzia Aurilia[1], Stefano Bonassi[2,3], Antonio Carnevale[4], Laura Di Clemente[5], Gabriella Egeo[1], Annalisa Gai[6], Isabella Ferdinanda Pestalozza[7], Stefania Proietti[3], Angelo Ranieri[8], Micaela Robotti[9], Giuliano Sette[10], Giorgio Spano[11], Carlo Tomino[12], Alessandro Valenza[13] and Piero Barbanti[1,2]

[1]*Headache and Pain Unit, IRCCS San Raffaele Roma, Rome, Italy*
[2]*San Raffaele University, Rome, Italy*
[3]*Clinical and Molecular Epidemiology, IRCSS San Raffaele Pisana, Rome, Italy., Rome, Italy*
[4]*Headache Center, Neurology Unit, San Filippo Neri Hospital, Rome, Italy*
[5]*Headache Center, Neurology Unit, San Camillo-Forlanini Hospital, Rome, Italy*
[6]*Neurology and Stroke Unit, Asti Hospital, Asti, Italy*
[7]*Neurology and Neurophysiopathology Unit, Sandro Pertini Hospital, Rome, Italy*
[8]*Neurology Unit and Stroke-Unit, AORN A. Cardarelli, Naples, Italy*
[9]*Headache Center, ASST Santi Paolo Carlo, Milan, Italy*
[10]*Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), "Sapienza" University of Rome, Sant"Andrea University Hospital, Rome, Italy*
[11]*Center for Headache and Intracranial Pressure Disorders, Neurology Unit, A.O.U. Mater Domini, Catanzaro, Italy*
[12]*Scientific Direction, IRCSS San Raffaele Pisana, Rome, Italy*
[13]*Neurological Unit, Ospedale Belcolle, Viterbo, Italy*

Objective: The Italian Migraine Registry (I-GRAINE) collects big data on sociodemographic characteristics, clinical features, treatment and healthcare resource use of migraine patients. The aim is to overcome disease misconceptions, improve clinical government, and rationalize economic resource allotment. The present study focuses on diagnostic investigations and specialist visits performed by migraine patients, considering their appropriateness and the impact on our National Health System (NHS).
Methods: The Italian Migraine Registry (I-GRAINE) is a multicenter ($n = 39$), prospective, observational, non-interventional study. We enrolled consecutive patients affected by episodic or chronic migraine, according to the systematic random method. Information on sociodemographic characteristics, migraine features, patient's journey and healthcare resource use were collected by headache specialists with face-to-face interviews using a shared web-based questionnaire.
Results: At the date of 31 December 2022, we enrolled 867 patients (M/F: 126/741; age 45.0 ± 12 yrs; EM/CM: 718/149; medication overuse: 131). Patient referred high migraine frequency (9.3 ± 7.8 days/month) and severe disability (MIDAS score: 48.3 ± 50.7; HIT-6 score: 60.9 ± 9.1). Most of them underwent to diagnostic investigations (lifetime: 81.8%; last 3 years: 68.8%; 2.5 ± 2.3) and to specialist visits (last 3 years: 63.1%; mean n: 2.4 ± 0.2), often self-prescribed, mostly inappropriate and subsidized by our NHS (Table).
Conclusion: A large number of diagnostic investigations and specialist visits for migraine are inappropriate, self-prescribed and subsidized by the NHS. The I-GRAINE registry is expected to contribute to improve the clinical management of migraine, rationalizing healthcare resource allocation, and reducing its economic burden.
Disclosure of Interest: Cinzia Aurilia received travel grants from Eli-Lilly, FB-Health, Lusofarmaco and Teva, honoraria from Novartis; Piero Barbanti received travel grants, honoraria for advisory boards, speaker panels or investigation studies from Alder, Allergan, Bayer, ElectroCore, Eli-Lilly, GSK, Lusofarmaco, MSD, Novartis, Stx-Med, Teva, Visufarma. Gabriella Egeo received travel grants and honoraria from Eli-Lilly, Novartis, New Penta

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	%	n per patient (mean + SD)	In agreement with current guidelines	Self-prescribed (%)	Subsidized by the NHS in at least 50% of cases (range)
Diagnostic investigations					
Brain MRI/CT scan	95.0	5.3 ± 3.5	No*	12.5	27.7–86.3
Spine MRI/X-Ray	22.8	2.2 ± 0.6	No	17.2	67.6–81.3
EEG	11.4	1.8 ± 1.4	No	2.8	84.7
Others	10.6	1.2 ± 0.7	No	6.2	83.3
Specialist visits					
Neurologist	85.6	3.5 ± 3.9	Yes	68.7	52.9
Ophtalmologist	33.6	1.5 ± 0.9	No	70.7	21.5
Physiotherapist	17.8	1.5 ± 1.2	No	83.0	13.6
Others	41.2	1.9 ± 1.5	No	74.3	66.1

*all patients had typical migraine picture and normal neurological examination

and Ecupharma; Angelo Ranieri received speaker honoraria from Teva, Lilly; Stefano Bonassi, Antonio Carnevale, Laura Di Clemente, Giulia Fiorentini, Bianca Orlando, Isabella Ferdinanda Pestalozza, Stefania Proietti, Micaela Robotti, Giuliano Sette, Giorgio Spano, Carlo Tomino, Alessandro Valenza have no disclosures to declare.

IHC23-PO-015

Treatment Profile of 2,642,286 Migraine Patients: Analysis of a Multicenter Electronic Medical Record (TrinetX)

Victor Wang[1], Mario Peres[1,2] and Hsiangkuo Yuan[1]

[1]*Jefferson Headache Center, Philadelphia, USA*
[2]*Institute of Psychiatry, University of São Paulo, São Paulo, Brazil*

Objective: Migraine remains a disabling and prevalent condition globally, with many patients having unmet acute and preventive treatment needs. Large multicenter electronic medical record cohorts, such as the TrinetX database, present an opportunity to study treatment profiles globally to identify opportunities to improve access to treatments. In this study, we aim to characterize the treatment profile of a large cohort of migraine patients, including abortive and preventive medication use.

Methods: Using the TrinetX database, we analyzed the profiles of a large multicenter cohort from a database containing information on over 127 million patients across 102 healthcare organizations. Cohorts of patients diagnosed by medical providers as migraine (episodic, chronic, and unspecified, with or without aura) were created. Information regarding patient demographics, medical comorbidities, and medication use was obtained.

Results: We identified 2,642,286 patients across 95 healthcare organizations with mean age 45 ± 18 years, with female:male ratio of 3.55:1, 67% of which were white, 12% were black/African American, and 7% Hispanic/Latino.

Data was available to analyze 668,068 (25.28%) of the total population. Of these patients, 164,492 (24%) were designated migraine without aura, 119,370 (18%) were designated as migraine with aura. Specific aura subtypes included: Ophthalmoplegic migraine (10,447, 2%), hemiplegic migraine (3,517, 1%).

We identified 2,332,985 episodic migraine patients with female:male ratio of 3.35:1, 66% were white, 12% were black/African American, and 7% Hispanic/Latino. 309,301 patients with chronic migraine were identified (11.7% of total population), with mean age 45 ± 17 years, female: male ratio of 4.56:1, 71% were white, 11% were black/African American, and 8% Hispanic/Latino. The episodic: chronic migraine ratio was 7.54:1.

Of the 668,068 out of 2,642,286 patients, 334,111 (50%) had been given opioid analgesics, 198,629 (30%) were prescribed antimigraine agents, including triptans, CGRP monoclonal antibodies, DHE, CGRP gepants, and lasmiditan. Sumatriptan was the most commonly prescribed of these options (132,166, 20%), followed by rizatriptan (53,672, 8%). CGRP monoclonal antibodies (erenumab, galcanezumab, fremanezumab and eptinezumab, in order of descending counts) and CGRP gepants (rimegepant, ubrogepant, and atogepant, in order of descending counts) were each prescribed 1% or less in this cohort. Dihydroergotamine and lasmiditan were also prescribed to 1% or less of this cohort. Other preventive agents included antidepressants (252,687, 38%), anticonvulsants (196,007, 29%), beta blockers (144,897, 22%), calcium channel blockers (82,220, 12%), and ACE inhibitors (65,403, 10%).

Of the chronic migraine patients analysis was available for 276,462 of 309,301 (89.4%), treatment profiles were as follows: opioid analgesics (168,838,61%) compared to antimigraine agents (173,327, 63%), including sumatriptan as the most common (107,592, 39%), followed by rizatriptan (63,325, 23%), followed by the CGRP monoclonal antibodies erenumab (25,830, 9%), galcanezumab (23,289, 8%), fremanezumab (15,254, 6%), and eptinezumab (1,721, 1%), and CGRP gepants rimegepant (17,363, 6%), ubrogepant (13,406, 5%), and atogepant (2,059, 1%). Other medications were prescribed as follows: onabotulinumtoxina (29,314, 11%), dihydroergotamine (12,042, 4%), and lasmiditan (1,173, 1%).

Conclusion: Based on results from a large multicenter electronic medical record analysis, we find that migraine may have higher rates of prescription of opioid analgesics relative to their prescriptions for antimigraine-specific agents. In chronic migraine patients, there are higher rates of antimigraine agent prescriptions than opioid analgesics. Further investigation is warranted into the barriers regarding lack of access and low prescription rates of the CGRP antagonist classes of medications (monoclonal antibodies and gepants).

Disclosure of Interest: None Declared

IHC23-PO-016

Demographics, patient's journey, clinical features and therapeutic management of people with migraine in Italy: insights from the Italian Migraine Registry (I-GRAINE) study.

Bianca Orlando[1], Giulia Fiorentini[1], Gabirella Egeo[1], Cinzia Aurilia[1], Cecilia Camarda[2], Roberta Messina[3], Rossella Cherchi[4], Valentina Favoni[5], Francesca Schiano di Cola[6], Licia Grazzi[7], Marco Russo[8], Simone Quintana[9], Antonio Carnevale[10], Roberto De Simone[11], Florindo D"Onofrio[12], Angelo Ranieri[13], Marco Bartolini[14], Miriam Tasillo[15], Alfonso Coppola[16], Fabio Frediani[17], Claudia Altamura[18], Rosario Grugno[19], Laura Di Clemente[20], Davide Bertuzzo[21], Fabrizio Vernieri[22], Stefania Proietti[23], Carlo Tomino[1] and Piero Barbanti[1,24]

[1]*Headache and Pain Unit, IRCCS San Raffaele, Via della Pisana 235, 00163, Rome, Italy*
[2]*Department of Biomedicine, Neuroscience and Advanced Diagnostics (BIND), University of Palermo, Palermo, Italy*
[3]*Neurology Unit, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy*
[4]*Neurology Unit, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy*
[5]*IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy*
[6]*Neurology Unit, Department of Clinical and Experimental Sciences, Università degli Studi di Brescia, Brescia, Italy*
[7]*Neuroalgology Unit and Headache Centre, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy*
[8]*Headache Centre, Neurology Unit, AUSL IRCCS Reggio Emilia, Reggio Emilia, Italy*
[9]*Headache Center, Neurology Unit, University Hospital of Parma, Via Gramsci 14, 43126, Parma, Italy*
[10]*Headache Center, Neurology Unit, San Filippo Neri Hospital, Rome, Italy*
[11]*University of Naples "Federico II", via S. Pansini 5, 80131, Naples, Italy*
[12]*Neurology Unit, San Giuseppe Moscati Hospital, Avellino, Italy*
[13]*Neurology and Stroke Unit, AORN A.Cardarelli, Naples, Italy*
[14]*Neurological Clinic, Marche Polytechnic University, Via Conca 1, 60020, Ancona, Italy*
[15]*Stroke Unit, S. Camillo de Lellis Hospital, Rieti, Italy*
[16]*Headache Center, G. Salvini Hospital, Garbagnate Milanese, Italy*
[17]*Headache Center, ASST Santi Paolo Carlo, Milan, Italy*
[18]*Headache and Neurosonology Unit, Neurology, Fondazione Policlinico Universitario Campus Bio-Medico Di Roma, Roma, Italy*
[19]*IRCCS Centro Neurolesi Bonino-Pulejo, Messina, Italy*
[20]*Headache Center, Neurology Unit, San Camillo-Forlanini Hospital, Rome, Italy*
[21]*Neurology and Stroke Unit, Asti Hospital, Asti, Italy*
[22]*Headache and Neurosonology Unit, Neurology, Fondazione Policlinico Campus Bio-Medico, Rome, Italy*
[23]*Clinical and MolecularEpidemiology, IRCCS San Raffaele, Rome, Italy*
[24]*San Raffaele University, Rome, Italy*

Objective: The Italian Migraine Registry (I-GRAINE) is a strategic project aimed at providing big-data on migraine to guarantee a proper clinical and therapeutic management of the disease. I-GRAINE investigates patient's socio-demographic characteristics, lifestyle and comorbidities, patient's journey, migraine features and clinical government, as well as healthcare resource use. Here we reported the findings of the second I-GRAINE report updated on 31 December 2022.

Methods: The Italian Migraine Registry (I-GRAINE) is a multicenter (n = 39), prospective, observational, non-interventional study. All consecutive adult patients affected by episodic migraine (EM) or chronic migraine (CM) seen at each participating headache center were enrolled. Participation to the study was proposed on each outpatient visit day to the first patient at his/her first visit (incident patient), and to the first patient at his/her first control visit (prevalent patient), according to the systematic random method. Information on socio-demographic characteristics, lifestyle, clinical features, and healthcare resource use were gathered in each patient with face-to-face

interviews by specifically trained board–certified neurologists using a shared web-based questionnaire.

Results: On 31 December 2022, we enrolled 867 patients (M/F: 126/741; age 45.0 ± 12yrs; EM/CM: 718/149; medication overuse: 131). Most of them had > high school degree (86.8%) and were employed/students (75.7%). Only 8.1% of the patients had consulted (lifetime) a general practitioner due to migraine and 36.2% a headache center (age at first headache center access: 31.5 ± 13.5 yrs; number of centers consulted: 1.3 ± 0.6), whereas 9.2% had been admitted to the ER within the last 12 months (on average 1.7 ± 1.5 admissions).

Age at migraine onset was 17.6 ± 8.7 yrs. Patients referred unilateral pain (70.3%), high migraine frequency (9.3 ± 7.8 days/month), and severe disability (HIT-6 score 60.9 ± 9.1, MIDAS score 48.3 ± 50.7). Many patients complained of osmophobia (42.1%), dopaminergic symptoms (40.4%), allodynia (40.3%), cephalalgiophobia (33.5%), unilateral cranial autonomic symptoms (25.8%) and vertigo (17.1%). Comorbidities were present in 41.4% of the patients.

Two/thirds of patients (66.7%) used triptan as acute treatment (responders: 74.6%). Migraine prophylaxis was taken by 67.0% of the patients. Most of them (46.9%) were treated with anti-CGRP monoclonal antibodies (mAbs) (erenumab 49.3%, galcanezumab 35.7%, fremanezumab 29.8%, eptinezumab 0.7%). The proportion of anti-CGRP mAbs responders ranged from 77.3% to 85.7%.

Conclusion: Low migraine awareness causes delayed diagnosis and treatment. Migraine phenotype frequently includes symptoms not listed in the current headache classification. Specific and selective acute and preventive drugs (triptans, anti-CGRP mAbs), currently the most widely used migraine treatments in Italy, are characterized by high responder rates.

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IHC23-PO-017

An computer-aided diagnosis model for primary headache disorders based on large-scale dataset using auto deep learning

Ziming Yin[1], Heng Li[1], Zhao Dong[2] and Shengyuan Yu[2]

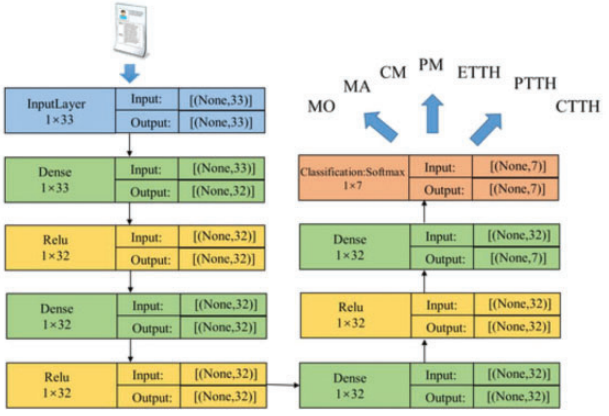
[1]*University of Shanghai for Science and Technology, Shanghai, China*

[2]*Chinese PLA General Hospital, Beijing, China*

Objective: Migraine and tension type headache (TTH) are the two kinds of primary headaches with the highest incidence rate in China, which seriously affect people's quality of life. There exists some overlap in terms of attack duration, number of attacks, attack intensity and accompanying symptoms between these two headaches. A considerable number of patients are in the middle of these two headaches, making it difficult to diagnose using ICHD-3 diagnostic criteria. Our goal is to establish a computer-aided diagnosis model based on large-scale headache dateset to help doctors distinguish migraine and TTH.

Methods: The study was carried out at headache or neurological clinics of 10 hospitals in China between April 2014 and December 2020. The research protocol was approved by the Ethics Committee of the Chinese PLA

General Hospital. The Institutional Review Board of each participating hospital approved this study. After de privacy processing, 8283 cases of migraine or TTH were screened by the headache experts of the PLA General Hospital, There are 32 headache features in each case. Some features are patient's personal information (such as sex, age, education, etc.); Another features are from the diagnostic criteria of migraine and TTH in ICHD-3, including headache characteristics and accompanying symptoms. We also added some cranial autonomic symptoms, because some migraine attacks can be associated with cranial autonomic symptoms; The following are personal habits (such as smoking, drinking, exercise, etc.), inducing factors, mitigating factors, and premonitory symptoms. Automatic deep learning (AutoDL) is currently the state-of-the-art machine learning method, especially for large-scale datasets. The Efficient Neural Architecture Search algorithm were used to search for the optimal deep neural network architecture and hyper-parameters. In this study, we input all 8283 headache cases into the AutoDL framework, which automatically constructed the optimal DL model for distinguish migraine and TTH. The optimal architecture of DL model is shown in Figure.



Results: Of the 8283 patients recruited, the AutoDL correctly recognized migraine without aura (MO) with accuracy of 91.56%, migraine with aura (MA) (99.79%), chronic migraine (CM) (98.31%), probable migraine (PM) (96.52%), episodic tension-type headache (ETTH) (97.98%), chronic tension-type headache (CTTH) (92.98%), and probable tension-type headache (PTTH) (98.78%).

Conclusion: The experimental results indicated that the proposed AutoDL model in this study diagnosed migraine and TTH with a high degree of accuracy. This system could be used as a diagnostic tool to assist general practitioners in distinguishing migraine and TTH at primary hospitals.

Competing interests: The authors declare that they have no competing interests.

Disclosure of Interest: None Declared

Abstract number: IHC23-PO-017

	ETTH	PTTH	CTTH	MO	MA	PM	CM
Accuracy (%)	97.98	98.78	92.98	91.56	99.79	96.52	98.31
(95%CI)	97.94–98.04	98.75–98.83	92.90–93.07	91.46–91.63	99.71–99.74	96.45–96.58	98.29–98.39
Precision (%)	90.46	95.43	79.21	72.63	98.96	88.58	94.82
(95%CI)	90.26–90.74	95.30–95.67	78.92–79.58	72.27–72.95	98.53–98.74	88.30–88.84	94.72–95.13
Sensitivity (%)	97.77	97.08	72.48	70.65	99.77	88.76	94.80
(95%CI)	97.64–97.90	96.91–97.22	72.10–72.96	70.21–71.02	99.58–99.69	88.48–89.05	94.66–95.07
Specificity (%)	98.02	99.12	96.59	95.28	99.79	97.92	99.00
(95%CI)	97.98–98.09	99.09–99.16	96.53–96.66	95.20–95.35	99.70–99.74	97.85–97.96	98.98–99.06

Cluster headache and other trigeminal autonomic cephalalgias

IHC23-PO-018

Onset age and clinical feature of headache according to severity of obstructive sleep apnea in cluster headache

Yooha Hong[1], Mi-Kyoung Kang[1], Min Kyung Chu[2], Hee-Jin Im[1] and Soo-Jin Cho[1]

[1]*Department of Neurology, Dongtan Sacred Heart Hospital, Hallym University Colleage of Medicine, Hwaseong, Korea, Republic of*
[2]*Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of*

Background: Cluster headache (CH) is characterized by severe pain accompanied with ipsilateral autonomic symptoms, and circadian rhythmicity of the attacks. Moderate-to-severe obstructive sleep apnea (OSA) is frequently associated with CH, hypoxemia and fatigue related to OSA can be the precipitating factor of cluster attacks. We investigated the headache characteristics and findings of polysomnography (PSG) in patients with CH according to the severity of OSA.

Methods: We retrospectively analyzed the data of patients with CH who underwent polysomnography on clinical suspicion of OSA between January 2020 and October 2022. Inclusion criteria were OSA diagnosed by

an apnea-hypopnea index (AHI) of 5 or more and experience of cluster period within two years. Basic demographic data, headache-related parameters, and sleep parameters were analyzed according to the severity of OSA. Severity was divided into mild, with an AHI of less than 15, and moderate-to-severe, with an AHI of 15 or more.

Results: A total of 12 CH patients with OSA were evaluated. All participants were male, and the median age was 42 years (range 24 to 62 years). The onset median age was 29 years (range 15 to 57 years), and the median disease duration of CH was 5 years (range 1 to 16 years). Six participants had mild OSA, and the remaining participants had moderate-to-severe OSA. The age at onset of CH in the moderate-to-severe OSA group was higher than in the mild OSA group (median 38.5 years vs. 19.0 years, $p = 0.010$). The maximal duration of cluster bout in the moderate-to-severe group was longer than that in the mild OSA group (median 156.6 days vs. 47 days, $p = 0.037$). A total of 10 participants (83.3%) reported diurnal periodicity.

Conclusions: The onset age of CH and maximal duration of cluster bout were associated with the severity of OSA in CH patients. This may be an indicator that PSG should be actively recommended to patients with CH with these features.

Disclosure of Interest: None Declared

IHC23-PO-019

Preventive Therapy with Galcanezumab for the Next Bout in Patients with Episodic Cluster Headache

Yooha Hong[1], Heejung Mo[1], Byung-Kun Kim[2], Heui-Soo Moon[3] and Soo-Jin Cho[1]

[1]*Departement of Neurology, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of*
[2]*Departement of Neurology, Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Korea, Republic of*
[3]*Department of Neurology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of*

Background: Cluster headache (CH) is one of the severe and disabling medical condition. FDA approved galcanezumab for the preventive therapy of episodic cluster headache. The aim of our study was to investigate the preventive efficacy of galcanezumab injection for recurrent episodic cluster bouts (CB).

Methods: This observational study enrolled 16 patients with episodic CH who received at least 1 time on 240 mg of galcanezumab during each CB in the 3 university hospitals from February 2020 to April 2022. The efficacy and adverse events of galcanezumab during each CB were analyzed and compared.

Results: Patients were 10 (62.5%) males, and the mean age was 38.7 ± 9.8 years. The galcanezumab was injected median 22 (6–63) days after the onset of the first episode of CB and 10.5 (3–49) days in second episode ($p = 0.038$). Among 16 patients, the proportion of patients with 50% or more reduction in daily headache frequency at week 3 from baseline were 62.5% during first episode and 68.8% during the second episode of CB. The frequency of transitional preventive therapies before GT is more (31.3%) during the first galcanezumab treated episode compared to second episode (0%). The improvement of clinical global impression of galcanezumab treatment (GT) was reported as feeling "very much better" or "much better" in 87.5% in the first episode of CB and 62.5% in the second episode. There were no serious adverse reactions and there were not statistically differences in the frequency of adverse effects according to episode of CB.

Conclusions: The patients with cluster headache who had been treated with galcanezumab tend to receive second treatment in the early stages of the next CB without transitional therapy. The efficacy of GT may be influenced by timing of therapy and transitional therapy between CBs in the same patient.

Disclosure of Interest: None Declared

IHC23-PO-020

Efficacy of oxygen treatment using home oxygen concentrators for the treatment of cluster headaches: A randomized, crossover, multicenter study

Soohyun Cho[1], Byung-Kun Kim[2], Min Kyung Chu[3], Heui-Soo Moon[4], Mi Ji Lee[5], Dae-Woong Bae[6], Junhee Han[7], Sang-Hwa Lee[8] and Soo-Jin Cho[9]

[1]*Uijeongbu Eulji Medical Center, Eulji University School of Medicine, Uijeongbu, Korea, Republic of*
[2]*Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Korea, Republic of*
[3]*Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of*
[4]*Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of*
[5]*Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*
[6]*St Vincent's Hospital, The Catholic University of Korea, Suwon, Korea, Republic of*
[7]*Hallym University, Chuncheon, Korea, Republic of*
[8]*Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea, Republic of*
[9]*Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of*

Objective: Oxygen treatment is the first-line acute treatment for cluster headaches; however, insurance coverage and oxygen tank maintenance can be an issue. Oxygen concentrators filter nitrogen from ambient air to produce oxygen-rich gas, so it can be an alternative for conventional oxygen therapy based on oxygen tank. We investigated the effectiveness and safety of oxygen using two home oxygen concentrators compared to oral zolmitriptan in the acute treatment of cluster headaches.
Methods: Forty patients with episodic cluster headaches who were in the active cluster period were enrolled in this randomized, crossover, multicenter study. During the cluster period, two attacks were treated with oxygen delivered by connecting two home oxygen concentrators, whereas the other two attacks were treated with oral zolmitriptan (5 mg) in a random sequence. The primary endpoint was substantial pain reduction (0–1 on a five-point rating scale [zero–four points]) at 15 min.
Results: In total, 125 attacks (63 attacks using oxygen and 62 attacks using zolmitriptan) in 32 patients were randomized and treated according to the study protocol. More attacks treated with oxygen reached the primary endpoint than those treated with zolmitriptan (31.7%, 20/63 attacks vs 12.9%, 8/62 attacks, $p = 0.013$). After 30 min, 58.1% of the patients reported pain relief using oxygen and 38.7% with zolmitriptan ($p = 0.082$). All patients treated with oxygen reported an improvement in pain, and 61.3% preferred oxygen compared to 9.7% who preferred zolmitriptan. No adverse events occurred during the oxygen treatment.
Conclusion: Oxygen administration using two home oxygen concentrators resulted in better pain relief than oral zolmitriptan in patients with episodic cluster headaches. Our results suggest that the home oxygen concentrator may be capable of efficiently supplying oxygen, similar to an oxygen tank.
Disclosure of Interest: Soo-Jin Cho has been the site investigator for a multicenter trial sponsored by Novartis, Allergan, Abbvie Pharma, Ildong Pharma, and Hyundai Pharma. She received honoraria as a speaker or moderator from Teva, Lilly Korea Ltd., Lundbeck, SK Chemical Pharm, Yuyu Pharma, Shinpoong Pharma, and Pfizer and the grant from JW Pharma. Byung-Kun Kim served on Lundbeck's Advisory Board. He received honoraria as a moderator and speaker from Lundbeck, AbbVie, Pfizer, Eli Lilly, Teva, Yuyu Pharm, and SK Pharm. He has been the principal investigator of clinical trials sponsored by Eli-Lilly, Novartis, Lundbeck, Teva, AbbVie, and Ildong Pharm.

IHC23-PO-021

Risk and Reward Seeking in Cluster Headache

Willemijn Naber, Roemer Brandt, Rolf Fronczek and Michel Ferrari

Leiden University Medical Center, Leiden, Netherlands

Objective: Anecdotally, patients with cluster headache (CH) have an increased tendency towards risk-reward seeking. We assessed risk-reward seeking behavior in people with CH, people with migraine, and headache-free controls using the Zuckerman Sensation Seeking Scale (ZSSS) and the Balloon Analogue Risk Task (BART).
Methods: In this single-center, cross-sectional, explorative study, all patients with episodic or chronic CH (eCH and cCH), or migraine from our Neurology outpatient clinic were screened for eligibility between September 2019–December 2020. Headache free controls were recruited through advertisements. All groups were matched for age and sex. Participants completed the ZSSS and two BART rounds. To stimulate risk-taking behavior, the second BART round "suddenly" included an actual reward. Results of the BART are expressed in terms of the number of balloon "pumps", as a measure of risk taking behavior. Between-groups outcomes were analyzed using a multivariate regression analysis, within-groups outcomes with a paired T-Test.
Results: 140 participants (35 eCH, 35 cCH, 35 migraine and 35 controls) were included. Participants with eCH scored higher compared to all groups on the total ZSSS (eCH adjusted mean: 21.8 SD $\pm$ 9.5; cCH: $+8.2$ (95% CI: 3.9; 12.4); Migraine $+6.9$ (95% CI: 2.9; -11.0); Controls: $+6.6$ (95% CI: 2.8; 10.4)), the "experience seeking" subscale and the "disinhibition" subscale. During the second BART, participants with cCH had a lower number of corrected mean pumps ($\Delta -10.6$, 95% CI (–20.9; -0.3)) and popped balloons ($\Delta -2.3$, 95% CI (–4.5; -0.1)) compared to eCH, and lower number of mean pumps ($\Delta -5.9$, 95% CI (–11.7; -0.05)) compared to controls, indicating a decrease in risk-reward behavior.
Conclusion: While the ZSSS points towards an increase in risk-reward seeking behavior in eCH compared to people with migraine and headache-free controls, the BART paradoxically shows a decrease in this behavior in cCH. We hypothesize that there is an inherent increase in risk-reward seeking behavior in CH, which is dampened due to the impact of the chronic form of the disease.
Disclosure of Interest: None Declared

Abstract number: IHC23-PO-021

Table 1 Psychometric measurements (raw means ± SD/median (IQR) when applicable)

		Cluster headache			
Psychometric measurement	Score	Episodic	Chronic	Migraine	Controls
Zuckerman SSS	Total score	19.5 ± 6.9	15.0 ± 6.6	14.9 ± 6.6	16.1 ± 7.5
	Thrill & Adventure Seeking	4.9 ± 2.9	4.1 ± 2.5	4.2 ± 2.6	4.9 ± 3.0
	Experience Seeking	5.5 ± 2.2	4.3 ± 1.9	4.1 ± 2.2	4.2 ± 2.2
	Disinhibition	4.8 ± 2.1	3.3 ± 2.6	3.2 ± 2.5	3.9 ± 2.7
	Boredom Susceptibility	4.3 ± 2.5	3.3 ± 2.3	3.4 ± 1.8	3.1 ± 2.4
Hospital Anxiety and Depression	Total	11.6 ± 5.6	15.0 ± 5.8	11.5 ± 5.1	8.7 ± 4.7
BART (Reward Round)	Mean pumps	36.4 ± 10.4	30.5 ± 12.3	34.0 ± 11.5	36.5 ± 11.8
	Corrected pumps	49.5 ± 20,6	39.7 ± 19.9	45.6 ± 20.2	49.9 ± 20.5
	Popped balloons	14.1 ± 4,2	12.1 ± 4.6	13.4 ± 4.1	14.2 ± 4.2

IHC23-PO-022

Disease Characteristics in Triptan Users and Non-users in a Swedish Cluster Headache Cohort

Felicia Jennysdotter Olofsgård[1], Caroline Ran[1], Katrin Wellfelt[1], Christina Sjöstrand[2,3], Elisabet Waldenlind[2,4], Anna Steinberg[2,4] and Andrea Carmine Belin[1]

[1]*Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden*
[2]*Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden*
[3]*Department of Neurology, Danderyd Hospital, Stockholm, Sweden*
[4]*Department of Neurology, Karolinska University Hospital, Stockholm, Sweden*

Objective: There is clear variation in triptan response between individuals diagnosed with cluster headache (CH) and roughly 25% of patients with CH do not adequately respond to triptans. The biological mechanisms behind non-response are still unknown and previous studies indicate there are differences in CH clinical characteristics between responders and non-responders. For this study we investigated the differences in clinical characteristics between triptan users vs non-users to better understand potential underlying mechanisms.
Method: All study participants had a CH diagnosis validated by a neurologist. 660 of the study participants used triptans in the form of nasal spray or injections (Users) and 142 used no forms of triptans (Non-users). All study participants answered a questionnaire on lifestyle, clinical characteristics, and family history. Chi-square analyses and Wilcoxon test were used for statistical analysis.
Results: Triptan non-users were less likely to have alcohol as an attack trigger (41.6% vs 57.2%, $P = 0.001$) and less likely to have autonomic symptoms accompanying the attacks (88.5% vs 95.0%, $P = 0.007$). Triptan users on the other hand were more likely to have a younger age at onset (31.0 (6–69) vs 35.0 (14–70) years, $P = 0.009$). There was a significant difference in attack frequency ($P = 7.8e-05$) with users more likely to be in groups with higher attack frequency. There was also a significant difference in smoking status ($P = 0.034$) with users more likely to be current smokers (27.7% vs 20.4%) and non-users more likely to be previous smokers (52.1% vs 40.5%).
Conclusion: As expected, we found that triptan usage positively correlates with attack frequency. Furthermore, there are differences in disease characteristics between triptan users and non-users which could indicate biological differences between the two groups, specifically characteristics involving vascular mechanisms seemed more pronounced in the triptan users.
Disclosure of Interest: None Declared

IHC23-PO-023

The enigmatic triangle of cluster headache attacks, sleep and the biological clock: rationale and protocol of the CIESTA study

Paulien J. van Tilborg[1], Else A. Tolner[1,2], Onno C. Meijer[3], Mariëtte R. Boon[3], Thomas J. Upton[4], Stafford L. Lightman[4], Walter Karlen[5], Gisela M. Terwindt[1], Gert J. Lammers[1,6] and Rolf Fronczek[1]

[1]*Department of Neurology, Leiden University Medical Center, Leiden, Netherlands*
[2]*Department of Human Genetics, Leiden University Medical Center, Leiden, Netherlands*
[3]*Department of Endocrinology, Leiden University Medical Center, Leiden, Netherlands*
[4]*University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom*

[5]Institute of Biomedical Engineering, Ulm University, Ulm, Germany
[6]Sleep Wake Centre SEIN, Heemstede, Netherlands

Objective: The aetiology of cluster headache is unknown. Several studies show a clear relationship between attacks, sleep and the circadian rhythm, indicating a pivotal role of the hypothalamus. However, results up until now have been inconsistent, mostly based upon single-night measurements in a hospital setting with a limited number of samples. We aim to determine whether cluster headache attacks occur in relation to specific characteristics and time-points of sleep and the circadian rhythm using a one-week ambulatory study protocol.
Methods: During a one-week baseline period, people with chronic or episodic cluster headache ($n = 24$) will fill out an electronic headache journal to determine if they meet the required number of nocturnal attacks ($\geq$4/week). Baseline will be followed by seven consecutive days of neurophysiological measurements. To approximate regular home-sleep, all measurements will be conducted with wearable devices in a remote setting. Polysomnography will be performed with "MHSL-SleepBand v3", a head worn biopotential (i.e. EEG, EOG and EMG) monitoring device. "U-RHTYHM", a novel micro-dialysis device allowing for subcutaneous cortisol and melatonin levels at twenty minute intervals, will be used to record the circadian rhythm. Additionally, actigraphy, skin and core body temperature, and heart rate variability will be measured with dermal and ingestible sensors. Timing of attacks will be recorded with the electronic diary and wearable headband.
Results: Primary outcome will be the sleep stage (N1, N2, N3, REM) directly prior to attack onset. Secondary outcomes will include mean cortisol and melatonin levels at attack onset, time from zenith and nadir respectively to attack onset, and time from sleep stage transition to attack onset. Additionally, differences in sleep macrostructure (including sleep-related EEG features of excitability) as well as melatonin and cortisol rhythms, during versus outside a cluster episode will be assessed.
Conclusion: The CIESTA study aims to create a unique ambulatory neurophysiological dataset: cluster headache attacks in relation to sleep and clock time-series data. Unravelling the role of the hypothalamus and increased knowledge of sleep and clock rhythms in cluster headache will be of great value for evolving hypotheses and can create a target for new treatments.

IHC23-PO-024

The Spectrum of Disease: A Case Report of Epicrania Fugax Preceded by Reverse Ascending Cluster Headache with Successful Response to Fremanezumab

Thanakit Pongpitakmetha[1,2,3], Sekh Thanprasertsuk[3,4], Wanakorn Rattanawong[5], Kammant Panthumjinda[1] and Prakit Anukoolwittaya[1,3]

[1]Division of Neurology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[2]Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3]Chula Neuroscience center, King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[4]Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[5]Department of Medicine, Faculty of Medicine, King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand

Objective: Epicrania fugax (EF) is characterized by brief electrical linear trajectory pains in different nerve distributions, which 30% of the patients experience autonomic features at the end of the pain. In contrast, cluster headache (CH) is characterized by severe, strictly unilateral pains in the orbital, supraorbital, or temporal area, lasting from 30 minutes to 3 hours. The pain is associated with restlessness and ipsilateral autonomic features. A variant of CH that starts as mild-to-moderate pain at the occipital region and gradually moves towards the orbital area is called the ascending CH reported by Senna-Candel et al. Ascending CH fulfills the criteria of CH but has a pain character of trajectory pain in different nerve distributions like EF. We report a patient who was diagnosed with reverse ascending CH followed by EF and much improved with anti-calcitonin gene-related peptide (CGRP) therapy.
Methods: We report a patient who was diagnosed with EF preceded by trajectory backward pain projection. We proposed the opposite pain projection of ascending CH as "reverse ascending CH". Informed consent was obtained from patient.
Results: A 39-year-old female patient with a 12-year history of high-frequency episodic migraine with visual aura sought consultation at a neurology clinic due to the emergence of a new type of headache over the last 4 years. These new headache attacks always occurred in the late afternoon around 3 P.M., and each episode started with moderately severe stabbing pain (intensity 6/10 on a visual analog scale (VAS)) at the left eyebrow. Then, the pain moved backward along a linear trajectory, reaching the ipsilateral occipital area in 10 minutes. During the peak of headache, the pain at her eyebrow became sharp and

excruciating (intensity 10/10 on VAS), accompanied by tearing, conjunctival injection, ptosis of the left eye, and restlessness. Without treatment, the pain lasted from 30 minutes to 3 hours. The patient sought treatment where she was diagnosed with CH and was treated by a combination of 400 mg/day of gabapentin, 25 mg/day of nortriptyline, 480 mg/day verapamil, sumatriptan, naproxen, and paracetamol/tramadol as needed. Despite the effective dose of treatment, the headaches persisted with the same character. However, they became just a few seconds in duration and had a higher frequency, occurring up to 50 times on certain days. As a result, the patient decided to seek further evaluation at our hospital. Her headache medications were then adjusted to 1200 mg/day of gabapentin, 30 mg/day of propranolol, 40 mg/day of nortriptyline. Other past medical illnesses included nonactive Grave's disease which was treated with 7.5 mg/day of methimazole. Physical and neurological examinations showed unremarkable findings. Brain magnetic resonance imaging was unremarkable.

She was diagnosed with EF due to the short duration and linear trajectory of the headache, which started at the left orbital region and projected towards the occipital region, as defined by ICHD-3. Additionally, the pain from 4 years ago was nearly similar to ascending CH but showed a backward projection, which we defined as "reverse ascending CH". Due to more frequent and disabling episodic migraines, she was administered a 225 mg subcutaneous injection of fremanezumab for 3 months. Three months after the administration of fremanezumab, she reported the resolution of the symptom of EF and ascending CH as well as less frequent episodes of migraines.

Conclusion: EF and ascending CH may not be distinct entities but rather a spectrum of disease that involves peripheral mechanisms such as trigeminal and cervical afferent fibers, as well as central mechanisms such as the trigeminocervical complex, trigeminal-parasympathetic pathway, and hypothalamus. Although the EF pathogenesis remains unclear, the possible pathogenic mechanism was explained by the ascending pain pathway of the peripheral pain generator from the pericranial nerve, in which CGRP plays role in the pain pathway. EF and ascending CH may play a dominant role in peripheral mechanisms, while migraine may play a dominant role in central mechanisms. The anti-CGRP terminating pain transmission in the peripheral pathway can be used in treating the refractory migraine and reverse ascending CH like this case. Further study of the correlation between EF and ascending CH is needed.

Disclosure of Interest: None Declared

IHC23-PO-025

Clinical characteristics and demographics of cluster headache. What are we able to learn from this National Health Service – based sample?

Helin Gosalia[1], Diana Y. Wei[2] and Peter J. Goadsby[1,3]

[1]NIHR King's Clinical Research Facility, & SLaM Biomedical Research Centre, and Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom
[2]Department of Neurology, King's College Hospital, London, United Kingdom
[3]Department of Neurology, University of California, Los Angeles, CA, USA

Objective: To report findings from a cluster headache questionnaire-based study from a National Health Service (NHS)-based sample, detailing diagnosis timelines, cranial autonomic symptoms, premonitory symptoms, clinical characteristics and demographic details.

Methods: A questionnaire-based study was conducted and distributed amongst NHS home-oxygen users across 14 Health Boards in Scotland, UK with a sample size of 95 patients. The diagnosis of cluster headache was established using the criteria of the International Classification of Headache Disorders (ICHD-3).

Results: At the interim analysis, 514 adult patients were on the database receiving oxygen, 198 patients consented to receiving questionnaires of which 95 returned a completed response. All responders met the criteria in ICHD-3. The male to female ratio was 2:1. For the cohort, 53% had episodic and 47% had chronic cluster headache. The mean age of cohort reported was 52 (SD: 15), median age of onset 35 (IQR: 29) and the median time to diagnosis 2 (IQR: 9) months. Of the cohort, 73% were diagnosed by a neurologist, 20% by a general practitioner, 1% by other physician and 6% by other means. Of responders, those who have never smoked accounted for 40%, 27% ex-smokers and 26% current smokers. Of studied subjects, 40% reported alcohol consumption and 60% stated they had no alcohol consumption. The mean duration of attacks was 116 (SEM: 34) minutes. Of the cohort, 100% reported at least one cranial autonomic symptom, most prominent were congestion (85%), aural discomfort (70%) and miosis (63%). The median number of cranial autonomic symptoms reported were 6 (IQR: 3). The presence of premonitory symptoms was reported by 80% of the cohort, most prominent being: cravings (52%), irritability (47%) and neck stiffness (46%). The median number of premonitory symptoms was 4 (IQR: 5). In terms of family history of migraine 47% reported yes, 38% no and 15% unsure. Of the studied population, 37% reported yes for a diagnosis of migraine. The most effective prophylactic treatment

was verapamil, and the most common dose of 240 mg. The most effective acute treatment was oxygen, average rate 12 L/min. Of the cohort, 92% reported migrainous associated symptoms, most prominent: photophobia (61%), phonophobia (54%) and nausea (50%).

Conclusion: We concluded there is a comparatively reduced time to diagnosis, to what has been previously reported. Furthermore, identifying and tracking premonitory symptoms can be helpful in managing the condition, as it may allow for earlier intervention. Demographic and clinical data collected as above can facilitate clinical decision making and understand better the evolving patient population.

Disclosure of Interest: Helin Gosalia has nothing to declare. Diana Y. Wei has nothing to declare. Peter J. Goadsby reports, over the last 36 months, grants a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly, Epalex, GlaxoSmithKline, Impel Neuropharma, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee.

IHC23-PO-026

A comparison of the use of oxygen between the subtypes of cluster headache in a National Health Service – based sample

Helin Gosalia[1], Diana Y. Wei[2] and Peter J. Goadsby[1,3]

[1]*NIHR King's Clinical Research Facility, & SLaM Biomedical Research Centre, and Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[2]*Department of Neurology, King's College Hospital, London, United Kingdom*
[3]*Department of Neurology, University of California, Los Angeles, CA, USA*

Objective: Inhalation of 100% high flow oxygen is a first-line acute therapy for the indication of cluster headache. Given its place as a treatment option, very little is known about the differences between the two subtypes with regard to oxygen consumption and efficacy.

Methods: A questionnaire-based study was conducted and distributed amongst National Health Service (NHS) home-oxygen users across 14 Health Boards in Scotland, UK with a sample size of 95 patients. The diagnosis of cluster headache was established using the criteria of the International Classification of Headache Disorders (ICHD-3). Detailed questions about their use of oxygen, mask type, rate, use of instructions, rebound effect and satisfaction rates were explored.

Results: At the interim analysis, 514 adult patients were on the database receiving oxygen, 198 patients consented to receiving questionnaires of which 95 returned a completed response. All of the responders met the criteria in ICHD-3. Episodic cluster headache (ECH) patients made up 54% ($n = 51$) and chronic cluster headache (CCH) 46% ($n = 44$) of the cohort. Of ECH patients, 96% reported the use of oxygen and of CCH patients, 96%. The range for rate of oxygen use was 8–14 L/min in ECH patients and 6–12 L/min in CCH patients. Of ECH patients, 44% reported the use of a simple face mask, 47% non-rebreather mask and 9% demand valve. Of CCH patients, 28% simple face mask, 62% non-rebreather mask and 10% demand valve. Average time of use of oxygen for ECH patients was 22 (SEM: 2) minutes and for CCH patients 23 (SEM: 2) minutes. Of ECH patients 90% received instructions for the use of oxygen and of CCH patients, 83%. For ECH patients, 47% endorsed oxygen as the most effective acute treatment and of CCH patients, 50%. Of ECH patients, 53% reported rebound headache with mean time 33 (SEM: 11) minutes after oxygen use. Of CCH patients, 54% reported rebound headache with mean time 17 (SEM: 4) minutes. A significant association between oxygen as the most effective acute treatment and taking verapamil as a preventive was seen for ECH patients. We conducted Fisher's exact test with a $P < 0.001$. To corroborate this finding, we conducted a chi-square test which was significant ($P < 0.001$) and this was also significant after Yates's continuity correction ($P < 0.001$).

Conclusion: From this interim analysis, we found important differences between the two subtypes, specifically that there are synergistic effects between verapamil and oxygen for episodic users. Both treatments are unique to this disorder only, further indicating that taken together may yield better efficacy and clinically demonstrate to be a better treatment plan.

Disclosure of Interest: Helin Gosalia has nothing to declare. Diana Y. Wei has nothing to declare. Peter J. Goadsby reports, over the last 36 months, grants a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly, Epalex, GlaxoSmithKline, Impel Neuropharma, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press,

UptoDate and Wolters Kluwer, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee.

IHC23-PO-027

SUNCT Following Lateral Brainstem Infarction: Two Case Reports

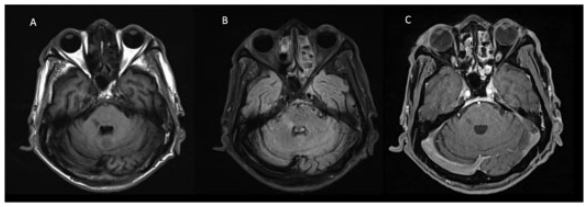
Priabprat Jansem[1], Nattapat Watanapa[1], Sekh Thanprasertsuk[2,3], Wanakorn Rattanawong[4] and Prakit Anukoolwittaya[5,2]

[1]Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[2]Chula Neuroscience Center, King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3]Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[4]Department of Medicine, Faculty of Medicine, King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand
[5]Division of Neurology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

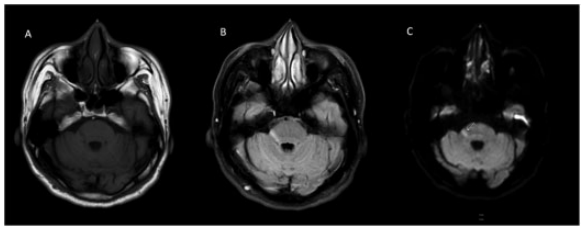
Objective: Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) are rare headache syndromes categorized in trigeminal autonomic cephalalgias by the International Classification of Headache Disorders 3 (ICHD-3). These syndromes are characterized by headache attacks accompanied by autonomic symptoms, such as conjunctival injection and tearing, among others. Existing literature suggests that these pathologies may be triggered by certain cerebral pathologies, with modern neuroimaging techniques assisting in the discovery of these associations. Emerging clinical knowledge has identified vascular etiologies to at least some cases of these headaches. Therefore, we seek to clarify these associations. We present two cases of patients who have suffered SUNCT following a lateral brainstem infarction documented on magnetic resonance imaging (MRI) and proposed pathogenesis SUNCT after brainstem stroke.

Method: We report two cases of patients who have suffered SUNCT following a lateral brainstem infarction. Informed consent was obtained from patients.

Result: Case 1: A 70-year-old Thai male with dyslipidemia presented with headache progressing over five years. He described the pain as an electrical shock-like sensation from his right frontal area radiating to his cheek lasting 30 seconds. Associated symptoms included ipsilateral lacrimation, conjunctival injection, facial erythema, and rhinorrhea. After the first evaluation, the diagnosis of trigeminal neuralgia was made at a local community hospital, and Gabapentin 300 mg was initiated. Interestingly, the patient reported that his symptoms recurred annually, and subsided for the rest of the year. He decided to reevaluate his headache at King Chulalongkorn memorial hospital (KCMH). The patient's physical examination was unremarkable, with no sinus tenderness or trigger zone, no facial sensory loss or hyperesthesia. His headache characteristics were compatible with the criteria for SUNCT.
MRI brain revealed a lesion at the right lateral aspect of pons and right cerebellar peduncle involving the course of the fascicular segment of the right trigeminal nerve, suggesting a previous ischemic lesion.
Treatment with Gabapentin 900 mg daily, Carbamazepine 400 mg daily, Lamotrigine 25 mg daily, Aspirin 81 mg daily, and Simvastatin 20 mg daily was initiated, resulting in significant improvement in symptoms.



Case 2: A 55-year-old Thai male with hypertension presented with a persistent right-sided headache progressing over seven years. The pain was described as a sharp stabbing around the right eye, lasting 30 seconds and occurring 1–2 times daily around the time of presentation. He sought medical attention at King Chulalongkorn Memorial Hospital.
During an attack of pain, the patient exhibited ipsilateral conjunctival injection, lacrimation, and hemifacial spasm. Outside an attack, the physical examination was unremarkable, including no facial tenderness or trigger zone. The neurological examination was normal, with no facial sensory loss or hyperesthesia. His headache was compatible with the criteria for SUNCT.
An MRI brain performed seven years prior showed a lesion at the right lateral aspect of the pons, suspected to be due to subacute infarction. The patient was prescribed a daily dose of 1200 mg of gabapentin and 25 mg of lamotrigine, which resulted in a notable improvement in his symptoms.



Discussion: Both cases had stroke confirmed by imaging at the lateral pons. Therefore, we propose a mechanism in

which these headache syndromes are attributable to lateral brainstem lesions. From a clinical point of view, the pain location and associated symptoms follow the trigeminal nerve distribution indicating a point of origin at the trigeminocervical complex which is located in the lateral brainstem, coinciding with the stroke location seen in our cases. Involvement of the nearby superior salivary nucleus, which provides parasympathetic innervation to the lacrimal gland and conjunctiva, can explain the associated lacrimation and conjunctival injection found in SUNCT.
Since the time between the onset of headache and stroke is different as shown by our two cases, the etiology of these headaches could possibly be due to either direct damage to the trigeminocervical complex or later remodeling of the brain tissue after infarction, presumably abnormal neuroplasticity. We propose one possible mechanism of SUNCT: dysfunctional remodeling of the trigeminocervical complex and autonomic neural pathways in the lateral brainstem.
Disclosure of Interest: None Declared

IHC23-PO-028

The New Prophylactic Treatment for Episodic Cluster Headache by Administration of Live Attenuated Zoster Vaccine ~including recurrence cases related frequent vaccinations for COVID 19 or affection to COVID 19

Toshihiko Shimizu[1] and Ichiro Arakawa[2]

[1]*Department of Neurosurgery Neurological Institut, Tokyo Women's Medical University, Tokyo, Japan*
[2]*Former Teikyo Heisei University, Tokyo, Japan*

Back ground and aims: We had ever reported that episodic cluster headache (ECH) might be probably triggered by reactivation of subclinical Varicella Zoster Virus (VZV) in trigeminal ganglion which would induce abnormal CGRP release of perivascular region, and vaccination of live attenuated zoster were effective prophylactic method for over100 patients suffering from ECH. We are continuing observation the efficacy of vaccination for about 84 months (7years), and also re-evaluated the timing and indicator for second look vaccination by measuring immunoglobulin G tighter (IgG) and complement fixation method tighter(CF) of VZV.
Method: This time, diagnosed ECH by the International Classification of Headache Disorder III Edition over 160patients suffering from episodic cluster headache (ECH), visiting our clinic, had annually experienced 1.12-time seizure with 4.79-week period per seizure on average before vaccinated. Almost all patients were prescribed as prophylactic treatment in pre-vaccinated. All patients were checked antibody of VZV (IgG and CF) before and after vaccinated, to confirm the efficacy for the prevention of ECH.
Result: The Survival analysis revealed that time to have first seizure in effective group gained sufficient antibody by vaccinated was statistically longer than that in ineffective group ($p < 0.0001$).After vaccinated, to be kept antibody values stable for a few months or over. The Survival analysis revealed that time to have first seizure in COVID 19 non-infected group tended to be longer than that in infected group ($p = 0.29/0.41$) after vaccination of herpes zoster. A few patients experienced the recurrence of very slight and short-term cluster headache attack who was vaccinated within 6 months after last cluster period. Also, COVID 19 infection and several times vaccination for COVID 19 may be considered as worsened factor of recurrence of ECH, because of break the balance of immunoglobulin or stimulation of spike proteins existing in surface of COVID 19 virus for brain vessels in human being.
Discussion: Furthermore, long term and large number evaluation will be needed to confirm the certain efficacy of Zoster vaccine to the prophylactic effect for ECH.
Disclosure of Interest: None Declared

IHC23-PO-029

Chiari-TAC; A Surgically Cured Symptomatic Trigeminal Autonomic Cephalalgia

Devasmitha Wijesundara, Shiran Paranavitane and Bimsara Senanayake

Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka

Background: Trigeminal autonomic cephalalgia (TAC) encompasses four primary headache disorders according to the International Classification of Headache Disorders 3β (ICHD3β). Rarely, TAC headaches may occur secondary to structural pathology. We describe a patient with TAC headache as the initial manifestation of Type I Chiari malformation, which resolved after decompressive surgery.
Case Presentation: A 36-year-old female presented with a one-month history of worsening headache. Headache frequency was 4- 5 times per week. She described a severe, left side locked headache with associated redness and tearing of the ipsilateral eye. She also complained of numbness of the ipsilateral face and weakness of the body. Duration of the headache was unusual, lasting between 4–6 hours and occurring 2- 3 times per day. She denied any increase in headache with the Valsalva maneuver. Examination revealed left- sided partial ptosis and conjunctival suffusion (figure 1). However, there was no pupillary involvement. She had impaired pain sensation over the ophthalmic and maxillary divisions of the left

trigeminal nerve. Fundoscopy was normal and there were no other cranial nerve abnormalities. Hoover's test uncovered that her hemiparesis was a functional neurological deficit. Magnetic resonance imaging (MRI) of the brain revealed a 6mm tonsillar descent, compatible with the diagnosis of Type I Chiari malformation (figure 2). She was started on a combination of indomethacin, verapamil, and prednisolone, to which she had suboptimal control of headaches. A neurosurgical input was obtained, after which she underwent successful cranio-vertebral decompression. She remains headache free at 2 months of follow up.

Discussion: All patients with trigeminal autonomic cephalalgia should undergo MRI as symptomatic TAC headaches may be indistinguishable from primary headache disorders. However, the presence of atypical features, such as in our patient suggest the former. We wish to highlight that although symptomatic TAC headaches are rare, they may be amenable to surgery with excellent outcomes.

Figure 1

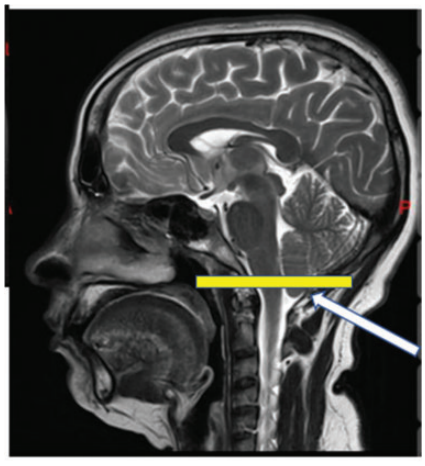


Figure 2

Disclosure of Interest: None Declared

IHC23-PO-030

Greater Occipital Nerve Stimulation for Refractory Chronic Cluster Headache: Is there life after the Implant?

Davide Mascarella[1], Giulia Giannini[1,2], Lorenzo Giusti[1], Valentina Favoni[2], Giulia Pierangeli[1,2] and Sabina Cevoli[2]

[1]Departement of Biomedical and Neuromotor Sciences (DIBINEM) – University of Bologna, Bologna, Italy
[2]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Background: Cluster Headache (CH) is an unbearably painful and rare condition that can be resistant to standard medical treatments. Occipital nerve stimulation (ONS) has shown promising results for refractory Chronic CH in both open-label studies and randomized clinical trials. However, more research is needed to fully understand the long-term effectiveness and safety of this treatment, as well as the optimized stimulation protocol. This study aims to evaluate the effectiveness and safety of ONS in refractory Chronic CH patients during a one-year period.

Methods: We included all patients diagnosed with refractory Chronic CH who underwent bilateral greater occipital nerve stimulation implantation between April 2018 and November 2022 at the Headache Center of Bologna. The stimulation parameters (contacts polarity, intensity, pulse width, and frequency) were programmed following a developing stepwise protocol to optimize clinical effects. Patients were then followed up for a minimum period of 12 months. Patients kept a daily diary of headaches during the whole study period. The following parameters were evaluated: baseline and demographic features at baseline, attack frequency, pain intensity, latency between implantation and achievement of maximum benefit, stimulation parameters that led to maximum benefit, and adverse events. The primary endpoint was a 50% reduction in headache frequency.

Results: 9 patients were included (8 males, 1 female), the mean age was 55 (SD $\pm$ 15.3) and the mean latency from chronicization to implant was 10 years (SD $\pm$ 8.5). The median number of previous prophylactic medications was 7 (IQR 6–9). After six months 7 out of 9 patients achieved the 50% reduction in headache frequency, while after 9 months 50%-responders were 8 of the total 9 patients. Among the 7 patients who completed one year of follow-up, six patients no longer had a diagnosis of Chronic CH but had reverted to episodic CH. Regarding pain intensity, the NRS scale mean values declined from 9.6/10 pre-implant to 6.5/10 one year after. Assessing personal satisfaction expressed as a percentage, 8 out of 9 patients defined themselves as satisfied at 60% or more, with 5 of those 8 reporting satisfaction levels of 90% or

100% after one year. The mean latency from surgery to best effect was 3.8 months (SD ± 2.6) following our stimulation programming protocol. One patient experienced a loss of effectiveness due to leads migration and needed an explant of the GONS after two years.
Conclusions: The Occipital Nerve Stimulation (ONS) has demonstrated to be a highly effective and well-tolerated therapy in a severely disabled population with few therapeutic alternatives. In our study, a significant proportion of refractory patients showed a rapid and sustained response, highlighting the role of a thorough programming protocol. Adverse effects were negligible, and surgical removal was required in only one case.
Disclosure of Interest: None Declared

IHC23-PO-031

Burden of disease in cluster headache: An online survey for patients and relatives of patients

Charly Gaul[1], Mirjana Slijepcevic[2] and Janosch Fox[3]

[1]*Headache Center Frankfurt, Frankfurt, Germany*
[2]*Benedictus Hospital, Feldafing, Germany*
[3]*University of Göttingen Medical Centre, Department of Psychosomatic Medicine and Psychotherapy, Göttingen, Germany*

Objective: To evaluate the (1) burden of disease, (2) satisfaction with diagnostic and treatment and (3) interventional needs in episodic and chronic cluster headache (eCH, cCH) as well as the (4) burden on the relatives of sufferers. Herein we focus on the data of the relatives.
Methods: Data were obtained systematically with an online survey in January and February 2023 among cluster headache patients and relatives of sufferers. Diagnoses were made by treating physicians and rechecked by asking the ICH-3 criteria1. The survey included the CHS (Cluster Headache Scales)3 to assess psychosocial factors in patients and the DASS (Depression, Anxiety, and Stress Scale) 2 to assess psychological burden in patients and relatives of patients.
Results: Out of 869 participating patients, complete data sets from 640 patients could be included (354 eCH; 287 cCH; male (m): 373, female (f) 265, age 18–86 years). For relatives, 147 complete data sets could be included (m: 42, f: 104, age 18–79 years) out of 232. The relatives were mostly partners or family members (partners 72,8%, parents 10.2%, children 6.1%, siblings 2.0%, near friends 5.4%, colleagues 0.7% and others or unknown 2.7%). They had been in contact with the patients for a mean duration of 20.8 years (SD = 13.7) and 80% live together with the patients in a household. The relationship with the patient was found to be burdened by 68.7% of the relatives due to the CH. 90.5% felt a feeling of helplessness when present during a cluster headache attack. In 31.3% of cases, patients were perceived by relatives to be aggressive during attacks. 87.1% of relatives reported that the disease was associated with psychological burden in patients. 85% were afraid of the further course of the disease, which was similar to the patients: 80.9% ($p > 0.05$).
Regarding the psychological burden a score $\geq$ 10 on the DASS depression scale was shown by 42.1% of patients and 50.3% of relatives, a score $\geq$ 6 on the DASS anxiety scale was shown by 54.8% of patients and 10.2% of relatives, a score $\geq$ 10 on the DASS stress scale was shown by 54.0% of patients and 32.7% of relatives. Patients had higher mean scores for anxiety (7.0 (5.1) vs. 3.2 (4.0), $p < 0.01$, $d = 0.77$) and stress (10.6 (6.1) vs. 7.1 (5.6), $p < 0.01$, $d = 0.59$) compared to relatives; for depression, relatives'' mean scores were higher than patients'' (11.3 (4.9) vs. 8.4 (6.7), $p < 0.01$, $d = 0.49$).
Conclusion: This is the first study obtaining data on the psychological burden of CH patients and relatives of CH patients in Germany. Using screening questionnaires, a high level of psychological burden was found in both groups. CH disease can strain the relationship between patient and relatives. During CH attacks, aggressive behavior in patients and a feeling of helplessness in relatives are important characteristics. Anxiety about further progress of the disease is frequent among patients and relatives equally. Caregivers (neurologists, psychologists) should focus on these aspects and consider the psychological burden, as well as the need for education of patients and relatives.
Disclosure of Interest: There was no funding of this study. C.G. has received honoraria for consulting and lectures within the past three years from Allergan Pharma, Lilly, Novartis Pharma, Hormosan Pharma, Grünenthal, Sanofi-Aventis, Chordate, Lundbeck Perfood, and TEVA. He is honorary secretary of the German Migraine and Headache Society. He does not hold any stocks of pharmaceutical Companies. J. F. has no conflict of interest M. S. has received compensation for travel expenses and regirstations fees for several congresses from TEVA.

IHC23-PO-032

Melatonin in Hemicrania Continua: a cohort of 56 patients

Sing Ngai Cheung[1,2] and Peter J Goadsby[1,3]

[1]*NIHR King's Clinical Research Facility & SLaM Biomedical Research Centre, and Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[2]*Department of Medicine and Geriatrics, Hong Kong SAR, Hong Kong*
[3]*Department of Neurology, University of California, Los Angeles, USA*

Objective: Hemicrania continua is an uncommon primary headache disorder. One of the diagnostic criteria is the absolute response to the therapeutic dose of indomethacin. However, some patients cannot continue on indomethacin due to their intolerance to its side effects. Melatonin, a pineal hormone, which shares similar chemical structure to indomethacin has been reported to have some efficacy for hemicrania continua in previous case reports and series. We aimed to describe the clinical use of melatonin in patients of hemicrania continua as an alternative preventive treatment.
Method: Audit of patient data extracted from routinely collected clinical records in consecutive patients with hemicrania continua seen in King's College Hospital from September 2014 to April 2023.
Results: Fifty-six patients were included with mean age 52 ($\pm$ 16, SD) years; 43 of 56 (77%) patients were female. All patients were diagnosed with hemicrania continua according to the International Classification of Headache Disorders – third edition. Melatonin was taken by 23 (41%) patients. Fifteen (65%) patients had a positive intramuscular indomethacin test, while the remaining 8 (35%) showed a positive response to an oral indomethacin trial. The equivalent daily dose of indomethacin ranged from 75 mg to 225 mg. Of 23 patients, 19 (83%) stopped indomethacin with different side effects. Commonly reported side effects of indomethacin included nausea, stomach discomfort and peptic ulcer. The doses of melatonin used ranged from 0.5 mg to 21 mg. Fourteen (61%) patients reported some positive relief for headache, while the remaining 9 (39%) patients reported no headache preventive effect. None of the patient reported they were completely pain free with melatonin treatment. Two patients continued on indomethacin and melatonin concurrently for better symptom relief. Eight patients stopped indomethacin due to intolerance and continued on melatonin as the single preventive treatment. Side effects from melatonin were rare. One patient reported fatigue and one patient reported sleepiness after the use of melatonin. Two patients reported worsening of headache after taking melatonin and one patient stopped because of a wish for pregnancy.
Conclusion: Melatonin showed some efficacy in the treatment of hemicrania continua with a well-tolerated side effect profile. It does not have the same absolute responsiveness as indomethacin, at the doses used, although it does offer a well-tolerated option that can having significant ameliorating effects in a substantial cohort of patients.
Disclosure of Interest: SNC reports nil disclosure of interest. PJG reports, over the last 36 months, a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly and Company, Epalex, GlaxoSmithKline, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer, and for medicolegal advice in headache, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee.

IHC23-PO-033

The phenotype of cluster headache patients changed in time: From the perspective of a Taiwanese cluster headache registry

Yi Chia Liaw[1], Yen-Feng Wang[1,2,3], Wei-Ta Chen[1,2,3,4], Shih-Pin Chen[1,2,3,5,6], Jr-Wei Wu[1,2], Shu-Ting Chen[2,7], Kuan-Lin Lai[1,2], Jong-Ling Fuh[1,2,3] and Shuu-Jiun Wang[1,2,3]

[1]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Department of Neurology, Keelung Hospital, Ministry of Health and Welfare, Keelung, Taiwan*
[5]*Division of Translational Research, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan*
[6]*Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[7]*Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan*

Objective: Since recent studies of cluster headache (CH) showed a decreasing male-to-female ratio over time, we hypothesized that clinical characteristics may have

changed. However, no data exists in investigating the trend. Thus, we aim to investigate the trend of clinical presentations of cluster headache in a large cohort in Taiwan.

Methods: Patients with CH were consecutively enrolled from headache clinics in Taipei-Veterans General Hospital from 1997 to 2021. Patients were recruited if they fulfilled the diagnostic criteria of CH by the International Classification of Headache Disorders (ICHD). They were asked to fill in an intake questionnaire which included demographic data, clinical profiles, and psychological burdens. To describe the trend, the patients were designated into three epochs according to the onset year of their first cluster period, namely years ≦1996, 1997 to 2004, and ≧ 2005. The trend of demographical and clinical profiles as well as psychological burdens throughout different epochs were compared. To remove the potential confounding factors, regression models including onset age, age at diagnosis, sex, diagnostic delay and smoking status were established. We also tested the relationship between clinical presentations and diagnostic delay or smoking status.

Results: This retrospective cohort study enrolled 791 patients in total. The proportions of male patients did not change (80.6%, 84.4%, and 82.5%, p for trend = 0.555). Throughout the three epochs, the proportions of ever smokers decreased from 63.7% to 55.0% (p for trend < 0.046), the mean onset age became older from 22.4 to 29.5 years old (p for trend < 0.001), and the mean diagnostic delay became shorter from 19.1 years to 4.1 years (p for trend <0.001). The mean severity of CH has decreased from 8.4 to 7.6 on the 0–10 scale (p for trend < 0.001). Patients reporting cranial autonomic features including conjunctival injection and/or lacrimation (from 86% to 70.9%, p < 0.001), nasal congestion and/or rhinorrhea (from 61.6% to 32.4%, p < 0.001), eyelid edema (from 23.3% to 15.0%, p = 0.017), forehead and facial swelling (from 41.1% to 28.7%, p = 0.003), ptosis and/or miosis (from 31.0% to 22.3%, p = 0.024) have declined, and the average number of CAS also decreased (from 2.1 to 1.7, p < 0.001). Migrainous features, which included nausea (from 61.5% to 48.2%, p = 0.003), vomiting (from 45.0% to 25.6%, p < 0.001), photophobia (from 63.7% to 53.8%, p = 0.024) and phonophobia (from 66.2% to 51.6%, p = 0.001) decreased. The anxiety and depression burden as assessed by the Hospital Anxiety and Depression Scale (HADS) also declined (from 16.0 to 13.0, p < 0.001).

We also noted that diagnostic delay is positively correlated with headache severity (β = 0.029, p < 0.001), the proportion of conjunctival injection and/or lacrimation (OR = 1.004, p = 0.020), nasal congestion and/or rhinorrhea (OR = 1.007, p = 0.001), eyelid edema (OR = 1.004, p = 0.014), forehead and facial swelling (OR = 1.005, p = 0.007), and the average number of CAS (β = 0.02, p < 0.001). For smokers, there is an increased risk for forehead and facial swelling (OR = 1.10, p = 0.005), ptosis and/or miosis (OR = 1.07, p = 0.041) and increased average number of CAS (β = 0.270, p = 0.002).

After controlling for potential confounding factors, the headache severity remained a declined trend (β for epoch = −0.395, p = 0.003). The proportions of patients reporting conjunctival injection and/or lacrimation (OR = 0.89, p < 0.001), nasal congestion and/or rhinorrhea (OR = 0.83, p < 0.001) and the average CAS count (β for epoch = −0.332, p < 0.001) remained a declined trend throughout the epochs. HADS score has also decreased (β for epoch = −3.15, p < 0.001).

Conclusion: Our study did not show the change of male-to-female ratios by dividing patients into three epochs according to their disease onset. However, the severity of CH decreased, and there was a decline in patients reporting CAS or migrainous features. These positive changes might be partly due to a reduced smoking rate and shorter diagnostic delay among patients. Nevertheless, there are still unknown socio-environmental factors that could be influencing the trend of CH phenotype.

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IHC23-PO-034

Are migraine and cluster headache one spectrum? Implications from cyclical migraine

Mingjie Zhang[1], Ziming Yin[2], Zihan Zhang[1], Ye Ran[1], Shuhua Zhang[1], Ke Li[1], Jingrui Mao[1], Wei Zhao[1], Huanxian Liu[1], Yajun Lian[3], Yanmei Xu[4], Yajie Li[5], Jiale liu[6], Qun Gu[7], Fanhong Yan[8], Zhaoli Ge[9], Yu Lian[10], Dongmei Hu[11], Sufen Chen[12], Xiaolin Wang[1], Rongfei Wang[1], Xiaoyan Chen[1], Zhihua jia[1], Jing Liu[1], Xun Han[1], Dong Zhao[1] and Shengyuan Yu[1]

[1]*Department of neurology, The first medical center, The Chinese PLA general hospital, Beijing, China*
[2]*School of Medical Instrument and Food Engineering, University of Shanghai for Science and Technology, Shanghai, China*
[3]*Department of Neurology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*
[4]*Department of Neurology, Dingyuan general hospital, Anhui, China*
[5]*Diagnostic ultrasound centre, The centre hospital of jilin city, Jilin, China*
[6]*Department of neurology, The centre hospital of jilin city, Jilin, China*
[7]*Department of Neurology, Huzhou first peolple's hospital, Zhejiang, China*
[8]*Department of Neurology, linyi jinluo hospital, Shandong, China*
[9]*Department of Neurology, Shenzhen second people's hospital, Guangdong, China*
[10]*Department of Neurology, Inner Mongolia xing"an league people's hospital, Inner Mongolia, China*
[11]*Department of Neurology, The second affiliated hospital of Shandong first medical university, Shandong, China*
[12]*Department of Neurology, Changsha central hospital affiliated to university of south china, Hunan, China*

Objectives: Cyclical migraines (C-M) are occasionally met in the clinic, but not well studied. The aim of the study was to define the characteristics of C-M and compare these features with cluster headache (CH) and migraine without aura (MO).
Methods: We collected patients who could be diagnosed as migraine or probable migraine but have definite cluster period between 2014 and 2020 in our headache center. Patients who diagnosed as cluster headache (CH) and migraine without aura from our cross-sectional standardized survey during the same period was collected as control. Data including demographics, headache characteristics, triggers and relieving factors.
Results: Forty-seven patients with C-M were identified. We found that C-M had a higher percentage of women, less severe than CH. We also found C-M had a lower percentage of women, earlier onset, shorter duration of headache attack, more severe, less in proportion of parietal region and more in proportion of orbital region than migraine. Patients with C-M had similar percentages of migraine-like accompanying features like nausea, vomiting, photophobia and phonophobia to CH, but were less than in MO. Except for miosis and eyelid oedema, the incidence of other CH-like accompanying features in C-M patients were significantly lower than CH. Except for miosis, the incidence of other CH-like accompanying features in C-M patients were significantly higher than MO. Triggers and relieving factors in C-M were more likely to CH but not to migraine. Alcohol were more often induced headaches in C-M and CH compared to MO and stress were more often induced headaches in MO compared to CH and C-M. Hormones, noisy environment and specific odor were common triggers for MO than CH. Rest or sleep and pregnancy were more useful for MO patients compared to CH and C-M, and cold compress and exercises were more useful for CH patients compared to MO.
Conclusions: The largest series of C-M defines it as a transition stage between migraine and CH. Less differences were found between C-M and CH indicated that C-M may be more similar to CH.
Disclosure of Interest: None Declared

IHC23-PO-035

Factors associated with bout frequency in episodic cluster headache

Byung-Su Kim[1], Mi Ji Lee[2], Pil-Wook Chung[3], Byung-Kun Kim[4], Min Kyung Chu[5], Kwang-Yeol Park[6], Dae Woong Bae[7], Tae-Jin Song[8], Jong-Hee Sohn[9], Kyungmi Oh[10], Daeyoung Kim[11], Jae-Moon Kim[11], Jeong Wook Park[12], Jae Myun Chung[13], Heui-Soo Moon[3], Soohyun Cho[14], Jong-Geun Seo[15], Soo-Kyoung Kim[16], Yun-Ju Choi[17], Chin-Sang Chung[18] and Soo-Jin Cho[19]

[1]*Ewha Womans University Mokdong Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of*
[2]*Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*
[3]*Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of*
[4]*Eulji Hospital, Eulji University, Seoul, Korea, Republic of*
[5]*Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of*
[6]*Chung-Ang University Hospital, Seoul, Korea, Republic of*
[7]*College of Medicine, The Catholic University of Korea, Suwon, Korea, Republic of*
[8]*Seoul Hospital, Ewha Womans University Seoul Hospital, College of Medicine, Seoul, Korea, Republic of*
[9]*Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea, Republic of*

[10]Korea University College of Medicine, Seoul, Korea, Republic of
[11]Chungnam National University College of Medicine, Daejeon, Korea, Republic of
[12]Uijeongbu St.Mary's Hospital, The Catholic University of Korea College of Medicine, Uijeongbu, Korea, Republic of
[13]Inje University College of Medicine, Seoul, Korea, Republic of
[14]Eulji University, Uijeongbu, Uijeongbu, Korea, Republic of
[15]School of Medicine, Kyungpook National University, Daegu, Korea, Republic of
[16]Gyeongsang National University College of Medicine and Gyeonsang National University Hospital, Jinjoo, Korea, Republic of
[17]Dr. Choi's Neurology Clinic, Jeonju, Korea, Republic of
[18]Neuroscience Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of
[19]Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of

Background: Cluster headache (CH) is rare, but the most painful primary headache disorder. Cluster bout is not only the distinct key feature from other headache disorders but also a core element of disease course. Nevertheless, little data are currently available which factors are important in determining the frequency of bout. The aim of this study is to investigate factors associated with bout frequency in patients with episodic CH (ECH).
Methods: In this cross-sectional study, we analyzed data from a prospective multicenter CH registry over a 4-year period. We enrolled ECH patients with $\geq$2 years of lifetime disease duration and $\geq$2 times of lifetime bout. Bout frequency was defined as number of bouts per year (number of lifetime bout divided by lifetime disease duration). These key variables were ascertained at baseline enrollment period based on recall in memory. Eligible patients were categorized into three groups along with the tertiles of bout frequency (1st tertile, $\leq$0.6; 2nd tertile, $>$0.6 and $\leq$1; and 3rd tertile, $>$1). Ordinal logistic regression analysis was conducted to identify factors associated with bout frequency.
Results: Of 316 eligible patients, the median bout frequency was 0.88 (interquartile range: 0.5–1.10). In terms of age, the median bout frequency was highest in the 20s, while lowest in the 50s (1.0 vs. 0.6). In univariable analysis, age (odds ratio [OR] = 0.95, 95% confidence interval [CI] = 0.93–0.97) and body mass index (BMI; OR = 0.89, 95% CI = 0.83–0.95) were inversely correlated with the tertiles of bout frequency, while seasonal rhythmicity was associated with the tertiles of bout frequency (OR = 1.87, 95% CI = 1.23–2.83). After multivariable adjustment, the association of age, BMI, and seasonal rhythmicity with the tertiles of bout frequency remained significant (multivariable-adjusted OR [aOR] = 0.96, 95% CI = 0.94–0.98; aOR = 0.89, 95% CI = 0.84–0.96; and aOR = 1.74, 95% CI = 1.14–2.65, respectively).
Conclusions: Age, BMI, and seasonal rhythmicity were independently associated with the tertiles of bout frequency in ECH patients. These findings suggest that bout may become less frequent as getting older in ECH, and obesity status and chronobiology may be further connected to determining bout frequency. Further preclinical and clinical studies are required to confirm our findings.
Disclosure of Interest: None Declared

IHC23-PO-036

Clinical characteristics and diagnostic delay in Cluster headache, An Egyptian study.

Mona K. Moawad, Mona AF Nada and Salsabil Abo Al-Azayem

Cairo University Kasr Alainy Faculty of Medicine, Cairo, Egypt

Objective: Cluster headache (CH) is the least common primary headache disorder. Despite its low prevalence, it is associated with the most severe and disabling pain among primary headache disorders and known as suicidal headache. We aim to present for the first time in Egypt, the clinical characteristics of cluster headache and assess the diagnostic delay.
Methods: The study is a cross sectional investigation study that included all patients presenting with cluster headache diagnosed according to ICHD-III, who were consecutively recruited from all patients presenting with primary headache disorders based on data from two centers in Egypt (Cairo university hospital specialized headache clinic, and Specialized center in Alexandria) over 1 year with age from 18 to 60 years old. Demographic and clinical characteristics were collected. Rate of diagnostic delay in diagnosis was calculated. The protocol was approved by Cairo university ethical committee.
Results: Our data registry included 1187 patients with primary headaches with 23 patients with diagnosed as cluster headache which represents 1.9% of all patients. The majority of patients (82%) were males with male to female ratio 4.75:1. The mean age was 37.9 ± 10 years, while the mean age of disease onset was 25 ± 8 years. Twelve patients (52.2%) were smoker while 6 patients (26.1%) had comorbidities (hypertension, ischemic heart disease and diabetes). None of our patients reported family history of CH. Sixty-five percent of patients had episodic CH, while 34.8% had chronic CH. All the patients had unilateral periorbital excoriating severe pain, with significant autonomic manifestations. Most of patients (95.7%) had strictly unilateral pain (right side 52.2%, left side 43.5%), while only one patient had alternating pain.

The most common autonomic features were rhinorrhea (91%), ptosis (87%), and lacrimation (78%). Migrainous features as photophobia, phonophobia, nausea and vomiting were found in 26% of patients more in males (4 out of 6). Most of the attacks were nocturnal with infrequent attacks occurring in early morning. The median attack severity by Visual Analog Scale (VAS) was 10 (8–10). The bout duration of CH lasted average 1–4 months duration. The time interval of diagnostic delay ranged from 0.5–29 years, with mean diagnostic delay 9.8 $\pm$ 7.9 years. The longer diagnostic delay was associated with poorer response to prophylactic treatment and required polytherapy.

Conclusion: Our study showed a wide range of diagnostic delay that necessitate the importance of diagnostic awareness among non-neurologists.

Disclosure of Interest: None Declared

IHC23-PO-037

Clinical Characteristics of Patients with TAC-tic Syndrome from a Headache Clinic in Sri Lanka

Devasmitha Wijesundara and Bimsara Senanayake

Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka

Objective: TAC-tic syndrome is a peculiar entity where trigeminal neuralgia (tic douloureux) coexists with trigeminal autonomic cephalalgia (TAC). It is an exceptionally rare clinical entity whose cause is unclear. Mere coincidence or pathophysiological similarities could be responsible. If one of the two is overlooked it may lead to significant morbidity. Hence both conditions need to be recognized and treated simultaneously.

Methods: All consecutive patients diagnosed with TAC-tic syndrome attending a specialized headache clinic in a tertiary care hospital in Sri Lanka over a 1-year period were included. The diagnosis was made by a senior neurologist and patients were interviewed using a structured questionnaire.

Results: A total of 10 patients were included (mean age-54 years, 90% female). The average age at headache onset was 46 years. Chronic paroxysmal hemicrania (CPH) was the commonest TAC phenotype. With 3 Tesla Magnetic Resonance imaging, vascular anomalies (commonest in the right superior cerebellar artery) were found in 3 patients while another had a meningioma compressing the trigeminal nerve. Symptom relief was achieved in all by treating both trigeminal neuralgia and TAC headache simultaneously. One underwent meningioma excision. Patient characteristics are summarized in Table 1.

Conclusion: It is important to recognize and treat these two entities occurring concurrently. Underlying structural abnormalities too are not uncommon, hence should be searched for.

Disclosure of Interest: None Declared

IHC23-PO-038

Secular trend of sex ratio in subjects under randomized controlled trials for cluster headache

Pil-Wook Chung and Heui-Soo Moon

Department of Neurology, Kangbuk Samsung Hospital, Sungkyunkwan university school of medicine, Seoul, Korea, Republic of

Abstract number: IHC23-PO-037

Table 1 Patient characteristics

	Sex	Age (years)	Age at onset	Side	TAC phenotype	MRI	Medications
1	Male	62	59	Right	SUNCT	normal	carbamazepine, indomethacin, lamotrigine
2	Female	71	58	Right	CPH	Vascular loop – superior cerebellar artery	indomethacin, lamotrigine, pregabalin
3	Female	50	36	Left	CPH	normal	carbamazepine, indomethacin, pregabalin
4	Female	73	53	Right	Cluster	normal	carbamazepine, indomethacin, lamotrigine
5	Female	47	42	Right	CPH	normal	carbamazepine, indomethacin
6	Female	54	46	Right	Cluster	Meningioma along lateral wall of cavernous sinus	carbamazepine, lamotrigine
7	Female	35	35	Right	Cluster	normal	carbamazepine, indomethacin, pizotifen
8	Female	68	62	Right	CPH	Vascular loop – superior cerebellar artery	carbamazepine, indomethacin, pregabalin
9	Female	37	34	Right	CPH	Vascular loop – anterior inferior cerebellar artery	carbamazepine, indomethacin, pizotifen, verapamil
10	Female	42	41	Left	CPH	normal	carbamazepine, indomethacin, flunarizine

Introduction: Although cluster headache (CH) is well known as a disorder of predominantly young males, the male to female ratio decreased from 5∼7:1 before 1980s to ∼2:1 in the 2000s and afterward in Western observational studies. It is unclear whether this represents a true rise of CH in women or better recognition of CH in women. We sought to assess whether the sex ratio of CH were changing or not in randomized controlled trials (RCTs) over time in accordance with observational studies.
Methods: RCTs of CH with a comparator were included. Studies were eligible for inclusion if patients were adult with CH as defined by established criteria such as Ad Hoc criteria or International Classification of Headache Disorders of any edition. We included studies regarding pharmacologic medication, as well as procedural and surgical treatment, devices. Studies were excluded if total randomized subjects were small ($n < 20$) or demographic data did not present sex ratio.
Results: 21 acute treatment trials and 24 preventive treatment trials were initially selected for inclusion. 5 acute treatment trials and 10 preventive treatment trials were excluded due to small sample size ($n < 20$) and/or no demographic information for sex ratio. Finally 30 trials were included for analysis. All studies were underwent in western countries. Of 30 trials finally included, 10 studies were published between 1985 to 2000 (period 1), 8 studies were published from 2001 to 2010 (period 2), 12 studies were published after 2010 (period 3, 2011–2019). Of the 2237 patients, 80.8% were male patients (male to female ratio, 4.2:1). Secular tendency of decreasing male predominance was shown over time. 542 of 623 patients (87%) were male in period 1, 477 of 575 (83%) were male in period 2, and 788 of 1039 (75.8%) were male in period 3 ($p < 0.001$). Male to female ratio was 6.7:1 in period 1, 4.9:1 in period 2, and 3.1:1 in period 3.
Conclusions: As with observational and registry data suggested, RCT enrolled population also showed decreasing tendency of male predominance over time in CH.
Disclosure of Interest: None Declared

IHC23-PO-039

Can clinical data predict the outcome of occipital nerve stimulation in refractory chronic cluster headache?

Javier A. Membrilla[1], María-Luz Cuadrado[2], Nuria González-García[2], Jesús Porta-Etessam[2], Antonio Sánchez-Soblechero[3], Alberto Lozano-Ros[3], Alicia González-Martínez[4], Ana Beatriz Gago-Veiga[4], Sonia Quintas[4], Jaime S. Rodríguez-Vico[5], Alex Jaimes[5], Lucía Llorente-Ayuso[6], Javier Roa[7], Carlos Estebas[7] and Javier Díaz- de-Terán[7]

[1]*Hospital Francesc de Borja, Gandía, Spain*
[2]*Hospital Universitario Clínico San Carlos, Madrid, Spain*
[3]*Hospital Universitario Gregorio Marañón, Madrid, Spain*
[4]*Hospital Universitario La Princesa, Madrid, Spain*
[5]*Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain*
[6]*Hospital Universitario Infanta Leonor, Madrid, Spain*
[7]*Hospital Universitario La Paz, Madrid, Spain*

Introduction: Occipital nerve stimulation (ONS) is a surgical treatment with good clinical evidence for the treatment of refractory chronic cluster headache (CCH). However, the irregular response rate reported in different studies, and the associated cost make it necessary to investigate predictors of response.
Methods: We conducted a cross-sectional study through a review of the medical records of CCH patients in six hospitals in the Community of Madrid. Epidemiological data, comorbidities and clinical variables were collected and compared between ONS failure group and the rest. ONS failure was defined as the need for removal surgery or device shutdown due to nonresponse or adverse events.
Results: From a series of 88 CCH, 26 (29.6%) were treated with ONS. ONS failure was observed in 50.0% (13/26). All of them were due to lack of response. This group of patients had an earlier onset of headache (mean 27.7 years SD 6.9 vs mean 36.7 years SD 11.8, $p = 0.026$). Active smoking was more prevalent in ONS failure cases (100% vs 42.9%, $p = 0.006$), as well as occurrence of seasonal exacerbations (58.3% vs 7.7%, $p = 0.007$) and nocturnal worsening (91.7% vs 53.9%, $p = 0.035$). Diagnostic delay, years of evolution prior to surgery, opioid use, psychiatric comorbidity or history of other headache or other comorbid pain disorders did not differ between groups, nor did the previous response to occipital nerve block or other treatments.
Conclusion: Some clinical characteristics such as a younger age of onset, active smoking and fluctuations with seasonal or circadian pattern may be related to ONS failure in refractory CCH.

Disclosure of Interest: JA Membrilla has received honoraria as a consultant and speaker for TEVA and Novartis. Lilly, TEVA and Novartis have funded JA Membrilla's research and teaching activities.

IHC23-PO-040

Analysis of 29,458 Cluster Headache Patients from a Multicenter Electronic Medical Record Database (TrinetX)

Victor Wang[1], Mario Peres[1,2] and Hsiangkuo Yuan[1]

[1]*Jefferson Headache Center, Philadelphia, USA*
[2]*Institute of Psychiatry, University of São Paulo, São Paulo, Brazil*

Objective: Cluster headache remains a largely understudied primary headache disorder in comparison to migraine and tension headaches. Large multicenter electronic medical record cohorts, such as the TrinetX database, present an opportunity to study this rare population with previously defined cohorts totaling in the hundreds of patients. In this study, we aim to characterize the profile of cluster headache patients, including demographics, medical comorbidities, and medication use profiles.

Methods: Using the TrinetX database, we analyzed the profiles of a large multicenter cohort from a database containing information on over 135 million patients across 105 healthcare organizations. Cohorts of patients diagnosed by medical providers as cluster headache (episodic, chronic, and unspecified) were created. Patients with a diagnosis of migraine were excluded from these cohorts of cluster headache. Episodic cluster headache patient counts excluded chronic cluster headache co-existing diagnoses. Chronic cluster headache patient counts excluded episodic cluster headache co-existing diagnoses. Information regarding patient demographics, medical comorbidities and medication use was obtained.

Results: After exclusion of migraine diagnoses, we identified 29,458 patients with cluster headache, unspecified, 13,750 with episodic cluster headache, and 7,483 with chronic cluster headache yielding a prevalence of 0.02%, 0.01%, and 0.0055% across the global network population (135,552,436), respectively. The episodic to chronic ratio was 1.84:1.

Mean age in cluster headache patients overall was 51 ± 19 years, with a minimum age of 3 and maximum age of 90, with a female to male ratio of 1.08:1, 64% of which were white, 15% black/African American and 8% Hispanic/Latino. Mean age in episodic cluster headache patients was 48 ± 19 years with a female to male ratio of 1.08:1, 62% were white, 19% were black/African American and 10% Hispanic/Latino. Mean age in chronic cluster headache patients was 49 ± 20 years with a female to male ratio of 1.27:1, 63% were white, 17% were black/African American and 10% Hispanic/Latino.

In the overall cluster headache patient population, associated conditions were observed in the population as follows: hypertension (11,213, 38%), vascular headache (otherwise unspecified) (5,420, 18%), sleep apnea (6,942, 24%), obesity/overweight state (6,375, 22%), chronic sinusitis (3,387, 11%), diabetes mellitus (4,210, 14%), ischemic heart disease (3,844, 13%), cerebrovascular disease (3,283, 11%), tobacco use (1,735, 6%), chronic rhinitis (1,260, 4%), glaucoma (1,227, 4%), and peptic ulcer disease (256, 1%).

Observed counts of potentially secondary causes of cluster headache include: injuries to the head (4,447, 15%), concussion (696, 2%), cerebral aneurysm (unruptured, 401, 1%), traumatic brain injury (232, 1%), benign neoplasm of pituitary gland (201, 1%), and malignant neoplasm of pituitary gland (10, $<$1%).

Treatment profiles included a) acute: opioid analgesics (fentanyl, oxycodone, and hydrocodone most commonly), antimigraine agents (16,178, 55%), prednisone (7,471, 25%), and sumatriptan (4,398, 15%), and b) preventives: gabapentin (5,681, 19%), verapamil (3,265, 11%), melatonin (2,177, 7%), topiramate (1,811, 6%), valproate (802, 3%), galcanezumab (359, 1%), olanzapine (578, 2%), lithium (289, 1%), greater occipital nerve blocks (255, 1%), and clomiphene (69, $<$1%). The remainder of the following other medications were all $<$1% of the total cohort: erenumab, fremanezumab, eptinezumab, rimegepant, ubrogepant, atogepant, lasmiditan, onabotulinumtoxina).

Conclusion: From this large database of approximately 30,000 cluster headache patients globally, we find a near even female to male ratio in overall cluster headache patients, episodic cluster, and chronic cluster headache patients, with the highest female to male ratio in chronic cluster headache patients, in contrast to previously published studies. We find that current prescribing practices may undertreat cluster headache with preventive medications and overtreat with opioid analgesics. Further investigation is warranted into a potentially shifting patient population than previously described in the literature and into the barriers to accessing preventive treatments for this population.

Disclosure of Interest: None Declared

IHC23-PO-041

Epidemiology, clinical features and treatment of refractory chronic cluster headache: Results of a multicenter registry

Javier A. Membrilla[1], María-Luz Cuadrado[2], Nuria González-García[2], Jesús Porta-Etessam[2], Antonio Sánchez-Soblechero[3], Antonio Lozano-Ros[3], Alicia González-Martínez[4], Ana Beatriz Gago-Veiga[4], Sonia Quintas[4], Jaime S. Rodríguez-Vico[5], Alex Jaimes[5], Lucía Llorente-Ayuso[6], Javier Roa[7], Javier Roa[7] and Javier Díaz-de-Terán[7]

[1]*Hospital Francesc de Borja, Gandía, Spain*
[2]*Hospital Universitario Clínico San Carlos, Madrid, Spain*
[3]*Hospital Universitario Gregorio Marañón, Madrid, Spain*
[4]*Hospital Universitario La Princesa, Madrid, Spain*
[5]*Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain*
[6]*Hospital Universitario Infanta Leonor, Madrid, Spain*
[7]*Hospital Universitario La Paz, Madrid, Spain*

Introduction: Cluster headache (CH) is a relatively rare primary headache disorder in which large series of the chronic form are lacking. In this study, we aimed to describe the characteristics of chronic CH (CCH) patients.
Methods: We conducted a cross-sectional study through a review of the medical records of CCH patients in six hospitals in the Community of Madrid. Epidemiological, clinical, treatment, and outcome variables were described.
Results: 88 CCH patients were included in the registry. Diagnostic criteria of refractory CCH (as defined by the European Headache Federation Consensus statement) were met in 68.2% (60/88). Mean debut age was 33.6 (SD 12.9), with a mean diagnostic delay of 4.2 (SD 6.3) years. Verapamil, lithium and topiramate were used in 98.9% (87/88), 42.1% (37/88) and 84.1% (74/88), but they were discontinued in 41.4% (36/87), 71.2% (37/52) and 63.5% (47/74), respectively. OnabotulinumtoxinA and galcanezumab were initiated in 77.3% (68/88) and 5.7% (5/88), but discontinued in 52.9% (36/68) and 60.0% (3/5), respectively. Occipital nerve stimulation (ONS) was implanted in 29.6% (26/88), with 50.0% (13/26) still active. Most treatment discontinuations were due to inefficacy. At the date this work was conducted, 60.2% (53/88) had poor clinical outcomes (having at least three severe attacks per week). ONS and onabotulinumtoxinA were the therapies that achieved good clinical evolution in most rCCH patients.
Conclusion: CCH is a disorder with poor prognosis, meeting refractoriness criteria in more than half. OnabotulinumtoxinA and ONS could be the best treatment to offer in these cases.
Disclosure of Interest: JA Membrilla has received honoraria as a consultant and speaker for TEVA and Novartis. Lilly, TEVA and Novartis have funded JA Membrilla's research and teaching activities.

IHC23-PO-042

Prevalence of Cluster Headache and other Trigeminal Autonomic Cephalalgias (TACs) in the United States: Results from 254,700 Individuals in the National Institutes of Health All of Us Research Program

Victor Wang[1], Mario Peres[1,2] and Hsiangkuo Yuan[3]

[1]*Jefferson Headache Center, Philadelphia, USA*
[2]*Institute of Psychiatry, University of São Paulo, São Paulo, Brazil*
[3]*Jefferson Headache Center, Philadelphia, Brazil*

Objective: Trigeminal autonomic cephalagias (TACs) are a group of primary headache disorders including cluster headache (CH), hemicrania continua, paroxysmal hemicrania, and Short-lasting, Unilateral, Neuralgiform headache attacks with either conjunctival injection and tearing (SUNCT) or with cranial autonomic symptoms (SUNA), characterized by unilateral pain in the head and face accompanied by cranial autonomic symptoms. Despite its impact on quality of life, the prevalence of CH and other TACs in the general population remains poorly understood. We aimed in this study to estimate the prevalence of CH and other TACs in the All of Us Research Program.
Methods: The All of Us (AoU) Research Program is a large-scale medical research initiative launched by the National Institute of Health (NIH) seeking to engage at least one million diverse participants to advance precision medicine and improve human health. Data from 409,420 participants were included as of early May 2023. Of these, 254,700 individuals with electronic medical records data were available for medical diagnosis encoded by a health care provider. We identified all participants with a confirmed diagnosis of CH and TACs. We also assessed the demographics and temporal patterns (episodic or chronic) of CH patients.
Results: A total sample of 155,060 women and 94,480 men was analyzed. 897 CH patients were identified, 578 women, 302 men. The estimated prevalence of CH was 352 ± 59 per 100,000 individuals (0.35%), 0.37% in women, 0.32% in men, the women:men (W:M) ratio was 1.17:1. Prevalence of hemicrania continua was 47 ± 10 per 100,000 (0.05%), W:M 2.14:1. Prevalence of paroxysmal hemicrania was 106 ± 12 per 100,000 (0.11%), W:M 2:1. Prevalence of SUNCT/SUNA syndrome was 14 ± 4/100.000 (0.01%), W:M 1.6:1.
Conclusion: Our results show the prevalence of CH in the All of Us cohort is similar to other population-based studies. However, the male preponderance typically seen in CH was not found. Our study provides valuable insights into the prevalence and characteristics of CH, hemicrania

continua, paroxysmal hemicrania, and SUNCT/SUNA syndrome in a large, diverse population. These findings have important implications for the diagnosis and management of CH, as well as for future research on this debilitating condition.
Disclosure of Interest: None Declared

IHC23-PO-044

Actigraphy and self-assessed sleep study show increased sleep latency and sleep related stress in cluster headache

Caroline Ran[1], Felicia Jennysdotter Olofsgård[1], Anna Steinberg[2,3], Katrin Wellfelt[1], Christina Sjöstrand[2,4], Elisabet Waldenlind[2,3], Anna Dahlgren[2] and Andrea Carmine Belin[1]

[1]*Centre for Cluster Headache, Dept. of Neuroscience, Karolinska Institutet, Stockholm, Sweden*
[2]*Dept. of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden*
[3]*Dept. of Neurology, Karolinska University Hospital, Stockholm, Sweden*
[4]*Dept. of Neurology, Danderyd Hospital, Stockholm, Sweden*

Objective: Cluster headache (CH) is a primary headache disorder characterized by excruciatingly painful headache attacks which often occur with a clear circadian pattern and previous studies have found CH to be linked with sleep disturbances. It is unclear if the attacks lead to a worse quality of sleep or if common biological mechanisms account for both CH and the sleep disturbances. To better understand the link between sleep and CH, we performed a study comparing the sleep of CH patients, both during an active (attack) period as well as in a remission (attack free) period, with controls.
Method: 50 study participants with validated CH and 42 controls were included in the study. Participants were asked to wear a MotionWatch 8 actigraph unit (CamNTech) for 2 weeks, which can detect sleep and wakefulness. Participants filled out sleep diaries daily during the 2 weeks evaluating subjective ratings of disturbed sleep, worry/stress at bedtime, waking up too early, and sleep quality.
Results: The objective measurements of sleep showed a difference in time spent in bed (CH: 8.1 h vs controls: 7.7 h, $P = 0.03$) and time it took to fall asleep, known as sleep latency (CH: 17.4 min vs controls: 7.8 min, $P < 0.001$). These differences persisted when individuals with nightly CH attacks were removed from the analysis. However, there was no difference in sleep efficiency or in hours slept between CH and controls (CH: 6.7 h vs controls: 6.5 h, $P = 0.3$). CH patients reported a significantly worse sleep than controls in the sleep diaries with more worry/stress at bedtime, more often waking up too early, more disturbed sleep, and worse sleep quality. Patients in an active phase scored worse on subjective sleep scores than patients in remission. Interestingly, patients in remission still scored worse than controls on several sleep parameters.
Conclusion: Our analysis suggests that sleep is affected in CH though hours slept per night remained similar to controls. This study stresses the importance of considering sleep when treating CH patients and that differences in sleep persist in the remission phase.
Disclosure of Interest: None Declared

IHC23-PO-045

Association between calcitonin gene-related peptide and disease stages in cluster headache. A prospective and controlled study.

Anja Petersen[1], Nunu Lund[1], Sarah Louise Christensen[1], Mads Barloese[2], Niklas Rye Jørgensen[3] and Rigmor Jensen[1]

[1]*Danish Headache Center, Department of Neurology, University of Copenhagen, Rigshospitalet-Glostrup, Glostrup, Denmark*
[2]*Department of Clinical Physiology and Nuclear Medicine, Centre for Functional and Diagnostic Imaging and Research, University of Copenhagen, Hvidovre Hospital, Hvidovre, Denmark*
[3]*Department of Clinical Biochemistry, Rigshospitalet-Glostrup, University of Copenhagen, Glostrup, Denmark*

Objective: We investigated if plasma levels of CGRP differed between disease stages defined as episodic cluster headache in bout, episodic cluster headache in remission and chronic cluster headache and differed from healthy controls matched for sex and age.
Methods: The study design was a prospective observational case-control study in which plasma was collected from 201 cluster headache patients and 100 controls. Episodic cluster headache patients were sampled twice (during a bout and in remission). Plasma CGRP concentrations were measured with a fully evaluated radioimmunoassay for human CGRP.
Results: Plasma levels of CGRP were higher in bouts than in remission (mean:17.8 pmol/L, 95%CI:6.6–28.0, $p = 0.002$), but plasma CGRP levels showed no difference among patients with current attacks e.g., in bout or chronic ($p = 0.238$). Throughout all three disease stages (bout, remission and chronic), plasma levels of calcitonin gene-related peptide were found significantly reduced when compared to controls ($P < 0.001$). In a linear regression

model, plasma CGRP levels did not correlate with attack frequency or use of acute medication (oxygen or sumatriptan) within the 24 hours preceding the sampling.

Conclusion: We have identified that plasma CGRP is dependent on the remission phase but does not differ among patients with current attacks e.g. chronic cluster headache versus episodic cluster headache in bout. These results support the hypothesis that the CGRP system is disrupted in cluster headache patients even in the passive phase as compared to controls. Our results support the pathophysiological reasoning for targeting the CGRP in episodic cluster headache.

Disclosure of Interest: Anja Sofie Petersen have received a restricted research grant from Lundbeck and is current or former investigator in trials for Lundbeck and Eli Lilly Nunu Lund: Nothing to declare Mads Barloese: Nothing to declare Sarah Louise Christensen: Contract research for Cephagenix and DSM/Glycom and advisor/consultant for y-mAbs Therapeutics Niklas Rye Jørgensen: Nothing to declare Rigmor Jensen: Given lectures for Pfizer, Eli-Lilly, Merck, TEVA, Novartis, Lundbeck and Allergan. Investigator in clinical trials with Eli-Lilly, Novartis and Lundbeck. Director of Danish Headache Center, Lifting The Global Burden of Headache and Founder of Master of Headache Disorders at University of Copenhagen. Recieved research funding from University of Copenhagen, Rigshospitalet, Lundbeck Foundation, Lundbeck Pharma, The Medical Society in Copenhagen, NovoNordisk Foundation and Tryg Foundation

IHC23-PO-046

The China Cluster Headache Register Individual Study (CHRIS): Study Design and Baseline Characteristics

Shuhua Zhang[1], Chunfu Chen[2], Suiyi Xu[3], Hongru Zhao[4], Yuanrong Yao[5], Shengyuan Yu[1] and Zhao Dong[1]

[1]*Chinese PLA General Hospital, Beijing, China*
[2]*Department of Neurology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, China*
[3]*Department of Neurology, First Hospital of Shanxi Medical University, Taiyuan, China*
[4]*The First Affiliated Hospital of Soochow University, Shanxi, China*
[5]*Department of Neurology, Guizhou Province People's Hospital, Guiyang, China*

Background: There is currently a paucity of comprehensive multicenter cohort studies exploring cluster headache (CH) in China. Consequently, the establishment of a representative and prospective cohort for the purpose of multidimensional analysis in the future is deemed indispensable.

Methods: CHRIS is an ongoing multi-centered, prospective, and longitudinal cohort study taking place in 31 provinces of China. It was first implemented as a multicenter study in January 2019 before its official launch in August 2022. Multidimensional data, comprising demographic characteristics, medical history, previous therapeutic regimens, comorbidities (including anxiety, depression, and sleep disorders), biospecimens, imaging, and electrophysiological data, were collected at baseline. The patients were followed-up every six months, both in the cluster and non-cluster periods, for outcomes, treatment patterns, and prognoses. The study protocol has been approved by the ethics committee of the Chinese PLA General Hospital, and was registered at the Chinese Clinical Trial Registry. All patients are required to provide written informed consent.

Results: A total of 816 patients with CH were enrolled, of whom 663 were males and 153 were females, with a mean age of 35.05 ± 9.85 years. Among these patients, 19 (2.33%) were categorized as chronic CH. The average age of onset of CH was 24.89 ± 9.77 years, and only 57 (6.99%) patients had a family history of CH. The most common frequency of cluster occurrences was found to be 1–2 times per year (45.96%), and the majority of the clusters persisted for 2 weeks to 1 month (44.00%). Additionally, 68.50% patients ($n = 559$) experienced clusters once or twice a day, with a duration of 1–2 hours (45.59%). Most of the cluster episodes were observed to be strictly unilateral (94.00%), often having locations of retro-orbital (75.98%) and temporal (74.39%). Lacrimation (78.80%) was the most common autonomic symptom seen in CH, followed by conjunctival injection (53.19%), rhinorrhea (49.63%), and nasal congestion (38.97%). The most common additional symptoms in CH included a sense of restlessness and agitation (55.88%), nausea (57.48%), photophobia (55.02%), and phonophobia (53.55%). Further analysis showed that cluster episodes occurred most frequently in spring and winter, and least commonly in summer. Moreover, 704 (86.32%) patients reported experiencing "clock" attacks, commonly at 9 am to 11 am (37.2%) and 1 am to 2 am (18.16%). A total of 11.03% patients ($n = 90$) had received a pertinent diagnosis of CH in the past. In the latest research, more than16.00% patients were accurately diagnosed with CH within a year. It was found that 67.65% patients previously implemented acute treatment, of which oxygen (23.56%) and zolmitriptan (17.02%) were used most often. In addition, around 57.41% patients had received preventive treatment in the past, with oral glucocorticoid (16.67%) and verapamil (6.4%) being the most common options used.

Conclusion: As the first China CH patient registry study, the large baseline data is the basis for revealing the characteristics of CH in mainland China, and could further help guide the intervention and management of CH patients. Long-term follow-up and multidimensional data analysis will be crucial

for developing and optimizing the diagnosis and treatment system that fits the characteristics of Chinese patients.

Keywords: Cluster headache, registry study, protocol, baseline characteristics

Figure 1 Map of the study centers.

Figure 2 Seasons and times of cluster attacks.

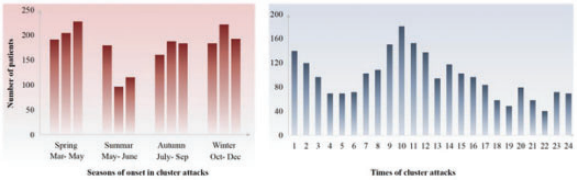

Figure 3 Treatment and response in CH patients.

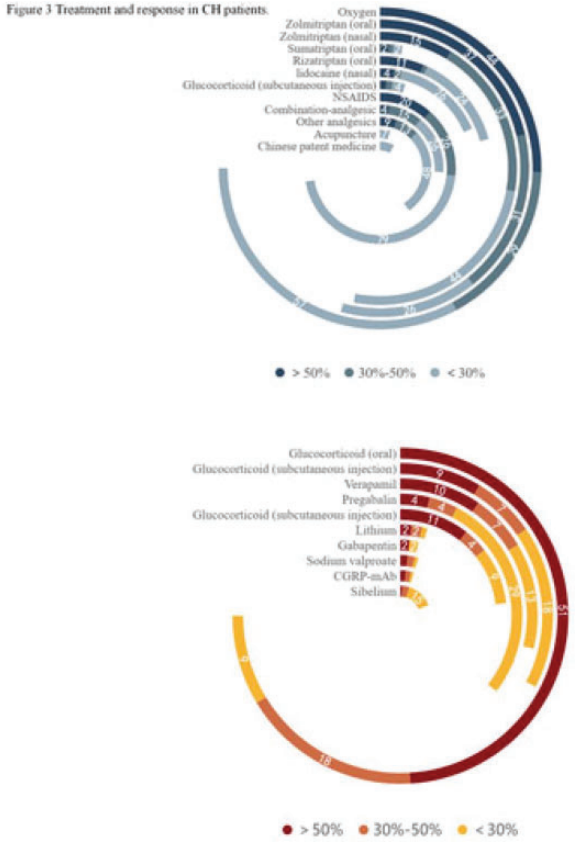

Table 1. Demographics of patients with CH (n=816).

Demographics	Male (n=663)	Female (n=153)	Total (n=816)	*p*- Value
Type of CH, n (%)				0.610
Episodic	648 (97.8)	149 (97.4)	797 (97.6)	
Chronic	15 (2.3)	4 (2.6)	19 (2.33)	
Age in years, Mean (SD), y	35.23 (9.82)	34.27(9.95)	35.05 (9.85)	0.278
Age at onset, Mean (SD), y	25.31 (9.71)	23.09 (9.86)	24.89 (9.77)	0.011*
Educational background, n (%)				0.720
Primary school or below	11 (1.67)	4 (2.61)	15 (1.84)	
Junior or senior high school	320 (48.27)	72 (47.06)	392 (48.04)	
University or higher	332 (50.08)	77 (50.33)	409 (50.12)	
Family History of CH, n (%)	40 (6.03)	17 (11.1)	57 (6.99)	0.026*
Smoking, n (%)	321 (48.42)	17 (11.1)	338 (41.42)	<0.001
Drinking, n (%)	179 (27.00)	11 (7.29)	190 (23.28)	<0.001

*$p < 0.05$; CH: cluster headache

Table 2. Clinical characteristics of CH patients (n=816).

Characteristics	Male (n=663)	Female (n=153)	Total (n=816)	*p*- Value
Frequency of clusters, n (%)				0.147
Less than 1 time/year	272 (41.03)	54 (35.29)	326 (40.10)	
From 1 to 2 times/year	300 (45.25)	75 (49.02)	375 (45.96)	
More than 2 times/year	58 (8.75)	20 (13.07)	78 (9.56)	
Fist experience of cluster	33 (4.98)	4 (2.61)	37 (4.53)	
Duration of clusters, n (%)				
Less than 2 weeks	121 (18.25)	28 (18.30)	149 (18.26)	0.539
From 2 weeks to less than 1 month	285 (42.99)	74 (48.37)	359 (44.00)	
From 1 month to 2 months	146 (22.02)	33 (21.15)	179 (21.94)	
More than 2 months	78 (11.76)	14 (9.15)	92 (11.27)	
Fist experience of cluster	33 (4.98)	4 (2.61)	37 (4.53)	
Frequency of attacks, n (%)				
Less than 1 time/day	90 (13.57)	20 (13.07)	110 (13.48)	0.956
From 1 to 2 times/day	451 (68.02)	106 (69.28)	559 (68.50)	
More than 2 times/day	122 (18.40)	27 (17.65)	149 (18.26)	
Duration of attacks, n (%)				
Less than 1 h	212 (31.98)	51 (33.33)	263 (32.23)	0.962
From 1 hour to less than 2 hours	305 (46.00)	67 (43.79)	372 (45.59)	
From 2 hours to 3 hours	82 (12.22)	19 (13.07)	101 (12.38)	
More than 3 hours	6 (9.65)	16 (10.46)	80 (9.80)	
Laterality of pain				0.09
Right- side only	345 (52.03)	76 (49.67)	421 (51.59)	
Left- side only	284 (42.84)	62 (40.52)	346 (42.40)	
Side-alternating	34 (5.13)	15 (9.80)	49 (6.00)	
Sites of pain				
Retro-orbital	500 (75.41)	120 (78.43)	620 (75.98)	0.431
Temporal	503 (75.87)	104 (66.67)	607 (74.39)	0.044*
Forehead	252 (38.01)	59 (38.56)	311 (38.11)	0.899
Parietal	191 (28.81)	45 (29.41)	236 (28.92)	0.882
Occipital	171 (25.79)	49 (32.03)	220 (26.96)	0.117
Teeth	65 (9.80)	37 (24.18)	102 (12.50)	<0.0001*
Cheek	69 (10.41)	26 (16.99)	95 (11.64)	0.022*
Ear	26 (3.92)	16 (10.46)	42 (5.16)	0.001*
Pain Intensity (VAS)	8.69±1.31	8.78±1.53	8.71±1.36	0.461

CH: cluster headache

Table 3. Autonomic and additional symptoms of CH patients (n=816).

	Male (n=663)	Female (n=153)	Total (n=816)	*p*- Value
Autonomic symptoms, n (%)				
Lacrimation	529 (79.79)	114 (74.51)	643 (78.80)	0.150
Conjunctival injection	370 (55.81)	64 (41.83)	434 (53.19)	0.002*
Rhinorrhea	343 (51.73)	62 (40.52)	405 (49.63)	0.012*
Nasal congestion	254 (38.31)	64 (41.83)	318 (38.97)	0.421
Facial sweating	242 (36.50)	44 (28.76)	286 (35.05)	0.070
Ptosis/miosis	242 (36.50)	42 (27.45)	284 (34.80)	0.034*
Eyelid oedema	87 (13.21)	61 (39.87)	118 (14.46)	0.024*
Additional symptoms, n (%)				
Nausea	371 (55.96)	98 (64.05)	469 (57.48)	0.068
Vomiting	212 (31.98)	50 (32.68)	262 (32.11)	<0.0001*
Photophobia	366 (55.20)	83 (54.25)	449 (55.02)	0.830
Phonophobia	354 (53.39)	83 (54.25)	437 (53.55)	0.848
Osmophobia	98 (14.78)	33 (21.57)	131 (16.05)	0.039*
Allodynia	108 (16.29)	25 (1.31)	133 (16.30)	0.988
Sense of restless and agitation	371 (55.96)	85 (55.56)	456 (55.88)	0.928
Aggravation by physical activities	85 (12.82)	33 (21.57)	118 (14.46)	0.006*

CH: cluster headache

Table 4. Time delay for correct diagnosis of CH (N=816)

	Total （n=816）, n (%)
Less than 1 year	90 (11.03)
1 year	47 (5.76)
2 years	39 (4.78)
3 years	65 (7.97)
4 years	44 (5.39)
5 years	64 (7.84)
6 years	48 (5.88)
7 years	38 (4.66)
8 years	43 (5.26)
9 years	18 (2.21)
10 years	89 (10.91)
More than 10 years	231 (28.31)

CH: cluster headache

Disclosure of Interest: None Declared

Comorbidity of primary headaches

IHC23-PO-047

Comorbidity of Migraine, depression, fibromyalgia, and insomnia; A population-based study

Wonwoo Lee[1,2], Jiyun Lee[1,2], Kyung Min Kim[1], In Kyung Min[1], Kyoung Heo[1] and Min Kyung Chu[1]

[1]*Yonsei University College of Medicine, Seoul, Korea, Republic of*
[2]*Yongin Severance Hospital, Yongin, Korea, Republic of*

Migraine, depression, fibromyalgia, and insomnia are reportedly comorbidities. Nevertheless, no study has evaluated the comorbidity of all four of these disorders. This study aimed to investigate the comorbidity of these four disorders using the data from a nationwide population-based study.

Baseline assessment data of Circannual Change in Headache and Sleep study, a web-based questionnaire survey on circannual change headache and sleep was used. The study participants were comprised of similar distribution of age, sex and socioeconomic factors compared to that of the total Korean population. Validated questionnaires for depression, fibromyalgia, insomnia and migraine were assessed.

The prevalence rates of migraine, depression, fibromyalgia, and insomnia were 5.6%, 7.2%, 5.8%, and 13.3%, respectively. Among the 3,030 included participants, 494 (16.3%), 164 (5.4%), 40 (1.3%), and 6 (0.2%) had one, two, three, and four of these conditions, respectively. The number of headache days per 30 days (Jonckheere–Terpstra trend test, $p = 0.011$) and migraine-related disability (migraine disability assessment score, $p = 0.021$) increased with an increase in the number of comorbidities but not with the intensity of headache (visual analogue scale, $p = 0.225$) among participants with migraine. The severity of insomnia (Insomnia Severity Index, $p < 0.001$) and fibromyalgia (fibromyalgia severity score, $p = 0.002$) increased with additional comorbidities; however, depression (Patient Health Questionnaire-9, $p = 0.384$) did not show such as increase.

The findings confirmed significant comorbidity between migraine, depression, fibromyalgia, and insomnia. Health professionals should be aware of the probable comorbidity of migraine, depression, fibromyalgia, and insomnia when caring for individuals with any of these four disorders.

Disclosure of Interest: Min Kyung Chu was a site investigator for a multi-center trial sponsored by Allergan Korea, Biohaven Pharmaceuticals, and Lundbeck Korea. He has received lecture honoraria from Allergan Korea, Handok-Teva, Eli Lilly and Company, and Yuyu Pharmaceutical Company in the past 24 months.

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IHC23-PO-048

Migraine and REM sleep behavior disorder: a cross-sectional study

Kristin Sophie Lange[1], Pia Kull[1], Jasper Mecklenburg[1], Lucas Hendrik Overeem[1], Mira Pauline Fitzek[1], Anke Siebert[1], Maureen Steinicke[1], Paul Triller[1], Lars Neeb[1,2], Jens P. Dreier[1], Daniel Kondziella[3], Uwe Reuter[1] and Bianca Raffaelli[1,4]

[1]*Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany*
[2]*Helios Global Health, Berlin, Germany*
[3]*Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark*
[4]*Clinician Scientist Program, Berlin Institute of Health at Charité (BIH), Berlin, Germany*

Objective: Migraine and sleep disorders are known to occur comorbidly with a bidirectional relationship. While altered patterns of rapid eye movement (REM) sleep have been documented in migraine patients, little is known about the prevalence of REM sleep disturbances. We aimed to assess the prevalence of REM sleep behavior disorder (RBD) in patients with migraine.
Methods: This analysis is part of a cross-sectional survey study conducted at the Headache Center of the Charité – Universitätsmedizin Berlin between August 2020 and March 2022. At the end of their regular medical appointment, patients who had been diagnosed with migraine were requested to fill out a series of electronic questionnaires. We used the validated RBD Screening Questionnaire (RBDSQ) to screen for RBD, with an RBDSQ score $\geq$5 considered indicative of RBD. Symptoms of depression, anxiety, and stress were assessed using the Depression, Anxiety and Stress Scale 21 (DASS-21). Primary endpoint was the percentage of patients with a positive screening score for RBD. Subgroup analyses included comparison of patients with episodic vs. chronic migraine, migraine with vs. without aura and positive vs. negative scores for depression, anxiety and stress, as well as correlation of RBDSQ scores with age, mean number of monthly headache days (MHD) and monthly migraine days (MMD), and DASS-21 scores.
Results: Of 808 patients with migraine who completed the survey, 751 patients (44.1 $\pm$ 13.2 years; 87.4% female) with complete RBDSQ were included in this analysis. Chronic migraine was diagnosed in n = 190 patients (25.3%), and migraine with aura in n = 325 patients (43.3%). The mean RBDSQ score was 5.2 ($\pm$2.4), and 443 (59%) of participants scored positive for RBD. The RBDSQ score was negatively correlated with age ($r = -0.11$, $p = 0.002$) and positively correlated with the number of MHD ($r = 0.08$, $p = 0.028$), but did not differ between episodic and chronic migraine. The prevalence of RBD was significantly higher in migraine with aura (63% vs. 56%, $p = 0.047$), and in patients with depression, anxiety, and stress (69.6% vs. 51.5%, 73.7% vs. 48.3%, 77.5% vs. 47.4%; $p < 0.001$, respectively). RBDSQ scores were positively correlated with all three DASS-21 scales scores ($r = 0.25$ for depression, $r = 0.36$ for anxiety, $r = 0.36$ for stress; $p < 0.001$, respectively).
Conclusion: RBD is frequent in patients with migraine, and predominantly affects younger patients, patients with aura and with psychiatric comorbidities. Further studies including polysomnography are required to confirm an association of migraine and RBD, and to explore potential common pathophysiological mechanisms.
Disclosure of Interest: KSL reports personal fees from Teva and Acticor Biotech. PK has nothing to disclose. JM reports personal fees from Novartis. LHO has nothing to disclose. MPF reports personal fees from Teva. AS reports personal fees from Teva and Novartis. MS reports personal fees from Abbvie. PT has nothing to disclose. LN reports personal fees from Allergan, BIAL, Lilly, Grünenthal, Hormosan, Novartis, and Teva, and research funding from Lily and Teva. JPD has nothing to disclose. DK reports personal fees from Wiley, and research funding from among others the Lundbeck Foundation and the Novo Nordisk Foundation. UR reports personal fees from Amgen, Allergan, Abbvie, Lilly, Lundbeck, Novartis, electroCore, Medscape, StreaMedUp, and Teva, and research funding from Novartis. BR reports research grants from Novartis and personal fees from Abbvie/Allergan, Eli Lilly, Hormosan, Novartis, and Teva.

IHC23-PO-049

Near-death experiences are associated with REM sleep intrusion in migraine patients, independent of migraine aura

Bianca Raffaelli[1,2], Pia Kull[1], Jasper Mecklenburg[1], Kristin S. Lange[1], Lucas H. Overeem[1], Mira P. Fitzek[1], Anke Siebert[1], Maureen Steinicke[1], Paul Triller[1], Lars Neeb[1,3], Jens P. Dreier[1], Uwe Reuter[1,4] and Daniel Kondziella[5,6]

[1]*Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany*
[2]*Clinician Scientist Program, Berlin Institute of Health at Charité (BIH), Berlin, Germany*

[3]Helios Global Health, Berlin, Germany
[4]Universitätsmedizin Greifswald, Greifswald, Germany
[5]Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark
[6]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

Objective: Migraine aura, near-death experiences (NDE), and REM sleep intrusions might share common pathophysiological mechanisms. This study aimed to investigate the prevalence of NDE and REM sleep intrusions in patients with migraine. Our hypothesis was that the prevalence of NDE and REM sleep intrusions would be higher in patients with aura than in those without.
Methods: We conducted a cross-sectional survey study at a tertiary headache center in Germany. Patients with a diagnosed migraine were recruited after their regular consultation. Eligible participants completed the following questionnaires: 1) Survey about demographic and headache characteristics; 2) The 16-item Greyson NDE scale; 3) A 4-item questionnaire about REM sleep intrusions; 4) The Depression, Anxiety, and Stress Scale 21 (DASS-21).
Results: Based on a prespecified sample size calculation, we included 808 participants in the study, of which 353 (43.7%) had a current or previous history of migraine aura. Overall, 22 participants (2.7%) reported an NDE without differences between migraine with and without aura (2.8% vs. 2.6%, $p > 0.999$). The prevalence of REM sleep intrusions was 5.4% with similar occurrence rates in migraine with and without aura (6.3% vs. 4.9%, $p = 0.43$). NDE were reported significantly more often by participants with REM sleep intrusions than those without ($n = 5/44$, 11.4% vs. $n = 17/754$, 2.2%, $p = 0.005$). There was a positive correlation between the occurrence of REM sleep intrusions and symptoms of depression, anxiety, and stress.
Conclusion: Our findings do not support an association of migraine aura with NDE or REM sleep intrusions but provide further evidence for the relationship between NDE and REM sleep intrusions. Neuronal mechanisms underlying REM sleep intrusions may be causally involved in the development of NDE.
Disclosure of Interest: BR reports research grants from Novartis, Deutsche Forschungsgemeinschaft (RA 3907/1-1) and Deutsche Migräne- und Kopfschmerzgesellschaft and personal fees from Abbvie/Allergan, Eli Lilly, Hormosan, Novartis, and Teva. PK has nothing to disclose. JM reports personal fees from Novartis. KSL reports personal fees from Teva and Acticor Biotech. LHO has nothing to disclose. MPF reports personal fees from Teva. AS reports personal fees from TEVA and Novartis. MS reports personal fees from Abbvie. PT has nothing to disclose. LN reports personal fees from Abbvie/Allergan, BIAL, Lilly, Hormosan, Novartis, and Teva, and research funding from Lily and Teva. JPD reports research grants from Deutsche Forschungsgemeinschaft (DFG DR 323/10-1) and Bundesministerium für Bildung und Forschung (Era-Net Neuron EBio2, with funds from BMBF 01EW2004). UR reports personal fees from Amgen, Allergan, Abbvie, Lilly, Lundbeck, Novartis, electroCore, Medscape, StreaMedUp, and Teva, and research funding from Novartis. DK reports personal fees from Wiley, and research funding from among others the Lundbeck Foundation and the Novo Nordisk Foundation.

IHC23-PO-050

Comorbidity of primary migraine headache: Prevalence and differences between migraine subtypes

Thanin Asawavichienjinda

Department of Medicine, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Objectives: To determine the prevalence of comorbidity and the difference in comorbidities between migraine subtypes.
Methods: This retrospective study was conducted at the Chulalongkorn Comprehensive Headache Center, King Chulalongkorn Memorial Hospital, Thailand, between January 2007 and June 2022 and was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University. This center creates a case-record form to gather patient information. Every patient who visits this center is registered and asked for information to complete the case-record form. Patients with migraine according to the International Classification of Headache Disorders were recruited for the study. Information from the case-record forms was collected and analyzed. The comorbidities reported by the patients were confirmed by reviewing their electronic medical records. The sample size was calculated based on the previous report on the prevalence of migraine comorbidity, which was 44%, and the difference in the proportion of comorbidity between episodic and chronic migraine, which was 42% and 54%, respectively. The sample size for prevalence was 378 patients, and for the difference in comorbidity between episodic and chronic migraine, it was 271 patients per group, or 542 patients total. Statistical analysis was applied using an unpaired *t* test for continuous data with normal distribution, a Mann-Whitney *U* test for continuous data without normal distribution, and a chi-square test or Fisher exact test for categorical data. The significant *p*-value was 0.05, and the Benjamini-Hochberg procedure was applied to adjust for the family-wise error rate of multiple analyses.

Results: Of the 681 patients registered at the center, 572 were diagnosed with migraine and were analyzed. The mean age of the patients was 42.3 (SD 14.1) years, with an age range of 15 to 80 years. Most of the patients were female (84.1%) and were working or studying (85.3%). Nearly half of the patients had completed university education (44.8%). The proportion of migraine patients with aura was 29.9%, and the ratio of patients with episodic to chronic migraine was 1.02 to 1. This study found that patients with one comorbidity accounted for 36.7% of the total (210/572), and patients with two or more comorbidities accounted for 16.8% of the total (96/572). The prevalence of patients with existing comorbidities was 53.5%, and the highest prevalence was hypertension at 14.5%, followed by allergic rhinitis at 12.9% and dyslipidemia at 8.7%. The prevalence of patients with thyroid disease was 6.1%, and dizziness was 5.4%. Patients with episodic migraine had a significantly higher proportion of completed university education than those with chronic migraine, with an odds ratio of 2.28 (95% confidence intervals 1.63 to 3.19) and a p-value <0.001. In addition, patients with chronic migraine had a significantly higher proportion of comorbidities than those with episodic migraine, with an odds ratio of 1.51 (95% confidence intervals 1.09 to 2.10), as did those with hypertension comorbidity, with an odds ratio of 1.87 (95% confidence intervals 1.16 to 3.02) and a p-value <0.05. Comorbidities with thyroid disease and dizziness had odds ratios of 1.57 and 1.92, respectively, comparing patients with chronic and episodic migraine, but without statistical significance. There were no significant differences in comorbidities between migraine patients with and without aura.

Conclusion: This study confirmed the comorbidities that need to be taken into account when treating migraine. Other comorbidities and differences between migraine with and without aura, and episodic and chronic migraine, should also be proven to support their association.

Disclosure of Interest: None Declared

Abstract number: IHC23-PO-050

Table: Prevalence of comorbidity and the differences between migraine subtypes

	Migraine						
Comorbidity	Overall (572)	Episodic (289)	Chronic (283)	p-value	with aura (171)	without aura (401)	p-value
Comorbidity presence, n (%)	306 (53.5)	140 (48.4)	166 (58.7)	**0.018**	95 (55.6)	211 (52.6)	0.58
Hypertension, n (%)	83 (14.5)	31 (10.7)	52 (18.4)	**0.013**	24 (14.0)	59 (14.7)	0.94
Allergic rhinitis, n (%)	74 (12.9)	37 (12.8)	37 (13.1)	0.98	19 (11.1)	55 (13.7)	0.48
Dyslipidemia, n (%)	50 (8.7)	29 (10.0)	21 (7.4)	0.34	13 (7.6)	37 (9.2)	0.64
Thyroid disease, n (%)	35 (6.1)	14 (4.8)	21 (7.4)	0.27	14 (8.2)	21 (5.2)	0.25
Dizziness, n (%)	31 (5.4)	11 (3.8)	20 (7.1)	0.12	7 (4.1)	24 (6.0)	0.48
Depression, n (%)	16 (2.8)	4 (1.4)	12 (4.2)	0.069	5 (2.9)	11 (2.7)	0.88

IHC23-PO-051

Alice in Wonderland Syndrome (AIWS) and Migraine: Prevalence and characteristics of AIWS in adults with migraine

Mira Fitzek[1], Jasper Mecklenburg[1], Pia Kull[1], Kristin Lange[1], Lucas Overeem[1], Anke Siebert[1], Maureen Steinicke[1], Paul Triller[1], Lars Neeb[1,2], Jens Dreier[1], Daniel Kondziella[3], Uwe Reuter[1,4] and Bianca Raffaelli[1]

[1]*Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany*
[2]*Helios Global Health, Berlin, Germany*
[3]*Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark*
[4]*Universitätsmedizin Greifswald, Greifswald, Germany*

Objective: Alice in Wonderland syndrome (AIWS) is a rare perceptual disorder, characterized by distorted somatosensory and/or visual sensations of one's body or surroundings. In addition, altered sense of time, and feelings of derealization and depersonalization can occur. AIWS is associated with migraine and has been proposed as a variant of migraine aura, but pathophysiology, epidemiology and clinical characteristics remain poorly understood. Here we investigate the prevalence and features of AIWS in patients with migraine.

Methods: This analysis is part of a prospective cross-sectional cohort study conducted at a tertiary headache center. Migraine patients completed a series of questionnaires, including demographic and headache characteristics, AIWS characteristics, and different visual phenomena (e.g. fragmented vision, scotoma and tunnel vision).

Results: In total, 133 out of 808 (16.5%) migraine patients (mean age 44.4 ± 13.3 years, 87% women) reported lifetime experience of AIWS core symptoms lasting on average half an hour. Micro- and/or teleopsia (50.4%) were

reported most frequently followed by macro- and/or microsomatognosia (49.6%) and macro- and/or pelopsia (38.2%). Two thirds of patients (65.1%) indicated headache prior to, after, or during the AIWS symptomatic. More than half (53.7%) of the patients were 18 years or younger at initial occurrence of AIWS. Patients with AIWS were more often diagnosed with migraine with aura compared to those without AIWS (52% vs. 42%, $p = 0.04$) and reported an increased occurrence of 16 out of 22 visual phenomena investigated.

Conclusion: In this large cohort of migraine patients, AIWS was a frequent lifetime phenomenon. The association of AIWS with migraine with aura as well as a similar time course might indicate common pathomechanisms.

Disclosure of Interest: MPF reports personal fees from Teva. JM reports personal fees from Novartis. PK has nothing to disclose. KSL reports personal fees from Teva. LHO has nothing to disclose. AS reports personal fees from TEVA and Novartis. MS reports personal fees from Abbvie. PT has nothing to disclose. LN reports personal fees from Allergan, BIAL, Lilly, Grünenthal, Hormosan, Novartis, and Teva, and research funding from Lily and Teva. JD reports research grants from Deutsche Forschungsgemeinschaft (DFG DR 323/10-1) and Bundesministerium für Bildung und Forschung (Era-Net Neuron EBio2, with funds from BMBF 01EW2004). DK reports personal fees from Wiley, and research funding from among others the Lundbeck Foundation and the Novo Nordisk Foundation. UR reports personal fees from Amgen, Allergan, Abbvie, Lilly, Lundbeck, Novartis, electroCore, Medscape, StreaMedUp, and Teva, and research funding from Novartis. BR reports research grants from Novartis and personal fees from Abbvie/ Allergan, Eli Lilly, Hormosan, Novartis, and Teva.

IHC23-PO-052

Impact of headache on the quality of life of people living with epilepsy in a referral hospital in Cameroon

Daniel Gams Massi[1,2], Emma Anastasie Babe[3], Annick Mélanie Magnerou[3,4], Kuate Tegueu Callixte[4,5], Njankouo Yacouba Mapoure[3,1] and Mathieu Motah[3,6]

[1]*Douala General Hospital, Douala, Cameroon*
[2]*Faculty of Health Sciences, University of Buea, Buea, Cameroon*
[3]*Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon*
[4]*Douala Laquintinie Hospital, Douala, Cameroon*
[5]*Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon*
[6]*University of Bertoua, Bertoua, Cameroon*

Introduction: Headache occurs frequently in people living with epilepsy and it contributes greatly to an altered quality of life for these people. However, despite the frequent association between these two health conditions, there is limited data on this subject in Cameroon. The aim of this study was to assess the impact of headache on the quality of life of people living with epilepsy who were being followed up at the Douala General Hospital (DGH).

Methods: we conducted a 4-months cross-sectional and analytic study from February to May 2021 at the outpatient unit of neurology of the DGH. We included people living with epilepsy confirmed by a neurologist and who were aged 18 years and above. A previously designed questionnaire was administered. Data on sociodemographic characteristics, data clinical of epilepsy, data clinical of headache which makes it possible to determine the type of headache according to International classification headache, characteristics of headache and the period of occurrence during an epileptic seizure. Data on quality of life was assessed using quality of life in epilepsy-31 (QOLIE-31). Statistical analysis was performed using EPI info software version 7.2. Binary logistic regression analysis was used to determine the predictors of poor quality of life. $p < 0,05$ was considered significant.

Results: A total of 150 people living with epilepsy were recruited into the study. we included 100 and excluded 50 due to refusal of consent. Of 100 participants, 52.1% were males. The mean age of participants was 38 ± 16 years. A majority of our participants reported a history of generalized epileptic seizure with no significant difference between the two groups. Forty-eight (48%) of the participants had headache. The most frequent headache was migraine (50%) followed by tension-type headache (37%). Headache occurred more in the post ictal period (32%). Impaired emotional well-being ($p = 0.013$), impaired social functioning ($p = 0.047$) was significantly higher in those with headache. On multivariate analysis, having a family history of headache (OR 12.66, 95% CI 1.86–86.22) and lack of headache treatment (OR 16.28, 95% CI 2.31–114.41; $p = 0.005$) were found to be independent predictors of poor quality of life.

Conclusion: close to half of the people with epilepsy seen during the study period had headache, mainly migraine headache. Having a family history of epilepsy, not being on treatment for headache were independent predictors of poor quality of life in our participants. Thus, it is imperative to identify, counsel and treat headache and headache syndromes in these people so as to improve on their quality of life.

Keywords: epilepsy, headache, quality of life, Douala

Disclosure of Interest: None Declared

IHC23-PO-053

The Impact of Migraine on the Long-term Prognosis in Photosensitive Epilepsy

Tülay Yılmaz Erol, Esme Ekizoglu, Tuba Cerrahoglu Şirin, Nermin Görkem Şirin, Nerses Bebek and Betül Baykan

Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Turkey

Objective: Changes in cortical excitability may be the common pathophysiological mechanism of the frequent comorbidity of epilepsy and migraine, thus photosensitivity would be a clinical correlate of this association. The comorbidity of migraine with photosensitive idiopathic generalized epilepsy (P-IGE) has not been evaluated before. We aimed to investigate the impact of migraine and its accompanying symptoms on long-term prognosis in patients with P-IGE.
Methods: Epileptic patients, diagnosed with IGE or eyelid myoclonia with absences (EMA), with at least one EEG showing photoparoxysmal response, admitted during the period of 1976 to 2022 and followed up for at least ten years were retrospectively included. Migraine comorbidity was investigated by reviewing the files of the patients. Patients were divided into subgroups with remission, with remission and recurrence and without remission in terms of long-term prognosis. The clinical characteristics of the patients with and without migraine were statistically compared.
Results: A total of 108 patients with P-IGE (80 females, 74%) were included; the mean age at admission was 18.38 ± 8.4 years with a follow-up period of 16.79 ± 6.45 (range:10–42) years. Among them 43 patients (40%) had migraine and 33 (31%) had a family history of migraine. The majority (85%) of the P-IGE patients with migraine were female and migraine was significantly more frequent in women with P-IGE compared to males ($p = 0.031$). Migraine was present in 33% of the patients with remission, in 46.4 of those with remission and recurrence, and in 50% of those without remission. The longest duration of seizure freedom and generalized tonic-clonic seizure-free period, as well as the prognosis of P-IGE, did not differ between patients with and without migraine.
Conclusion: Migraine in P-IGE seems to be more frequent than expected, compared to the rates reported in the general population, and mostly seen in women. Although migraine was not associated significantly with the long-term prognosis in P-IGE, half of the patients without remission had migraine, strikingly.

IHC23-PO-054

FKN/CX3CR1 axis facilitates migraine-Like behaviour by activating thalamic-cortical network microglia in status epilepticus model rats

Zheman Xiao and Yanjie Zhou

Renmin Hospital of Wuhan University, Wuhan, China

Background: The incidence of migraines is higher among individuals with epilepsy than in healthy individuals, and these two diseases are thought to shared pathophysiological mechanisms. Excitation/inhibition imbalance plays an essential role in the comorbidity of epilepsy and migraine. Microglial activation is crucial for abnormal neuronal signal transmission. However, it remains unclear whether and how microglia are activated and their role in comorbidities after being activated. This study aimed to explore the characteristics and mechanism of microglial activation after seizures and their effect on migraine.
Methods: Model rats of status epilepticus (SE) induced by intraperitoneal injection of lithium chloride (LiCl)-pilocarpine and migraine induced by repeated dural injections of inflammatory soup (IS) were generated, and molecular and histopathologic evidence of the microglial activation targets of fractalkine (FKN) signalling were examined. HT22-BV2 transwell coculture assays were used to explore the interaction between neurons and microglia. LPS (a microglial agonist) and FKN stimulation of BV2 microglial cells were used to evaluate changes in BDNF levels after microglial activation.
Results: Microglia were specifically hyperplastic and activated in the temporal lobe cortex, thalamus, and spinal trigeminal nucleus caudalis (sp5c), accompanied by the upregulation of FKN and CX3CR1 four days after seizures. Moreover, SE-induced increases in nociceptive behaviour and FKN/CX3CR1 axis expression in migraine model rats. AZD8797 (a CX3CR1 inhibitor) prevented the worsening of hyperalgesia and microglial activation in migraine model rats after seizures, while FKN infusion in migraine model rats exacerbated hyperalgesia and microglial activation associated with BDNF-Trkb signalling. Furthermore, in neuron-microglia cocultures, microglial activation and FKN/CX3CR1/BDNF/iba1 expression were increased compared with those in microglial cultures alone. Activating microglia with LPS and FKN increased BDNF synthesis in BV2 microglia.
Conclusions: Our results indicated that epilepsy facilitated migraine through FKN/CX3CR1 axis-mediated microglial activation in the cortex/thalamus/sp5c, which was accompanied by BDNF release. Blocking the FKN/CX3CR1 axis and microglial activation are potential therapeutic strategies for preventing and treating migraine in patients with epilepsy.
Disclosure of Interest: None Declared

IHC23-PO-055

Migraine and Endometriosis: a comorbidity or secondary headache?

Catarina Fernandes[1], José Miguel Alves[1], Mariana Coelho[1], Helena Gens[1] and Isabel Luzeiro[1,2]

[1]*Neurology Department, Hospitalar and University Center of Coimbra, Coimbra, Portugal*
[2]*2- Coimbra Health School/ESTeSC, Coimbra, Portugal*

Objectives: The prevalence of endometriosis is estimated to be 7% to 10% of women, whereas migraine is a chronic condition with an estimated prevalence of 18%. An association between migraine and endometriosis has been postulated. The aim of this study is, from a clinical case, to review the literature on the relationship of migraine and endometriosis.
Methods: Describe clinical case of a patient diagnosed and performe a nonsystematic literature search in the PubMed, EMBASE and Cochrane Database of Systematic reviews databases. The search strategy included the following MeSH terms and all their variants, adapted to each database: "migraine" "headache" and "endometriosis".
Results: We present a 39-year-old woman who suffered from periorbital pulsating headache with photofobia during menstruation since her adolescence. When she was 29 years old, was referred to neurology department because of an increase in migraine days. At the same time, the patient complained of recurrent abdominal pain that occurred concurrently with the migraine attacks. The subsequent examination revealed endometriosis diagnose and she began treatment with combined hormone therapy. At this point, she began preventive treatment with amitriptyline, which she did not tolerate, and then propranolol was tried, followed by topiramate, which resulted in a good therapeutic outcome. Later, the migraine attacks worsened, were accompanied by dizziness and she was treated with venlafaxine. At age 36, the abdominal pain recurred, and the number of migraine days also increased. Endometriosis treatment was switched to GnRH analogs and onabotulinumtoxinA treatment was initiated. However, in March 2022, the migraine attacks and abdominal pain worsened again and we suggested preventive treatment with monoclonal anti-CGRP. Three months later, we decided to postpone treatment because she reported significant improvement in the number, fewer than two migraine attacks per month, and intensity of headache attacks after total hysterectomy and bilateral adnexectomy. Surgical treatment was decided due to refractory endometriosis. At follow-up twelve months later, the patient was free of migraine attacks and abdominal pain, with no need of preventive treatment.
There is evidence that patients with endometriosis, especially those with coexisting adenomyosis, are more likely to suffer from headaches and migraine. Studies have found a prevalence approximately 30% in patients diagnosed with endometriosis.
Although the comorbidity of migraine and endometriosis is recognized, the reasons for this association remain unclear. Both conditions are common in women of reproductive age and are influenced by ovarian hormones. Moreover, a relationship between the severity of the two conditions has been suggested.
When a pre-existing headache with the features of a primary headache disorder worsens significantly in close temporal relation to another disorder, a diagnosis of concomitant primary and secondary headache should be made. In our clinical case, we speculated on the possibility of secondary headache in endometriosis because the patient improved after surgical treatment for endometriosis. However, this also supports to the possible role of a hormonal influence in both conditions.
Conclusions: The mechanism behind the association between these two conditions is still unknown, but there is evidence that a hormonal influence and a chronic inflammatory process in the ectopic endometrial tissue are related to the pathophysiology of migraine attacks. The clinical case presented highlights the therapeutic challenges and allows speculation on the suggestive effect of invasive treatments in endometriosis patients with migraine comorbidity or on the possible role of a secondary headache with migraine-like features in endometriosis.
Disclosure of Interest: None Declared

IHC23-PO-056

The characteristics and burdens of vestibular symptoms in patients with migraine: A hospital-based retrospective study in Taiwan

Yi-Hsien Tu[1], Tzu-Chou Huang[2], Yen-Feng Wang[3,4,5], Shih-Pin Chen[3,4,5,6,7] and Shuu-Jiun Wang[3,4,5]

[1]*Tainan Municipal An Nan Hospital, China Medical University, Tainan, Taiwan*
[2]*Living Water Neurological Clinic, Tainan, Taiwan*
[3]*School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[5]*Brain Research Center and College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[6]*Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[7]*Division of Translational Research, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan*

Objective: To evaluate the clinical presentation and burden of vestibular symptoms (VS) in adult patients with migraine, comparing different migraine subtypes and presence or absence of medication overuse.
Methods: We conducted a retrospective study on adult patients with migraine who were treated at a headache clinic in a tertiary hospital and classified into different subtypes including migraine without aura (MWoA), migraine with aura (MWA), and chronic migraine (CM). Questionnaires were used to document the impact and burden of VS and headache characteristics, and various scales including the Migraine Disability Assessment (MIDAS), headache impact test-6 (HIT-6), Hospital Anxiety and Depression Scale (HADS), and the Beck Depression Inventory (BDI) were administered. Additionally, we compared the clinical features and disease burden between the groups with and without VS, as well as among different migraine subtypes.
Results: The study included a total of 2,580 patients with migraine, with a mean age of 37.9 years, of which 77.1% were female. Among all participants, 49.1% reported experiencing vestibular symptoms (MwV). Among MwV patients, the majority (58.7%) reported that the duration of VS was less than five minutes. Although the severity of VS was mostly moderate (mean $\pm$ standard deviation, 4.8 ± 2.5 on a scale from 0 to 10), 59.6% of MwV patients reported that VS interfered with or prohibited their daily activities. Additionally, 65.2% of MwV patients had less than a 50% chance of experiencing VS concomitant with headache. Among the three migraine subtypes, CM patients had the highest proportion of interference or prohibition of daily activities due to VS ($p = 0.012$), and the severity of VS in CM was higher than that in MWoA ($p < 0.001$). There were no significant differences in terms of the impact of VS on daily activities ($p = 0.596$), duration of VS ($p = 0.851$), and severity of VS ($p = 0.247$) when comparing CM patients with and without medication overuse headache. Compared to migraine patients without vestibular symptoms (MwoV), MwV patients had a higher occurrence of nausea/vomiting ($p < 0.001$), an earlier onset age ($p = 0.005$), higher headache frequency ($p < 0.001$), as well as increased rates of suicidal ideation ($p < 0.001$) and attempts ($p < 0.001$). Moreover, MwV patients had more severe psychiatric and disability symptoms than MwoV patients, as measured by MIDAS ($p < 0.001$), HIT-6 ($p < 0.001$), HADS ($p < 0.001$), and BDI ($p < 0.001$).
Conclusions: Vestibular symptoms were very common among patients with migraine, particularly among those with CM. Comorbidity with vestibular symptoms was associated with a higher disease burden, including psychological disturbance and disability. This study emphasizes the significance of evaluating and managing vestibular symptoms in patients with migraine.
Disclosure of Interest: None Declared

IHC23-PO-057

Clinical Differentiation of Chronic Migraine with and without Medication Overuse: Insights from a Retrospective Study

Gülcan Göçmez Yılmaz[1], Nevra Öksüz Gürlen[2], Asena Ayça Özdemir[2], Reza Ghouri[2] and Aynur Özge[2]

[1]*Mersin City Training and Research Hospital, Mersin, Turkey*
[2]*Mersin University School of Medicine, Mersin, Turkey*

Background: Medication overuse can significantly alter the phenotype of migraines, leading to refractory and resistant cases. Understanding the clinical features associated with chronic migraine (CM) and medication overuse headache (MOH) is crucial for effective management. The aim of this study was to analyze the clinical characteristics of CM patients with and without medication overuse and identify potential prognostic markers.
Methods: A retrospective analysis was conducted using the Mersin University headache database, which included a total of 824 patients who met the diagnostic criteria for CM according to the International Classification of Headache Disorders, 3rd edition (ICHD-3). Among the included patients, 85.3% were female, and the mean age was 41.98 ± 15.5 years. To compare the clinical features between CM patients with and without MOH, the control of normality of continuous variables was evaluated with the Shapiro Wilk test. The Mann-Whitney U test was used to compare VAS and pain frequency in those with and without excessive drug use. Chi-square test was used in the analysis of categorical data. The analysis of the data was evaluated in IBM SPSS 21 program. The statistical significance level was taken as 0.05.
Results: Out of the 824 patients, 143 reported the presence of MOH in addition to CM, while the remaining 681 patients did not have MOH. The analysis revealed several significant findings. Patients with MOH exhibited a significantly higher frequency of throbbing headaches compared to those without MOH ($p = 0.002$). Moreover, patients who reported bilateral pain location were more likely to develop MOH ($p = 0.033$). In terms of headache severity, patients with MOH experienced more frequent and severe attacks compared to those without MOH ($p = 0.001$, 0.010, respectively). The study also found significant associations between MOH and common migraine-associated symptoms. Patients with MOH were more likely to experience nausea, vomiting, photophobia, and phonophobia ($p = 0.004$, 0.008, <0.001, 0.004, respectively). Additionally, MOH showed a significant positive association with symptoms such as dizziness, osmophobia, and allodynia ($p = 0.039$, <0.001, 0.029, respectively).
Conclusion: This comprehensive analysis of CM patients with and without medication overuse provides valuable

insights into the clinical characteristics associated with MOH. The presence of medication overuse was found to be associated with distinct headache characteristics, increased severity, and a higher prevalence of common migraine-associated symptoms. These findings highlight the importance of considering medication overuse as a contributing factor in the management of chronic migraines and may serve as potential prognostic markers. Further research and validation of these findings are warranted to optimize the clinical management of CM patients with medication overuse.

Disclosure of Interest: None Declared

IHC23-PO-058

Study of the association of primary headaches and suicidal risks

Evgenii Sokolov, Alexey Sergeev, Dmitrii Petelin and Nadezhda Kovalchuk

Sechenov University, Moscow, Russian Federation

Background: Primary headaches (tension-type headache and migraine) are the most common neurological disorders. Moreover than 50% of the population expirience headaches on a regular basis.[1] Due to epidemiological studies 10,4% of Russians suffer from chronical forms of headache.[2] A targeted study of suicidal risks in patients with headaches is demanded because of severe levels of disadaptation, high levels of comorbidity with psychiatric disorders and because of how widely spread headaches are (especially in adolcents and young adults).

The purpose of the study: Analysis of suicidal risks in patients with primary headaches.

Materials and Methods: A survey of 103 respondents was conducted (n-90 (87,4%) – females (F) and n-13 (12,4%) – males (M)). The average age of the survey participants was 27.6 years. Validated questionnaires and scales were used in the course of the study, such as: ID-Migraine, Headache Impact Test (HIT-6), Hamilton Anxiety and Depression Rating Scale (HAM-A and HAM-D), also Columbia-Suicide Severity Rating Scale (C-SSRS) was used.

Results: Out of 103 respondents 90 (87,4%) have complained about having headaches at least once a month, meanwhile 44 (42,7%) respondents noted presence of a history of suicidal thoughts or actions. 39 patients with headaches (43,3% of patients with headaches) noted presence of a history of suicidal thoughts and/or actions. A group of patients with headaches and suicidal thoughts and/or actions (n-39, average age – $27,1 \pm 7,6$) and a group with headaches but with no history of suicidal thoughts and/or actions (n-51, average age – $28,6 \pm 7,2$) were comparable by age and gender composition (92,3% – F, 7,7% – M vs 86,3% – F, 13,7% – M). Apart from that, a group of patients without headaches, but with a history of history of suicidal thoughts and/or actions (n – 5, average age $22,8 \pm 4,5$), as well as a groupof patients with no headaches or history of suicidal thoughts and/or actions (control group) (n-8, average age – $26,5 \pm 5,6$) was included.

Statistical analysis revealed a significant predominance of anxiety and depression levels in patients with headaches and suicidal intentions (HAD-A – $21,0 \pm 7,1$, HAD-D – $17,1 \pm 5,9$, $p < 0,001$, ANOVA test) comparing to a group of patients with headaches (HAD-A – $14,7 \pm 8,3$, HAD-D – $11,4 \pm 6,4$) and control group (HAD-A – $8,1 \pm 3,4$, HAD-D – $6,0 \pm 4,6$). At the same time, indicators of level of anxiety and depression in groups with suicidal thoughts and/or behavior with headaches (HAD-A – $21,0 \pm 7,1$, HAD-D – $17,1 \pm 5,9$) and without headaches (HAD-A – $20,6 \pm 4,6$, HAD-D – $19,2 \pm 6,5$) were comparable and did not differ significantly.

Interestingly, due to Headache Impact Test (HIT-6) headaches affected quality of life inpatients with a history of suicidal thoughts and/or actions (HIT-6–$59,7 \pm 6,4$) and without one (HIT-6–$59,6 \pm 6,3$) equally. There is also a tendency of increased risks of suicidal behavior inpatients with headaches (43.3%) in comparison with the group with a history of suicidal intentions and/or actions, but without headache (38.5%). Besides, the conducted correlation analysis showed a direct association between the levels of anxiety, depression and headaches and an increase in the risks of suicidal ideation and actions (correlation coefficient 0,399, $p < 0,001$).

Conclusion: Patients with primary headaches (migraine and tension-type headache) have a significant association with high levels of anxiety and depression, as well as an increased risk of developing suicidal thoughts and/or behavior. The data obtained indicates the need for further detailed study of this problem and targeted analysis. Identification of psychiatric disorders in patients with headaches, especially chronic forms, is required.

Disclosure of Interest: None Declared

Literature

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IHC23-PO-059

Migraine Prevalence and Comorbidities in US Veterans: The Importance of Gender and Environmental Factors in The Million Veteran Program

Marianna Gasperi[1,2,3], Niloofar Afari[1,4,5] and Brooke Franklin[6,4]

[1]*UC San Diego, La Jolla, USA*
[2]*VA Puget Sound Healthcare System, Seattle, USA*
[3]*Mental Illness Research Education and Clinical Center, Seattle, USA*
[4]*VA San Diego Healthcare System, San Diego, USA*
[5]*Center of Excellence for Stress and Mental Health, San Diego, USA*
[6]*University of Utah, Salt Lake City, USA*

Objective: The study investigated the lifetime prevalence of migraine headache in US Veterans and its associations with health comorbidities, environmental risk factors, service history, and the impact of gender on these associations using data from the Million Veteran Program (MVP).
Methods: The MVP data (n = 450,625) and logistic regression models were used to establish the prevalence of migraine in male and female Veterans, along with the comorbidities, environmental factors, and service history.
Results: Migraine prevalence was higher in women (30.1%) than men (8.2%). Veterans with migraines had worse general health, more pain interference, and opioid use. They were significantly more likely to report neurological (OR range:1.68–5.76), psychiatric (OR range: 1.79–3.20), and digestive conditions (OR range: 1.41–2.99). Chemical and biological warfare, anti-nerve agent pills, and Agent Orange exposure were associated with higher migraine prevalence (OR range: 1.50–2.19). Women used more antimigraine medications, and men received more opioid prescriptions. Significant migraine-by-gender interactions ($p < .001$) were present for over half of the conditions assessed, indicating that the association with migraine varied by gender and, for neurological and psychiatric conditions, was stronger in men.
Conclusion: Our study highlights the impact of migraine on Veterans" health, with higher prevalence in women. Interdisciplinary approaches to migraine management and screening strategies for different populations, including Veterans with specific environmental exposures, are needed. Gender significantly affects the relationship between migraine and health comorbidities, warranting further study.
Disclosure of Interest: None Declared

IHC23-PO-060

Neck Pain disability on Headache impact and a link between sleep disturbance and Neck Pain in Migraine

Hee-Jin Im[1] and Soo-Jin Cho[2]

[1]*Dongtan Sacred Heart Hospital, Hallym University Medical Center, Hwaseoung, Korea, Republic of*
[2]*Dongtan Sacred Heart Hospital, Hallym University Medical Center, Hwaseong, Korea, Republic of*

Background: Neck pain (NP) is a prevalent symptom among migraine patients, but its disability on headache impact and the contributing factors for comorbid NP are poorly understood. This study aimed to investigate NP disability on the impact of headache among migraineurs and factors linked to comorbid NP, including sleep-related variables.
Methods: This cross-sectional study was conducted at a university hospital headache center, for headache patients at their first visits. 295 patients with migraine (217 females; 39.0 ± 10.8 years; 101 chronic migraine) were included in the study. Information on NP, history of physician-diagnosed cervical spine or disc disorders, detailed parameters of headache, and sleep and mood variables were collected. Logistic analysis of the severe impact of headache and contributing factors for NP were performed.
Results: NP was present in 153 participants (51.9%) with migraine, with high NP disability observed in 28 patients, and 125 patients had low NP disability. In multivariable analysis, NP disability, medication days per month, severe disability of migraine, and excessive daytime sleepiness were significant predictors for severe impact of headache. Thirty-seven patients with physician-diagnosed cervical spine or disc disorders were excluded from the NP analysis. Higher monthly headache days, female gender, and a high likelihood of obstructive sleep apnea were positively correlated with the presence of NP among migraineurs in multivariable analysis.
Conclusion: Overall, the study highlights that the potential impact of sleep-related variables and monthly headache days on NP in these patients. The high disability of NP was also associated with severe impact of headache.
Disclosure of Interest: None Declared

IHC23-PO-061

Factors Contributing to Changes in Chronic Migraine Patients with Fibromyalgia: A Comparative Analysis

Nevra Öksüz[1], Reza Ghouri[1], Fehmi Bilgiç[1], Asena Ayça Özdemir[1], Gülcan Göçmez Yılmaz[2] and Aynur Özge[1]

[1]*Mersin University School of Medicine, Mersin, Turkey*
[2]*Mersin City Training and Research Hospital, Mersin, Turkey*

Background: Migraine and fibromyalgia (FM) are prevalent pain disorders that often coexist, with several studies reporting a high proportion (20%–36%) of migraine patients also experiencing FM. Similarly, the occurrence of migraines in FM patients ranges from 45% to 80%, indicating its common occurrence in this population. Despite the well-established association, the reasons behind this co-occurrence remain largely unexplained. Furthermore, existing data suggests that individuals with migraine have a higher likelihood of developing FM compared to the general population. Building upon this knowledge, our study focused on chronic migraine (CM) patients and aimed to investigate the clinical features associated with FM in this specific group. Our primary objective was to analyze the clinical characteristics of CM patients, comparing those with and without FM, in order to identify potential prognostic markers.

Methods: A retrospective analysis was conducted utilizing the comprehensive Mersin University headache database, which encompassed a total of 824 patients meeting the diagnostic criteria for CM according to the International Classification of Headache Disorders, 3rd edition (ICHD-3). These patients were closely monitored between the years 2017 and 2023. Among the CM patients, 159 individuals were additionally diagnosed with fibromyalgia, in accordance with the diagnostic criteria set forth by the American College of Rheumatology (ACR) in 2016. To compare the clinical features between CM patients with and without fibromyalgia, thorough statistical analyses were performed. The TIBCO Statistica version 13.5.0.17 program was employed for data evaluation, with a statistical significance level set at $p < 0.05$. The normality of continuous variables was assessed using the Shapiro-Wilk test. The Mann-Whitney U test and t-test were utilized for comparing continuous variables in the two independent groups, i.e., CM patients with and without fibromyalgia. As for categorical data analysis, the Chi-Square test and Fisher's Exact test were applied.

Results: Out of the 824 patients included in the analysis, 159 individuals reported the coexistence of FM alongside CM, while the remaining 665 patients did not have FM. The findings of the analysis unveiled several noteworthy observations. As anticipated, FM was more prevalent among female migraineurs. CM patients with FM exhibited a higher likelihood of experiencing migraine-associated symptoms, including nausea, vomiting, photophobia, phonophobia, and osmophobia ($p < 0.001$, $p = 0.003$, $p < 0.001$, $p < 0.001$, $p < 0.001$, respectively). The characteristics of the headache, such as the throbbing pattern, were similar in both groups, showing no significant difference. However, certain factors such as family history of migraine, atopy, menstrual association, and seasonal relationship were more common in CM patients with FM ($p = 0.003$, $p < 0.001$, $p < 0.001$, and $p = 0.014$, respectively). Additionally, the presence of allodynia was significantly higher in this group ($p = 0.001$). Although there was no disparity between the groups in terms of depression rates ($p = 0.357$), which is known to often accompany FM, higher rates of anxiety were observed in the group with FM ($p = 0.033$). Furthermore, the FM group exhibited a higher frequency of metabolic syndromes ($p = 0.035$).

Conclusion: The presence of FM demonstrated a significant association with a higher prevalence of common symptoms related to migraines. The frequency of these accompanying symptoms in the FM group suggests a potential shared pathophysiological mechanism between FM and migraines. These findings emphasize the significance of acknowledging FM as a contributing factor in the holistic management of chronic migraines. To optimize the clinical care for CM patients with FM, it is crucial to comprehend the specific changes that FM introduces in these individuals. Therefore, further research is warranted to deepen our understanding in this regard. This comprehensive analysis offers valuable insights into the clinical characteristics associated with FM, aiding in the development of tailored management approaches.

Keywords: fibromyalgia, migraine, chronification, prevalence, allodynia

Disclosure of Interest: None Declared

IHC23-PO-062

The impact of sleep disturbances in patients with migraine – a prospective observational study from a tertiary care specialty hospital from South India

Sahil Mathur, DV Seshagiri, Sanjib Sinha, Girish B Kulkarni, Ravi Yadav, Nitish Kamble, Mailankody Pooja and Pritam Raja

NIMHANS, Bangalore, India

Objectives: Migraine is a common primary headache disorder that impairs the quality of life of patients. Sleep disturbances are known to affect the characteristics of migraine. The inter-relationship between headache and

sleep has not been studied in detail in Indian population. AIM: To study the impact of sleep disturbances in patients with migraine.

Methods: One hundred and seventeen adult patients of migraine visiting the neurology outpatient department, who were not on any prophylactic medication for migraine were assessed by personal interview. Headache severity was recorded by the verbal analogue scale (VAS) and the Migraine Disability Assessment (MIDAS) questionnaire. A comprehensive questionnaire was developed for the characterization of headache. The subjective sleep quality was recorded by the Pittsburgh sleep quality index (PSQI). Insomnia and excessive daytime sleepiness was graded by the Insomnia severity index (ISI) and Epworth sleepiness scale (ESS). The overall health related quality of life was assessed by the SF-36 total score. The data analysis was done using SPSS version 26.

Results: Out of 117 migraine patients, 85 were female (70.8%), with a mean age at presentation of 35.6 ± 9.8 years, mean duration of headache being 6.5 years. 90/117 patients had chronic migraine (76.9%), with a mean MIDAS score of 42.5. Mean ISI score was 10.2, and 34/117 patients had clinical insomnia. The mean PSQI score was 7.22 and 64/117 patients had poor sleep quality (PSQI score 5 or more). Comorbid anxiety was present in 42/117 patients (35.9%) and comorbid depression was present in 44/117 patients (37.6%). There was a significant correlation of MIDAS score with severity of insomnia – ISI score (Pearson's coefficient- 0.735, p- 0.001); overall sleep quality – PSQI (Pearson's coefficient – 0.657, p-0.001). The overall SF-36 score had a significant correlation with the total MIDAS score (Pearson's coefficient – 0.568, p-0.001), total ISI score (Pearson's coefficient – 0.788, p-0.001), and total PSQI score (Pearson's coefficient – 0.859, p-0.001).

Conclusion: In patients with migraine, the severity of headache correlates with the severity of insomnia and the overall sleep quality. This study emphasizes the need to address the sleep disturbances associated with migraine to improve the quality of life and reduce the overall disability related to the illness.

Disclosure of Interest: None Declared

IHC23-PO-063

Do migraine patients have higher levels of misophonia compared to healthy controls?

Aysenur Sahin[1], Seda Cakir[1], Elif Ilgaz Aydinlar[1], Mustafa Ertas[2] and Pinar Yalinay Dikmen[1]

[1]*Acibadem University School of Medicine, Istanbul, Turkey*
[2]*Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey*

Objective: Misophonia is characterized by a negative emotional response, such as anxiety, irritability, or restlessness, towards certain sounds, including but not limited to tapping, chewing, typing, breathing, swallowing, or foot tapping. Phonophobia is a subtype of misophonia characterized by fear as the dominant emotion. However, misophonia is characterized by other dominant emotions, such as irritation, stress and anxiety, aggravation, feeling trapped, and impatience.

Migraine is often associated with other neurological and psychiatric disorders such as depression, and anxiety. These comorbid conditions can significantly impact the frequency, severity, and duration of migraine attacks, as well as the response to treatment. Phonophobia may be related to both ictal and interictal phases of migraine. However, misophonia has not been studied in migraine yet. The aim of this study was to investigate whether misophonia is more prevalent in patients with migraine compared to healthy individuals. Additionally, we aimed to explore the association between misophonia and migraine-related disability, depression, anxiety, stress levels, and obsessive-compulsive traits.

Methods: We recruited 205 patients with migraine as a migraine group (MG) and 205 healthy subjects as a control group (CG). Demographics, Headache Impact Test-6 (HIT-6), Depression Anxiety Stress Scale (DASS-21), Misophonia Scale (total score and severity scale), Yale Brown Obsessive Compulsive Scale (Y-BOCS) were recorded from all participants. In the MG, clinical features of migraine, Migraine Disability Assessment Test (MIDAS) and Allodynia Symptom Checklist were also obtained.

Results: The mean age [36.5 (9.5) vs. 36.5 (10.1); $p = 0.956$] and gender distributions were similar between the MG and the CG. In the MG, the mean duration of migraine was 14.1 years and the mean number of headache days in the last month was 8.6 (6.7) days. The mean MIDAS score was found to be 19.1 (21.5). In the MG, 22.4% of the patients had chronic migraine.

The percentage of patients exceeding the Misophonia Severity Scale cut-off level (^{3}7) was found to be higher in the MG than the CG (44.9% vs. 17.6%, $p < 0.001$). The MG showed higher levels of interictal photophobia (53.7% vs. 37.6%, $p < 0.001$), interictal phonophobia (67.3% vs. 36.6%, $p < 0.001$), and interictal osmophobia (49.8% vs. 41.0%, $p > 0.001$) compared to the CG.

The MG also showed statistical difference in the HIT-6 scores [65.2 (6.4) vs. 42.9 (6); $p > 0.001$], the mean depression scores of DASS-21 [5.2 (4.7) vs. 3.93(3.5); $p > 0.001$], the mean anxiety scores of DASS-21 [4.6 (3.9) vs. 2.9 (2.8); $p > 0.001$], the mean stress scores of DASS-21 [7.8 (4.4) vs. 5.4 (3.5); $p > 0.001$], the Misophonia Scale total scores [34.7 (15.1) vs. 21.4 (13.7); $p > 0.001$] and the Misophonia Scale severity scores [6.7 (3.2) vs. 4.1 (2.5); $p > 0.001$] compared to the CG. No difference was observed in the mean Y-

BOCS scores [11.3 (9.0) vs. 9.4 (8.3); p = 0.317] between the two groups.

Conclusion: In our cohort, misophonia was more common in migraine patients compared to healthy controls. Besides, misophonia showed a positive correlation to the duration of migraine, depression, anxiety, stress levels and obsessive-compulsive traits in the MG. Therefore, it is recommended to consider misophonia when evaluating comorbidity in migraine patients. Future studies will reveal the relationship between migraine and misophonia and its effect on the course of migraine.

Disclosure of Interest: None Declared

IHC23-PO-064

Assesment of cephalic and extra-cephalic pain sensitivity in medication overuse headache patients with chronic migraine compared to the episodic migraine patients and healthy control

Nishana Zakharova[1] and Isin Unal-Cevik[2]

[1]Hacettepe University Faculty of Medicine Department of Neurology, ANKARA, Turkey
[2]Hacettepe University Faculty of Medicine Department of Neurology, Headache and Pain Unit, ANKARA, Turkey

Objective: Hypersensitivity to non-noxious stimulus is reported in migraine patients. We aimed to assess the demographical, clinical and headache characteristics, the comorbidities, the pain sensitivity characteristics and chronicity-related factors in medication overuse headache patients with chronic migraine (MOH+CM) compared to the episodic migraineurs (EM) and healthy control (HC).

Methods: Adult participants were prospectively enrolled in 3 groups. Demographical features, clinical, laboratory and neuroimaging findings, MIDAS, Allodynia Checklist (ASC), Beck Depression and Anxiety Inventory scores were recorded. To quantify the type of pain sensitivity and spatial characteristics of central sensitization; pinprick hyperalgesia, brush allodynia, cold allodynia, and temporal summation tests were applied to cephalic (left forehead region) and extra-cephalic (left forearm anterior surface) regions. Comparisons among the groups were analyzed.

Results: A total of 90 participants (30 in each group) were enrolled to the study. Age and sex (female dominance) did not differ among the groups. The MOH+CM patients revealed higher BMI, fasting glucose, total cholesterol levels, and lower iron binding capacity compared to the HC. The migraine disease history, attack duration, frequency, severity, triptan usage, combination analgesic usage, the MIDAS, Beck Depression and Anxiety, Allodynia Checklist scores were statistically significant and high in MOH+CM compared to the EM. All of the MOH+CM patients reported that they felt a compulsion to take their pain killers regularly for their attacks and the possibility of missing a dose made them anxious or disturbed. The 70% MOH+CM patients wished they could stop taking their painkillers and knew that painkillers could harm. On sensory examinations, MOH+CM and EM patients disclosed both cephalic and extra-cephalic cold allodynia (statistically significant high scores in MOH+CM compared to EM and HC).The pinprick hyperalgesia and wind-up phenomena were detected at cephalic region in both group migraineurs and statistically significant high scores in the MOH+CM compared to EM and HC groups. Among the ASC items, combing hair, wearing eyeglasses, wearing contact lenses, wearing a necklace, tight clothing, resting the face or head on a pillow, exposure to heat (e.g., cooking, washing your face with hot water) and exposure to cold (e.g., using an ice pack, washing your face with cold water) were correlated with pain sensitivity sensory examination modalities.

Conclusions: Pain sensitivity has significant implications for our understanding of the pathophysiology of headache. The MOH+CM patients revealed metabolic syndrome, depressive features, severe disability, and prominent cephalic and extra-cephalic pain hypersensitivity. The pain hypersensitivity is associated with chronicity and higher levels of disability. Pain modulation systems are prominently altered in MOH+CM compared to EM and HC. Identification of chronicity-related factors and quantification of central sensitization, may provide insight into personalized treatment options in chronic headache patients.

Disclosure of Interest: None Declared

IHC23-PO-065

Migraine and sleep quality

Ezgi Uludüz[1], Derya Uludüz[2], Aynur Özge[3] and Füsun Mayda Domaç[4]

[1]Koç University, School of Medicine, Medical Student, İstanbul, Turkey
[2]İstanbul University, Cerrahpaşa Medical Faculty, Neurology Department, İstanbul, Turkey
[3]Mersin University, Neurology Department, Mersin, Turkey
[4]University of Health Sciences, Erenköy Mental and Nervous Diseases Training and Research Hospital, Neurology Department, İstanbul, Turkey

Background and Aim: Several studies have shown a distinct relation between sleeping disorders and psychiatric disorders where accompanying headache is more severe in patients who have both disorders. In this study, our aim was to examine the sleeping quality of

migraine patiens and the effects of accompanying depression upon sleep.
Method: Patients that were followed up at headache outpatient clinics and diagnosed as episodic migraine according to ICHD-3 criteria were included. Healthy people with coherent ages were selecte as the control group. Subjects with a history of any psychiatric disease, another primary or secondary headache and patients under prophylactic treatment were excluded. Beck Depression Inventory, Pittsburg Sleep Quality Index (PTS) and Eppworth Sleepiness Scale were applied to both groups. Migraineous patients were also grouped as patients with depression (WD) and patients without depression (WOD). Duration of headache, frequency and severity, MIDAS and type of migraine were noted. Between the groups difference between PST total score and subgroups were examined.
Results: One hundred and ninety three patients with episodic migraine and 85 healthy subjects were included into the study. Thirthy three percent of of migraine patients were also diagnosed with depression. ESS and PSQ were significantly higher in migraine patients ($p = 0.001$ and $p = 0.000$) than the control group . All of the scores of subgroups of PSQ were higher in migrane patients than control group ($p = 0.000$). In patients with depression, it was found that the subjective sleep quality is worse ($p = 0.000$), sleep latency is longer ($p = 0.021$), use of sleep medication is more ($p = 0.005$) and daytime dysfunction was worse ($p = 0.001$) than the control group. No difference was found between PSQ, ESS and BDI scores and MIDAS in migraine patients with aura and without aura ($p > 0.05$). There was a positive correlation between headache frequency ($p = 0.000$) and intensity ($p = 0.000$).
Conclusion: Though regardless of depression quality of sleep is worse and daytime sleepiness is more in patients with migraine, comorbidity may worsen sleep and daily functions. Researches for existing of depression in patients with the diagnosis of migraine and choosing appropriate treatments will increase the sleep quality of the patient and also the quality of life as a result.

Genetics and biomarkers of headache disorders

IHC23-PO-066

Identification of an *ATP1A2* variant in a patient with childhood-onset of epilepsy and adulthood-onset of migraine

Iltsuki Oda[1], Daisuke Danno[2], Haruka Tada[1], Kazumasa Saigoh[1], Atsuko Ikegawa[1], Makito Hirano[3], Makoto Samukawa[3], Yoshiyuki Mitsui[3], Takao Takeshima[2] and Yoshitaka Nagai[3]

[1]*Department of Clinical Genetics, Kindai University Hospital, Osaka, Japan*
[2]*Department of Neurology, Tominaga Hospital, Osaka, Japan*
[3]*Department of Neurology, Kindai University, Osaka, Japan*

Introduction: Familial hemiplegic migraine (FHM) is primarily thought to be caused by genetic factors. Mutations in the *ATP1A2* gene are known to be associated with familial hemiplegic migraine type2 (FHM2), a form of hereditary migraine characterized by headaches, nausea, and sensitivity to light and sound, among other symptoms. This gene encodes the α-2 isoform of Na+K+-ATPase, a membrane protein essential for the electrochemical gradient of Na+ and K+ inside and outside the cell membrane and for its maintenance. The *ATP1A2* protein is an ATPase enzyme located on the cell membrane and is primarily expressed in the brain and eyes. In addition, mutations in the *ATP1A2* gene have also been reported to be involved in the onset of some neurodegenerative diseases, epilepsy, and autism spectrum disorder (ASD). We report here a case of migraine associated with typical absence seizure with a variant in *ATP1A2*.
Case: 24-year-old woman

At the age of 10, she visited the University Hospital A with a chief complaint of loss of consciousness from her surroundings. She was diagnosed with typical absence seizure and started treatment with valproic acid. She did well after that, but valproic acid use may increase the risk of birth defects, particularly affecting the development of the brain and heart. So, at the age of 19, when she reached the age of pregnancy, she was started on lamotrigine instead of valproate, and at the age of 20, she visited our hospital to enter university. At age 23, she began to have migraine headaches and was started on triptans. At the same time, genetic testing for migraine revealed the *ATP1A2* c.194G>T (p.Arg65Leu) variant.
Discussion: In this case, the *ATP1A2* p.Arg65Leu variant was present, but the patient did not have the hemiplegia characteristic of FHM2, and the migraine nature of the clinical symptoms was controllable with triptans. This variant is reported as conflicting interpretations in the ClinVar database. However, it is a variant similar to the familial hemiplegic migraine we reported (Oda I, Danno D,

et al. 2022) and is the second case of this variant in a Japanese migraine patient. The phenotype and clinical presentation of this variant may range from minor headache cases to those resulting in epilepsy and hemiplegic migraine, suggesting that there may be a wide range of clinical manifestations and penetrance.
Conclusion: We experienced a case of absence epilepsy with migraine with a variant in *ATP1A2*.
Disclosure of Interest: None Declared

IHC23-PO-067

Is an immediate CGRP-induced headache predictor for CGRP antagonism?

Marjan Zaletel and Gorazd Požlep

University Clinical Centre of Ljubljana, Ljubljana, Slovenia

αCGRP induces hemodynamic changes in cerebral circulation and CGRP-induced headache (CGRP-IH), which is classified into immediate and delayed CGRP-IH (iCGRP-IH and dCGRP-IH). A study showed cerebral hemodynamic responses to CGRP. It is unclear whether iCGRP-IH and dCGRP-IH are associated with CGRP-induced hemodynamic changes. Therefore, we studied the effects of αCGRP on cerebral hemodynamics, iCGRP-IH, dCGRP-IH. Twenty migrainours and healthy subjects participated in our study. Mean arterial velocity in MCA (vm MCA) and PCA (vm PCA), end-tidal carbon dioxide partial pressure (Et-CO2), mean arterial pressure (MAP), and heart rate (HR) were monitored using transcranila Doppler (TCD). We administered an intravenous infusion of CGRP. The vm MCA, vm PCA Et-CO2, HR, and MAP were determined at different time points and calculated the responses. We monitored the intensity of iCGRP-IH and dCGRP-IH using a visual analog scale (VAS).
We found a significant higher response in vm MCA ($p = 0.0028$) and vm PCA ($p = 0.022$) in iCGRP-IH of migrainours. In addition, we found positive association between Δvm MCA and iCGRP-IH ($p = 0.003$, $OR = 1.18$) as well as Δvm PCA and iCGRP-IH ($p = 0.002$, $OR = 1.16$). We did not find a significant association between Δvm MCA, Δvm PCA, and dCGRP-IH ($p = 0.170$, $OR = 1.05$, and $p = 0.228$, $OR = 1.08$) respectively. A significant relationship was found between Δvm PCA and VAS iCGRP-IH ($p = 0.045$), but not between Δvm MCA and VAS of dCGRP-IH ($p = 0.326$), nor between Δvm PCA and iCGRP-IH ($p = 0.279$).
We have concluded that hemodynamics after CGRP provocation is associated with iCGRP-IH but not with dCGRP-IH. iCGRP-IH could be a sensitive predictor for anti-CGRP therapy in migraine.
Disclosure of Interest: None Declared

IHC23-PO-068

Diagnostic yield of xanthochromia detection by visual inspection versus spectrophotometry

Ane Skaare Sjulstad[1], Ole-Lars Brekke[1,2] and Karl Bjørnar Alstadhaug[1,2]

[1]*Nordland Hospital Trust, Bodø, Norway*
[2]*Institute of Clinical Medicine, UIT The Arctic University of Norway, Tromsø, Norway*

Objective: There is still disagreement about whether to routinely use spectrophotometry to detect xanthochromia in cerebrospinal fluid (CSF) or if visual inspection is adequate. We aimed to assess the use of these two methods in detecting an aneurysmal subarachnoid haemorrhage (aSAH).
Methods: Having applied standard guidelines for analysis of bilirubin in the CSF, we identified patients who underwent both brain CT scan and CSF-spectrophotometry (CSF-SP) at our hospital due to acute headache in the period 2002–2020, scrutinized their medical journals, and evaluated the benefit of CSF-SP comparing with visual inspection. The net bilirubin absorbance (NBA) cut-off for support of subarachnoid haemorrhage (SAH) was set at NBA > 0.007 AU. CSF-SP was also considered positive if NBA ≤ 0.007 and net oxyhaemoglobin absorbance (NOA) was ≥ 0.1 AU.
Results: In total, 801 subjects were identified, but 32 were excluded. The remaining 769 had a mean age of $42{,}3 \pm 17{,}3$ years. Of these, 2% ($n = 15$) were finally diagnosed with SAH; six aSAH, seven perimesencephalic haemorrhage (PMH), and 2 other diagnoses. The number needed to lumbar puncture to detect a SAH was 51, and 128 to detect an aSAH. Post-dural puncture headache was registered in 80 subjects (10%), of whom 14 got a blood patch. Five subjects had other minor complications.
CSF-SP was positive in 31 subjects, in whom 18 also had visual detected xanthochromia (11 true positive). The mean NBA in the 13 samples with clear CSF was 0.0111 ± 0.0103 AU, compared to 0.0017 ± 0.0013 in CSF-SP negative patients ($p < 0.001$). The corresponding figures for oxyhaemoglobin were 0.0391 ± 0.0521 versus 0.0057 ± 0.0081 ($p < 0.001$). Four subjects (0.52%) had a SAH that was only detected by CSF-SP, two with an aSAH, one with PMH, and one with another diagnosis. One of these with aneurysmal haemorrhage died just before intervention and the other one got coiled an anterior communicating aneurysm.
The number needed to perform CSF-SP to detect a SAH was 192, and 385 to detect an aSAH. The sensitivity of CSF-SP was 100%, [95% CI, 78–100] compared to 73% [95% CI, 45–92] of visual xanthochromia detection, but both methods have high negative predictive values, 100% [95% CI, 99.5–100] versus 99.5% [95% CI, 98.6–99.9].

Conclusion: Using visual inspection to detect xanthochromia in the CSF among CT-negative patients with suspected aSAH has low sensitivity and is unreliable, but almost 400 spectrophotometric analyses have to be performed to detect one additional case. Spectrophotometry yielded four false positive results for each true positive in the present cohort, meaning a 20% probability of aSAH following a positive test.
Disclosure of Interest: None Declared

IHC23-PO-069

Genome-wide association study reveals a locus in *ADARB2* for complete freedom from headache

Isa Amalie Olofsson[1,2], Ragnar P. Kristjansson[1], Ida Callesen[1], Olafur Davidsson[3], Bendik Winsvold[4], Henrik Hjalgrim[3], Sisse R. Ostrowski[5], Christian Erikstrup[6], Mie Topholm Bruun[7], Ole Birger Pedersen[8], Kristoffer S. Burgdorf[9], Karina Banasik[9], Erik Sørensen[5], Christina Mikkelsen[5], Maria Didriksen[5], Khoa Manh Dinh[6], Susan Mikkelsen[6], Soren Brunak[9], Henrik Ullum[10], Mona Ameri Chalmer[1], Jes Olesen[1], Lisette J. A. Kogelman[1] and Thomas Folkmann Hansen[1]

[1]*Danish Headache Center, Copenhagen University Hospital, Copenhagen, Denmark*
[2]*Institute for Cellular and Molecular Medicine, University of Copenhagen, Copenhagen, Denmark*
[3]*Danish Cancer Society Research Center, Copenhagen, Denmark*
[4]*Department of Neurology, Oslo University Hospital, Oslo, Norway*
[5]*Department of Clinical Immunology, Copenhagen University Hospital, Copenhagen, Denmark*
[6]*Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark*
[7]*Department of Clinical Immunology, Odense University Hospital, Odense, Denmark*
[8]*Department of Clinical Immunology, Zealand University Hospital, Koge, Denmark*
[9]*Novo Nordic Foundation Center for Protein Research, University of Copenhagen, Copenhagen, Denmark*
[10]*Statens Serum Institute, Copenhagen, Denmark*

Authors
Isa Amalie Olofsson, Ragnar P. Kristjansson, Ida Callesen, Olafur Davidsson, Bendik Winsvold, Henrik Hjalgrim, Sisse R. Ostrowski, Christian Erikstrup, Mie Topholm Bruun, Ole Birger Pedersen, Kristoffer S. Burgdorf, Karina Banasik, Erik Sorensen, Christina Mikkelsen, Maria Didriksen, Khoa Manh Dinh, Susan Mikkelsen, **International Headache Genetic Consortium, DBDS Genomic Consortium,** Soren Brunak, Henrik Ullum, Mona Ameri Chalmer, Jes Olesen, Lisette J. A. Kogelman* & Thomas Folkmann Hansen*
*Contributed equally

Objectives: Headache disorders are the most common disorders of the nervous system. Yet, 4% of the Danish population have never experienced headache. The etiology of complete freedom from headache is not known. To assess genetic variants associated with complete freedom from headache, we performed the first genome-wide association study of individuals who have never experienced a headache.
Methods: We included 63,992 individuals (2,998 individuals with complete freedom from headache and 60,994 controls) in our discovery analysis and replicated any signal in a non-overlapping cohort, both from the Danish Blood Donor Study Genomic Cohort. We calculated genetic correlation between complete freedom from headache and migraine and calculated migraine polygenic risk scores for the entire cohort.
Results: We discovered a genome-wide significant association of the intronic variant rs7904615[G] in ADARB2 (OR = 1.20 [1.13–1.27], p = 3.92x10–9) and replicated the signal. ADARB2 is primarily expressed in the brain, in inhibitory neurons, but the function of the gene is poorly understood. We found a negative genetic correlation between complete freedom from headache and migraine and a low polygenic risk score for migraine in people with complete freedom from headache.
Conclusion: We show that complete freedom from headache has a genetic component, and we suggest that ADARB2 is involved in complete freedom from headache. The genomic locus was not associated with any headache disorders. The negative genetic correlation with migraine and the low polygenic risk score for migraine in people with complete freedom from headache might suggest a shared biology or indicate the existence of a biological continuum of susceptibility to headache. Further studies are needed before ADARB2 can be proven a gene contributing to protection from headache.
Disclosure of Interest: None Declared

IHC23-PO-070

Discovery of New Genetic Variants Associated with Migraine and Family History in Han Chinese in Taiwan

Yi Liu[1], Chia-Lin Tsai[1], Yu-Kai Lin[1], Ming-Chen Tsai[1], Kuo-Sheng Hung[2] and Fu-Chi Yang[1]

[1]*Department of Neurology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan*
[2]*Center for Precision Medicine and Genomics, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan*

Objective: Migraine is a common and debilitating neurological disorder with a strong genetic component. Family history is an important risk factor for migraine, but the genetic association between migraine and family history is still unclear. In this study, we aimed to identify novel genetic variants associated with migraine and its family history in a Han Chinese population in Taiwan.
Methods: We conducted a genome-wide association study in a cohort of 1561 Han Chinese outpatients with a family history of migraine. We collected structured headache histories from probands and their relatives and categorized them according to the International Classification of Headache Disorders. We identified multiple susceptibility loci for migraine, both with and without a family history, and analyzed data for subgroups based on sex, migraine type, and presence or absence of aura.
Results: Our results identified novel susceptibility loci, including rs2287637 in DDX1 and LINC01804 and rs12055943 in ELMO1, which correlated with a positive family history of migraine. We also found a locus downstream of MESP2 associated with episodic migraine and loci in the USP26 exonic region, DUSP9 and PNCK intergenic regions, and PARP1 and STUM associated with chronic migraine. Loci in the C9orf135, MAMDC2, SPRY4-AS1 and FGF1 intergenic regions, the SNAP25-AS1 ncRNA intronic region and the SLC5A11 intronic region were associated with the presence of aura. Loci upstream of LINC00676, downstream of MESP2, and in the RSU1 intronic region were associated with the absence of aura. A locus between LINC02561 and UCN3 was also found in female patients.
Conclusion: Our findings provide evidence for a potential genetic basis for migraine and its family history in the Han Chinese population. We also identified candidate genes for further investigation that may contribute to a better understanding of the pathophysiology of migraine.
Disclosure of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

IHC23-PO-071

Assessment of Proinflammatory Blood Markers in Migraine and their role in Cutaneous Allodynia

Mona Nada[1], Dalia Labib[1], Sahar Wahib[1] and Mohamed Edress[2]

[1]*Cairo University, Cairo, Egypt*
[2]*Cairo Univeristy, Cairo, Egypt*

The association between inflammatory markers and migraine needs to be well addressed because it could help in better understanding the pathophysiology and this could assist the development of new treatment options in migraineurs and thus reduce disability caused by migraine.
Methods: A prospective case control study that included 30 migraine patients and 30 age and sex-matched headache-free controls. Demographic, headache characteristics, and inflammatory markers (Interleukin- 6, Interleukin- 1 and Proinflammatory markers ratios) or both groups were obtained and correlated with each other. Cutaneous allodynia was assessed and correlated to headache characteristics and inflammatory markers.
Results: Regarding cutaneous allodynia, the majority of patients (70%) suffered from cutaneous allodynia (more in females than males) and the median degree of allodynia was 6 (Moderate cutaneous allodynia). There was no statistically significant difference in presence of cutaneous allodynia between migraine patients with and without aura. The duration of headache and headache frequency were higher in migraine patients with cutaneous allodynia (P value 0.047). The average albumin level as well as platelet level were significantly higher in migraine patients compared to controls (P value 0.025 and 0.040 respectively). Mean serum levels of interleukin 6, interleukin 1 and other proinflammatory markers ratios (NLR, PLR, CAR and ESR) were not significantly higher in migraine patients compared to normal subjects (P-value = 0.117, 0.375, 0.220, 0.836, 0.160, 0.835 respectively). Monocyte lymphocyte ratio (MLR) as well as monocyte % were significantly higher in controls compared to patients (P value 0.003, 0.023). Moreover, there are no statistically significant differences between patients" subgroups (migraine with aura versus migraine without aura) regarding serum level of Interleukin- 1b or Interleukin- 6 (P-value = 0.536, 0.245 respectively). Concerning MIDAS score, there was significant positive correlation with IL-1 level (r: 0.304). However, there wasn"t any significant correlation between pro-inflammatory markers with either disease duration or degree of allodynia.
Conclusion: There is no association between migraine and Inflammatory markers Interleukin- 6, Interleukin- 1 and Proinflammatory markers Ratio. Cutaneous allodynia

is very common and underestimated in migraine patients but no correlation between CA and inflammatory markers.
Disclosure of Interest: None Declared

IHC23-PO-072

FGF-21 and GDF-15 are increased in Migraine and associated with the severity of migraine-related disability

Kaiming Liu and Jiahui He

Department of Neurology, The Second Affiliated Hospital, Zhejiang University School of Medicine, No 88 Jiefang Road, Hangzhou, Zhejiang, China., HangZhou, China

Background: Migraine is a highly prevalent disorder that imposes a significant socioeconomic burden. The diagnosis of migraine is based on clinical features and lacks specific biomarkers. Some research has found that mitochondria play an important role in the pathogenesis of migraine. Fibroblast growth factor-21 (FGF-21) and growth differentiation factor-15 (GDF-15) are considered biomarkers for mitochondrial disorders. The aim of this study was to determine whether the serum levels of FGF-21 and GDF-15 in migraine sufferers differ from those in healthy controls and are associated with the severity of migraine-related disability.
Methods: The serum concentrations of FGF-21 and GDF-15 were measured using an ELISA-based approach. Clinical variables, including monthly headache days, peak headache pain intensity, the 6-item Headache Impact Test (HIT-6), and the Migraine Disability Assessment (MIDAS), were also addressed. The associations between the clinical variables of migraine patients and serum levels of FGF-21 and GDF-15 were studied.
Results: We collected serum samples from 221 migraine patients (153 episodic migraineurs and 68 chronic migraineurs) and 124 healthy controls. In the multiple regression that corrected for identified confounders, we found that the serum levels of FGF-21 and GDF-15 were significantly higher in migraine sufferers than in healthy controls. Regarding quality of life, higher scores on the HIT-6 and MIDAS were associated with higher levels of FGF-21 and GDF-15. For the ROC analysis, the diagnosis of migraine using GDF-15 showed that the area under the ROC curve (AUC) was 0.801 and the AUC of chronic migraine was 0.880.
Conclusion: The results revealed that FGF-21 and GDF-15 levels were significantly higher in migraine sufferers than in healthy controls and were strongly associated with the severity of migraine-related disability. Our findings may contribute to a better understanding of the underlying mechanisms of brain mitochondrial metabolism dysfunction in migraine.
Trial registration: China Headache Registry Study (CHRS), ClinicalTrials.gov ID: NCT04939922 (06/14/2021).
Keywords: GDF-15, FGF-21, migraine, mitochondrial dysfunction, migraine-related disability
Disclosure of Interest: Vice President, Headache Group, Neurologist Branch, Chinese Medical Association. Vice President, Youth Committee of Headache and Sensory Disorders, Chinese Research Hospital Association, 2019- present.

IHC23-PO-073

Both receptor and circulating monoclonal antibodies selectively normalize baseline increased serum alpha-CGRP levels in chronic migraine patients throughout 3-month treatment

Gabriel Gárate[1,2,3], Vicente González-Quintanilla[1,2,3], Andrea González[1,2,3], Marta Pascual[1,2,3], Sara Pérez-Pereda[1,2,3], Jorge Madera[1,2,3] and Julio Pascual[1,2,3]

[1]*University Hospital Marqués de Valdecilla, Santander, Spain*
[2]*Universidad de Cantabria, Santander, Spain*
[3]*IDIVAL, Santander, Spain*

Background: The interictal concentrations of serum CGRP levels in chronic migraine (CM) patients are controversial. Data on their status after treatment with antibodies against circulating CGRP or its receptor (mAB) are still scarce. Additionally, available studies have not differentiated between alpha (nervous system) or beta (gut) CGRP isoforms.
Objective: To analyse whether mAb therapies have an effect on alpha and/or beta-CGRP circulating levels in chronic migraine (CM) patients, increasing the number of subjects from our recent work (Gárate et al. 2023, Ann. Neurol, online), and to evaluate their correlation with parameters of treatment outcome.
Methods: We recruited 125 CM patients (age 49.6 ± 9.7, range 21–71 years; 87.2% women) beginning mAb treatment along with 78 sex and age paired healthy controls without history of migraine (HC). For CM patients, blood was extracted before, two-weeks (M0.5) and three months (M3) after first dose of mAb, always in 24 hour free-migraine and free-abortive medication periods. All patients were on preventives (average 1.5 ± 0.2), which were not modified during the study period. For HCs, blood was extracted once in a 24 free-medication period. Alpha and beta-CGRP serum levels were measured using ELISAs designed for the specific detection of

each isoform (Abbexa, UK, for alpha-CGRP and CUSABIO, China, for beta-CGRP).
Results: Baseline alpha-CGRP levels were significantly elevated in CM patients (mean ± SD: 56.0 ± 31.9 pg/mL) compared to HC (45.2 ± 27.1 pg/mL) and significantly decreased over the course of mAb treatment (n = 104; M0.5: 47.6 ± 27.4 pg/mL; M3: 47.1 ± 29.5 pg/mL). No differences were found between anti-CGRP (n = 49; galcanezumab n = 45, fremanezumab n = 4) and erenumab (n = 76) groups at any time point. Absolute decrease of alpha-CGRP throughout the treatments positively correlated with the decrease in monthly headache days ($p < 0.01$; 95% CI "r": 0.09–0.45). Negative modulation of alpha-CGRP at the third month significantly associated with positive scores (>4) at the patient global impression of change scale (PGIC) and with analgesic overuse reversal. Beta-CGRP did not differ at baseline between CM patients (4.2 ± 3.4 pg/mL) and HC (4.5 ± 2.6 pg/mL) nor was modulated by mAb treatment (n = 104) (M0.5: 4.3 ± 3.0 pg/mL; M3: 4.3 ± 2.9 pg/mL).
Conclusions: alpha-CGRP circulating levels are progressively normalized from basally increased concentrations to the range found in HC by the mAb therapies, regardless of their target. The decrease is specific for this isoform as beta-CGRP was not modulated nor found elevated at any time-point analysed. These results indicate that only alpha-CGRP reflects the status of the trigemino-vascular system and that the relevance of beta-CGRP is limited. They also highlight the importance of reporting the isoform measured, showing two different concentrations ranges which potentially could be the reason of the heterogenous findings in studies with CGRP measurements.
Grants: this work has been supported by Instituto de Salud Carlos III (PI20/01358), IDIVAL (INNVAL20/25) and Lilly (I5Q-NS-O002).
Disclosure of Interest: None Declared

IHC23-PO-074

Evaluating the chameleon role of beta-CGRP in gastrointestinal disorders and migraine patients with constipation due to anti-CGRP/CGRPr monoclonal antibodies

Marta Pascual[1,2,3], Gabriel Gárate[1,3], Vicente González-Quintanilla[1,3], Monserrat Rivero[1,2,3] and Julio Pascual[1,2,3]

[1]*University Hospital Marqués de Valdecilla, Santander, Spain*
[2]*Universidad de Cantabria, Santander, Spain*
[3]*IDIVAL, Santander, Spain*

Background: CGRP has two isoforms: alpha-CGRP is thought to be crucial for migraine pain pathophysiology, while beta-CGRP is located in the gastrointestinal system and its physiological role is mostly unknown. It is tempting to propose that diarrhea induced by iv CGRP infusion and the constipation seen with CGRP antibodies could be mediated by the beta-isoform. On the other hand, basic studies have suggested that beta-CGRP exerts a protective role in the gastrointestinal system.
Objective: To analyse and evaluate the relationship between beta-CGRP and gastrointestinal symptoms in patients with inflammatory bowel diseases (IBD), chronic migraine (CM) patients on anti-CGRP/CGRPr monoclonal antibody (mAb) treatment and subjects experiencing acute diarrhea due to COVID-19.
Methods: We recruited and extracted serum samples from 94 IBD, 104CM and 26 COVID-19 patients suffering from diarrhea along with 79 healthy controls (HC) with similar age and sex distribution to the other 3 groups. IBD patients were untreated and recently diagnosed when enlisted. CM patients were analysed before initiation of mAb and after three months, when the record of any adverse effect was made. IBD and COVID-19 patients were analysed once. Beta-CGRP was measured by ELISA (Cusabio, China).
Results: Circulating levels of the beta-CGRP were significantly lower in IBD (mean ± SD: 3.1 ± 1.9 pg/mL) compared to HC (4.5 ± 2.6 pg/mL; $p < 0.001$). In contrast, COVID-19 patients with darrhea presented higher levels (6.3 ± 2.6 pg/mL; $p < 0.01$) as compared with HC. Basal beta-CGRP levels in CM (4.4 ± 3.4 pg/mL) did not differ between HC nor at three months (4.3 ± 2.9). When classified between those who experienced constipation (n = 30, Basal: 4.9 ± 3.9 pg/mL; Month 3: 3.8 ± 2.2 pg/mL) and those who did not (n = 74, Basal:4.2 ± 3.2 pg/mL; Month 3:4.4 ± 3.1pg/mL), we found an average decrease at the third month (–22.4%) selective for the constipation group, although it did not achieve statistical significance.
Conclusion: Our results show that beta-CGRP levels vary depending on the underlying conditions. The elevation found in COVID-19 patients, concurring with what happens after iv CGRP administration, and the tendency to decrease found in mAB-treated patients with constipation suggest that the CGRP effects on gut motility are mediated by the beta-CGRP isoform. Our very consistent results in naïve IBD subjects strongly support a protective role for beta-CGRP in the homeostasis of the gut mucosa. By contrast, the normality of beta-CGRP levels in CM patients indicates that this peptide is not involved in migraine pain pathophysiology.
This work has been supported by grants from the Instituto de Salud Carlos III (PI20/01358), IDIVAL(INNVAL20/25) and Lilly (I5Q-NS-O002).
Disclosure of Interest: None Declared

IHC23-PO-075

Pupillary light response in migraine patients: a study of autonomic function.

Marina Romozzi[1], Costanza Sottani[1], Valeria Guglielmino[1], Serenella Servidei[2,1], Paolo Calabresi[2,1] and Catello Vollono[2,1]

[1]*Università Cattolica del Sacro Cuore, Rome, Italy*
[2]*Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy*

Objective: To assess the autonomic function through automated pupillometry, a non-invasive and rapid test able to provide objective and reproducible data on pupil size and reactivity in patients with migraine, compared to healthy controls (HC). We investigated whether the measurement of the pupillary light reflex provides further information on the pathophysiology of migraine.
Methods: We performed automated pupillometry in a cohort of patients with a diagnosis of migraine without and with aura in the interictal phase, compared to age-matched HC. The following pupillometric parameters were recorded: Baseline pupil diameter (BPD), Minimum Pupil Diameter (MPD), Constriction Index (CI), Reflex Latency (RL), Constriction Velocity (CV), Maximum Constriction Velocity (MCV), Dilation Velocity (DV) and Neuro-pupillary index (NPi). Demographical and clinical data on migraine were collected. The severity and disability of migraine were assessed through the headache impact test (HIT-6) and the migraine disability assessment (MIDAS) scale.
Results: We included 220 eyes from 110 patients with a diagnosis of migraine and a mean age of 38.1 ± 14.0 and 152 eyes from 76 HC with a mean age of 41.0 ± 12.8. In the migraine group, we found significantly lower values of NPi ($p < 0.001$), CH ($p < 0.001$), DV ($p = 0.021$) and MCV ($p = 0.043$) and significantly higher values of MPD ($p = 0.023$) compared to HC. We did not find significant correlations between pupillometric parameters and demographic, clinical features, HIT-6 and MIDAS in the migraine group. The pupil changes were not correlated with the interval since the last migraine attack.
Conclusion: The results suggest subtle sympathetic and parasympathetic pupil dysfunction in the interictal phase of migraine. Automated pupillometry may play a role as a reliable and non-invasive tool to evaluate patients with migraine and may also provide insights into the pathophysiology of migraine.
Disclosure of Interest: None Declared

IHC23-PO-076

Cutaneous allodynia as predictor for treatment response in chronic migraine

Judith A. Pijpers[1], Dennis A. Kies[2], Erik W. van Zwet[3], Irene de Boer[1] and Gisela M. Terwindt[1]

[1]*Dept. Neurology, Leiden University Medical Center, Leiden, Netherlands*
[2]*Dept. Radiology, Leiden University Medical Center, Leiden, Netherlands*
[3]*Dept. Medical Statistics, Leiden University Medical Center, Leiden, Netherlands*

Objective: Central sensitisation is an important mechanism in migraine chronification. It is presumed to occur in second and third order neurons sequentially, resulting in an analogous spatial distribution of cutaneous allodynia with cephalic and extracephalic symptoms. We investigated whether allodynia, and its subtypes based on spatial distribution and type of stimulus, predict response to treatment in chronic migraine patients.
Methods: This study was conducted as part of the CHARM study (NTR3440), a randomized, double-blind, placebo-controlled trial in chronic migraine patients with medication overuse. We included 173 patients. The presence of cutaneous allodynia at baseline was established with the Allodynia Symptom Checklist. Primary endpoint was reversion from chronic to episodic migraine.
Results: Of all patients, 129 (74.6%) reported cutaneous allodynia. Absence of allodynia compared to presence of allodynia was predictive for reversion from chronic to episodic migraine, odds ratio (OR): 2.45 (95%CI: 1.03–5.84, $p = 0.042$). The predictive value was more pronounced when subdivided for spatial distribution, for participants without allodynia versus cephalic (OR: 4.16 (95%CI: 1.21–14.30, $p = 0.003$) and extracephalic (OR: 7.32 (95%CI: 1.98–27.11, $p = 0.024$) allodynia. Mechanical (OR: 7.52 (95%CI 1.60–35.39, $p = 0.011$), but not thermal, allodynia, was associated with outcome.
Conclusions: Cutaneous allodynia, an important marker for central sensitization, has predictive value for treatment response in chronic migraine.
Disclosure of Interest: Irene de Boer reports independent support from the Dutch heart foundation. GMT reports consultancy support from Novartis, Allergan/Abbvie, Lilly, Teva, and Lundbeck and independent support from Dutch Organization for Scientific Research, the Dutch Heart & Brain Foundations and Dioraphte. The other authors report no relevant conflicts of interest

IHC23-PO-077

Circulating exosome microRNA profiles in migraine and healthy controls

Alicia Gonzalez-Martinez[1,2], Hortensia De la Fuente[2], Paula Vera[2], Álvaro Sierra[3], Yésica González Osorio[3], Álvaro Planchuelo-Gómez[4,5], Ángel Luis Guerrero-Peral[3], Ana Beatriz Gago-Veiga[1], David García Azorín[3], José Vivancos[3] and Francisco Sánchez-Madrid[2]

[1]Headache Unit, Hospital Universitario de la Princesa & Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain, Madrid, Spain
[2]Immunology Service, Hospital Universitario de la Princesa e Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain, Madrid, Spain
[3]Headache Unit, Hospital Clínico Universitario de Valladolid, Valladolid, Spain, Valladolid, Spain
[4]Cardiff University Brain Research Imaging Centre (CUBRIC), School of Psychology, Cardiff University, Cardiff, United Kingdom., Cardiff, United Kingdom
[5]Imaging Processing Laboratory, Universidad de Valladolid, Valladolid, Spain., Valladolid, Spain

Objective: In the last decade, different microRNA (miRNA) expression patterns have been associated to migraine. miRNAs are small, single-stranded, non-coding RNA molecules, containing 21 to 23 nucleotides that regulate gene expression at a posttranscriptional level. Exosomes are tiny sac-like structures containing miRNAs able to transfer miRNAs into other cells. In this exploratory study, we aimed to evaluate differentially expressed exosome serum miRNAs as biomarkers of migraine in patients with episodic (EM) and chronic migraine (CM) in a well-controlled homogeneous cohort of non-menopausal women.

Methods: A cohort of 30 participans-10 healthy controls, 10 patients with EM and 10 patients with CM- was recruited. Patients were diagnosed with migraine by neurologists at specialized in Headache according to the International Classification of Headache Disorders (ICHD-3); healthy controls were age-matched participants without familial history of headache disorders. Exosomes were first isolated from serum in all patients; levels of miRNA expression were measured using a human miRNA panels and compared between EM, CM and control groups. Afterwards, an in silico miRNA target prediction analysis was performed including the top three differentially expressed miRNAs contained in exosomes through experimentally validated miRNA interactions to identify pathways regulated by the miRNAs, using the Kyoto Encyclopedia of Genes Genomes (KEGG) pathway analysis.

Results: We included 30 women, mean age 30 (SD: 8.2) years old, mean time with migraine 17 (SD: 8.5) years. Mean monthly migraine days (MMD) and mean monthly headache days (MHD) was 4 (SD: 2.1) in patients with EM, while mean MMD was 22 (SD: 3.9) and mean MMD was 11 (SD:4.5) in patients with CM. The top three differentially expressed exosome miRNA levels were miR-375, miR-454-3p and miR-16-2-3p, which were lower in patients with migraine compared to healthy controls ($p < 0.05$) in the ANOVA or Kruskal-Wallis test. The functional enrichment analysis revealed that proteoglycans pathway is targeted by the three miRNAs performing a pathway intersection analysis with p-value threshold: 0.05. There were 43 genes targeted by the exosome contained miRNAs in this pathway.

Conclusion: Our results show differences in exosome miRNA expression between patients with EM, CM and healthy controls. Moreover, proteoglycans pathway is a putative pathway that might be associated with migraine pathophysiology according to the enrichment analysis. Further studies with a larger sample size to validate these findings are undergoing.

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IHC23-PO-078

Flow cytometry evaluation of peripheral monocytes subpopulations reveal lower inflammatory classical, transitional and nonclassical monocytes in patients with COVID-19 headache: a case-control study

Alicia Gonzalez-Martinez[1,2], Ildefonso Sánchez-Cerrillo[2], Ilya Tsukalov[2], Iris Fernández-Lázaro[1], Pedro Landete[3], Beatriz Aldave[3], Santiago Sánchez-Alonso[2], Ana Sánchez-Azofra[3], Ana Marcos-Jiménez[2], Elena Ávalor[3], Ana Alcaraz-Serna[2], Ignacio De los Santos[4], Tamara Mateu-Albero[2], Laura Esparcia[2], Celia López-Sanz[2], Pedro Martínez-Fleta[2], Ligia Gabrie[2], Luciana Del Campo Guerola[2], Hortensia De la Fuente[2], Francisco Sánchez-Madrid[2,5], María José Calzada[2,5], Isidoro González-Álvaro[6], Arantzazu Alfranca[2], Cecilia Muñoz-Calleja[2], Joan B Soriano[3], Julio Ancochea[3], José Vivancos[1,5], Enrique Martín-Gallo[2,5] and REINMUN-COVID and EDEPIMIC group[2]

[1]Headache Unit, Hospital Universitario de la Princesa & Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain, Madrid, Spain
[2]Immunology Service, Hospital Universitario de la Princesa & Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain, Madrid, Spain
[3]Pneumology Service, Hospital Universitario de la Princesa & Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain, Madrid, Spain
[4]Infectious Diseases Division, Hospital Universitario de la Princesa & Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain, Madrid, Spain
[5]Universidad Autónoma de Madrid, Madrid, Spain, Madrid, Spain
[6]Rheumatology Service from Hospital Universitario de la Princesa and Instituto de Investigación Sanitaria Princesa, Madrid, Spain., Madrid, Spain

Background: Headache is an important manifestation during SARS-CoV-2 infection. Prior studies have shown that headache is associated with a more benign course of the disease. However, the mechanisms underlying headache in COVID-19 patients are still under study. Monocytes are a link between innate and adaptative immune response, and circulating monocytes are important cell types involved in the renovation of macrophages and tissular dendritic cells. In this study, the aim was to study the presence of peripheral inflammation through the study of peripheral monocyte subpopulations and its relationship with other factors associated with headache in COVID-19 patients.
Methods: This case–control study includes COVID-19 hospitalized patients with pneumonia during March 2020. Controls comprise COVID-19 patients without headache and the cases are COVID-19 patients with headache. Demographic, clinical and laboratory data were obtained from the medical records. Monocyte subpopulations were evaluated using flow cytometry.
Results: Of a total of 58 COVID-19 patients, 33/58 (56.9%) women, among them, 11/58 (18.9%) developed headache. Mean age was 59.9 (AD:14.9), 60.7 (SD: 15.7) years old in patients with headache and 59.8 (SD: 14.6) in patients without headache; there were 6/11 (54.5%) women among patients with headache and 28/47 (59.6%) among patients without headache. Patients with headache had lower percentage of classical monocytes (762 vs 455; $p = 0.0022$), transitional monocytes (428 vs 297; $p = 0.001$), and non-classical monocytes (292 vs 193; $p = 0.002$). The percentage of total monocytes was similar between the two groups. There were no differences in C-reactive protein (CRP) levels nor IL-6 levels between patients with and without headache.
Conclusions: Our results show that COVID-19 headache is associated with lower levels of CD40 classical, CD40 transitional and CD40 non-classical monocytes, suggesting that, monocytes preferentially migrate from blood to another tissue in a higher proportion in patients with COVID-19 headache, pointing out towards a possible mechanism involved in COVID-19 headache due to SARS-CoV-2 infection.
Disclosure of Interest: Alicia Gonzalez-Martinez has received speaker honoraria from TEVA. Dr. José Vivancos has served as speaker, consultant, and advisory member for or has received research funding from MSD, Pfizer, Daychii-Sankyo, Bayer, Sandoz, Bristol Myers Skibb, Lilly, Boehringer Ingelheim, Almirall, Sanofi-Aventis and Ferrer Pharma. The rest of the authors report no disclosures relevant to the abstract.

IHC23-PO-079

Corneal nerve morphology as a potential objective biomarker of migraine

Nur Amalina Md Isa[1], Shyam Tummanapalli[1], Jeremy Chung Bo Chiang[1], Arun Krishnan[2,3], Alessandro Zagami[2,3], Eric Papas[1], Maria Markoulli[1] and Katherine Spira[2,3]

[1]School of Optometry and Vision Science, University of New South Wales, Sydney, Australia
[2]Institute of Neurological Science, Prince of Wales Hospital, Sydney, Australia
[3]School of Clinical Medicine, University of New South Wales, Sydney, Australia

Objective: The concentration of calcitonin gene-related peptide (CGRP) – a key biomarker in migraine – has been shown to be significantly elevated in the tears of those with migraine. CGRP in the tears is likely released by Aδ- and C- corneal nerve fibres, originating from the trigeminal ganglion that plays a significant role in migraine pain. Therefore, we compared the corneal nerves of patients with migraine and healthy controls to determine whether the cornea could give an objective assessment of migraine disorder.

Methods: Corneal nerve morphology of 34 migraine patients [16 episodic, 8 chronic, and 10 previously chronic-now-episodic (reversed progression)] and 32 controls were evaluated using in-vivo corneal confocal microscopy and automated ACCMetrics software.

Results: The corneal nerve fibre density (CNFD) at the inferior whorl region was significantly reduced in chronic (11.8 ± 8.8 number/mm^2) compared to episodic migraine patients (20.1 ± 7.4 number/mm^2, $p = 0.009$), and to controls (23.4 ± 6.7 number/mm^2, $p < 0.001$). Similar observations were identified in corneal nerve fibre length (CNFL) of the same region (chronic: 11.1 ± 5.3 mm/mm^2 vs. episodic: 16.3 ± 5.6 mm/mm^2, $p = 0.01$; vs. control: 17.5 ± 4.7 mm/mm^2, $p = 0.001$). No difference was found between the episodic migraine and reversed progression groups in CNFD (reversed progression: 14.4 ± 6.9 number/mm^2, $p = 0.08$) or CNFL (reversed progression: 12.9 ± 4.3 mm/mm^2, $p = 0.21$).

Table. Distribution of age, gender, and corneal nerve morphology.

	Control (n = 32)	Migraine group			ANOVA
		Episodic Migraine (n = 16)	Chronic Migraine (n = 8)	Reversed Progression (n = 10)	
Age	50.6 ± 15.7	39.1 ± 14.7	43.0 ± 14.1	52.9 ± 18.3	p = 0.06
Gender, n					N/A
Female	21	15	6	9	
Male	11	1	2	1	
Inferior Whorl Morphology					
CNFD (number/mm²)	23.4 ± 6.7	20.1 ± 7.4	11.8 ± 8.8	14.4 ± 6.9	*p < 0.001
CNFL (mm/mm²)	17.5 ± 4.7	16.3 ± 5.6	11.1 ± 5.3	12.9 ± 4.3	*p = 0.002

N/A, not applicable; *p < 0.05

Conclusion: The significant differences in corneal nerve morphology between chronic and episodic migraine groups suggests that the frequency of migraine may impact corneal nerve morphology, while the non-significant difference between the reversed progression and episodic migraine groups may suggest the regeneration of the nerves after receiving effective migraine treatment. Together, these findings suggest the potential of corneal nerve morphology as an objective biomarker for migraine frequency and response to treatment.

Disclosure of Interest: None Declared

IHC23-PO-080

Exploratory study of the molecular neuroaxonal integrity in chronic migraine: the role of neurofilament light chain protein

Víctor J. Gallardo[1], Marta Vila-Pueyo[1], Laila Asskour[1], Edoardo Caronna[1], Marta Torres-Ferrus[1,2], Alicia Alpuente[1,2] and Patricia Pozo-Rosich[1,2]

[1]*Headache Research Group, Vall d"Hebron Research Institute, Barcelona, Spain*
[2]*Department of Neurology, Vall d"Hebron University Hospital, Barcelona, Spain*

Objective: To study the presence of the neurofilament light chain protein (NfL) as a neuronal damage molecular biomarker in chronic migraine (CM) patients.

Background: In chronic migraine there is functional, structural, and molecular evidence of changes that occur in the brain, some of which could be linked to the presence of neuroaxonal damage. The NfL detects neuroaxonal damage, and has emerged as a potentially valuable biomarker in neurodegenerative conditions providing a sensitive diagnostic and prognostic tool.

Methods: We recruited healthy controls (HC) and patients diagnosed with CM with or without aura according to the ICHD-3 for this exploratory study. Demographics, migraine clinical data and participant-reported outcomes were recorded during the screening visit and blood samples were also collected. Serum NfL levels were determined by ELISA (UmanDiagnostics AB) according to the manufacturers" recommendations. Statistical inference of NfL quantification between study groups was assessed with unpaired t-tests; the relationship between NfL and related-clinical data was analyzed with correlation analysis; and finally, linear mixed effect models, adjusted by participants" intra-individual variability, were conducted in order to study the change of NfL between study groups and clinical data. Because of the exploratory nature of this study, effect size measurements were also computed. All analysis were performed with specific R libraries.

Results: A total of 38 age-matched female participants (19 HC and 19 CM) were recruited with a median [IQR] age of 39.0 [33.0–45.0] years. Patients presented statistically significantly higher presence of anxiety (BAI score; HC: 3.0 [1.0–4.5] vs. CM: 11.0 [7.0–22.5]; $p < 0.0001$) and depression (BDI-II score; HC: 2.0 [0.0–5.5] vs. CM: 11.0 [5.5–17.0]; $p < 0.0001$) symptoms. Median monthly headache frequency (MHD) was 19.0 [17.5–21.5] days/month and monthly acute medication intake (MAMI) was 11.0 [8.5–15.0] days/month. Statistically significant correlations were found between NFL & age ($rp = 0.511$; $p = 0.001$), MHD & BAI ($rp = 0.658$; $p < 0.0001$), MHD & BDI-II ($rp = 0{,}628$; $p < 0.0001$) and BAI & BDI-II ($rp = 0{,}818$; $p < 0.0001$).

However, we found a non-statistical trend between MHD & NFL ($rp = 0.278$; $p = 0.090$) and, in the comparison of NfL quantification between study groups: HC, 6.1 [4.8–7.6] pg/mL vs. CM, 7.9 [6.1–8.9] pg/mL; $p = 0.092$ (Cohen's d [95% CI]: 0.561 [–0.110–1.231]). Finally, as NFL was correlated with age, a linear model was performed between study groups adjusted by age. Anxiety and depression were also introduced (separately) in the model as a covariables but they did not increase model performance (based on AIC and R2). We also did not find a statistically significant association between NfL and study groups.

Conclusion: Although the results reported in this exploratory study do not provide sufficient evidence to support the presence of NfL as a biomarker of molecular neuroaxonal damage in chronic migraine, the medium effect size observed suggests that further studies with larger sample sizes should be conducted to investigate this potential relationship.

IHC23-PO-081

Genetic variability in vitamin D receptor and migraine susceptibility: a case-control study

Maria Papasavva[1,2], Michael Vikelis[3], Vasileios Siokas[4], Emmanouil Dermitzakis[5], Martha-Spyridoula Katsarou[1], Efthymios Dardiotis[4] and Nikolaos Drakoulis[1]

[1]*Research Group of Clinical Pharmacology and Pharmacogenomics, Faculty of Pharmacy, School of Health Sciences, National and Kapodistrian University of Athens, Athens, Greece*
[2]*School of Sciences, European University Cyprus, Nicosia, Cyprus*
[3]*Headache Clinic, Mediterraneo Hospital, Glyfada, Greece*
[4]*Department of Neurology, University Hospital of Larissa, Faculty of Medicine, University of Thessaly, Larissa, Greece*
[5]*Euromedica General Clinic, Thessaloniki, Greece*

Objective: Migraine is a common primary headache disorder with significant environmental and genetic inputs. Emerging evidence suggests an association between vitamin D and migraine, as vitamin D has a potential key role in the pathways involved in migraine pathogenesis. Understanding the role of vitamin D and its receptor in migraine pathophysiology can ultimately contribute to more efficacious disease management. The current study aimed to investigate the association of three genetic variants in vitamin D receptor (VDR) i.e., FokI-rs2228570, BsmI-rs1544410 and TaqI-rs731236 with the susceptibility to develop migraine in a case-control population residing in Greece.

Methods: DNA sample was collected and extracted from 191 patients diagnosed with migraine according to the ICHD3 criteria and 265 headache-free subjects. The genotyping of the three *VDR* variants under investigation was carried out by the real-time polymerase chain reaction method (melting curve analysis).

Results: According to the statistical analysis (SPSS v28.0), a significant association between migraine susceptibility and TaqI-rs731236 and BsmI-rs1544410 ($p < 0.05$) variants was indicated. Furthermore, subgroup analysis among subsets of patients and controls showed significant association of the TaqI-rs731236 and BsmI-rs1544410 variants with migraine without aura susceptibility ($p < 0.05$).

Conclusion: The current study provided evidence of an association between migraine susceptibility and the *VDR* TaqI-rs731236 and BsmI-rs1544410 variants, which reinforces the emerging role of vitamin D and its receptor in migraine.

Disclosure of Interest: None Declared

Headache classification

IHC23-PO-082

No machine learning required: a number theory diagnostic methods for primary headache disorders

Pengfei Zhang

Rutgers University, New Brunswick, USA

Objective: Objective: Significant interests have been generated in the past years in applying machine learning techniques to headaches diagnosis. Here we propose that differentiating between primary headaches disorders using ICHD3 can be translated to a prime factorization problem, requiring only a working hand held calculator. We demonstrate our method with an example involving migraine without aura and tension type headaches.

Methods: We assigned each statement of headache characteristic in the ICHD3 criteria to a unique prime number. (Table 1). Notice that prime number operations is analogous to logical conjunction (AND) and logical disjunction (OR) in the following manner: 1) If the logic AND is required, we multiply the two numbers. 2) If the logic OR is required, we document both numbers in a list. For example: A statement requiring both photo and phono-phobia is models as 61*67, or 4087. A statement requiring nausea/vomiting or presence of both photo and phonophobia is modeled as a list of two number: [37, 4087]. Using this observation, each ICHD3 diagnosis criterion can be decomposed to logic statements, which then in turn can be used to generate a list of non-prime, i.e. composite, numbers (Table 2).

To use the algorithm, the user answers yes or no to each of the headache characteristics in Table 1; then the user

raises the corresponding prime numbers to 1st power if the answer is yes and 0th power if the answer is no, effectively excluding the latter from the calculation. These numbers are then multiplied together to form a number i. (As a patient's complete profile can be thought of as logical conjunctions.) If a number associated with a headache criterion divides i without remainder, then that criteria is diagnostic.
For example, a patient with with greater than 5 episodes (19) of pulsating (71), unilateral headaches (73) lasting 5 hours each (17) with nausea (37) but no photo/phonophobia (43*47) can be represented by a score of 19*17*37*43*47*71*73 = 125184848693. This number can be divided by 61942033 without remainder. Since 61942033 is a number in the migraine without aura list under Table 2, the diagnosis is therefore migraine without aura.
Results: We applied the above method to migraine without aura as well as infrequent, frequent, and chronic tension type headaches as a pilot study. For migraine without aura, infrequent, frequent, and chronic tension type headaches, 22 composite numbers represent each of the diagnostic criteria.
Conclusion: Applying headache diagnosis according to the ICHD3 criteria can be translated to a prime factorization problem. Our method represents a bridge between number theory and clinical medicine. Further applications of this methodology to analysis of co-diagnosis among primary headache disorders is also submitted as an abstract to the meeting.

Table 1

Statement Number	Description of Criteria
2	1 to 14 episodes per month
3	10 episodes but less than 1 per month
5	15 days per month
7	30 min to 7 days in duration
11	aggravated by physical activity
13	bilateral location
17	duration between 4 to 72 hours
19	greater than 5 episodes
23	hours to days or unremitting
29	mild to moderate pain
31	moderate to severe
37	nausea/vomiting
41	no nausea/vomiting
43	no phonophobia
47	no photophobia
53	not pulsating
59	not aggravated by activity
61	Phonophobic
67	Photophobic
71	pulsating
73	unilateral

Table 2

Encodings for Migraine without Aura:
4075291, 9333731, 9596653, 26304151, 27045113, 61942033, 289345661, 297496243, 450154441, 681362363, 1030998881, 1060041103, 1920203023, 2905542301, 2987388563, 6842083483, 21122233253, 31960965311, 32861274193, 75262918313, 212104587973, 2333150467703
Encodings for Infrequent Tension Type Headache:
13957671, 15256059, 25508847, 27881763, 28396641, 31038189, 56904351, 62197779, 63346353, 69239037, 115770921, 126540309, 739756563, 808571127, 823502589, 900107481, 1505021973, 1645024017, 3357356709, 3669668961, 43645637217, 47705696493
Encodings for Frequent Tension Type Headache:
9305114, 10170706, 17005898, 18587842, 18931094, 20692126, 37936234, 41465186, 42230902, 46159358, 77180614, 84360206, 493171042, 539047418, 549001726, 600071654, 1003347982, 1096682678, 2238237806, 2446445974, 29097091478, 31803797662
Encodings for Chronic Tension Type Headache:
76434865, 83545085, 139691305, 152685845, 155505415, 169971035, 311619065, 340606885, 346896695, 379166155, 633983615, 692958835, 4051047845, 4427889505, 4509657035, 4929160015, 8241786995, 9008464855, 18385524835, 20095806215, 239011822855, 261245480795

Disclosure of Interest: PZ: He has received honorarium from Alder Biopharmaceuticals, Board Vitals, and Fieve Clinical Research. He collaborates with Headache Science Incorporated without receiving financial support.

IHC23-PO-083

Improving the Efficiency of ICHD3

Pengfei Zhang and Roger Cheng

Rutgers University, New Brunswick, USA

Introduction: What is the minimum number of questions necessary to diagnose any primary headache disorder? The answer to this question may provide clinicians with a more efficient approach to history taking and a more concise form of ICHD3. In this project, we attempt to address this problem mathematically.
Methods: We define a headache phenotype as a collection of characteristics, variables that can take on a Boolean (true/false) value and correspond to the diagnostic criteria for each headache in ICHD3. There may be multiple phenotypes (each consisting of a slightly different set of characteristics) that fit a given diagnosis in the ICHD3. Defined this way, each diagnosis in the ICHD3 is a set of sets.
First, we extracted all characteristics used to describe the primary headaches up to two levels deep in the hierarchy in the ICHD3, though 1.3) Chronic migraine, 1.4) Complications of migraine, and 1.6) Episodic syndrome that may be associated with migraine were excluded because these require a primary diagnosis of migraine. Overlaps and duplications were removed, resulting in a set of unique characteristics which can be used in various combinations to describe all the theoretically possible headache phenotypes based on the presence/absence of criteria in ICHD3.
For each headache diagnosis, we can then determine its "necessary true" (NT) characteristics, which is the set of characteristics that all must be true to make that given diagnosis. We then attempted to optimize further by algorithmically identifying the smallest set of NT characteristics needed to differentiate between all primary headache diagnoses – that is, reducing these to the minimum number needed such that no two diagnoses share the exact same combination.
Since a patient's full headache phenotype contains multiple characteristics, it may satisfy the NT criteria for more than one diagnosis. To address this, we next found a list of "necessary false" (NF) characteristics by identifying the ones that logically contradict the NT characteristics for each given diagnosis. This set of NF characteristics was likewise minimized such that no two diagnoses share the exact same combination.
Now, any ICHD3 headache phenotype can be tested against the combined NT and NF criteria for each headache diagnosis – as long as both are satisfied, it is sufficient to make the diagnosis, with the remaining characteristics not contributing towards diagnosis. We verified this by translating all the possible conditions described by the

ICHD3 criteria to our phenotype encoding scheme and verifying equivalence between the two systems.
This is done with the prime number encoding method, which assigns each characteristic to an arbitrary prime to leverage the unique properties of primes to help with sorting (see https://hal.science/hal-03723482). The search algorithms for the above procedures were then implemented on the encoding through Haskell.
Results: There are 103 unique characteristics and 294 unique headache phenotypes that can fit a diagnosis in the ICHD3.
We were able to minimize the NT criteria to a set of 21 characteristics and NF to 6; there were 4 overlaps between the NT/NF groups, resulting in a final set of 23 unique characteristics. Though an even smaller NT set may be possible, we are limited by computational power.
One solution to our problem is presented in Table 1; the 23 necessary characteristics can be defined by using the following 15 questions to generate a headache phenotype: 1) duration, 2) frequency 3) sudden/rapid onset, 4) laterality, 5) clearly remembered onset, 6) sharp contour, 7) severity, 8) relationship to sleep/awakening 9) reversibility of aura, 10) stabbing quality, and whether the headache can be triggered by 11) sex, 12) compression, 13) traction, 14) cold, or 15) exercise.
For validation, we took the 294 headache phenotypes as defined by the full ICHD3 criteria and validated that they all still corresponded one-to-one with the original diagnosis when processed through our simplified descriptor set.
Conclusion: Fifteen questions are necessary and sufficient to diagnose the primary headache disorders in ICHD3. A smaller set may be possible, but we cannot prove its existence. Using this reduced set of questions, clinicians may be able to more efficiently arrive at ICHD3 diagnoses.

Table 1: Criteria sufficient to diagnose ICHD3 Primary Headache Disorders (bold represents necessary true, italics represents necessary false)

Paroxysmal Hemicrania	**17**	**523**	*23*	*97*	*547*		
Primary Sex Headache	**71**	*97*					
Hypnic Headache	**101**	*97*	*5*	*23*			
Cluster Headache	**11**	**523**	*5*	*23*	*97*	*547*	
Migraine with aura	**131**						
SUN	**5**	**523**	*7*	*23*	*199*	*97*	*547*
Chronic TTH	**139**	*5*					
Primary Stabbing	**491**	*7*	*97*	*23*	*547*		
Exercise Headache	**67**	*7*	*97*				
Thunderclap Headache	**223**	*547*					
Infrequent TTH	**199**	*5*	*97*				
Frequent TTH	**3**	*5*	*97*	*199*			
Compression Headache	**433**						
Traction Headache	**439**						
Cold Induced Headache	**443**						
Nummular Headache	**487**						
Primary cough headache	**503**	*23*	*97*				
Hemicrania Continua	**97**	**523**	*5*	*7*	*23*	*199*	*547*
New Daily Persistent Headache	**97**	**83**	*5*	*7*	*23*	*199*	*547*
Migraine without aura	**23**	*5*	*97*	*7*			

Key:
3 = 1 to 14 days per month, 5 = 1 to 600 seconds, 7 = 15 min up to 4 hours after waking, 11 = 15 to 180 minutes, 17 = 2 to 30 minutes, 23 = 4 to 72 hours, 67 = brought on by exercise, 71 = brought on by sex, 83 = clearly remembered onset, 97 = constant, 101 = developing only during sleep and causing wakening, 131 = fully reversible aura, 139 = greater than 15 days per month, 199 = less than 12 days per year, 223 = max within 1 minute, 433 = resolve within 1 hour after removal of compression, 439 = resolve within 1 hour after removal of traction, 443 = resolve within 30 min after removal of cold, 487 = sharply contoured, 491 = single or series of stabs, 503 = sudden, 523 = unilateral, 547 = up to 72 hours with mild headaches

Disclosure of Interest: PZ has received honorariums from Lundbeck Biopharmaceuticals, Board Vitals, and Fieve Clinical Research. PZ collaborates with Headache Science Incorporated without receiving financial support. PZ has ownership interest in Cymbeline LLC. RC received research funding from Biogen.

IHC23-PO-084

Visual aura in non-migraine headaches: a population study

Hye Jeong Lee[1], Seung Jae Kim[2], Sue Hyun Lee[3], Soomi Cho[2], Kyung Min Kim[2] and Min Kyung Chu[2]

[1]*Department of Neurology, Chung-Ang University Gwangmyeong Hospital, Gwangmyeong, Gyeonggi-do, Korea, Republic of*
[2]*Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of*
[3]*Department of Neurology, Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Gangwon-do, Korea, Republic of*

Background: Visual aura (VA) occurs mostly in migraine with aura (MA), but some case studies have reported aura in non-migraine headaches. Thus, information of VA in non-migraine headaches is scarce. Aim of this study is to investigate the prevalence and impact of VA in non-migraine headache and compare it with that of migraine headache.

Methods: This study was a nationwide population-based study. We used an internet-based headache diagnosis questionnaire to diagnose headache, and various modules to evaluate clinical features and comorbidities of participants with headache. We defined migraine headache as migraine and probable migraine (PM), whereas non-migraine headache was defined as a headache but not migraine or PM. VA was defined as a self-reporting VA rating scale (VARS) score $\geq$3.
Results: Of the 3,030 participants, 1,431 (47.2%) and 507 (16.7%) had non-migraine headache and migraine headache, respectively. VA prevalence was much lower in the non-migraine headache group than in the migraine headache group (14.5% [207/1431] vs. 26.0% [132/507], ***$P < 0.001$). In subjects with non-migraine headache, those with VA had a markedly higher number of headache days per 30 days (median [25th–75th percentiles]: 2.0 [1.0–5.0] vs. 2.0 [1.0–3.0], ***$P < 0.001$), and headache-related disability (6.0 [3.0–16.0] vs. 2.0 [0.0–7.0], ***$P < 0.001$) than those without VA. VA prevalence did not differ significantly according to age and sex.
Conclusion: Non-migraine headache with VA patients had more severe symptoms than those without VA. These findings may improve the understanding of VA and the management of individuals with non-migraine headache.
Disclosure of Interest: Min Kyung Chu was a site investigator for a multicenter trial sponsored by Biohaven Pharmaceuticals, Allergan Korea, and the Ildong Pharmaceutical Company. He has received lecture honoraria from Eli Lilly and Company, Handok-Teva, and Ildong Pharmaceutical Company over the past 24 months. He received grants from Yonsei University College of Medicine (6-2021-0229) and the Korea Health Industry Development Institute (KHIDI) (grant number: HV22C0106). The other authors have no conflicts of interest to declare. Seung Jae Kim, Hye Jeong Lee, Sue Hyun Lee, Soomi Cho, and Kyung Min Kim have no conflicts.

IHC23-PO-085

Proposed general diagnostic criteria for secondary headaches

Jes Olesen

Rigshospitalet, Copenhagen, Denmark

Background: Distinction between a pre-existing primary headache and a secondary headache at the onset of a disorder is important and has not been taken into account in the International Classification of headache disorders-3 (ICHD-3). The purpose of our study was to analyse the results of our previous studies of headache attributed to transient ischemic attack (TIA) and ischemic stroke and to propose a revision of the general diagnostic criteria for secondary headaches.
Materials and Methods: We analysed clinical characteristics of headache including change of 7 characteristics of pre-existing headache (change in intensity, duration, frequency, localization and side of headache, development of new accompanying symptoms, and therapeutic response) at onset of TIA (n = 120, mean age 56.1, 55% females) and ischemic stroke (n = 550, mean age 63.1, 56% females) compared to a control group (n = 192, mean age 58.7, 64% females).
Results: Headache of a new type occurred in 8,4% of ischemic stroke patients and 5% of TIA patients on the day of admission but did not occur at all in the control group. Pre-existing headache with a change of at least one of seven characteristics occurred significantly more often in stroke (5.4%) and TIA (7.5%) than in the control group (1%) ($p = 0.01$ and $p = 0.003$ respectively).
Conclusion: The presence of a new type of headache and a pre-existing headache with altered characteristics in close temporal relation to a disorder indicates causality. Based on these data we propose revised general diagnostic criteria for secondary headaches.
Disclosure of Interest: Holds stock in Cephagenix and H.Lundbeck

IHC23-PO-086

Matrix Representation of the Primary Headache Syndromes in the International Classification of Headache Disorders (ICHD3): a basis for automated diagnosis and analysis of criteria

Pengfei Zhang and Roger Cheng

Rutgers University, New Brunswick, USA

Background: Primary headache disorders are unique in that they are classified entirely by the presence/absence of clinical features as defined in ICHD3. We attempt to represent the ICHD3 mathematically in a binary matrix form and show that this representation allows for additional insights into headache classification.
Methods: Each primary headache diagnosis in the ICHD3 is defined by a list of *characteristics*, features/symptoms of that headache type. Combinations of characteristics form *phenotypes*. Multiple phenotypes may fit a given headache diagnosis as not all characteristics are required simultaneously. First, we translated all of the characteristics used to describe the primary headache diagnoses up to 2 levels deep in the ICHD3 into logical (true/false) statements. Duplicates were removed, but required "negative" characteristics (such as "not photophobic") were

represented independently from their inverse, resulting in 103 unique characteristics. Next, we extracted all the combinations of characteristics leading to valid ICHD3 diagnoses, creating 578 unique headache phenotypes. Using these, we generated a matrix as follows:
1. Each row of the matrix represents a headache phenotype.
2. Each column of the matrix represents a diagnostic characteristic.
3. If any phenotype (row) contains a characteristic (column), then that element of the matrix at that intersection is encoded as 1. Otherwise, it is encoded as 0.
From this matrix, we first generated a bipartite projection to identify hidden affiliations between characteristics and phenotypes. We then applied non-negative matrix factorization (NMF) and Markov clustering to search for non-obvious clusters of characteristics. Conceptually, ICHD3 itself defines diagnoses with clusters of characteristics, so other clusters identified by these analyses may represent alternative classifications.
Finally, if rows corresponding to "probable" diagnoses are removed, the matrix representation can be interpreted as the space of all headache phenotypes. We therefore applied row reduction to derive the basis vectors that span this space.
Results: Our matrix allows for automated diagnosis in the following fashion: each row in the ICHD3 matrix (i.e. a headache phenotype) is compared with a patient's headache phenotype. If all the 1's in that row (required characteristics) correspond with 1's in the patient phenotype (i.e. all the required characteristics are present), the patient's headache matches the ICHD3 diagnosis described by that phenotype. Note that the patient phenotype may have other 1's, but these would not contribute to the diagnosis.
The strongest associations between characteristics based on the bipartite projection are all within the migraine diagnoses. "Greater than 15 days per month" and "more than 3 months" are most commonly associated, followed by the pair "fully reversible" and "greater than 2 episodes."
NMF clustering for 10 to 25 topics roughly replicates the canonical ICHD3 diagnoses without any surprises. Markov clustering yields 77 clusters. The elements of each cluster are either phenotypes (30 clusters) or characteristics (47 clusters), but not both. Among the phenotype clusters, canonical ICHD3 diagnoses are clustered together as expected; however, "probable hemicrania continua" and "probable cluster headache" are also clustered together, as are "paroxysmal hemicranias" with "cluster headache," and "short lasting unilateral neuralgiform headaches" with "hemicrania continua." Most clusters of characteristics describe single ICHD3 diagnoses; however, the presence/absence of individual autonomic features also appear to form additional clusters not seen within ICHD3. Finally, row reduction of our matrix yields 55 basis vectors, implying that all headache diagnoses in the ICHD3 can be represented as linear combinations of 55 characteristics. These characteristics describe 14 features – duration, frequency, triggers, sharply contoured border, aura, laterality, clearly remembered onset, autonomic features, severity, phonophobia, pulsating quality, nausea, restlessness/aggravation with activity, and triptan responsiveness.
Conclusion: This work demonstrates the potential analytical value of a matrix representation of the ICHD3 criteria. Our result demonstrates that the most tightly associated characteristics are the ones for migraines. Although NMF clustering does not add much insight to headache classification, Markov clustering suggests the possibility for reclassification of the trigeminal autonomic cephalalgias. Finally, our project suggests that the defined headache disorders are fully defined by using only 55 of the 103 currently used characteristics, which may allow for simplification of ICHD3. In addition to potential use as an automated diagnostic tool, internal analysis of the headache classification system may be a novel research approach to provide insight into the system itself.
Disclosure of Interest: PZ: He has received honorarium from Alder Biopharmaceuticals, Board Vitals, and Fieve Clinical Research. He collaborates with Headache Science Incorporated without receiving financial support. He has ownership interest in Cymbeline LLC.

IHC23-PO-087

Accurate classification of episodic migraine with structural MRI using a novel fractal dimension analysis

Chi Ieong Lau[1,2,3,4], Yu-Te Wu[3], Wei-Hung Chen[1], Jiann-Horng Yeh[1,4], Pei-Hsin Lee[3], Vincent Walsh[2] and Chi-Wen Jao[3]

[1]Department of Neurology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan
[2]Applied Cognitive Neuroscience Group, Institute of Cognitive Neuroscience, London, United Kingdom
[3]Institute of Biophotonics, National Yang Ming Chiao Tung University, Taipei, Taiwan
[4]College of Medicine, Fu-Jen Catholic University, New Taipei City, Taiwan

Objective: Despite numerous studies using advanced imaging techniques to identify potential biomarkers, the diagnosis of migraine still relies on clinical criteria established by expert consensus. This study aimed to investigate whether using fractal dimension (FD) analysis of structural MRI is superior to traditional cortical thickness

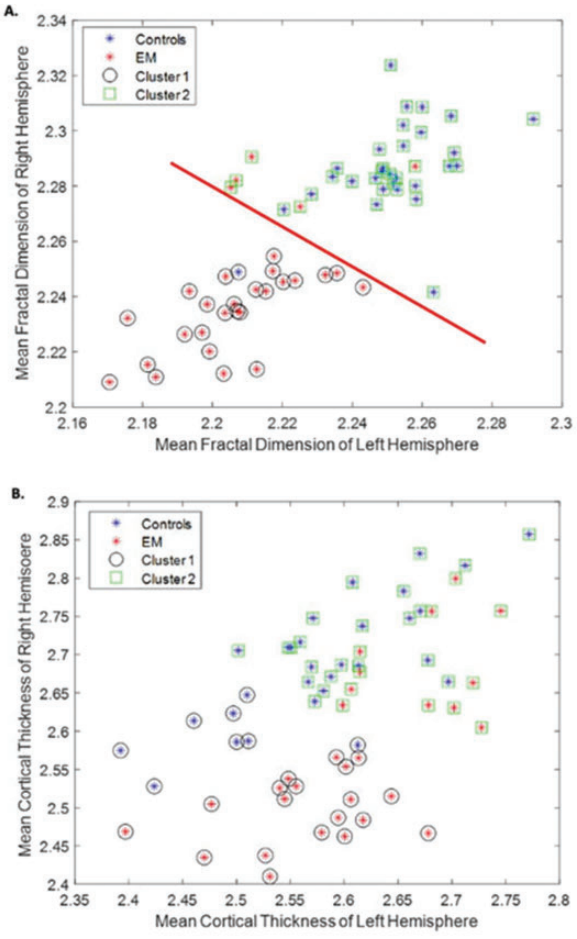
(CTh) analysis and whether it could serve as a biomarker for identifying migraine.

Methods: FD and CTh analyses were compared to assess morphological changes in cerebral lobes and 68 parcellated focal regions of the cerebral cortex in 30 patients (30% female, 45.5 ± 10.4 years) with episodic migraine (EM) (7.4 ± 4.6monthly headache day) and 30 healthy controls (HC) (50% female, 44.3 ± 11.3 years). We then used the results of both methods to establish unsupervised discriminants for the two groups.

Results: Our results showed that FD outperformed CTh in detecting morphological changes in migraine. Patients with EM had significantly decreased morphological complexity in their limbic, temporal, and occipital lobes compared to HC, as indicated by the FD measure. In contrast, CTh analysis revealed significantly decreased GM thickness in the frontal, limbic, and occipital lobes of patients with EM, but not in the temporal lobe. In addition,

FD analysis detected 11 focal regions with significantly decreased FD values in EM, including the left anterior cingulate (rostral and caudal), posterior cingulate, insula, entorhinal, temporal (superior and middle), and lateral occipital regions, as well as the right medal orbitofrontal, lateral orbitofrontal, and lingual regions. Meanwhile, EM had nine focal regions with significantly lower cortical GM thickness, comprising the left rostral anterior cingulate, isthmus cingulate, pars triangularis, rostral middle frontal, caudal middle frontal, medial orbitofrontal, and lingual regions, along with the right caudal anterior cingulate and posterior cingulate. Notably, only the FD method detected alteration of the insula between the groups. The FD values of each lobe for both EM and HC groups had denser data distribution with smaller standard deviations compared to CTh results, highlighting the effectiveness of FD in detecting morphological brain changes. Using the FD classifier, we achieved high accuracy of 91% in discriminating between EM and HC (Figure 1A), whereas the CTh classifier yielded a lower accuracy of 67% (Figure 1B).

Conclusion: Our findings suggest that FD analysis using structural MRI is a promising and superior method to differentiate EM from HC, and could potentially serve as an imaging biomarker for EM.



Disclosure of Interest: None Declared

IHC23-PO-088

The Clinical Profile in Patients with Idiopathic Intracranial Hypertension: A Retrospective Study in Taiwan

Hsiang-Ting Hsu[1,2], Yen-Feng Wang[1,2,3], Tsung-Wei Hou[4], Yi-Shiang Tzeng[1], Jong-Ling Fuh[1,2,3], Shih-Pin Chen[1,2,3,5,6], Wei-Ta Chen[1,2,3,7], Yi-Chung Lee[1,2,3], Hsiangkuo Yuan[8] and Shuu-Jiun Wang[1,2,3]

[1]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Department of Neurology, Neurological Institute, Taichung Veterans General Hospital, Taichung, Taiwan*
[5]*Division of Translational Research, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan*
[6]*Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[7]*Department of Neurology, Ministry of Health and Welfare Keelung Hospital, Keelung, Taiwan*
[8]*Jefferson Headache Center, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA*

Objective: Idiopathic intracranial hypertension (IIH) is characterized by signs and symptoms secondary to increased intracranial pressure (IICP). The clinical profile of IIH in Asians remained to be characterized as only limited data were available. There are discrepancies in the requirement of cerebrospinal fluid (CSF) open pressure (OP) for the diagnosis of IIH in different criteria, i.e. >250 mmCSF in the third edition of International Classification of Headache Disorders (ICHD) (ICHD-3) and the criteria by Friedman et al., and >200 mmCSF in the non-obese and >250 mmCSF in the obese in the second edition of ICHD (ICHD-2). We aimed to clarify the clinical profile of IIH patients in Asia and to identify differences in clinical and radiologic features between patients with OP > 250 mmCSF and ≤250 mmCSF.

Methods: This was a retrospective study involving consecutive patients hospitalized in two tertiary medical centers, i.e., Taipei Veterans General Hospital and Taichung Veterans General Hospital, with a final diagnosis of IIH, benign intracranial hypertension, pseudotumor cerebri, or intracranial hypertension. Patients with secondary causes for IICP or with OP <200 mmCSF were excluded. Clinical profiles were retrieved by chart review, including headache features, ophthalmologic examinations, and four prespecified MRI features according to the criteria by Friedman et al. Comparisons were made between patients with OP > 250mmCSF and ≤250 mmCSF.

Results: A total of 101 patients (70 F/31M, mean age 33.4 ± 12.3 years, mean body-mass index [BMI] 29.15 ± 6.18 kg/m^2) were identified. In addition to headache (90.1%), the most commonly reported symptoms were visual blurring (49.5%), transient visual obscuration (24.8%), pulsatile tinnitus (22.8%), horizontal diplopia (21.8%) and neck stiffness (25.7%). The mean OP was 282.7 ± 74.9 mmCSF, and 56 patients (55.4%) had papilledema. Patients with OP > 250 mmCSF (n = 61) (60.4%) were more likely to have papilledema (63.9% vs. 42.5%, p = 0.026), transient visual obscuration (32.8% vs. 12.5%, p = 0.007) and horizontal diplopia (29.5% vs. 10.0%,

	All patients (n = 101)	OP > 250 mmCSF (n = 61)	OP ≤ 250 mmCSF (n = 40)	P value
Age (yrs)	33.4 ± 12.3	32.3 ± 11.4	35.1 ± 13.4	0.288
Gender	M = 31; F = 70	M = 17; F = 44	M = 14; F = 26	0.447
Body-mass index (kg/m^2)	29.15 ± 6.18	28.91 ± 5.88	29.55 ± 6.74	0.865
Opening pressure (mmCSF)	282.7 ± 74.9	325.9 ± 68.9	220.0 ± 14.3	***<0.001***
Papilledema	55.4%	63.9%	42.5%	***0.026***
Headache feature	90.1%	86.9%	95.0%	0.104
Migrainous	34.7%	32.8%	37.5%	
Tension-type	40.6%	44.3%	35.0%	
Thunderclap	5.0%	1.6%	10.0%	
Visual symptoms				
Visual blurring	49.5%	57.4%	37.5%	0.059
Transient visual obscuration	24.8%	32.8%	12.5%	***0.007***
Horizontal diplopia	21.8%	29.5%	10.0%	***0.008***
Average of MRI signs	2.6 ± 1.2	2.8 ± 1.1	2.2 ± 1.3	***0.023***
Retinal nerve fiber layer (μm)	144.8 ± 80.9	175.1 ± 97.9	106.4 ± 16.9	***0.011***
Surgery	8.9%	14.8%	0.0%	***0.011***

$p = 0.008$) when compared with those with OP $\leq$ 250 mm CSF. These patients had more MRI signs (2.8 ± 1.1 vs. 2.2 ± 1.3, $p = 0.023$) and thicker retinal nerve fiber layer ($175.1 \pm 97.9\mu m$ vs. $106.4 \pm 16.9\mu m$, $p = 0.011$), as well as more likely to have surgical intervention (14.8% vs. 0.0%, $p = 0.011$). However, the demographics and most of the other clinical characteristics were similar.

Conclusions: IIH patients in the Asian population are characterized by a lower BMI, lower opening pressure, and less papilledema and visual problems. Patients with OP > 250 mmCSF and OP $\leq$ 250 mmCSF shared similar clinical features. However, patients with OP > 250 mmCSF are more likely to have ophthalmologic abnormalities and surgical intervention.

Headache disorders in children and adolescents

IHC23-PO-089

Tension-type headache and migraine in adolescents with internet gaming disorder

Sergey Tereshchenko[1], Margarita Shubina[1], Nina Gorbacheva[1], Marina Smolnikova[1] and Ivan Novitckii[1,2]

[1]*Scientific Research Institute for Medical Problems of the North, Krasnoyarsk, Russian Federation*
[2]*Dmitri Hvorostovsky Siberian State Academy of Arts, Krasnoyarsk, Russian Federation*

Somatic symptoms prevalence in Internet-addicted adolescents are not studied well. We aimed to investigate tension-type headache (TTH) and migraine comorbidity with Internet gaming disorder (IGD) in Central Siberia urban adolescents.

Methods: 282 urban Siberian (Krasnoyarsk) adolescents (age 14.52 ± 1.52; boys/girl ratio 46.4%/53.6%) were tested with "Game Addiction Scale for Adolescents" (Lemmens J.S. et al., 2009) and primary headaches (TTH (frequent episodic TTH+chronic TTH) and migraine). The chi-square test was used.

Results: No associations IGD with TTH (15.6% (38/244) in "No IGD" group vs. 10.5% (4/38) in "IGD presence" group, $p > 0.05$) and migraine (16.8% (41/244) in "No IGD" group vs. 23.7% (9/38) in "IGD presence" group, $p > 0.05$) were found.

Conclusions: No association IGD with primary headaches was found in our sample. Further investigation is needed to assess the association of primary headaches with other types of Internet addiction in adolescents, such as problematic social media use.

IHC23-PO-090

Children under 6 years with acute headache in Pediatric Emergency Departments. A 2-years retrospective exploratory multicenter Italian study

Gabriele Monte[1], Umberto Raucci[2], Pasquale Parisi[3], Valentina Ferro[2], Erika Margani[3], Nicola Vanacore[4], Vincenzo Raieli[5], Claudia Bondone[6], Lucia Calistri[7], Agnese Suppiej[8], Antonella Palmieri[9], Duccio Maria Cordelli[10], Salvatore Savasta[11], Amanda Papa[12], Alberto Verrotti[13], Alessandro Orsini[14], Renato D"Alonzo[15], Piero Pavone[16], Raffaele Falsaperla[17], Mario Velardita[18], Raffaella Nacca[2], Laura Papetti[1], Roberta Rossi[6], Daniela Gioè[7], Cristina Malaventura[8], Flavia Drago[19], Cristina Morreale[9], Lucia Rossi[10], Thomas Foiadelli[11], Sonia Monticone[20], Chiara Mazzocchetti[21], Alice Bonuccelli[14], Filippo Greco[16], Silvia Marino[17], Antonella Versace[6], Stefano Masi[7], Giovanni Di Nardo[3], Antonino Reale[2], Alberto Villani[2] and Massimiliano Valeriani[1]

[1]*Developmental Neurology Unit, Bambino Gesù Children's Hospital, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Rome, Italy*
[2]*Department of Emergency, Acceptance and General Pediatrics, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*
[3]*Chair of Pediatrics, NESMOS Department, Faculty of Medicine and Psychology, Sapienza University, c/o Sant"Andrea Hospital, Rome, Italy*
[4]*National Centre for Epidemiology, Surveillance, and Health Promotion, National Institute of Health, Rome, Italy*
[5]*Child Neuropsychiatry Unit – ISMEP- ARNAS CIVICO, Palermo, Italy*
[6]*AOU Città della Salute e della Scienza – Regina Margherita Children's Hospital – Department of Pediatric Emergency, Turin, Italy*
[7]*Pediatric Emergency Unit, Anna Meyer's Children Hospital, Florence, Italy*
[8]*Department of Medical Sciences, Pediatric Section, University of Ferrara, Ferrara, Italy*
[9]*Pediatric Emergency Department, Giannina Gaslini Children's Hospital, IRCCS, Genova, Italy*
[10]*IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy*
[11]*Clinica Pediatrica, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*
[12]*S.C.D.O. Neuropsichiatria Infantile AOU Maggiore della Carità, Novara, Italy*
[13]*Department of Pediatrics, University of Perugia, Perugia, Italy*
[14]*Paediatric Neurology, Paediatric Department, Pisa University Hospital, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy*

[15]*Pediatric and Neonatological Unit, Maternal and Child Department, Nuovo Ospedale San Giovanni, Foligno, Italy*
[16]*Section of Pediatrics and Child Neuropsychiatry, Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy*
[17]*Unit of Pediatrics and Pediatric Emergency, AOU "Policlinico", PO "San Marco", Catania, Italy*
[18]*Department of Pediatrics, Gravina Hospital, Caltagirone, Italy*
[19]*Child Neuropsychiatry Unit- Dept. Pro.Mi.Se. "G. D"Alessandro" University of Palermo, Palermo, Italy*
[20]*Division of Paediatrics, Department of Health Sciences, University of Piemonte Orientale, Novara, Italy*
[21]*Department of Pediatrics, University of L"Aquila, L"Aquila, Italy*

Objective: Headache is common in children and represents one of the main neurological causes of admission in the pediatric Emergency Departments (ED). Age under 6 years (i.e. preschool-age) makes diagnosis challenging and is generally considered a "red flag" that requires more in-depth investigations to exclude potentially urgent intracranial conditions (PUIC), as brain tumors, cerebral vascular diseases, intracranial hypertension, central nervous system inflammatory disorders and malformation. The aim of this study was to investigate clinical characteristics of headache in preschool age in the emergency setting in order to find features associated with secondary "dangerous" headaches that should require brain CT. We also evaluated the etiology of headache to estimate the prevalence of life threatening conditions.
Methods: We performed a multicenter exploratory retrospective study in 14 Italian pediatric hospitals from January 2017 to December 2018. Patients were selected from electronic databases using the keyword "headache" in the fields "history", "clinical examination" and "diagnosis". Preschoolers with new-onset non-traumatic headache admitted to ED were included and were divided into two groups: hospitalized and discharged. These two groups were compared to identify variables associated with a higher risk of hospitalization. Hospitalized patients were further divided in two subgroups – patients with and without PUIC- and were compared to detect predictive variables associated with a higher risk of PUIC. A logistic regression analysis model was performed.
Results: We included 1455 preschoolers with acute headache. Ninety-five patients (6.5%) were hospitalized. Ataxia, ocular motility disorders, torticollis, nocturnal awakening, the presence of neurological signs or symptoms and vomiting were significantly associated to hospitalization, having an odds ratio of 5.46, 5.76, 5.98, 2.37, 5.22 and 1.80 respectively. Based on headache etiology, the 95 hospitalized children were divided in two groups – patients with PUIC and without PUIC – and were compared: presence of neurological symptoms and signs, ataxia, cranial nerves paralysis, nocturnal awakening, papilledema, comorbidities and vomiting were significantly associated with PUIC (Figure 1). Nevertheless, on multivariate logistic regression analysis, we found that only ataxia and vomiting were predictive of PUIC. Only 34 patients had PUIC (2.3%).

Characteristics of hospitalized patients Total =95	Not-potentially urgent intracranial conditions n=61	Potentially urgent intracranial conditions n= 34	*P value*
Age (months), median (IQR)	54 (40-64)	55 (46-64)	0.57
Sex, n (%) · Male · Female	 35 (57.4) 26 (42.6)	 25 (73.5) 9 (26.5)	0.12
Time of onset (days), median (IQR)	2 (1-12)	4.5 (2-20)	0.15
Comorbidities, n(%)	19 (31.2)	4 (11.8)	**0.028**
History of headache, n(%)	19 (31.2)	9 (26.5)	0.32
Fever, n(%)	15 (24.6)	8 (23.6)	0.90
Papilledema, n(%)	2 (3.3)	5 (14.7)	**0.05**
Vomiting, n(%)	25 (41.0)	25 (73.6)	**0.002**
Nystagmus, n(%)	2 (3.3)	3 (8.8)	0.24
Ataxia, n(%)	1 (1.6)	10 (29.4)	**<0.001**
Disturbance of ocular motility, n(%)	4 (6.6)	4 (11.8)	0.38
Torticollis, n(%)	4 (6.6)	0	0.13
Disturbance of consciousness, n(%)	16 (26.2)	12 (35.3)	0.35
Paralysis of cranial nerves, n(%)	1 (1.6)	4 (11.8)	**0.05**
Dizziness, n(%)	5 (8.2)	6 (17.7)	0.15
Nocturnal awakening, n(%)	14 (23.0)	15 (44.1)	**0.032**
Occipital localization (headache), n(%)	7 (11.5)	4 (11.8)	0.97
Asthenia, n(%)	10 (16.4)	7 (20.5)	0.60
Presence of neurological symptoms or/and signs, n(%)	21 (34.4)	22 (64.7)	**0.004**

Conclusion: Our study identified clinical features that should be careful evaluated in the ED in order to obtain a prompt diagnosis and treatment of PUIC. If they are present, they could represent an indication to perform brain CT, considering the limitation in the detection of posterior fossa alteration, and the patient must be hospitalized. We confirmed that, even under six years of age, benign conditions are the most frequent causes of headache in the ED. The prevalence of PUIC was low, which may suggest that age under six should not be considered an important risk factor for malignant causes as previously thought, but this needs to be confirmed in future studies.
Disclosure of Interest: None Declared

IHC23-PO-091

Prevalence and impact of primary headaches among students aged 8 to 12 in Sub-Saharan Africa

Annick Melanie Magnerou[1,2], Jacques Doumbe[1], Paule Rose Delima Tchombe[1] and Callixte Kuate-Tegueu[2]

[1]*University of Douala, Douala, Cameroon*
[2]*Laquintinie Hospital, Douala, Cameroon*

Introduction: Primary headache is the most common neurological disease and carries a considerable burden. Yet in Africa, epidemiological data in children are scarce. The aim of this study was to investigate the prevalence and impact of primary headache among students aged 8 to 12 years-old in the city of Douala (Cameroon).

Methods: From January to May 2022, we conducted a cross-sectional analytical study in 52 primary schools randomly selected from 5 districts in the city of Douala. The study population consisted of primary school pupils regularly enrolled in level III classes (CM1, CM2, Class 5, Class 6) aged between 8 and 12 years. The diagnosis of primary headache was made according to the ICHD-3 criteria and the paediatric version of the HARDSHIP questionnaire used for recruitment. Data were analysed using SPSS version 23.0 software.
Results: A total of 2056 students participated of which 55.9% were female, with a median age of 11 years. The prevalence of headache in the last 12 months was 85.7%, migraine 26.1% and tension-type headache (TTH) 15.1%. About the impact of primary headaches, 32.8% of migraine sufferers were absent from school compared to 22.5% of students with TTH ($p = 0.03$); 57.6% of migraine sufferers had a break in their activities compared to 47.3% of students with TTH ($p < 0.01$). Students with headaches were at higher risk of poor quality of life than those without headaches.
Conclusion: Primary headaches are common among 8 to 12-year-old students in the city of Douala. They are responsible for a considerable impact on the child who suffers from them and his family, particularly for migraines.
Keywords: primary headache, students, prevalence, burden or impact, migraine
Disclosure of Interest: None Declared

IHC23-PO-092

Prevalence and burden of migraine headache in children in a Sub-Saharan African country

Callixte Kuate-Tegueu[1,2], Mélanie-Annick Magnerou[1,3], Jacques Doumbe[3], Paule-Rose Delima-Tchombe[3], Paul Mbonda[2], Daniel Massi-Gams[4], Yannick Fogang-Fogoum[5] and Emmanuel Essomba[3,6]

[1]*Neurology Department, Laquintinie Hospital Douala, Douala, Cameroon*
[2]*Faculty Of Medicine and Biomedical Sciences, The University of Yaoundé 1, Yaoundé, Cameroon*
[3]*Faculty of Medicine and Pharmaceutical Sciences, The University of Douala, Douala, Cameroon*
[4]*Faculty of Health Sciences, The University of Buea, Buea, Cameroon*
[5]*Faculty of Medicine and Pharmaceutical Sciences, The University of Douala, Dschang, Cameroon*
[6]*Laquintinie Hospital Douala, Douala, Cameroon*

Objective: The aim of this study was to investigate the prevalence and impact of migraine headache among students aged 8 to 12 years-old in the city of Douala, Cameroon.
Methods: From January to May 2022, we conducted a cross-sectional analytical study in 52 primary schools randomly selected from 5 districts in the city of Douala. The study population consisted of primary school pupils regularly enrolled in level III classes (CM1, CM2, Class 5, Class 6) aged between 8 and 12 years. The diagnosis of migraine was made according to the ICHD-3 criteria and the paediatric version of the HARDSHIP questionnaire used for recruitment. Data were analysed using SPSS version 23.0 software.
Results: A total of 2056 students participated of which 55.9% were female, with a median age of 11 years. The prevalence of headache in the last 12 months was 85.7%, and that of migraine 26.1%. Concerning the impact, 32.8% of migraine sufferers were absent from school; 57.6% had a break in their activities and 22% never participate on leisure activities due to the headache. 33.4% of children with migraine had poor quality of life compared to those without headache (15%) ($p < 0.001$).
Conclusion: Primary headaches, especially migraine are common among 8 to 12-year-old students in the city of Douala, Cameroon. They are responsible for a considerable impact on the affected children as well as their family.
Keywords: primary headache, migraine, children, prevalence, burden or impact
Disclosure of Interest: None Declared

IHC23-PO-093

Clinical profile of headache among children attending emergency department Atalexandria University Children's Hospital

Marwa Abd Elmaksoud

Pediatric Neurology, Department of Pediatrics, Faculty of Medicine, Alexnadria University, Alexandria, Egypt

Introduction: Headache is a pain located in the head above the orbitomeatal line and/or nuchal ridge. It is the most common somatic complaint in children and adolescents both in clinical and epidemiological databases. Recent Findings suggest that headache prevalence in children and adolescents has been increasing in the last recent years.
Objectives: To study the clinical profile of headaches, and to estimate their burden among children attending the emergency department (ED) of Alexandria University Children's Hospital.
Methods: A Descriptive observational study conducted at the ED at Alexandria University Children's Hospital included all children presented with headache as their primary complaint over six months duration, through

a structured sheet that was designed, through literature review, and implemented to the studied children.

Results: During the study period, 22662 visits were made to the pediatric emergency department (PED); the chief complaint was a headache in 164 patients (0.72%). But only 46 patients (1.17%) were admitted either to the ward PICU or died at PED meaning that 28.01% of admitted patients were complaining mainly of headaches. A family history of headaches is usually present in children with a primary headache that is usually in first-degree relatives. Clinical characteristics of headaches, and clinical examination of studied children, including fundus examination, were statistically significant between children with primary and secondary headaches. While ENT assessment is not significantly related to headache etiology. Unnecessary laboratory investigations, neuroimaging, and other investigations mainly EEG were done for many children. The most common initial diagnosis of the children before coming to PED was epilepsy.

Conclusion: We concluded that headache among children is not an uncommon cause of visits to PED and hospital admissions. After discharge from the PED, most studied children were followed-up at the outpatient clinics. Among studied children primary headaches comprised the most frequent cause of headaches, secondary serious headaches represented the most frequent cause of secondary headaches, while non-life-threatening causes of secondary headaches represented the least frequent cause of headaches.

Disclosure of Interest: None Declared

IHC23-PO-094

Diet and pediatric migraine

Mansoureh Togha[1,2] and Soodeh Razeghi Jahromi[3,1]

[1]*Department of Headache, Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of*
[2]*3. Department of Headache, Neurology Ward, Sina University Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of*
[3]*Department of Clinical Nutrition and Dietetics, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran, Islamic Republic of*

Introduction: The importance of diet as a non-pharmacological approach in pediatric headaches cannot be underestimated. Many patients and care-givers have interest in this topic, but, evidence limitation makes it difficult to have strong recommendation about diet to pediatric migraineurs. In this review, we summarized new evidence, regarding dietary interventions for the prevention and treatment of pediatric migraine. We divided this review into two parts. In first part we discuss recent cross-sectional studies exploring the diet Patterns. In second part we go through clinical trials based on dietary interventions.

Method: To explore the efficacy and safety of different diets for severe migraine, we conducted a comprehensive search of PubMed/Medline, ISI Web of Science, and Scopus databases, from inception to 30 January 2023.

Results: In an observational study from Ankara University, Turkey on children in grades four to twelve, 52% of children with migraine, compared to 28% of their non-migraineurs copartners, did not have breakfast regularly. Comorbid eating disorders that are more common in children with migraine, might also make regular eating plan challenging. According to recent evidences "trigger foods" not play a big role as it was believed previously. In a prospective study which omit biases due to retrospective origin of the study like recall bias, especially tyramine-containing foods appeared to be not associated with headache. One reason that people believe that trigger foods cause headaches might be that the body is more sensitive to different stimuli prior to a migraine. Functional MRI revealed that 4 h prior to a migraine attack, the signaling between the hypothalamus and the hub areas for pain sensation is changing. Our team performed a cross-sectional study in Iran on 290 children aged from 7 to 14 years old. According to our observations after matching for age, sex, weight, and other confounders, greater amount of low-fat dairy intake may attenuate the odds of having migraine attacks in pediatrics and adolescents who might be at risk of headache (Odds of 0.48 in the second tertile and 0.46 in the third tertile of low fat dairy consumption respectively). In another case-control study performed on childeren and adolescents by our team, the findings confirmed a protective role of dietary vegetables and fruits against the risk of pediatric migraine, which can be attributed to the probable effect of dietary fiber. After controlling for all confounders, the odds of migraine was 50% lower in second tertile of vegetable consumption and 70% lower in the third tertile of fruits consumption compared to first tertile.

Our data about dietary interventions for controlling migraine headache in children is very limited. A multicenter 12 month-long clinical trial on obese adolescents with migraine (14–18 years old) assessed the effect of a weight reduction program consists of physical exercise, dietary education, and behavioral therapy on headache outcomes. They reported that weight reduction significantly reduced headache intensity, frequency, PedMIDAS, and use of abortive medication, were decreased after 6 and 12 month. A majority of clinical trials on pediatric migraineurs were conducted on elimination diet eliminated Aspartame, Monosodium Glutamate, and Nitrites, Alcohol, chocolate and caffeine. The reports are highly controversial. There

are some studies case-reports and small clinical trials with controversial results on ketogenic diet (KD) for treating pediatric migraine. KD is difficult to follow and have different side effects. Dietary interventions with less side effects and greater compatibility like Low-fat diet, Low-Glycemic-Index diet, and Dietary-Approach-to-Stop-Hypertension (DASH) diet that had promising results in adults need to be studied in children and adolescents with migraine headache.

Conclusion: A universal pediatric migraine diet with elimination of all potential trigger food is generally not advised in practice. Weight control and a well-balanced regular meal plan with ample amount of high fiber foods including plenty of fruits and vegetables, as well as low-fat dairy products is encouraged, with avoidance of skipped meals especially breakfast.

IHC23-PO-095

Do neuropsychiatric comorbidities influence the outcome of Greater Occipital Nerve Injections for headache prevention in paediatric patients? Preliminary results from a UK experience

Ilaria Frattale[1], Francesca Puledda[2] and Prab Prabhakar[3]

[1]*Child Neurology and Psychiatry Unit, Department of Neurosciences, Policlinico Tor Vergata Foundation Hospital, Rome, Italy*
[2]*Wolfson Centre for age-related diseases, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom*
[3]*Department of Paediatric Neurology Great Ormond Street Hospital for Children NHS Foundation, London, United Kingdom*

Objective: Primary headaches are the most common cause of pain in childhood and adolescence, and present major repercussions on the quality of life and daily activities of patients. Migraine prevalence in childhood is around 10%, with comorbidities such as major depressive disorders and anxiety ranging from 10 to 20%. Greater occipital nerve injections (GONI) are an effective, safe and well tolerated treatment, which can be used for primary headache prevention both in adults and in children. We aim to evaluate if the presence of neuropsychiatric comorbidities influences GONI response.

Methods: We retrospectively analysed the clinical history and therapeutic response of all paediatric patients with a primary headache diagnosis who underwent GONIs from June to December 2022 at the Headache Centre of Great Ormond Street Hospital in London, UK. GONI were performed unilaterally using a mixture of 40 mg methylprednisolone and 30 mg 1% lidocaine. We analysed demographic characteristics including gender, age at first injection, headache diagnosis, psychiatric diagnosis, considering separately mood disorders (anxiety/depression) and neurodevelopment comorbidities (autism, ADHD, learning disabilities). Our primary outcome was response to treatment, considered as a >50% reduction in monthly headache days following twelve weeks from the GONI.

Results: A total of n = 85 patients were included, of whom 80% were female. Mean age at first injection was 14 years ± 1,6. The most frequent headache diagnosis was migraine without aura (n = 44), followed by migraine with aura (n = 25), NDPH (n = 8), TTH (n = 1) and cluster headache (n = 1). The number of past GONIs administrations was 5 ± 2.5for each patient. Forty patients had previously received a neuropsychiatric diagnosis, n = 25 had mood disorders and n = 15 neurodevelopment comorbidities, of which the most frequent were learning disabilities (47%), ADHD (40%), autism (20%) and eating disorders (20%). For our primary outcome, n = 57 (67%) patients showed >50% reduction in monthly headache days.

There was no significant difference in GONI response in patients with mood comorbidity respect to those without ($\chi 2 = 1.007$). We also found no difference in response in patients with neurodevelopment comorbidity ($\chi 2 = 0.884$).

Conclusion: In our sample the presence of psychiatric comorbidities (e.g. mood disorders, anxiety, neurodevelopmental conditions) did not influence the effect of greater occipital nerve injections for primary headache prevention. GONIs are helpful in adolescents with and without neuropsychiatric comorbidities.

Demographic characteristics of patients received GONI

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	N	%	Migraine without aura (n, %)	Migraine with aura (n, %)	NDPH (n, %)	TTH (n, %)	HC (n, %)	Total Chronic Headache
Female/male	68/17	80/20						
Years of headache at 1° injection	14							
Past Medication	2.5							
Type of Headache Diagnosis	85	100%	44 (52%)	25 (29%)	8 (9%)	1 (1%)	1 (1%)	77 (90%)
Patients with psychiatric comorbidities	40	47%	21 (53%)	12 (30%)	4 (10%)	1 (3%)	0 (0%)	
Response to GONIs	57	67%	33 (58%)	15 (26%)	4 (7%)	1 (2%)	1 (2%)	

IHC23-PO-096

Pediatric Migraine in Egypt: Clinical characteristics and challenges

Mona Nada

Cairo University, Cairo, Egypt

Background: Approximately 3 to 5% of young children and 18% of adolescents experiences migraine attacks. Prophylactic treatments present challenge to physicians to convince parents to start these drugs.
Aim: To study the clinical features of migraine in children and assess challenges in their management.
Methods: A cross sectional study was performed over 2 years in a tertiary hospital and private center in Egypt. Diagnosis of migraine in pediatric age group with aura (MA) or without aura (MO) was based on the ICHD-III criteria. Patients were classified into 3 groups according to educational status: Group I: preschool age (Up to 6 years), Group II: primary school (7 to 12) and Group III: Middle and secondary School (13 to 18 years).
Results: Migraine was diagnosed in 80 children (16.8% MA, 83.2% MO). The majority of diagnoses were made in group II and III with almost 42% in group III. Females were more common in Group II and III while males were more in preschool age. Monthly migraine days were higher in group III. Headache severity, using visual analog scale, was more in group I followed by group III. Photophobia was present in 86.4%, followed by nausea/vomiting, phonophobia, dizziness and osmophobia. Parents refused or delayed prophylactic treatment in 45% of patients especially in group I.
Conclusion: Characteristics of pediatric migraine differ in different age groups. Management carries a lot of challenges related to diagnostic inertia, impact on quality of life and challenges in prophylactic medications.
Disclosure of Interest: None Declared

IHC23-PO-097

Disordered eating attitudes, psychological symptoms and migraine severity: which relationship?

Samuela Tarantino[1], Martina Proietti Checchi[1], Laura Papetti[1], Fabiana Ursitti[1], Gabriele Monte[1], Giorgia Sforza[1], Michela Ada Noris Ferilli[1] and Massiamiliano Valeriani[1,2]

[1]*Developmental Neurology Unit, Bambino Gesù Children's Hospital, Rome, Italy*
[2]*Center for Sensory-Motor Interaction, Aalborg University, Aalborg, Denmark*

Objective: Data on disordered eating attitudes in pediatric migraine are, so far, sparse. We aimed to investigate: 1) the prevalence of disordered eating behaviors and their association with the severity of migraine and body weigh; 2) the possible mediating role of anxiety and/or depression in the association between disordered eating attitude and frequency of migraine attacks in children.
Methods: We included 103 adolescent girls with migraine (mean age 14.2 ± 1.6 years). The frequency of migraine was divided in: 1) high frequency (from weekly to daily episodes) and 2) low frequency ($\leq$4 episodes per month). According to their Body Mass Index, patients were divided in "underweight" ($<$5th percentile), "normal weight" (from $\geq$5 to $<$85 percentile), "overweight" (from $\geq$85 to $<$95) and "obese" ($\geq$95). Given the low number of obese patients, overweight and obese groups were considered together in the "Overweight" group. Due to their low frequencies, "underweight" patients were not included in our analysis. The Italian Self-Administrated Psychiatric Scales for Youths and Adolescents battery (SAFA) was used to investigate eating disorder risk (SAFA-P), anxiety (SAFA-A) and depression (SAFA-D).
Results: In our sample, 20.4% of patients had scores above the normal range in SAFA-P Total scale. We found bulimic and anorexic attitudes respectively in 17.5% and 22.3% of patients. Perfectionism was high in 46.6% of patients. We found higher bulimic symptoms in patients with high frequency of attacks ($p = 0.040$). Overweight patients showed higher levels of disordered eating attitudes as compared with normal weight patients (SAFA-P Tot: $p = 0.011$). We found a mediating role between bulimic and anorexic attitudes and high frequency for school anxiety (respectively, $p = 0.040$ and $p = 0.045$).
Conclusions: Our data suggest an association between bulimic attitudes and the frequency of migraine. We suppose that, in our sample, school anxiety may lead to disordered eating attitudes which may influence the frequency of migraine.
Disclosure of Interest: None Declared

IHC23-PO-098

Coping strategies to stressful events in adolescents with migraine

Martina Proietti Checchi[1], Samuela Tarantino[1], Laura Papetti[1], Fabiana Ursitti[1], Gabriele Monte[1], Giorgia Sforza[1], Michela Ada Noris Ferilli[1], Romina Moavero[1,2], Alessandra Voci[1] and Massimiliano Valeriani[1,3]

[1]*Developmental Neurology, Bambino Gesù Children Hospital, IRCCS, Rome, Italy*

[2]Child Neurology and Psychiatry Unit, Tor Vergata University of Rome, Roma, Italy
[3]Center for Sensory-Motor Interaction, Aalborg University, Aalborg, Denmark

Objective: We aimed to explore: 1) coping responses to stressful events and their possible association with migraine severity (frequency of attacks and pain intensity) and the use of prophylactic treatments in adolescents with migraine; 2) the association between coping strategies, anxiety and depression levels.
Methods: We included 81 adolescents (m.a. 13.8 ± 1.6 years; 18 M and 63 F). They were divided into: (1) high frequency (weekly to daily episodes) and low frequency ($\leq$4 episodes per month); (2) mild and severe pain; (3) need for prophylactic treatment or not. To evaluate patients'' anxiety, depression and coping strategies we used respectively SAFA-A, SAFA-D and CRI-Y questionnaires.
Results: In our sample, high frequency of attacks was associated with ''Logical Analysis'' ($p = 0.012$) and ''Positive Reappraisal'' ($p = 0.002$) strategies of coping. Patients with severe intensity of pain showed levels above the normal range in ''Problem Solving'' ($p = 0.050$) and ''Cognitive Avoidance'' ($p = 0.034$) subscales. No significant association was found between the use of a prophylactic treatment and coping responses. We found higher symptoms of ''Total anxiety'' ($p = 0.025$), ''School anxiety'' ($p = 0.024$) and ''Feeling of hopeless'' ($p = 0.029$) in patients with the tendency to use a ''Positive Reappraisal'' strategy of coping; on the other hand, higher symptoms of depression were associated with ''Cognitive Avoidance'' ($p = 0.033$) style.
Conclusion: Adolescents with migraine tend to use a coping style characterized by an approach to the problem. In particular, cognitive coping strategies may be more prevalent in high frequency patients, while behavioral coping strategies could be more commonly used in severe intensity patients.
Disclosure of Interest: None Declared

IHC23-PO-099

Characteristics of postual orthostatic tachycardia syndrome (POTS) and headache as a symptom of POTS in children, before and after the COVID-19 pandemic

Yuko Omata, Yoshiko Takahashi and Tomoko Nakazawa

Seikeikai Chiba Medical Center, Chiba City, Japan

Background: It is reported that approximately 90% of patients with POTS have headache. POTS can be caused by viral infections, and recent reports suggest that POTS can develop within 6–8 months after infection with COVID-19. There are relatively fewer clinical and research studies about POTS in children compared with adults.
Objective: We investigated 1) whether the number of pediatric POTS patients has increased after the COVID-19 pandemic in children, 2) the percentage of children suspected of having COVID-19 as a trigger for the onset of POTS, and (3) whether there were differences in sex, frequency of headache symptoms, and complication rate of migraine as a comorbidity in pediatric POTS patients compared with previous reports of adults.
Methods: We retrospectively studied the medical records of pediatric POTS patients who were treated pharmacologically at our hospital between April 2017 and March 2023. Diagnosis was based on a sustained elevated pulse rate of 40 beats per minute or more within 10 min while standing and no orthostatic hypotension.
Results: A total of 22 patients were included. There were 12 patients in the three years before the pandemic and 10patients in the three years after the pandemic. The average age was 12.4 years and the proportion of female patients was 36.4%. Headache symptoms were present in 81.8% of the cases. Migraine was a comorbidity in 45.5% of the cases. The trigger was unknown in 90.9% of cases, and no cases were attributed to infectious diseases, including COVID-19.
Discussion: Headache is also a common symptom of POTS in children, and approximately 45% of the children also have migraine. Headache was similar to that reported in adults. Nearly 80% of the patients are female, which has been seen in studies of adults. However, unlike previous reports in adults, in our study headache was more frequent in male patients. Among patients with POTS onset in childhood, 20% of men and 50% of women continue to have symptoms into adulthood. This is believed to increase the proportion of adult female patients. Unexpectedly, in our study the number of pediatric POTS patients remained unchanged before and after the pandemic, and none of the cases could be attributed to COVID-19. There have been some reports of POTS onset in children after COVID-19, but the numbers are few compared to adults. Given that the rate of severe COVID-19 infection in children is relatively low compared with that in adults, it is possible that immunological stressors associated with the development of POTS are less involved. POTS after COVID-19 may be less likely to occur in children; however, this may be due to the small number of cases.
Conclusion: As a symptom of POTS, headache and the complication rate of migraines were similar to those reported in adults. Compared with previous reports on adults, the proportion of female patients in this study was lower. POTS after COVID-19 may be less likely to occur in children. The limitations of this study include the small number of cases. In the future, it will be desirable to conduct studies with larger sample sizes.
Disclosure of Interest: None Declared

IHC23-PO-100

Effect of COVID-19 infection on primary headache in children and adolescents

R.Gokcen Gozubatik-Celik and Banu Bayramoglu

Department of Neurology, Bakirkoy Research and Training Hospital for Neurologic and Psychiatric Diseases, University of Health Science, Istanbul, Turkey

Introduction: Primary headache is extremely common in children and adolescents. Although an increase in the frequency of headaches has been reported with COVID-19 infection, it has been reported that all clinical symptoms generally regressed and completely resolved in the first 3 months.

Objective: In this study, children and adolescents with a previous diagnosis of primary headache who had COVID-19 infection were included in the study. We aimed to investigate the clinical presentation of COVID-19, neurological symptoms, presence of additional/new headaches during the infection period, triggering factors, characteristics of current primary headaches during and after the disease, and treatment options. The patients were evaluated retrospectively with a questionnaire created by the researchers.

Results: 43 children and adolescents with primary headaches, 28 of whom were girls, were included in the study. The mean age was 13 ± 4.2 years. The mean disease duration was 3.4 years (min:2 months; max:4 years). Twenty-five (58.1%) patients were diagnosed with tension-type headaches, 15 (34.8%) migraine, and 3 (7.1%) chronic daily headaches. In 60% (n:26) of the patients, the COVID-19 clinic started with a new headache, 18% of them anosmia (n:19), and 85% of them respiratory symptoms (n:37) accompanied the clinic. They described a new headache in the temporo-occipital region in 11 of the patients (n:26), on the vertex in 8, and a headache in the occipital region in 7 of them, often bilaterally. It was observed that this new headache period lasted between 15 days and 2 months. When the characteristics of primary headache during the infection period were evaluated, an increase was observed in frequency in 12 of 43 patients and severity in 24. The most common trigger factor was screen usage time, and stress was the second most frequent factor. When primary headaches were compared among themselves, the increase in the frequency and severity of post-COVID headaches was most frequently observed in migraine patients ($p < 0.001$). The most common treatment option was paracetamol.

Conclusion: Headache presentation was frequently observed in children and adolescents with a diagnosis of primary headache in COVID-19 infection, and it was noted that they experienced a different type of headache from primary headaches during the infection period. Also, COVID-19 worsened the headaches of migraine sufferers the most.

Disclosure of Interest: None Declared

IHC23-PO-101

OnabotulinumtoxinA for the prevention of chronic migraine in adolescents: the experience of an italian third level headache center

Ilaria Frattale[1], Laura Papetti[2], Fabiana Ursitti[2], Giorgia Sforza[2], Gabriele Monte[2], Michela Ada Noris Ferilli[2], Samuela Tarantino[2], Martina Proietti Checchi[2] and Massimiliano Valeriani[2,3]

[1]*Child Neurology and Psychiatry Unit, Department of Neurosciences, Policlinico Tor Vergata Foundation Hospital, Rome, Italy*

[2]*Developmental Neurology, Bambino Gesù Children Hospital, Rome, Italy*

[3]*Center for Sensory-Motor Interaction, Aalborg University, Aalborg, Denmark*

Objective: Migraine is the main cause of headache in children with the possibility of turning into a chronic form in up to 5% of cases, causing severe disability and daily activities impairment. The use of onabotulinumtoxinA (BT-A) for the treatment of chronic migraine in adults represents one of the greatest efficacy treatments with many safety data collected. Only few data to date about the use in evolutive age. The present study aims to describe the experience with BT-A for the treatment of chronic migraine in adolescents.

Methods: All patients under the age of 18 treated with BT-A at the Headache Center of the Bambino Gesù Children Hospital from November 2018 to November 2022 were included. The patients underwent BT-A injections according to PREEMPT protocol.

Parameters considered were demographic characteristics, number of injections received, adverse effects and treatment efficacy. For the latter parameter, the subjects were classified as responders if a reduction in the monthly frequency of attacks greater than 50% was observed, partial responders if between 30 and 50% and non-responders if $<30\%$.

Results: The treated population consisted of 37 females and 9 males with a mean age of 14.7 ± 1.5 standard deviation (SD) years.

Patients had a mean disease duration from onset to BT-A initiation of 29.3 ± 9.1 SD months. Before starting the BT-A, all subjects had previously attempted at least one prophylactic therapy and 58,7% discontinued them due to side effects. From botox initiation to last clinical

observation, the mean duration of follow up was 17.6 ± 13.7 SD (range 1–48) months. The number of BT-A administrations were 3.4 ± 3 SD. Five patients discontinued the therapy after the first administration because of untoleration to the injections. No treated patients reported major side effects. One patient reported neck muscle weakness lasting 5 days, 3 patients reported injection site redness or mild oedema lasting approximately 24 hours. 68% of subjects responded to treatment within the first three administrations of the BT-A. Proceeding with the number of administrations, a progressive improvement in frequency is observed.

Conclusions: this case series shows the excellent safe profile and effectiveness of BT-A in pediatric age of preventive treatment of chronic migraine.

Demographic Characteristics of 46 Patients (Table1)

Age (years)	Mean 14.7 ± 1.5 SD
Sex	9 males (19.6%); 37 females (80.4%)
Duration of migraine history (months)	Mean 29.3 ± 9.1 SD
Monthly Migraine Days	Mean: 26.5 ± 5.8 SD
Previous prophylactic treatment (%)	Amitriptyline (95.7%); Topiramate (47.8%); Flunarizine (39.1%) Valproate (34.8%); Duloxetine (26.1%); Propanolol (6.5%) Pregabalin (4.3%); Ultra-micronized palmitoylethanolamide (um-PEA) (15.2%) Cognitive behavioral therapy (65.2%)

Table 1

Headache education for clinicians and patients

IHC23-PO-102

Analysis of chronic headache patients referred to psychiatry

Tatsuya Monzen[1] and Fumihiko Sakai[2]

[1]*Ota Memorial Hospital, gunma, Japan*
[2]*Saitama International Headache Center, Saitama, Japan*

Objective: Headache attributed to psychiatric disorders (the International Classification of Headache Disorders, 3rd edition) and psychogenic factors exacerbate other chronic headaches, often lead to headache clinic visits. Such headaches are often refractory and time consuming to treat. At our headache outpatient clinic, we are trying to improve the condition in cooperation with local psychiatrists. In the past, from 2015 to 2021, we analyzed and examined the patients who were referred to psychiatry for headache treatment, and aimed to establish a headache diagnosis process.

Methods: Among the patients who were referred to psychiatric departments at eight medical institutions from April 2014 to November 2021, we analyzed age, gender, background of referral, presence or absence of reply to the letter of referral, and diagnosis at the psychiatric department.

Results: A total of 64 patients (25 males and 39 females) were referred to psychiatry, with an average age of 39 years. The average number of visits before referral to a psychiatrist was two. Reason for referral to psychiatry were (1) suicidal ideation or suicide attempt, (2) Insomnia, (3) Frequent symptoms other than headache, (4) Awareness that it is psychogenic. The causes of mental disorders were often family problems, personal relationship problems, and work/school problems. Medical information from the psychiatric department was necessary for examination of psychiatric patients. There were 26 responses from the psychiatrists we introduced. Diagnoses included 2 depressive states, 8 depression, 1 bipolar disorder, 5 adjustment disorders, 4 somatoform disorders, 1 neurosis, 1 conversion disorder, and 1 psychogenic headache. 1 patient with hypersensitivity, 1 patient with decreased attention, and 1 patient with negative symptoms. There were 14 who did not receive a reply, but confirmed that they had started oral treatment, and 2 who had previously been to a psychiatric hospital.

Conclusion: 1. Patients visiting a psychiatric hospital should visit a headache outpatient clinic under the direction of their attending psychiatrist. 2. Evaluating (1) family relationships, (2) private interpersonal relationships, and (3) stress at work or school, and if necessary, seeing a psychiatrist early, can reduce medical time and medical costs.

IHC23-PO-103

A survey of Greek primary care physicians on their likeability of migraine and other common diseases

Michail Vikelis[1], Andreas A. Argyriou[2], Anastasia S. Antoniou[3], Konstantinos C. Spingos[4], Athanasios E. Skliros[5], Konstantinos Bilias[6], Aikaterini Kouroudi[6], Emmanouil V. Dermitzakis[7] and Efstathios A. Skliros[5]

[1]*Glyfada Headache Clinic, Glyfada, Greece*
[2]*Agios Andreas State General Hospital, Patras, Greece*
[3]*Attikon General University Hospital, Athens, Greece*
[4]*Corfu Headache Clinic, Corfu, Greece*
[5]*Hellenic Society for Primary Care Research and Continuing Education, Athens, Greece*
[6]*Greek Society of Migraine and Headache Patients, Athens, Greece*
[7]*Euromedica General Clinic, Thessaloniki, Greece*

Worldwide, migraine care is provided in most cases by primary care physicians. The aim of our study was to access the likeability of Greek primary care physicians to treat migraine, compared to other common neurological and general medical disorders.

We surveyed 182 Greek primary care physicians with the use of a 5-point questionnaire regarding their likeability to treat ten common medical conditions, including migraine, hypertension, hyperlipidemia, upper respiratory tract infections, diabetes mellitus, low back pain, dizziness, transient ischemic attack, diabetic peripheral neuropathy and fibromyalgia.

Overall, migraine scored very low (3.57 ± 1.02) next to diabetic peripheral neuropathy (3.57 ± 1.0) and third from last to fibromyalgia (3.25 ± 1.06). On the contrast, participants reported a much higher likeability to treat hypertension (4.66 ± 0.60) and hyperlipidemia (4.64 ± 0.65).

Our results indicate that Greek primary care physicians dislike to treat migraine, but also other neurological diseases. It remains to investigate the reasons for this dislike and if it is associated to poorest patient satisfaction, treatment results or both.

Disclosure of Interest: None Declared

IHC23-PO-104

The implementation of a headache and movement disorders skills workshop for neurology trainees in Australia

Jason Ray[1,2,3], Victor Zhang[1,2], Josephine Baker[1] and Melissa Tang[1]

[1]*Alfred Health, Melbourne, Australia*
[2]*Austin Health, Melbourne, Australia*
[3]*Monash University, Melbourne, Australia*

Objective: To survey the existing education of neurology trainees to headache medicine, and implement a headache skills workshop in Victoria, Australia.

Methods: A 4.5-hour workshop was designed consisting of four practical skills stations and two didactic lectures delivered to neurology trainees in Victoria, Australia. They were invited to complete a survey evaluating self-reported knowledge and experience of the workshop.

Results: A total of 43 trainees attended the weekend workshop in January 2023. Of the participants, 52.2% reported less than two hours formal teaching in headache medicine and 65.2% reported less than two hours in movement disorders at their local institution. Prior to the course, the level of self-rated competence for procedural skills was below the level of independence in 43.8% of respondents for Greater Occipital Nerve (GON) blocks, and 90.6% for botulinum toxin for headache disorders.

On a five-point scale, significant improvements were reported in knowledge of GON blocks (mean change 1.1, SD 0.9, $p < 0.001$), as well as botulinum toxin (mean change 1.6, SD 1.0, $p < 0.001$). All respondents reported that they would attend a similar course again.

Conclusion: The development of a headache skills workshop in Australia was well received. The workshop resulted in significant improvements in the comfort and knowledge of headache medicine skills in neurology trainees. Replication of the intervention in other jurisdictions may improve healthcare delivery to improve outcomes for people with headache disorders.

Disclosure of Interest: Dr. Ray has received funding for educational presentations Allergan, Novartis and has served on medical advisory boards for Pfizer, Viatris and Lilly. Dr Raviskanthan has no conflict of interest to declare.

IHC23-PO-105

International Headache Training Symposium in Cambodia

Liza Smirnoff[1] and Soma Sahai-Srivastava[2]

[1]*University of Miami Health, Miami, USA*
[2]*University of Southern California Keck School of Medicine, Los Angeles, USA*

Background: Cambodia experienced significant setbacks in medical education and care due to unrest and the loss of many doctors during and following the 1970's Khmer Rouge regime. As a result, the burden of migraine in Cambodia is currently unknown and education regarding headache management has been limited.

Methods: In December 2022, we organized a one-day symposium on headache medicine as part of a weeklong

Neurology teaching program in Phnom Penh, Cambodia. The symposium was attended by a group of 70 residents, fellows and attending physicians, and included optional surveys on headache epidemiology, classification, and treatment.
Results: Of the 14 who completed surveys, they reported seeing on average 4 patients per week for headache management, with patients reported to be predominantly female, with an average age of 35. Respondents reported knowledge of the diagnosis of migraine and tension-type headaches as well as established acute and preventative therapies such as NSAID's, acetaminophen and tricyclic antidepressants, but demonstrated limited knowledge of other headache disorders and additional treatments.
Conclusions: Based on initial data, knowledge of headache management by physicians in Cambodia focuses on basic diagnosis and treatment of migraine and tension-type headaches. Further didactics on headache classification and treatment are needed to improve headache care in this population.
Disclosure of Interest: None Declared

IHC23-PO-106

A survey on headache education curriculum in college of dentistry

Jinkyu Kang[1], Ji-Won Ryu[2] and Seong-Taek Kim[3]

[1]*Wonkwang University Dental Hospital, Daejeon, Korea, Republic of*
[2]*Chosun University, Gwangju, Korea, Republic of*
[3]*Yonsei University, Seoul, Korea, Republic of*

Headache is a common pain disease that can be easily encountered in clinical practice. Not only in the medical field but also in dentistry, patients often come to the hospital with headaches or complaints of headaches accompanied by a toothache or facial pain. However, it has been reported that education on headaches is insufficient in medical schools, which is believed to be a more serious problem in dental schools. In this study, the current status of headache education in 11 dental schools in Korea was investigated to be used as data for future student education and clinical application. As a result of the study, headache was included in the curriculum of orofacial pain and oral medicine at most dental colleges. Lectures were given for 1–2 hours by professors of oral medicine. Most universities were using "Orofacial Pain and Temporomandibular Disorder" textbook, published in 2012, reflecting the 2nd edition of the International Classification of Headache Disorders, so the latest diagnostic classification needs to be educated. At only one university, neurologists gave a lecture with discretionary materials, and only two universities had headache lectures in their graduate school curriculum. Considering the specificity of dentists who are in charge of pain in oral and facial region, continuous discussions and mutual cooperation with the neurology department are necessary to ensure sufficient education related to headaches during the undergraduate course.
Keywords: dental education, dental school, facial pain, headache, toothache.

IHC23-PO-107

Knowledge on headache disorders among neurology residents in Kyrgyzstan

Asel Jusupova

Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan

Background: The training program for clinical neurology in Kyrgyzstan lasts only 3 year and does not include specific headache program. Knowledge in headache management must therefore be acquired during everyday clinical training. The objectives of this study were to investigate neurology residents" knowledge of headache.
Methods: A questionnaire survey was undertaken among neurology residents.
Results: Overall 45 residents of second and third year study of Neurology Department of Kyrgyz State Medical Academy responded. 85% were women, 15% – men, mean age was 28 years. 38% knew the approximate prevalence of migraine and chronic headache. 75% never heard about the International Classification of Headache Disorders as well as about the third line medications for an acute migraine treatment. Further, only 20% have tried preventive therapy for chronic migraine. About 1/4 of respondents have used headache diaries for diagnostic purposes, and 90% requested an MRI for all long-lasting headaches referred to neurological outpatient clinics.
Conclusion: Overall knowledge on headache disorders amongst neurology residents in Kyrgyzstan do not meet the expectations set out by international recommendations. There is a relative lack of formal education and training in headache of Kyrgyz residents. There is unmet need for a structured headache training in residents program in order to improve clinical outcomes of headache patients.
Keywords: education, guidelines, migraine, neurology training, tension-type headache
Disclosure of Interest: None Declared

IHC23-PO-108

Survey of Headache Education and Training Exposure Amongst Neurology Trainees in Australia

Usman Ashraf[1], Jasmin Tilling[1] and Emma Foster[2]

[1]*St Vincent's Hospital Sydney, Sydney, Australia*
[2]*The Alfred Hospital, Melbourne, Australia*

Background: Headache remains a major public health concern, with patients experiencing difficulty accessing optimal, evidence-based care.
Objective: To evaluate perceptions of gaps in education and training in headache amongst Neurology Advanced Trainees in Australia
Methods: An 18 question survey was created using REDCap software. The survey was distributed to Neurology Trainees in Australia with a participation information sheet explaining the aims of the study, that participation was voluntary and that respondents would remain anonymous. Data were collected from Sept-October 2022.
Results: The response rate was 28.6% (n = 22/77). Respondents comprised 50.0% first year and 50.0% second year trainees. Amongst the respondents, 59.1% had less than 2 hours of exposure to headache education throughout their medical degree and 63.6% had no exposure to headache clinics during neurology training. 68.2% of trainees spend over 2 hours managing patients with headaches every week and 72.3% of trainees would consider headache as an area of subspecialty focus in their future careers. Only 13.6% felt adequately prepared to manage headache disorders in either the inpatient or outpatient setting.
Conclusions: Few neurology trainees who responded to the survey felt adequately prepared to manage headache disorders in the inpatient or outpatient setting. Gaps in education and training were identified from medical school through to advanced training. Addressing these gaps is an avenue to optimize the management of headache disorders in Australia.
Disclosure of Interest: None Declared

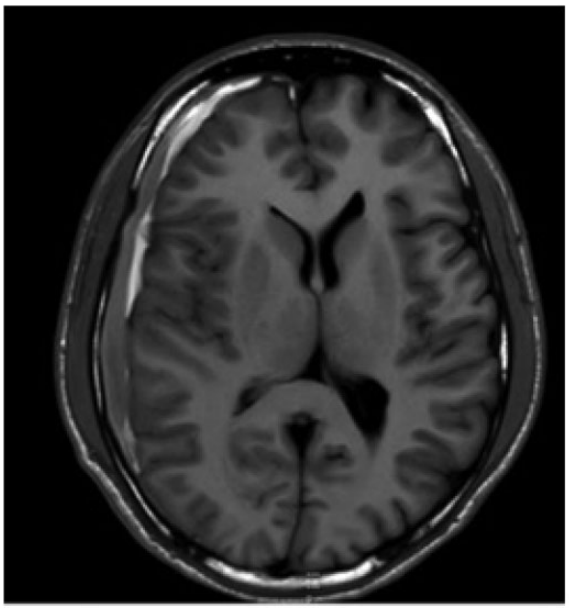
IHC23-PO-109

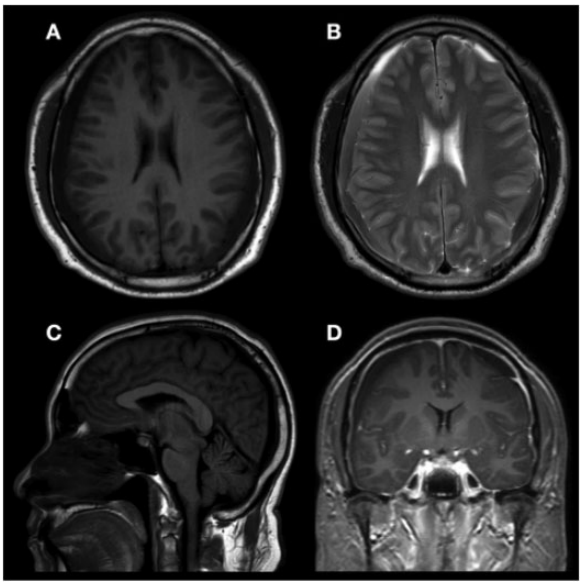
Alarming headache self-thought to be benign: a flaw of being a doctor

Wanakorn Rattanawong[1,2], Prakit Anukoolwittaya[3,2] and Sekh Thanprasertsuk[4,2]

[1]*Faculty of Medicine, King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand*
[2]*The Thai Headache Society, Bangkok, Thailand*
[3]*Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
[4]*Faculty of Physiology, Chulalongkorn University, Bangkok, Thailand*

Background and Objective: Headache is among the most common clinical presentations of neurological disorders. Unfortunately, it is also one of the most misdiagnosed conditions. Not only do doctors struggle to make a diagnosis for their patients, but doctors who experience headaches also struggle to make a correct diagnosis for themselves. Research suggests that doctors are more likely to misdiagnose and delay management of their own illnesses. Here, our goal is to educate and discuss the pitfalls that doctors encounter when diagnosing their own illnesses.
Methods: We reported two cases of doctor who suffered a secondary headache but thought to be primary. There clinical presentations are alarming in views of headache specialists. However, misdiagnosed. Informed consent was obtained from both doctors.
Results: Case 1
A 20–year-old medical student presented with a one-month history of right-sided headache, which was described as throbbing and radiating to the occiput. The patient reported that physical activities were precipitating factors. He denied nausea, vomiting, photophobia, or phonophobia, and there was no obvious history of trauma. He visited a doctor and was diagnosed with myofascial pain syndrome. During a follow-up visit, he reported 80% improvement in his symptoms but still experienced ongoing headaches (Later, he told us that he reported this decrease because he did not want to skip rounds). Later, he experienced a worsening headache. Neurological examinations were unremarkable. The magnetic resonance imaging (MRI) of the brain revealed evidence of an acute to subacute subdural hematoma (SDH) overlying the right cerebral hemisphere with midline shifting to the left about 1.1-cm (Fig 1). The patient was admitted to the hospital for conservative therapy. He later recall riding a roller-coaster before the onset of the headache.





Case 2

A 50-year-old administrative doctor presented with persistent diffused headache for 6 weeks. He had suffered episodic tension-type headache (TTH) for 10 years. 6 weeks PTA, the headache changed to a persistent pattern. He noticed that the pain is worsened by physical activities, coughing, and changing position from supine to upright. He thought his headache got worse as a result of chronic sinusitis and a chronification of TTH. Thus, he self-prescribed oral amitriptyline 10–25 mg before bedtime everyday along with acetaminophen. He reported that the medications partially eased his headache. At last, one of the authors incidentally talked with him about his headache. Intracranial pressure (ICP)-related headache was suspected. He was urgently appointed for a brain MRI. The MRI results revealed bilateral subdural collections (Fig 2A–2B), diffused pachymeningeal thickening, midbrain sagging and mild pituitary enlargement (Fig 2C–2D), consistent with intracranial hypotension. MR cisternography did not reveal any CSF leakage. Epidural blood patch was done. The headache with ICP-related features resolved thereafter.

Discussion and Conclusion: From a headache specialist's point of view, these clinical presentations are considered a straightforward secondary headache. The first scenario showed a side-locked headache with aggravating pain when changing position, which should have led to doubt of meningeal irritation. The second scenario showed numerous red flag signs of intracranial hypotension. The question arises: why were these patients delayed and misdiagnosed?

One possibility is that both patients are doctors. When facing their own illnesses, physicians usually delayed their own diagnosis. This problematic phenomenon has been explained by multiple factors, including doctors" belief that they have immunity to severe illness, judging certain symptoms as insignificant. Findings have shown that this thought process might be due to a lack of time, impact on work, confidentiality, and embarrassment. Another factor is self-treatment. In a systematic review, it was found that doctors tend to self-prescribe between 25%–100%, with 78% of doctors inappropriately treated themselves. Self-prescription also enhances the false belief of improvement. In our opinion, to overcome the pitfalls, it is crucial that doctors diagnose based on medical knowledge of anatomy and physiology without bias, even if the patient is a physician. Seeking other doctors for help should be encouraged. In addition, mnemonics like SNOOP might be used in case of misguided diagnosis.

Disclosure of Interest: None Declared

IHC23-PO-110

Revolutionizing Headache Treatment: The Impact of Tele-Education on Collaborative Care Between Neurology and Algology Specialists

Elif Kocasoy Orhan[1], İbrahim Kamaci[1], Macit Selekler[2], Halil Cetingok[3], Gul Goknel Talu[3], Suleyman Ozyalcin[3] and Aynur Ozge[4]

[1]*Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Turkey*
[2]*Kocaeli University, Faculty of Medicine, Department of Neurology, Izmit, Turkey*
[3]*Istanbul University, Istanbul Faculty of Medicine, Division of Algology, Department of Anesthesiology and Reanimation, Istanbul, Turkey*
[4]*Mersin University, Medical Faculty, Department of Neurology, Mersin, Turkey*

Introduction: Headache management requires a multidisciplinary approach, and Algology and Neurology physicians play a significant role in diagnosing and treating headache patients. The study aimed to compare the headache management approaches of Algology and Neurology physicians and evaluate the impact of telehealth education on their practices.
Methods: A questionnaire was developed, consisting of three sections, and sent to Algology and Neurology physicians through social media and email addresses. The survey collected data on demographic information, diagnostic and treatment approaches to a headache case, and the impact of telehealth education. Data were analyzed using descriptive statistics and chi-square tests.
Results: Eighty-two Algologists and 97 Neurologists completed the survey. Both groups gave similar responses to questions about the headache patient, and there was no significant difference between the diagnostic and differential diagnostic possibilities. However, the examination methods differed, with the Neurology Group relying on history and the Algology Group suggesting further investigations. Both groups agreed on the application of prophylaxis to the patient, with botulinum toxin administration and classical prophylactic agents being accepted in both groups. The newest preventive treatment method, CGRP-antagonists, was used more frequently in the Neurology Group than in the Algology Group. Participants reported that online meetings had a positive impact on their daily practices, with 48% stating that they were reflected in their practice. Those who attended online meetings marked more up-to-date treatment options such as CGRP antagonists and Botulinum toxin.
Conclusion: The study showed that Algology and Neurology physicians had similar approaches to headache management, with differences in examination methods and the use of newer preventive treatment methods. Telehealth education had a positive impact on the participants, improving their knowledge of up-to-date treatment options.
Disclosure of Interest: None Declared

IHC23-PO-111

Investigating the Management of Headaches and Self-Medication Practices among Healthcare Professionals and Students in Karachi, Pakistan: Implications for Enhancing Healthcare

Muhammad Liaquat Raza[1,2] and Hifza Ale-Ibrahim[3]

[1]*Al Fatima Hospital, Karachi, Pakistan*
[2]*Dept. of Health Management, IoBM, Karachi, Pakistan*
[3]*Benazir Bhutto Shaheed University Lyari, Karachi, Pakistan*

Objective: Headaches are a common neurological symptom experienced by people worldwide, but limited research has been conducted on headache management and self-medication practices in Karachi, Pakistan. In this study, we aimed to explore the prevalence, self-medication, and management practices of headaches among healthcare professionals and students in Karachi.
Methods: A cross-sectional survey was conducted among 140 healthcare professionals and students in Karachi, Pakistan. The survey questionnaire consisted of questions about demographic characteristics, types of headaches experienced, self-medication, and management practices for headaches.
Results: The study participants included 55% female and 53.6% unmarried respondents. The majority of respondents (62.8%) reported experiencing tension-type headaches, followed by migraines (44.6%), and other types of headaches (5.9%). Self-medication was common among the respondents, with 38.5% reporting reliance on over-the-counter medications or home remedies to manage their headaches.
The findings suggest that there is a lack of awareness or access to appropriate medical care for headaches among the surveyed population. Greater education and awareness campaigns could help improve headache management and reduce reliance on self-medication. Furthermore, the study emphasizes the need for further research to explore the prevalence and impact of headaches in other settings and populations, as well as to identify effective interventions for improving headache management and reducing the burden of headaches on individuals and society.
Conclusion: In conclusion, this study highlights the importance of examining headache management and self-medication practices among healthcare professionals and students in Karachi, Pakistan. The findings can serve as a

basis for healthcare professionals and policymakers to work together to address the issues identified and improve headache management in the region. Moreover, raising awareness of the importance of seeking medical care for headaches can lead to better headache management and a healthier population.

Disclosure of Interest: None Declared

Headache epidemiology, outcomes and burden

IHC23-PO-112

Potential burden of migraine in migraineurs: assessment of the number of days compelled to work or perform private activities

Noboru Imai[1] and Yasuhiko Matsumori[2]

[1]*Department of Neurology and Headache Center, Japanese Red Cross Shizuoka Hospital, Shizuoka, Japan*
[2]*Sendai Headache and Neurology Clinic, Sendai, Japan*

Objective: In Japan, migraineurs lose an estimated 2.2 trillion yen annually due to absenteeism. We hypothesize that these huge losses due to absenteeism are attributed to many migraineurs unable to take a break even if they wanted to. Moreover, we also believe that many migraineurs are also compelled to conduct private activities, such as housework and leisure activities, during their break due to their migraine attacks. To clarify our hypothesis, we investigated the number of days migraineurs are compelled to work or perform private activities over a 3-month period.

Methods: We collected data from 1717 migraineurs who visited two headache education centers accredited by the Japanese Headache Society between March 2021 and March 2022. The number of days compelled to work (NDCW) and the number of days compelled to perform private activities (NDCPPA) over a 3-month period were collected from questionnaires at the first visit. Baseline demographic data, such as the Visual Analog Scale (VAS) score, and psychiatric assessments results, such as the Japanese version of the Generalized Anxiety Disorder-7 (GAD-7) and the Japanese version of the Patient Health Questionnaire-9 (PHQ-9), were also collected. We compared NDCW and NDCPPA and examined whether there were differences in NDCW and NDCPPA according to age at first consultation, sex, and migraine type (episodic migraineurs [EM] and chronic migraineurs [CM]) using the Mann–Whitney U test (IBM SPSS Statics version 29.0).

Results: We excluded six patients due to lack of data from NDCW or NDCPPA. Finally, we analyzed data from 1711 migraineurs (1226 women, 485 men; 1327 EM, 384 CM). Baseline demographics and headache disability/psychiatric assessments are shown in the following table.

Baseline demographics and headache disability/psychiatric assessments

	n	Median	IQR*	Range
Age at first consultation	1711	31.0	23–43	6–76
VAS	1674	70.0	50–80	0–100
GAD-7	1711	5.0	2–8	0–21
PHQ-9	1711	5.0	2–9	0–26
NDFW	1711	6.0	3–11	0–90
NDFPA	1711	10.0	10–11	0–90

*Interquartile range

NDCPPA was significantly higher than NDCW (mean difference 1.9, 95% confidence interval [CI]: 1.4 to 2.4, $p < 0.001$, Mann–Whitney U test). The percentages of patients without NDCW and NDCPPA were 11.0% and 6.9%, respectively. NDCPPA was clustered around 10 (42.8%) and 11 (33.3%), respectively. CM had a significantly higher NDCW (11.6; CI: 10.1 to 13.1) and NDCPPA (10.4; CI: 9.5 to 11.2) than EM (7.2; CI: 6.8 to 7.6, 10.0; CI: 9.8 to 10.3. $p < 0.001$ each, Mann–Whitney U test), and females (8. 6; CI: 8.0 to 9.1, 10.3; CI: 9.9 to 10.7) had a significantly higher NDCW and NDCPPA than males (7.3; CI: 6.5 to 8.1, 9.7; CI: 9.3 to 10.1, $p < 0.001$ each, Mann–Whitney U test). NDCPPA was higher than NDCW in females, males, EM, and in all decades (by age), but NDCPPA was lower than NDCW in CM.

Conclusion: This study revealed that many migraineurs were compelled to work or conduct private activities even when they are desirous of a break. NDCPPA was higher than NDCW without CM.

Disclosure of Interest: None Declared

IHC23-PO-113

The analysis of precipitating factors related severity of migraine attacks using the headache diary mobile application (Smile Migraine Application)

Surat Tanprawate[1,2], Koth Charoensri[1], Angkana Nudsasarn[2] and Ronnakorn Vaiyavuth[3]

[1]*Chiang Mai University, Chiang Mai, Thailand*
[2]*The Northern Neuroscience Center, Chiang Mai, Thailand*
[3]*Chulalongkorn University, Bangkok, Thailand*

Introduction: Migraine is a prevalent neurological disorder that affects millions of people worldwide. Various factors, such as stress, hormonal changes, weather changes,

and food triggers, can precipitate or worsen migraine attacks. Understanding these precipitating factors and their impact on the severity of migraine attacks is crucial for the effective management of the condition. Headache diary mobile applications provide an effective tool for recording the frequency, duration, and severity of migraine attacks, as well as identifying potential triggers. This research aims to analyze the relationship between the precipitating factors and the severity of migraine attacks using headache diary mobile applications.

Methods: A retrospective cohort study was conducted among migraine patients who regularly used a smartphone headache diary application (the Smile Migraine application) to record details about headache trigger factors and severity for at least 1 month from May 2022 through September 2022. Eligible participants will be required to have a migraine diagnosis by a healthcare professional or online ID migraine screening tool. Data collection will involve participants completing demographic characteristics on their applications. Descriptive statistics will be used to summarize demographic and clinical characteristics, migraine features, and precipitating factors. A chi-square test will be used to examine the differences in migraine features and precipitating factors between participants with different migraine severity levels.

Results: In a retrospective cohort study, 778 individuals (mean age, 31 years; 88.9% women; mean duration of illness, 11 years) kept a one-month diary. There were 10,584 headache records in this data set (2,637 mild, 4,810 moderate, and 3,137 severe headaches); of these, 9,408 headache events contained trigger variables, while 1,176 occurrences did not. On headache days, the most prevalent trigger variables were present. 9.78% stress, 9.11% heat, 8.63% eye strain, 8.53% sleep deprivation, 7.83% sunlight, 7.63% muscle pain, 6.48% weather changes, and 6.33% menstruation were all mentioned.

Cheese (odd ratios [OR]: 5.95), chocolate (OR: 3.42), coffee (OR: 2.80), Monosodium glutamate (OR: 2.40), vaccination (OR:2.37), fatigue (OR: 2.17), exercise (OR: 2.15), bread (OR:2.13), noise (OR: 2.09), muscle pain (OR: 1.97), cold (OR: 1.96), odors (OR: 1.88), sunlight (OR: 1.82), hot (OR: Not sleeping on time (OR: 1.52), alcohol drinking (OR: 1.48), being moist (OR: 1.43) and eye strain (OR: 1.34) were significantly associated with the severity of headache.

We found a linear relationship between the number of triggers (2–7 triggers) and the intensity of the headache score, which showed the greater the number of triggers, the more severe the pain detected.

In conclusion, this study highlights the value of utilizing smartphone headache diary applications in identifying migraine trigger variables. The common trigger factors were not strongly associated with the severity of headaches, but mostly they were related to foods (cheese, chocolate, coffee, and foods containing monosodium glutamate). The findings suggest that migraine attacks with trigger factors tend to be more severe, and a higher number of identified triggers are associated with increased pain intensity. These results underscore the importance of investigating trigger variables to enhance our understanding of migraine occurrence and inform effective management strategies. Overall, the use of headache diary mobile applications may provide valuable insights for individuals with migraine and healthcare professionals in the management of this debilitating condition.

Disclosure of Interest: None Declared

IHC23-PO-114

Concurrent Validity and Minimal Clinically Important Difference (MCID) of the Smile Migraine Impact score (SMIs) for Headache Impact Evaluation in Migraine Patients.

Nopdanai Sirimaharaj[1], Surat Tanprawate[1], Chatree Chai-Adisaksopha[1], Phichayut Phinyo[1], Siwahdol Chaimano[1], Ronnakorn Vaiyavuth[2], Atiwat Soontornpun[1], Angkana Nudsasarn[1], Kitti Thiankhaw[1], Chayasak Wantaneeyawong[1] and Chutithep Teekaput[1]

[1]*Chiang Mai University, Chiang Mai, Thailand*
[2]*Chulalongkorn University, Bangkok, Thailand*

Introduction: Migraine impairs physical function, work productivity, leisure activities, lifestyle, and mental health. The MIDAS and HIT-6 are two of the most commonly used instruments to measure migraine's impact on an individual's life. Both instruments have pros and cons. The MIDAS and HIT-6 questionnaires capture the patient's assessment of how migraines affect their life, but patient interpretation and perception of symptoms may bias them, and headache attacks may be inaccurate if based on patient recall. Due to this, we developed and validated a score using the Smile Migraine application, an automated electronic headache diary, to assess migraine effects more accurately.

Objectives: To evaluate the concurrent validity of a newly developed impact assessment score used for clinical monitoring in migraine patients, named Smile Migraine Impact Score (SMI), using automatic calculation of an electronic headache diary (the Smile migraine application) with HIT-6 and EQ-5D-5L scores and to determine its minimal clinically important difference (MCID) threshold.

Materials and Methods: SMI Score Development: The development of the algorithm for the SMIs was based on a combination of clinical guidelines and research evidence. The algorithm was designed to take into account the frequency and severity of migraine headaches over a 30-day

period, as recorded in an electronic migraine diary. The frequency and severity criteria were based on established clinical guidelines for the initiation of migraine prevention, which recommend that individuals with moderate-to-severe migraine headaches occurring on at least 4 days per month with moderate intensity and 2 days per month with severe intensity should consider preventive treatment. The score of 3 (from 1 to 5; very mild to very severe) was rated as having a moderate impact based on the recommendation of headache frequency and severity that determine the starting dose of preventive medication for migraine. In addition, expert opinion was sought in the development of the algorithm by comparing it with the HIT-6 score to ensure that the criteria used in the SMIs were clinically relevant and meaningful. The algorithm was also designed to incorporate the HIT-6, which is a widely used tool for measuring the impact of headaches on individuals.

Participants and Design: Patients diagnosed with migraine at Maharaj Nakorn Chiang Mai Hospital were prospectively recruited. The study duration was from September 2021 to March 2022. Patients were instructed to record the frequency and severity of their headache symptoms for 60 consecutive days using the Smile Migraine application. The SMIs, HIT-6 score, and EQ-5D-5L questionnaires were assessed on the 30th and 60th days of follow-up. The concurrent validity of the SMIs with HIT-6 and EQ-5D-5L was evaluated using Spearman's correlation. The MCID of the SMIs was determined using three recommended approaches: consensus-based, distribution-based, and anchor-based.

Results: A total of 50 patients diagnosed with migraine were enrolled. The majority of the patients were female (80%), with a mean age of 36.6 10.7 years old. More than half of the participants had migraine without aura (68%) while the rest had migraine with aura, which presented most often as a visual aura (30%). Also, participants mostly used non-migraine-specific acute medications (68%). Lastly, over half of the participants had prior migraine prevention medications (64%). Prior migraine days were in the range of 5–10 days per month.

The SMIs showed a significant positive monotonic correlation with the HIT-6 score (Spearman's 0.89 [p 0.001] at the 1st visit and 0.84 [p 0.001] at the 2nd visit) and the EQ-5D-5L (Spearman's –0.83 [p 0.001] at the 1st visit and –0.82 [p 0.001] at the 2nd visit). All three approaches to determining the MCID of SMIs yielded the same value of –1 SMI score point.

Conclusion: Based on our results, the SMIs were concurrently valid with the HIT-6 score and the EQ-5D-5L score. With three different methods for determining the minimal clinically significant difference (MCID), a one-point change in the SMI score could be considered clinically significant. As a newly developed instrument, the SMIs are a useful tool for clinical monitoring of migraine patients due to their usability and capacity to measure both the frequency and severity of headache symptoms. In addition, they suggest that SMIs may be useful for identifying patients who could benefit from preventive migraine treatment.

Disclosure of Interest: None Declared

IHC23-PO-115

Current treatment and follow-up of Giant Cell Arteritis: A retrospective multi-center study

Mi-kyoung Kang[1], Yoo-ha Hong[1], Yoo Hwan Kim[2], Hong-Kyun Park[3], Soo-Kyoung Kim[4], Jong-Hee Sohn[5], Jiyoung Kim[6], Ki-Han Kwon[1] and Soo-Jin Cho[1]

[1]*Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of*
[2]*Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea, Republic of*
[3]*Inje University Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea, Republic of*
[4]*Gyeongsang National University College of Medicine and Gyeonsang National University Hospital, Jinju, Korea, Republic of*
[5]*Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea, Republic of*
[6]*Pusan National University, Pusan National University School of Medicine, Busan, Korea, Republic of*

Objective: Giant cell arteritis (GCA) is a serious disease with a high risk of blindness and long-term recurrence. Data to guide long-term management of GCA patients in Korea are very scarce. The purpose of this study is to analyze the treatment and follow-up status, relapse and remission rates of GCA patients.

Methods: This study is retrospective medical record analysis of the patients with GCA in 6 university hospitals in Korea from February 2009 to November 2022. GCA was initially diagnosed based on the existing 1990 American College of Rheumatology (ACR) and selected the cases by the 2022 ACR diagnosis criteria.

Results: A total of 18 patients were analyzed and median follow-up period was 3.5 months; 5 patients were currently followed-up and 13 patients were dropped-out. Seven patients suffered with arteritic anterior ischemic optic neuropathy (AAION). Initial treatment was prednisolone in all patients, and adverse effect of prednisolone occurred in 4 patients (25.0%). Methotrexate and azathioprine were used as adjuvant treatment in 9 patients, and no patients used tocilizumab. Relapses occurred in 2 patients (11.1%) and 9 patients (50.0%) showed remission. Patients with AAION had lower remission rates than those without AAION, and sustained remission occurred in 4 patients

without AAION. There were no differences in the follow-up period according to visual symptoms or the other clinical factors.
Conclusions: In this multicenter study, GCA had a high dropout rate, short follow-up period, with many being discontinued before 3 months. Adverse drug responses in about 1/4 of patients and recurrence in 1/10 of patients occured. Regular monitoring and long-term follow-up of GCA patients are needed.

IHC23-PO-116

Headache education and headache virtual consultation in the workplace at an information technology company of more than 70,000 employees

Masako Yokoyama[1], Hisaka Igarashi[2], Hirohisa Kato[1], Yasuhiro Azuma[1], Satoko Nagumo[1] and Hitoshi Miyake[1]

[1]*Health Promotion Unit at Fujitsu Co. Ltd, Kasaki, Japan*
[2]*Fujitsu Clinic, Kasaki, Japan*

Background: Headaches are more common among the working age population and affect productivity losses in the workplace.
Method: 81,159 employees of an IT company group were invited to participate in an e-learning course on headache, and 73,432 (90.5%) took the course. Of those who completed the e-learning, 20-minute headache virtual consultations were provided to those employees who requested it (https://doi.org/10.1177/03331024231165682).
Results: In a questionnaire before the course, 7.8% of the participants stated that their attitude towards headaches was "not a disease", 30.3% "mild", 46.8% " diseases with significant disruption to daily life", 13.1% "life-threatening" and 1.9% "other diseases." Younger generations had a lesser perception of headaches and the perceptions of headaches became greater with age ($P = 0.000$). Women were also more likely to perceive headaches as "diseases with significant disruption to daily life", ($P = 0.000$). In the post-course questionnaire, 94.5% recognised a need for the course. 82.9% of participants without headache said that their attitude toward colleagues with headache would change, and 70.6% said that their perception of headache was "diseases with significant disruption to daily life".
2,971 people (4.1% of the total; 6.2% of 48,238 people who experienced headaches) were interested in the headache virtual consultation, and 362 (202 males, 162 females) consulted. 292 (80.4%) had suffered from headaches for years. 43% had been aware of headaches since their teens. 47 (29 males, 18 females 11.8%) reported having headaches "almost every day" (the chronic headache group: CH). The mean age of CH (both chronic migraine and chronic tension-type headache) was older (43.4 ± 11.2 years) CH), compared with 315 (173 males, 142 females), mean age 40.7 ± 10.3 years, in the episodic headache group (EH). The number of days missed from work due to headache was 1.80 ± 3.60 in CH and 0.59 ± 1.33 in EH ($p < 0.001$). 61.7% of CH and 42.5% of EH answered "yes" to the question, "Does prolonged use of a computer cause headaches?" Only 14.9% of the chronic headache sufferers visited a doctor regularly for headaches, 55.3% said they lie down or sleep to cope with headaches, and 53.2% said they manage with headache medicine bought at a pharmacy. The most common reason for not seeing a doctor was that they thought they had no choice but to endure headaches (29%). Headache consultation reduced the number of headache days in the chronic headache group from 48.00 ± 24.57 days to 10.93 ± 9.18 days ($P = 0.000$).
Conclusion: E-learning on headache education increased employees" awareness and understanding of headaches. Headache virtual consultation improved headaches, especially in the chronic headache group.

IHC23-PO-117

Headwork as innovative tool for monitoring mAbs efficacy in migraine and their influence on work activity:a multicentric experience

Danilo Antonio Montisano[1], Gloria Vaghi[2], Alberto Raggi[1], Grazia Sances[2], Cristina Tassorelli[2], Claudia Altamura[3], Fabrizio Vernieri[3], Carlo Ferrarese[4] and Licia Grazzi[1]

[1]*Headache Center, IRCCS Besta Foundation, Milan, Italy*
[2]*Headache Center, IRCCS Mondino, Pavia, Italy*
[3]*Headache Unit, Campus Bio-Medico, Rome, Italy*
[4]*Neurology dpt, Milano Bicocca University, Milan, Italy*

Objective: The efficacy of monoclonal antibodies anti-CGRP (mAbs) is generally rated with disease related metrics, but the impact of treatment on the global burden needs to be assesed. HeadWork(HW) is an evaluation tool developed to value the impact on work tasks and reduced productivity of migraineurs.Aim of this study is to test the validity of HW and to compare its performance with usually used clinical indexes.
Methods: We enrolled 108 patients treated with mAbs at the Headache Centres of Besta(Milan), Mondino(Pavia) and Campus-Biomedico(Rome).They were followed up on a 3 month basis, at each time point they filled in diaries about headache frequency(MMD), medication intake(MMI) and HW.HW questionnaire consists:"Work-related difficulties"(HW1), to rate the degree of difficulty in general skills, problems solving or starting new task;"Factors contributing to work-related difficulties"(HW2), to rate

the degree to which some factors (i.e. noise, brightness of the workplace) impact work activities. Friedman and Wilcoxon repeated measure tests were used for the analysis ($p < .005$), SpermanRho for delta (T0-T3/T6) correlations.
Results: A total of 108 patients (79%females, average age $50y \pm 9$) completed the 6-months evaluation. For each parameters a significant reduction was observed at 3 and 6 months of treatment($p < .001$). MMD decreased from 16.8 ± 6.5 to 8.1 ± 6.2; MMI from 17.8 ± 9.7 to 7.8 ± 6.5; HW1 from 23.8 ± 10.5 to 15.2 ± 10.0; HW2 from 11.3 ± 6.3 to 8.1 ± 5.4. 60 patients out of 108 (56%) reduced monthly headaches by 50% or more, and 29 (27%) by 75% or more. The correlation for HW1 and HW2 is moderate and significant with deltas 0–3 and 0–6 for MMD and MMI.
Conclusion: HW has a parallel reduction with indexes usually used to monitor treatment efficacy in clinical practice, suggesting good reliability and fidelity. Also the observed reductions in MMD, MMI and HW were moderately correlated.With HW we can highlight and evaluate the effectiveness of these treatments in relation to work productivity.
Disclosure of Interest: None Declared

IHC23-PO-118

Headache profiles of patients who were referred to neurology clinics: A subgroup analysis of the Head-MENAA study

Hamit GENC[1], Hayrunnisa Bolay[2], Betul Baykan[3], Derya Uluduz[4], Isin UNAL-CEVIK[5], Najib Kissani[6], Otgonbayar Luvsannorov[7], Mansoureh Togha[8], Asena Ayça Ozdemir[9], Aynur Ozge[10] and The Head-MENAA Study Group[11]

[1]*Gaziantep Dr. Ersin Arslan Training and Research Hospital, Gaziantep, Turkey*
[2]*Gazi University, Medical Faculty, Department of Neurology and Algology, NÖROM, Ankara, Turkey*
[3]*Istanbul University, Istanbul Faculty of Medicine, EMAR Medical Center, Istanbul, Turkey*
[4]*Istanbul University, Cerrahpasa Faculty of Medicine, Istanbul, Turkey*
[5]*Hacettepe University Faculty of Medicine, Ankara, Turkey*
[6]*Neuroscience Research Laboratory in Marrakesh Medical School, Cadi Ayyad University, Marrakech, Morocco*
[7]*Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia*
[8]*Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of*
[9]*University of Mersin, Department of Biostatistics and Medical Informatics, Mersin, Turkey*
[10]*Mersin University Faculty of Medicine, Mersin, Turkey*
[11]*-, -, Turkey*

Objective: The lifetime prevalence of headache disorders is over 90%, one of the most important diseases that cause disability. Since headache is a clinical finding frequently encountered by other physicians except for neurologists, failure to provide a precise diagnosis may affect diagnostic and therapeutic approaches. This situation may increase the disabling effect of headaches and lead to unnecessary consultations. This study primarily aims to define the referred patient profile to optimize diagnostic and therapeutic approaches.
Methods: In this cross-sectional multicenter international study, sixty-nine headache specialists from 13 countries evaluated headache patients who were referred to neurology clinics. Researchers recruited patients on different weekdays selected by the research randomizer program for five consecutive weeks in April and May 2022. The researchers collected data on various factors such as age, sex, headache characteristics, and accompanying symptoms using the Head-MENAA study questionnaire and ICHD-3 criteria. Patients were categorized according to the areas such as emergency service, other services, and private offices in which they were evaluated.
Results: A total of 3722 of 12043 evaluated to neurology clinics on chosen days had headache complaints. 15.07% of the patients with headaches consisted of patients who were referred to neurology. 14.8% (83/561) of patients were referred from emergency services, 16.58 (93/561) from other services, and 68.64% (385/561) were applied to private neurology offices ***(Figure 1)***. The proportion of male patients in the emergency department (49.4%) was higher than the proportion of male patients in other services (26.9%) and private clinics (23.1%) **($p < 0.001$)**. There wasn"t a significant difference between groups regarding mean age ($p = 0.266$). Primary headaches were the reason for consultation in 89.2% of patients in the emergency department, 90.3% of patients in other services, and 93.5% of patients in private clinics. The most common headache subtype was migraine without aura in all groups. TTH rate in patients consulted from other services; was more than in private clinics **($p = 0.047$)**. Headache attributed to psychiatric disorder was observed higher ratio in the emergency service than in the private office **($p = 0.028$)**. There was no difference in the incidence of other headache types in terms of the areas where the patients were evaluated. Headache severity was higher in the emergency services and private offices than in the other services and neurology outpatient clinics **($p < 0.001$)**.

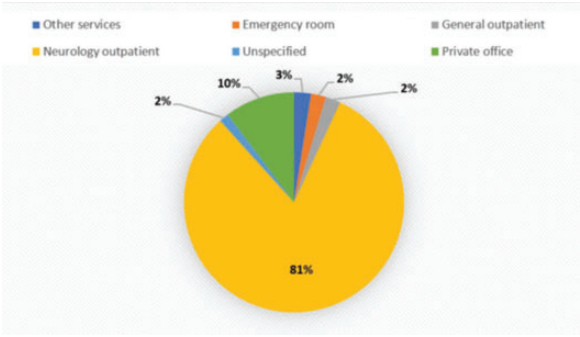


Figure 1: Distribution of patients according to areas where they were evaluated.

Conclusion: According to our study, primary headache disorders consisted of up to 90% of patients with headaches who were referred to neurology clinics, and migraine was the most common headache type. This study can inform that preferences for headache treatment may vary depending on personal characteristics, type, and severity of the headache, as well as accessibility and availability of different treatment options. Also, It can contribute to more effective disease control strategies by identifying critical focus areas and potential challenges.

Keywords: Head-MENAA study, primary headaches, neurology clinics, disease control, emergency service, other services, private office

Disclosure of Interest: None Declared

IHC23-PO-119

Headache-Related Disability Among Medical Students in Nepal: A Cross-Sectional Study

Ayush Chandra[1,2], Avinash Chandra[3] and Sudikshya Acharya[4]

[1]*Pokhara Academy of Health Sciences, Pokhara, Nepal*
[2]*Tianjin Medical University, Tianjin, China*
[3]*National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal*
[4]*Annapurna Neurological Institute and Allied Sciences, Kathmandu, Nepal*

Introduction: Headache is a common health issue that can affect the quality of life and productivity of individuals, including medical students who are exposed to various stressors during their training. Nepal, a country located in South Asia, has a unique cultural and environmental context that may impact the health of medical students. However, there is limited research on the burden of headache-related disability among medical students in Nepal. Therefore, this cross-sectional study aims to investigate the prevalence and impact of headache-related disability among medical students in Nepal.

Methods: A cross-sectional study will be conducted among medical students in Nepal. According to criteria established by the International Headache Society, data will be collected using validated tools such as the HIT-6 questionnaire, which assesses headache-related disability, and the Migraine Disability Assessment (MIDAS) questionnaire, which measures migraine-related disability. The questionnaire will also collect information on socio-demographic characteristics, headache characteristics, and perceived stress levels. Data will be analyzed using descriptive statistics, chi-square test, t-test, and regression analysis as appropriate.

Results: 150 medical students from different medical colleges were evaluated. 21.62% of cases of migraine headache, 10.30% of probable migraine, and 28.35% of tension headaches were detected. 9.51% reported an absence of headache, and another 10.22% had secondary headache. According to the HIT-6 questionnaire, in 5.23% and 12.45% of them, headaches were classified as having substantial to severe impact, respectively.

Conclusion: Tension headache and migraine headaches had higher scores than the other types of headache and, hence, led to higher levels of disability. The present study did not find a significant correlation between student semester, age or extracurricular activities on the impact generated by headache.

Disclosure of Interest: None Declared

IHC23-PO-120

Premonitory Symptoms in Migraine: A REFORM Study

Janu Thuraiaiyah, Håkan Ashina, Rune H. Christensen, Haidar M Al-Khazali, Astrid Wiggers, Faisal M Amin and Messoud Ashina

Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark

Objective: The objective of this cross-sectional study was to compare the relative frequency of premonitory symptoms in people with migraine using two methods (prompted and unprompted) and to investigate the relationship between premonitory symptoms and disease burden.

Methods: Participants with migraine were recruited from a tertiary headache center and were asked to report their premonitory symptoms during a semi-structured interview. They were first asked to report all premonitory symptoms experienced within 2 to 48 hours before the onset of headache or aura (unprompted) followed by a list

of 17 items (prompted). Disease burden was assessed using validated questionnaires including Headache Impact Test (HIT-6), Migraine Disability Assessment (MIDAS) and World Health Organization Disability Assessment 2.0 (WHODAS 2.0).

Results: A total of 632 participants (mean age of 44.6 years, 89% were female, 31% had migraine with aura, 98% has migraine without aura and 60% were diagnosed with chronic migraine) were included in the analysis, of whom 449 (71%) reported at least one premonitory symptom. More participants reported the presence of premonitory symptoms when using the prompted reporting compared to the unprompted (70% vs. 43%). The prompted method revealed a greater number of premonitory symptoms compared to the unprompted method (median: 1 [IQR 0–1] vs. 2 [IQR 0–6], $P < 0.001$). Disease burden was positively correlated with the number of prompted premonitory symptoms as measured by HIT-6 ($\rho = 0.14$; $P < 0.001$) and WHODAS scores ($\rho = 0.09$; $P = 0.041$) but not MIDAS ($\rho = -0.05$; $P = 0.24$).

Conclusion: Our study revealed that a prompted method for assessing premonitory symptoms in individuals with migraine yielded a higher frequency of reported symptoms than using an unprompted method with an open-ended question. This highlights the importance of employing standardized guidelines for evaluating premonitory symptoms in future research, to improve our understanding of the symptoms and their impact on disease burden.

Disclosure of Interest: JT, RHC, HMA and AW report no conflict of interest. HA reports personal fees from Teva, outside of the submitted work. FMA has received personal fees from Pfizer, Teva, Lundbeck, Novartis, Eli Lilly, outside of the submitted work. MA reports receiving personal fees from AbbVie, Amgen, Eli Lilly, Lundbeck, Novartis, Pfizer and Teva Pharmaceuticals outside of the submitted work. MA received institutional grants from Lundbeck Foundation, Novo Nordisk Foundation, and Novartis. MA reports serving as associate editor of Cephalalgia, associate editor of The Journal of Headache and Pain, and associate editor of Brain.

Withdraw

IHC23-PC-121

The global prevalence of migraine, it's subtypes, severity and predictors in the residents of high altitude

Prajjwol Luitel[1], Nishcal Neupane[1] and Rajeev Ojha[2]

[1]*Maharajgunj Medical Campus, Tribhuvan University, Institute of Medicine, Kathmandu, Nepal*
[2]*Department of Neurology, Tribhuvan University, Institute of Medicine, Kathmandu, Nepal*

Objective: The aim of this systematic review was to review the prevalence, predictors, subtypes, and symptom indices (attack frequency, attack length, and pain severity) of migraine at high altitude in order to investigate the relationships between migraine and altitude.

Background: Migraine is a poorly understood common phenomenon. Migraine at high altitude may be erroneously included under acute mountain sickness or chronic mountain sickness.(1) Most studies have estimated the prevalence of migraine among narrowly defined populations and only a few have addressed large samples of population.(2) Among risk factors for headache and migraine, the role of chronic exposure to high altitude has been invoked but is not established so far.(2)

Methods: This systematic review was performed till March 23, 2023 adhering to PRISMA guidelines.(3) Article selection was performed by searching all related articles using appropriate search strategy from inception till date in the electronic bibliographic databases MEDLINE (PubMed), Scopus, and EMBASE. Cross-sectional, prospective study reporting cases or prevalence or incidence of migraine at high altitude with n >2 patients published in the English language as full or abstracts were considered eligible to be included in this review.

Results: This review comprised 8436 individuals from four full-text papers, all being epidemiological studies. Prevalence of migraine at high altitude was 5.3% to 45.5%. Prevalence at high-altitude population was higher (12% vs. 4%) than that of the sea-level population. Median attack frequency of migraine increased from 1.3 to 3.0 days per month from the lowest altitude to 2500 m. Prevalence increased from 30.1% at ages 20–29 years to 36.5% at ages 50–59 years, and dropped to 34.5% after 60 years of age. Migraine with aura was more prevalent than migraine without aura (12% vs. 7%). Migraineurs with aura at an altitude of 1310 m had a significantly elevated hematocrit as compared to migraineurs with aura at sea level (42.2% vs 38.2%).

Conclusions: At high altitude, the prevalence of migraine was 5.3% to 45.5%. Prevalence and symptom severity increased with altitude. Prevalence increased with age till 60 years and dropped thereafter. Migraines with aura were more common than those without. Rising hematocrit was the only predictor of migraine.

Disclosure of Interest: None Declared

Abstract number: IHC23-PO-121

Author name	Country	Time of study	Altitude	Setting	Diagnostic criteria	Total number of cases	Headache prevalence	Migraine prevalence
Arregui	Peru	1994	4300 m	Epidemiological study	IHS	379	47.10%	32.20%
Linde	Nepal	2013	2000 m and above	Multistage stratified nationwide population-based survey	ICHD-3 beta	2100	NA	27.9–45.5%
Jaillard	Peru	NA	3380 m	Epidemiological study	IHS	3246	28.70%	5.30%
Arregui	Peru	1991	4300 m	Epidemiological study	NA	2263	NA	12.40%

ICHD-3 = International Classification of Headache Disorders 3rd edition
IHS = International Headache Society
NA = Not Available

IHC23-PO-122

Comparison between knowledge, attitude, and practice assessment toward migraine patients among doctors: A cohort retrospective study

Cita Mayorita, Selviana Pratiwi, Henry Sofyan, Irma Savitri and Tiara Aninditha

DKI Jakarta, DKI Jakarta, Indonesia

Objective: This research aimed to assess comparison between knowledge, attitude and practice toward migraine patients among specialists and general practitioners in Indonesia.
Methods: A cohort retrospective study was performed among doctors attending national neurology symposium. Data were collected by using a structured questionnaire that consists of 9-items of knowledge, 5-items of attitude and 5-items of practice related migraine patients. Subject's knowledge, attitude and practice data toward migraine patients were divided into 2 groups of general practitioners (GP) and neurologists. All data were analyzed by using SPSS.
Results: The study involved 318 subjects with an average age of 42 years (neurologist) and 28 years (GP) which were dominated by women (65.4%). Both GP and neurologists had good knowledge (94%) and a positive relationship between attitude and practice in the management of abortive migraine at the early onset of symptoms ($P < 0.001$, $r = 0.461$). However, only 24.2% of subjects had good knowledge regarding migraine diagnosis based on International Headache Society (IHS) criteria and only 12.9% of subjects had good knowledge related indications for migraine prophylaxis. 77% of the subjects were familiar about the headache diary (HD), 100% of the subjects agreed that HD was needed for migraine treatment and evaluation but only used by 24.2% subjects in daily practice.
Conclusion: This study showed that more than half of GP and neurologists had poor knowledge regarding migraine diagnosis and indications for prophylaxis administration. There was also a relatively low application rate of HD in daily practices among GP as well as neurologists. Continuous education regarding diagnosis and therapy of migraine may be required to improve knowledge and awareness.
Keywords: migrain, knowledge, attitudes, practice, headache diary
Abbreviation: General Practitioner (GP), Headache Diary (HD), International Headache Society (IHS)
Disclosure of Interest: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

IHC23-PO-123

Weather impact on migraine: an Emergency Department retrospective study

Costanza Sottani[1], Marina Romozzi[1], Eleonora Rollo[1], Paolo Calabresi[1,2], Serenella Servidei[1,2] and Catello Vollono[1,2]

[1]*Dipartimento di Neuroscienze, Università Cattolica del Sacro Cuore, Rome, Italy*
[2]*Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Dipartimento di Neuroscienze, Organi di Senso e Torace, UOC Neurologia, Rome, Italy*

Objective: Migraine is a relapsing, remittent pleomorphic disorder characterized by recurrent attacks that may be triggered or precipitated by several factors. About half of migraineurs identified weather conditions changes as a trigger for the headache onset, or as a cause of worsening of ongoing headache symptoms. Aim of the present study was to assess the influence of some meteorological parameters on migraine attacks.
Methods: We retrospectively evaluated the clinical data of all patients with headache who presented to the Emergency Room (ER) of Policlinico Gemelli from 20th

March 2010 to 20th March 2012. Primary and secondary headaches were classified according to the International Headache Society (IHS) criteria. Weather data were obtained from the Italian National Weather Service, analyzed, and correlated with clinical data, using Spearman's correlation coefficients.

Results: During the 24 months period, 1615 patients with migraine without aura and 127 with migraine with aura were admitted to the ER. Number of emergency admissions were directly correlated with the increase of temperature compared to the previous day and the humidity level two days before the attack, and inversely correlated with the atmospheric pressure two days before.

Conclusion: Our data confirm that a subgroup of migraineurs is highly sensitive to variations of meteorological factors. We could hypothesize that any variation of weather parameters may interfere with neuronal excitability of the trigeminal-vascular system directly, or with structures to it correlated, facilitating the onset of attacks. Alternatively, it could be possible that quantitative variations of trigger factors may enhance the response of migraineurs to environmental stimuli.

Disclosure of Interest: None Declared

IHC23-PO-124

Impact of Chronic Pain on Work Performance and Well-being Among Individuals in Nursing Homes: Initial Insights from Turkey's First Established Facility

Aynur Özge[1], Nil Tekin[2], Halil Çetingök[3], Sera Çetingök[4], Hatice Selin Irmak Yaşar[4], Derya Temiz[5], Istanbul University Department of Gerontology Students[6], Hayal Boyacıoğlu[7] and Esin Karakuş[8]

[1]*Mersin University School of Medicine, Department of Neurology, Mersin, Turkey*
[2]*Health Sciences University, Izmir Faculty of Medicine, Department of Family Medicine, İzmir, Turkey*
[3]*Istanbul University, Istanbul Faculty of Medicine, Algology, Istanbul, Turkey*
[4]*Istanbul University-Cerrahpaşa Faculty of Health Sciences, Department of Gerontology, Istanbul, Turkey*
[5]*Global Migraine and Pain Society, Istanbul, Turkey*
[6]*Istanbul University Department of Gerontology, Istanbul, Turkey*
[7]*Ege University, Faculty of Science, Department of Statistics, İzmir, Turkey*
[8]*Darülaceze Nursing Home Directory, Istanbul, Turkey*

Objective: This study aimed to assess the status of employees with chronic painful conditions at Darulaceze, the first established nursing home in Turkey.

Methods: Research guidelines and forms were developed under the institutional cooperation protocol. Gerontology students, trained by the Global Migraine and Pain Association, aided in online data collection using the Google Forms application. A total of 247 participants took part in the study. Descriptive statistics were used to analyze the data, and chi-square analysis was conducted to examine intergroup relationships.

Results: Among the 247 individuals employed at Darülaceze, 71.7% were aged 31–50, and 55.3% were male. The prevalent chronic health problems reported by the workers were headaches (59.9%) and low back and neck pain (14.9%). Lifetime headache frequency was 90.7%, and current ongoing headache frequency was 44.1%. A statistically significant relationship was found between age and the occurrence of headaches during one's lifetime ($p = 0.032 < 0.05$). Additionally, a statistically significant relationship was found between gender and experiencing headaches within the last three months ($p = 0.001 < 0.05$), with 97% of females and 85% of males reporting headaches. Furthermore, employees reported that headaches negatively affected work performance and disrupted daily activities for 19% of the participants. Pain medication was required by 47% of employees due to pain within the past month. Overall, recurrent body pain was reported by 39.3% of employees, with higher prevalence observed among women ($p = 0.00 < 0.01$). Of these cases, 21.1% were moderate, and 9.3% were severe. The primary cause of pain, as reported by employees, was a lack of physical activity or exercise (10.12%).

Conclusion: Chronic pain and its ineffective management processes significantly impact the productivity and well-being of employees in elderly care centers. This study provides the first evaluation of painful conditions among nursing home workers in Turkey. Detailed analysis of various factors such as pain causes, headache frequency, and age and gender differences is believed to contribute to alleviating the burden of care.

Disclosure of Interest: None Declared

IHC23-PO-125

Identifying Chronic Pain among Residents of Darulaceze Nursing Home: Preliminary Findings from Turkey's First Established Institution

Aynur Özge[1], Nil Tekin[2], Halil Çetingök[3], Sera Yiğiter Çetingök[4], Hatice Selin Irmak Yaşar[4], Derya Temiz[5], Istanbul University Department of Gerontology Students[6], Hayal Boyacıoğlu[7] and Esin Karakuş[8]

[1]*Mersin University School of Medicine, Department of Neurology, Mersin, Turkey*
[2]*Health Sciences University, Izmir Faculty of Medicine, Department of Family Medicine, İzmir, Turkey*
[3]*Istanbul University, Istanbul Faculty of Medicine, Algology, Istanbul, Turkey*
[4]*Istanbul University-Cerrahpaşa Faculty of Health Sciences, Department of Gerontology, Istanbul, Turkey*
[5]*Global Migraine and Pain Society, Istanbul, Turkey*
[6]*Istanbul University Department of Gerontology, Istanbul, Turkey*
[7]*Ege University, Faculty of Science, Department of Statistics, İzmir, Turkey*
[8]*Darülaceze Nursing Home Directory, Istanbul, Turkey*

Objective: The inadequate and ineffective treatment of pain worldwide has a detrimental impact on the quality of life of the elderly and places an increased burden on caregivers. This study aimed to assess the prevalence of chronic painful conditions among residents of Darülaceze, the first established nursing home in Turkey.
Methods: Research guidelines and forms were developed in accordance with the institutional cooperation protocol. Gerontology students, trained by the Global Migraine and Pain Association, assisted in data collection using both online and face-to-face methods, utilizing the Google Forms application. The collected data were analyzed appropriately.
Results: Among the 142 elderly individuals residing in Darülaceze Nursing Home, 63.4% were between 66 and 84 years old, and 69% were male. Approximately 35.2% had been living in the facility for 1–5 years. A substantial 88.8% of the residents reported experiencing some form of pain throughout their lifetime. Of these, 23.9% described experiencing current pain for 1–5 days, while 17.7% reported short-lived pain lasting from minutes to one hour. A significant relationship was observed between the average duration of headaches and gender ($0.027 < 0.05$). While 87.3% of the respondents indicated having experienced a headache at some point in their lives, the rate of residents with headaches in the past 3 months was 34.3%. Moreover, 21.1% reported using painkillers and/or migraine medication to alleviate their headaches. Recurrent body aches were described by 58.5% of the elderly population. Approximately 42.3% of the respondents stated that their quality of life had been negatively impacted by pain. However, no significant relationship was found between the effect of pain on quality of life and age ($p = 0.608 > 0.05$). Interestingly, a similar proportion of the elderly (26.7%) believed that pain is a natural consequence of aging, while one third (30.2%) believed that the pain would never dissipate.
Conclusion: Pain among the elderly remains an issue that is often overlooked despite the advancements in modern medicine, resulting in insufficient awareness and rational solutions. This first-of-its-kind study in our country highlights the need for increased efforts in raising awareness and developing effective solutions, emphasizing the importance of international cooperation in addressing this pressing issue.
Disclosure of Interest: None Declared

IHC23-PO-126

Prevalence and disability of migraine among medical staff

Suzuka Toi[1], Tatsuya Monzen[1] and Fumihiko Sakai[2]

[1]*Ota Memorial Hospital, Ota, Japan*
[2]*Saitama International Headache Center, Saitama, Japan*

Object: The annual prevalence of migraine in Japan is reported to be 8.4%. There is a possibility that the social and economic loss due to absenteeism and presenteeism will be greater among medical staff than that of general population. Workers at the hospital are nurses, and many women in their 20s to 50s of high prevalence of migraine. We conducted a questionnaire survey at the hospital and evaluated the social and economic loss by migraine among workers.
Method: At the time of the annual health checkup for employees (total of 967 workers: 674 females, 293 males) held in February 2022, we conducted two types of self-administered questionnaires, a questionnaire on headache prepared by our department and HIT-6.
Result: A total of 584 responded (401 females and 183 males). The recovery rate was 60.4%. The overall mean age of valid responses was 38.5 years(female: 38.4, male: 38.5). Of these workers, 237 (195 females, 42 males) met the diagnostic criteria for migraine. The average HIT-6 score was 55.3, HIT-6 above 50 were recommended to visit physician, but only 67 actually visited clinic for headache. 170 people (71.1%) suffered from absenteeism, but only 43 people reported presenteeism.
Conclusion: While the prevalence of migraine is high among workers at medical institutions, there are few

who ask for sick to have a rest or see a doctor. It was suggested that there is a high possibility that migraine is not diagnosed or is not considered to be a disabling disease. Social and economic losses by migraine is not aware well enough to advocate sufferers of migraine.

IHC23-PO-127

Day-to-day changes in headache frequency in patients with migraine peri-COVID-19 infection

Jiunn-Tyng Yeh[1], Yen-Feng Wang[2], Yi-Shiang Tzeng[2], Shih-Pin Chen[2], Li-Ling Hope Pan[3] and Shuu-Jiun Wang[2]

[1]*Department of Internal Medicine, Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan*
[2]*Department of Neurology, The Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*

Objective: Headache is a common symptom during the COVID-19 infection. However, the changes in the headache pattern in migraine patients during infection are unclear. In this study, we utilized the headache diary of the migraine patient to investigate the effect of COVID-19 infection on headache.
Methods: Migraine patients with documented COVID-19 infection and headache diaries were enrolled. A Bayesian change-point detection algorithm was used to identify the changes in daily headache or migraine frequencies of this cohort from 28 days before (day -28) to 28 days after (day 28) the infection. The headache and migraine frequencies were grouped into pre-, peri- and post-infection periods if potential change-points were detected, and then compared using ANOVA followed by Tukey's test. The frequencies of analgesics usage were also analyzed.
Results: A total of 463 patients with 93 males and a median age of 41 were enrolled. The change-point algorithm identified changes in headache frequencies on day -4 and day 12. For migraine, the change points were day -2 and day 11. After the grouping based on these change points, the headache and migraine frequencies in the peri-infection period increased by $\sim$20% compared with those of pre- and post-infection periods ($p < 0.05$), whereas the frequencies of pre- and post-infection periods were similar. We then stratified the cohort by gender and age 40. For the female patients, the change points were identical to the original cohort, and the frequencies of headache and migraine for the peri-infection period also increased by $\sim$20% ($p < 0.05$). In contrast, no change points were found for male patients. Those older than 40 years exhibited a delayed peri-infection period (day -2 to 14 for headache, and day 2 to 11 for migraine) with a $\sim$20% ($p < 0.05$) increase in frequencies compared with pre- and post-infection, whereas patients younger than 40 showed no significant changes. For the frequencies for analgesics use, we found a $\sim$2-fold increase since day -4 ($p < 0.05$).
Conclusion: In migraine patients, we found significant increases in headache and migraine frequencies and analgesics usage during acute COVID-19 infection, especially for females and those older than 40. Delayed diagnosis of COVID-19 may occur for up to 4 days in our migraine patients.
Disclosure of Interest: None Declared

IHC23-PO-128

Prevalence of headache in patients with Influenza infection: A twelve-surveillance seasons study

Laura Santana López[1], Jose Eugenio Lozano Alonso[2], Ana Ordax Díez[2], Ivan Sanz Muñoz[3], Yesica Gonzalez Osorio[1], Silvia Rojo Rello[4], José María Eiros Bouza[4], Javier Sánchez Martínez[5], Diego Macías Saint-Gerons[6], Álvaro Sierra[1], Andrea Recio García[1], Ángel Guerrero Peral[1] and David García-Azorín[1]

[1]*Department of Neurology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[2]*Dirección General de Salud Pública/Consejería de Sanidad/ Junta de Castilla y León, Valladolid, Spain*
[3]*National Influenza Centre, Valladolid, Spain, Valladolid, Spain*
[4]*Department of Microbiology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[5]*Centro Nacional de Gripe de Valladolid, Hospital Clínico Universitario Valladolid, Valladolid, Spain*
[6]*Department of Medicine, University of Valencia; INCLIVA Health Research Institute and CIBERSAM, Valencia, Spain, Valencia, Spain*

Objective: Headache is a common symptom in systemic infections. We aimed to evaluate the prevalence of headache in patients with influenza.
Methods: Observational study with cross-sectional design. The study population was the population surveyed by the Acute Respiratory Infection Surveillance Network. Approximately 100 healthcare providers conduct active monitoring over a population of 27,074–58,299 people. The eligibility criteria were: 1) acute respiratory illness with onset during the last seven days; 2) presence of at least one of the following symptoms: fever, malaise, headache, or myalgia; 3) presence of at least one of the following symptoms: cough, odynophagia and/or dyspnea. The study was done including twelve consecutive influenza seasons, from 2010–2011 to 2021–2022. The following variables were included: type of diagnosis (clinical vs.

microbiologically confirmed), sex, age, and prior vaccination status. Prevalence of headache was estimated as the proportion of patients who reported headache during the course of the Influenza disease over the total of patients, including the 95% confidence interval (CI).
Results: During the study period 8171 fulfilled the eligibility criteria. Headache was reported by 5402/8171 (66.11%; 95% CI: 65.07–67.14%) of Influenza patients. The prevalence varied between 49.6% (season 2021–2022) and 80.1% (season 2010–2011). Headache was present in 997/1671 (59.7%) cases with a confirmed influenza infection. There were subtle differences regarding patients'' sex (women: 67.93% vs. men 65.76%; $p = 0.0379$); and no differences regarding the vaccination status (65.01% vs. 65.51%; $p = 0.845$). The age group with the lowest prevalence was 00–04 years (33.51%), and the highest was observed in patients aged 15–24 (78.26%).
Conclusion: Headache is a highly prevalent symptom in patients with influenza. The prevalence remains high, regardless of patients'' sex or vaccination status.
Disclosure of Interest: None Declared

IHC23-PO-129

Secondary Headache Disorders in Turkey, the Middle East, Asia, and Africa: A Cross-Sectional, Multicenter Study

Ahmet Evlice[1], Hamit Genc[2], Derya Uludüz[3], Betül Baykan[4], Hayrunisa Bolay[5], Işıl Ünal Çevik[6], Najib Kissani[7], Otgonbayar Luvsannorov[8], Mansoureh Togha[9], Aynur Ozge[10] and Head-MENAA study group[10]

[1]*Cukurova University Faculty of Medicine, Department of Neurology, Adana, Turkey*
[2]*University of Health Sciences, Van Training and Research Hospital, Department of Neurology, Van, Turkey*
[3]*Istanbul University, Cerrahpasa Faculty of Medicine, Department of Neurology, istanbul, Turkey*
[4]*Istanbul University, Istanbul Faculty of Medicine, EMAR Medical Center, istanbul, Turkey*
[5]*Gazi University Faculty of Medicine, Department of Neurology, Ankara, Turkey*
[6]*Hacettepe University Faculty of Medicine, Department of Neurology, Ankara, Turkey*
[7]*Neuroscience Research Laboratory in Marrakesh Medical School, Cadi Ayyad University, Marrakesh, Morocco*
[8]*Mongolian National University of Medical Sciences, Department of Neurology, Mongolia, Mongolia*
[9]*Tehran University of Medical Sciences, Department of Neurology, Tehran, Iran, Islamic Republic of*
[10]*Mersin University Faculty of Medicine, Department of Neurology, Mersin, Turkey*

Background: The aim of this multicenter cross-sectional study was to determine the prevalence and characteristics of secondary headaches in different geographic regions, including Turkey, the Middle East, Asia, and Africa.
Methods: The patients diagnosed with secondary headaches according to the ICHD-3 criteria were included ($n = 1249$) from Turkey ($n = 1039$), Middle East ($n = 80$), Asia ($n = 51$), and Africa ($n = 79$). The study was conducted in two stages. In the first stage, the data of secondary headaches were compared between the regions. In the second stage, the sub-diagnoses of secondary headaches were analyzed only in Turkey.
Results: The prevalence of secondary headaches did not differ significantly between the regions ($p > 0.05$). The most common subtype of secondary headaches was headache attributed to substance or its withdrawal in all regions. There was a female predominance in all regions, but it was lower in Africa than in Turkey. The severity and frequency of headaches differed significantly between the regions, with African patients reporting milder pain than patients from other regions. In Turkey, the most common sub-diagnoses of secondary headaches were medication overuse headache (MOH), idiopathic intracranial hypertension (IIH), and cervicogenic headache (CGH).
Conclusion: Headache attributed to substance or its withdrawal was the most common subtype of secondary headaches in Turkey, the Middle East, Asia, and Africa. The female predominance of secondary headaches was lower in Africa than in Turkey. The severity and frequency of headaches differed significantly between regions, with African patients reporting milder pain.
Disclosure of Interest: Acknowledgments We thank the Global Migraine and Pain Society for collaboration. Funding information The authors did not receive support from any organization for the submitted work.

IHC23-PO-130

Characterizing healthcare utilization patterns in a Danish population with headache: Results from the nationwide Headache in Denmark (HINDER) panel

Thien Phu Do[1,2,3], Mikala Dømgaard[2], Simon Stefansen[2], Timothy Steiner[3,4,5] and Messoud Ashina[1,2,3]

[1]*Danish Headache Center, Copenhagen, Denmark*
[2]*Danish Knowledge Center On Headache Disorders, Glostrup, Denmark*
[3]*University of Copenhagen, Copenhagen, Denmark*
[4]*Norwegian University of Science and Technology, Trondheim, Norway*
[5]*Imperial College London, London, United Kingdom*

Objective: Worldwide, far from all of those who would benefit make use of headache services, largely because of clinical, social, and political barriers to access. Our purpose here is better to characterize healthcare utilization patterns in Denmark.
Methods: The Headache in Denmark (HINDER) study is a nationwide cross-sectional survey of people with headache, conducted using SurveyXact (Rambøll Group A/S, Copenhagen). Healthcare utilization was assessed in a study sample generated by population screening and recruitment. Data collection occurred over two weeks, from September 23rd until October 4th, 2021. The questions enquired into disease characteristics, management, burden, medication intake and healthcare utilization.
Results: The number of participants included in the HINDER panel was 4,431, with 2,990 (67.5%: 2,522 [84.3%] female, 468 [15.7%] male; mean age 40.9 ± 11.6 years) completing the survey. One quarter of participants (27.7%) disagreed or strongly disagreed that they were able to manage their headache attacks. Most participants (81.7%) agreed or strongly agreed that their headache was a burden in their everyday lives. The most reported acute medications, by 87.2% of participants, were simple analgesics; of note, 8.6% reported using opioids for their headache. One quarter of participants (24.4%) had never consulted a medical doctor for their headache; one in six (16.5%: more than two thirds of the 24.4%) had never done so despite agreeing or strongly agreeing that their headache was a burden in their everyday lives. Two thirds (65.3%) of participants overall, and almost three quarters (72.4%) of those with weekly headache, had tried one or more complementary or alternative therapies outside conventional medical care.
Conclusions: Our findings are indicative of inadequate delivery of headache care in a country that provides free and universal coverage for all its residents. The implications are twofold. First, it is not sufficient merely to make services available: public education and increased awareness are necessary to encourage uptake by those who would benefit. Second, educational interventions in both pre- and postgraduate settings are necessary, but a prerequisite for these is a resetting of policy priorities, properly to reflect the very high population ill-health burden of headache.
Disclosure of Interest: Thien Phu Do has received honoraria or personal fees from Teva for lecturing. Mikala Dømgaard reports no conflicts of interest. Simon Stefansen reports no conflicts of interest. Timothy J. Steiner reports no conflicts of interest. Messoud Ashina is a consultant, speaker, or scientific advisor for AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva and a primary investigator for ongoing AbbVie/Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva trials. Messoud Ashina has no ownership interest and does not own stocks of any pharmaceutical company. Messoud Ashina serves as associate editor of Cephalalgia, associate editor of the Journal of Headache and Pain, and associate editor of Brain.

IHC23-PO-131

Design of the ContemporAry ProspecTive Understanding of Migraine Real-world Evidence (CAPTURE) Study

Michel Lanteri-Minet[1], Cristina Tassorelli[2], Messoud Ashina[3,4], Peter J. Goadsby[5,6], Zaza Katsarava[7], Manjit Matharu[8], Mario Peres[9], Richard J. Stark[10], Jessica Ailani[11], Elizabeth Leroux[12], Laurent Delahaye[13], Huy Ha[14] and Patricia Pozo-Rosich[15]

[1]*Pain Department and FHU InovPain, CHU Nice and Côte Azur University, Nice, France*
[2]*Headache Science Centre, C. Mondino Foundation and University of Pavia, Pavia, Italy*
[3]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark*
[4]*Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*
[5]*King's College London, London, United Kingdom*
[6]*University of California, Los Angeles, CA, USA*
[7]*Evangelical Hospital Unna, Unna, Germany*
[8]*Queen Square Institute of Neurology, London, United Kingdom*
[9]*University of São Paulo, São Paulo, Brazil*
[10]*Alfred Hospital and Monash University Melbourne, VIC, Australia*
[11]*MedStar, Georgetown University Hospital, Washington, DC, USA*
[12]*Brunswick Medical Center, Montreal, QC, Canada*
[13]*AbbVie, Rungis, France*
[14]*AbbVie, Toronto, ONT, Canada*
[15]*Headache Unit, Neurology Department, Vall d'Hebron University Hospital; Headache and Neurological Pain Research Group, Vall d'Hebron Institute of Research, Universitat Autonoma de Barcelona, Barcelona, Spain*

Objective: To fill a gap in the longitudinal evidence describing the impact of migraine, this global study will assess how headache/migraine frequency, disability, and treatment patterns change over a 2-year period in individuals being treated for migraine.
Methods: ContemporAry ProspecTive Understanding of Migraine Real-world Evidence Study (CAPTURE) is a 2-year, global, observational, longitudinal, prospective study that will enroll individuals $>=18$ years of age being treated for migraine. Participants will be stratified into 3 baseline monthly headache day (MHD) cohorts: 4–7 days; 8–14 days; $>=15$ days. Eligibility criteria include

men/women diagnosed with migraine for >=1 year, <=50 years of age at migraine onset, taking >=1 migraine medication, and a history of >=4 MHDs in the 3 months prior to screening, which was confirmed prospectively with headache e-diary data in the 30-day screening period. The burden of illness in migraine will be evaluated every 3 months beginning with the baseline visit until the end of the study (i.e., 24 months). Visits will be clinical visits, aside from the month 9, 15, and 21, to be conducted over the phone. Key study design elements and endpoints are depicted in the Table.

Results: The target enrolled sample size is approximately 2000 (cohort 1: 30% [n = 600]; cohorts 2–3: 35% [n = 700 each]). Patients will be enrolled from approximately 135 sites in 15 countries. The target for first patient enrollment is early 2023 and the last patient completion date is anticipated to be late 2025. The study will collect clinical outcomes, patient-reported outcomes, and changes in the number of patients among the migraine cohorts. Only the methodology of this study will be described.

Conclusion: CAPTURE will provide a better understanding of headache/migraine frequency, disability, and treatment patterns in individuals being treated for migraine and will be one of the first global prospective longitudinal studies of its kind.

Abbreviations: HAD-S, Hospital Anxiety and Depression Scale; HIT-6, Headache Impact Test-6; MIBS-4, Migraine Interictal Burden Scale-4; MIDAS, Migraine Disability Assessment; MSQ v2.1, Migraine-Specific Quality of Life Questionnaire version 2.1; mTOQ-6, Migraine Treatment Optimization Questionnaire-6; PGI-S, Patient Global Impression – Severity; WPAI, Work Productivity and Activity Impairment Questionnaire.

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Table. Study Populations and Endpoints

Cohorts	**Definition**
Cohort 1 (30% [n = 600])	4–7 headache days/month
Cohort 2 (35% [n = 700])	8–14 headache days/month
Cohort 3 (35% [n = 700])	≥15 headache days/month
Endpoints	**Timepoints Assessed**
E-diary Outcomes	
Change from baseline in:	
Monthly headache days	Months 3, 6, 9, 12, 15, 18, 21, and 24
Monthly migraine days	
Monthly acute medication use days	
Patient-Reported Outcomes	
Change from baseline in:	
HIT-6	Months 3, 6, 12, 18, and 24
MSQ v2.1 Role Function–Restrictive, Role Function–Preventive, Emotional Function domain scores	
WPAI:MIGRAINE Absenteeism, Presenteeism, Overall work productivity loss, and Activity impairment	
PGI-S score	
HAD-S	
mTOQ-6	
MIBS-4	
MIDAS total score	
Changes Among Migraine Cohorts	
Number of patients changing among migraine cohorts	Months 12 and 24
Switching from current to subsequent migraine treatment	Months 6, 12, 18, and 24
Switching from monotherapy to combination therapies	

Medtronic, Novartis, Pfizer, ReckittBenckiser, Saint-Jude, Sanofi-Aventis, SUN Pharma, Teva, UPSA, Zambon. He has received research grants from the French Ministry of Health, the French Pain Society, the APICIL Foundation, and the Migraine Research Foundation. He has served as an associate editor for The Journal of Headache and Pain. Cristina Tassorelli, MD, PhD, has participated in advisory boards for AbbVie, Dompé, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva. She has lectured at symposia sponsored by AbbVie, Eli Lilly, Novartis, and Teva. She is principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva. She has received research grants from the European Commission, the Italian Ministry of Health, the Migraine Research Foundation, and the Italian Multiple Sclerosis Foundation. She serves as an associate editor for Cephalalgia and The Journal of Headache and Pain. Messoud Ashina, MD, PhD, DMSc, reports personal fees from AbbVie, Amgen, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva; has received research funding from Lundbeck Foundation, Novo Nordisk Foundation, and Novartis; and serves as an associate editor for Cephalalgia, an associate editor for The Journal of Headache and Pain, and associate editor for Brain. Peter J. Goadsby, MD, PhD, DSc, reports personal fees from AbbVie; grants and personal fees from Eli Lilly; a grant from Celgene; personal fees from Aeon Biopharma, Biohaven Pharmaceuticals, CoolTech, Dr Reddy's, Epalex, Impel NeuroPharma, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, and Teva; personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI MedPartners, and Vector Metric; fees for educational materials from CME Outfitters, Omnia Education, and WebMD; publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UpToDate, and Wolters Kluwer; and fees for medicolegal advice in headache. Zaza Katsarava, MD, has been a speaker and/or consultant for, and/or received research support from, Allergan, Amgen/Novartis, Eli Lilly, Merck, and Teva. Manjit Matharu, MD, serves on advisory boards for Abbott, AbbVie, Eli Lilly, Medtronic, Salvia, and Teva; has received payment for the development of educational presentations from AbbVie, Eli Lilly, and Teva; and has received research grants from Abbott, Medtronic, and Ehlers Danlos Society. Mario Peres, MD, PhD, has received personal fees as a consultant for AbbVie, Ache, Eli Lilly, Eurofarma, Libbs, Lundbeck, Novartis, Pfizer, Sanofi-Aventis, and Teva Pharmaceuticals. Richard Stark, MB, BS, FRACP, has received speaker fees and consulting fees from Allergan/Abbvie, Eli Lilly, Lundbeck, Pfizer and Teva. Jessica Ailani, MD, has served as a consultant for AbbVie, Aeon, Amgen, Biohaven, Eli Lilly, GlaxoSmithKline, Impel, Lundbeck, Miravo, Nesos, Neurolief, Pfizer, Satsuma, Teva, and Theranica; received stock options from CtrlM; provided editorial services to Current Pain and Headache Reports, SELF, and Medscape; and received clinical trial support from AbbVie, Biohaven, Eli Lilly, Satsuma, and Zosano. Elizabeth Leroux, MD, has received speaker fees and consulting fees from Allergan/AbbVie, Eli Lilly, Lundbeck, and Teva Neuroscience; consulting fees from Aralez Pharmaceuticals, Lin-Pharmaceuticals, McKesson Canada, Medscape, and Paladin; speaking fees, consulting, and reimbursement for travel from Novartis; and reimbursement for travel from IHS-GPAC. Laurent Delahaye, PhD, and Huy Ha, RPh, are employees of AbbVie and may hold AbbVie stock.

IHC23-PO-132

Subjective Cognitive Impairment During Migraine or Severe Headaches: Multi-country Results From the CaMEO-International Study

Richard B. Lipton[1], Kristina Fanning[2], Sait Ashina[3], Elizabeth Seng[4], Manjit Matharu[4], Brett Dabruzzo[5], Katherine Sommer[6], Michael Seminerio[7] and Dawn C. Buse[1]

[1]*Albert Einstein College of Medicine, Bronx, NY, USA*
[2]*MIST Research, Wilmington, NC, USA*
[3]*Department of Neurology and Department of Anesthesia, Critical Care and Pain Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA, USA*
[4]*Institute of Neurology, London, United Kingdom*
[5]*AbbVie, Madison, NJ, USA*
[6]*AbbVie, Irvine, CA, USA*
[7]*AbbVie, North Chicago, IL, USA*

Objective: Although symptoms of cognitive impairment, such as difficulty thinking, reasoning, or remembering, are common among people with migraine, they are not cardinal symptoms included in the diagnostic criteria. Cognitive difficulties occur most commonly in the premonitory and headache phases but may also occur in the postdrome and the inter-ictal phases. The objective of this analysis is to describe subjective cognitive impairment during migraine attacks or severe headaches in a representative international sample of people with migraine.

Methods: Chronic Migraine Epidemiology and Outcomes – International (CaMEO-I) was a cross-sectional, web-based survey conducted in 2021 in Canada, France, Germany, Japan, the United Kingdom (UK), and the United States (US). A validated questionnaire (the American Migraine Study/American Migraine Prevalence and Prevention study diagnostic questionnaire) identified respondents with migraine, based on modified *International Classification of Headache Disorders*, 3rd edition, criteria. In this analysis, using the subjective Migraine Cognitive Impairment Questionnaire, 6 questions related to the frequency of subjective cognitive impairment during migraine

Table. Subjective Cognitive Impairment During Migraine Attacks Across Countries

	US (N = 2404)	Canada (N = 2382)	Germany (N = 2397)	France (N = 2464)	UK (N = 2436)	Japan (N = 2409)	Total (14,492)
1st Category	28.6%	28.5%	31.8%	31.4%	26.4%	32.7%	29.9%
2nd Category	22.7%	26.8%	27.6%	28.4%	21.8%	34.5%	27.0%
3rd Category	18.5%	18.0%	20.3%	19.4%	19.5%	19.1%	19.1%
4th Category	30.2%	26.7%	20.3%	20.7%	32.2%	13.7%	24.0%
Chi^2 (vs US)	NA	13.742	64.798	62.616	4.623	216.556	368.050[a]
P value (vs US)	NA	0.003	<0.001	<0.001	0.202	<0.001	<0.001[a]

[a]Chi^2 test among all 6 countries.

attacks or severe headaches were assessed. We asked about severe headache because severe headaches in people with migraine are almost always migraine, whether or not the participant knows the term. Responses ranged from "never" (0), "rarely" (1), "less than half the time" (2), to "half the time or more" (3). Items were summed and rescaled to have a range of 0 to 100. Using the pooled sample (N = 14,492), quartile scores were calculated to represent ordered categories of subjective cognitive impairment: 1st quartile: ≤33.33, 2nd quartile: 33.33–55.56, 3rd quartile: 55.57–72.22, and 4th quartile: >72.22. Using an overall chi-square test and paired country chi-square testing, differences in cognitive impairment quartiles across the 6 countries were tested.

Results: The proportion of people with migraine reporting subjective cognitive impairment occurring "more than rarely" varied by symptom of cognitive impairment and among countries. In total, 11,752 of 14,492 (81.1%) individuals reported at least one symptom of cognitive impairment more than rarely. The proportion of people with migraine with particular symptoms of cognitive impairment averaged across the countries studied was 74.1% for difficulty concentrating, 62.6% for trouble thinking clearly, 57.8% for difficulty remembering things, 49.8% for trouble recalling words, 39.9% for confusion, and 29.0% for getting easily lost. Overall, the proportion of people with subjective cognitive impairment during migraine attacks was lowest in Japan and highest in the UK based on the percentage of respondents in the highest (4th) category of cognitive complaints (13.7% and 32.2%, respectively; **Table**). The difference among countries in the overall distribution of cognitive impairment was statistically significant (Chi-squared = 368.1, $P < 0.001$). Paired post hoc comparisons with the US revealed that the distribution of cognitive impairment did not differ between the US and UK. People in the US had greater cognitive impairment during migraine attacks compared with all the other countries besides the UK (all $P < 0.01$).

Conclusion: Among people with migraine, subjective cognitive impairment during migraine attacks was common across all 6 countries. Difficulty concentrating and trouble thinking clearly were the most commonly reported subjective cognitive impairments in each country. Differences among countries on subjective cognitive impairment during migraine attacks may reflect differences in language and culture or differences in the use of medication, among other factors.

Disclosure of Interest: Allergan (prior to its acquisition by AbbVie) Disclosures: Richard B. Lipton, MD, has received research support from the National Institutes of Health, the FDA, and the National Headache Foundation. He serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee. Kristina Fanning, PhD, is Managing Director of MIST Research which has received research funding from AbbVie, Allay Lamp, GlaxoSmithKline, Juva Health, and NYC Langone Health via grants to the National Headache Foundation. Sait Ashina, MD, has received honoraria for consulting from AbbVie/Allergan, Amgen, Biohaven, Eli Lilly, Impel NeuroPharma, Lundbeck, Novartis, Percept, Satsuma, Supernus, Teva, and Theranica. Elizabeth Seng has consulted for Click Therapeutics and GlaxoSmithKline and has served on an advisory board for AbbVie and for Theranica. Manjit Matharu, MD, serves on the advisory board for Abbott, Allergan, Eli Lilly, Medtronic, Novartis, and Teva, and has received payment for the development of educational presentations from Allergan, electroCore, Eli Lilly, Novartis, and Teva. Dawn C. Buse, PhD, has received grant support and honoraria from AbbVie, Amgen, Biohaven, Eli Lilly and Company, Collegium, Lundbeck, and Teva and for work on the editorial board of Current Pain and Headache Reports. Brett Dabruzzo, PharmD, Katherine Sommer, PhD, and Michael Seminerio, PhD, are employees of AbbVie and may hold AbbVie stock.

IHC23-PO-133

Association of Hypertension with Pain Intensity in Migraineurs: A Cross-sectional Study

Yu-Chen Cheng

Fu Jen Catholic University Hospital, New Taipei City, Taiwan

Objective: Hypertension and migraine are both public health concerns. While hypertension has been linked to chronic pain condition, the relationship between hypertension and migraine remains controversial. We aimed to investigate the relationship between migraine, hypertension, and pain intensity.

Methods: Cross-sectional data from the New York City Longitudinal Survey of Well-Being (Poverty Tracker), 2015–2018 were analyzed. In-person interviews were conducted with 3908 adults ages $\geq$18 years. Prevalence of hypertension was evaluated in migraineurs and non-migraineurs. Linear regression was used to examine the associations of pain intensity and hypertension in migraineurs, after adjusting for demographic factors, psychological factors, and comorbidities.

Results: In total, 3449 participants were enrolled in our study, of whom 492 (14.27%) had a migraine history. The prevalence of hypertension did not differ between migraineurs and non-migraineurs (36.59% versus 32.81%, $p = 0.100$). After adjusting for covariates, pain intensity was positively associated with hypertension ($\beta = 0.495$, $SE = 0.248$, $p = 0.047$) in migraineurs.

Conclusions: Although the prevalence of hypertension did not differ between migraineurs and non-migraineurs, our findings suggest that hypertension may contribute to pain intensity in migraineurs. These results highlight the potential for a shared underlying mechanism between hypertension and migraine, which warrants further investigation. Regular assessment and management of hypertension could enhance treatment outcomes in headache clinics.

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IHC23-PO-134

Mental Health Conditions and Headache Frequency Using the National Health Interview Survey (NHIS) 2019 – A Descriptive Analysis

Jenny Lee[1], Karla Minota[1], Joshua Li[2], Keren Chen[2], Nicholas Jackson[2], Andrew Charles[1] and Adys Mendizabal[1]

[1]*Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, USA*
[2]*Department of Medicine Statistics Core, David Geffen School of Medicine at UCLA, Los Angeles, USA*

Objectives: Previous studies have shown significant comorbidity of headache disorders and psychiatric conditions. Prior research has also demonstrated a strong association between migraine and a number of social determinants of health (SDH), but the specific mechanisms underlying these associations remain poorly understood. We aimed to evaluate the relationship between anxiety and depression severity and headache frequency and to identify sociodemographic factors associated with this relationship.

Methods: This cross-sectional study used the 2019 National Health Interview Survey (NHIS) data from adult respondents aged 18 and older. Respondents reported a diagnosis of anxiety and depression and disease severity as measured by the GAD7 and PHQ9. Respondents also reported headache frequency in the previous three months. Multivariable logistic regression models assessed the association of frequent headache with anxiety, depression, and SDH, including sex, age, race, region, household income, level of education, and insurance status.

Results: Among 31,603 respondents, 6,540 and 7,540 had a history of current anxiety and depression, respectively. Of them, 24.3% and 23.6% reported frequent headache. Severe anxiety and depression were both associated with a greater frequency headache. Females, individuals in the lowest income quartile, uninsured respondents, and those with military or Medicaid insurance had higher odds of reporting frequent headache (OR 2.6, 1.52, $p < 0.001$ and 1.54, 1.53, 2.34 $p < 0.05$). Factors associated with lower odds of frequent headache included high-income quartile, and higher educational attainment (OR 0.73, 0.73, $p < 0.001$).

Conclusion: Anxiety and depression diagnosis and severity were associated with headache frequency even after adjusting for sociodemographic factors. SDH, such as income and level of education, were tied to a higher frequency of headache. It is imperative to acknowledge the impact of SDH on those with mental health disorders and headache and to better understand the interactions between these factors to optimize patient care.

Disclosure of Interest: None Declared

IHC23-PO-135

Retrospective analysis of patients seen at an Australian Headache Clinic

Brett Travers and Benjamin Tsang

Sunshine Coast University Hospital, Birtinya, Australia

Objectives: A growing number of headache clinics exist in Australia for specialist management of complex headache disorders. Previous international data have shown that before specialist review there is low use of headache preventative treatments and high rates of analgesic medication overuse. This study aims to characterize the patients seen in an Australian headache clinic, with particular emphasis on these two issues.
Methods: A retrospective analysis of all patients seen at a tertiary hospital headache clinic was completed over a four-and-a-half-year period. Data were collected from electronic medical record notes. The details recorded include patient demographics, final headache diagnosis, presence of medication overuse, previous preventer medication use, and brain imaging performed.
Results: 425 sequential patients were reviewed from July 2017 to December 2021. 80% were female with median age of 44 years. 35% had not received a formal diagnosis prior to clinic other than 'headache'. The final clinic diagnosis by ICHD-3b criteria was a class 1 headache (migraine) in 91%. Medication overuse was present in 46% – most commonly with simple analgesia (17%) or combination analgesia (15%). 41% had not trialled any preventer medication before the clinic, and 14% more had inadequate preventer trials (defined as less than 3 months use or inadequate dosage of a single appropriate medication). 91% had brain imaging pre-clinic with incidental findings in 34%.
Conclusions: Significant potential exists to improve primary care headache treatment in Australia. Increased knowledge of medication overuse and first line preventer medications would be the first steps towards this.
Disclosure of Interest: None Declared

IHC23-PO-136

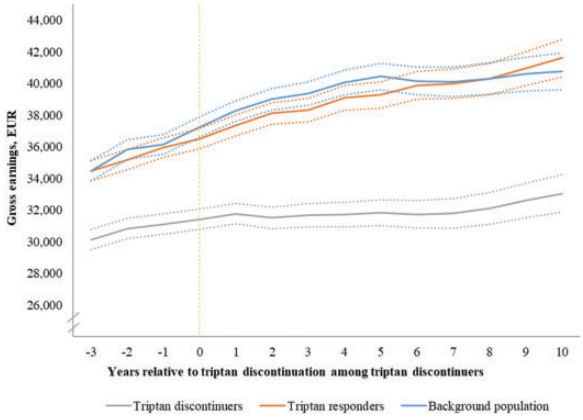
Reduced earnings among triptan non-responders with migraine

Messoud Ashina[1,2,3], Jakob Møller Hansen[4], Thomas Folkmann Hansen[1], Daniel Sloth Hauberg[5], Ulla Sofie Lønberg[5], Nanna Hovelsø[5] and Timothy J. Steiner[1,6,7]

[1]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark*
[2]*Danish Knowledge Center On Headache Disorders, Glostrup, Denmark*
[3]*Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*
[4]*Private Neurology Practice, Slagelse, Denmark*
[5]*Pfizer Denmark ApS, Ballerup, Denmark*
[6]*Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway*
[7]*Division of Brain Sciences, Imperial College London, London, United Kingdom*

Objective: In this population-based study using data from Danish national registries, we estimated difference in earnings among people with migraine who discontinued triptan treatment compared to triptan responders and the background population.
Methods: We included all triptan discontinuers between 18 and 65 years who redeemed prescriptions for three or more distinct triptans but fewer than ten prescriptions of the last consumed triptan between 1998 and 2019. Each individual was matched, when possible, by year of birth, declared gender, region of residence and year of first triptan prescription redemption with three triptan responders and three individuals from the background population with no recorded triptan use. Average individual gross earnings were calculated yearly from three years before to 11 years after the last triptan prescription redemption. Linear regression models were applied to determine differences and significance between triptan discontinuers and the matched comparison groups.
Results: We identified 4,979 triptan discontinuers with significantly lower gross earnings than either triptan responders and the background population throughout the study period, reflecting their detachment from the labour market even before discontinuation of triptans (Figure 1). In the tenth year after triptan discontinuation, triptan discontinuers earned 21% less than triptan responders (EUR 33,056 vs EUR 41,605) and 19% less than the background population (EUR 33,056 vs EUR 40,754). For the 14-year period from three years before to 11 years after triptan discontinuation, triptan discontinuers averaged

EUR 93,684 and EUR 99,485 lower earnings than triptan responders and the background population respectively, while triptan responders had no significant difference in average gross earnings compared with the background population over each year in the study period.



Conclusion: Triptan discontinuation was assumed to be due to non-response. The findings supported this, as triptan discontinuation was associated with substantially reduced earnings compared to both triptan responders and the background population. The study highlights the economic impact of inadequately treated migraine on both society and affected individuals, indicating an important and unmet need for further treatment options to potentially restore these losses.

Disclosure of Interest: MA reports receiving personal fees from AbbVie, Amgen, Eli Lilly, Lundbeck, Novartis, Pfizer and Teva Pharmaceuticals and reports serving as associate editor of Cephalalgia, associate editor of The Journal of Headache and Pain, and associate editor of Brain. JMH reports receiving personal fees from Pfizer. TFH reports no conflicts. DSH, USL and NH are employees of Pfizer Denmark. TJS is co-editor of the Journal of Headache and Pain, a director and trustee of Lifting The Burden, and reports receiving personal fees from Eli Lilly and Pfizer.

IHC23-PO-137

Cost of illness among patients with migraine discontinuing triptan treatment – a Danish nationwide register study

Messoud Ashina[1,2,3], Jakob Møller Hansen[4], Thomas Folkmann Hansen[1], Daniel Sloth Hauberg[5], Ulla Sofie Lønberg[5], Nanna Hovelsø[5] and Timothy J. Steiner[1,6,7]

[1]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark*

[2]*Danish Knowledge Center On Headache Disorders, Glostrup, Denmark*

[3]*Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*

[4]*Private Neurology Practice, Slagelse, Denmark*

[5]*Pfizer Denmark ApS, Ballerup, Denmark*

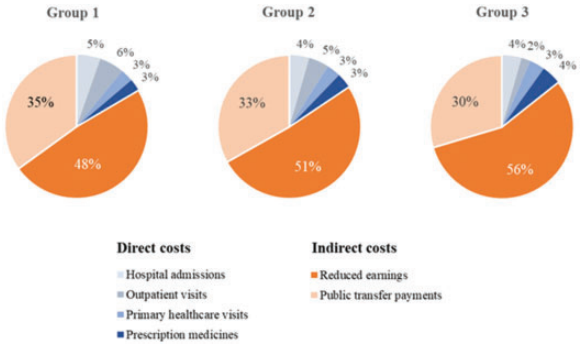
[6]*Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Trondheim, Norway*

[7]*Division of Brain Sciences, Imperial College London, London, United Kingdom*

Objective: To determine the difference in healthcare costs and monetary loss among patients with migraine who had discontinued triptan treatment and the background population, using routinely collected data from Danish nationwide registries.

Methods: We analysed data from all individuals aged 18 years or older who discontinued triptan treatment after redeeming one or more triptan prescriptions between 1998 and 2019 and grouped them according to the number of distinct triptans (one, two, or three or more) for which prescriptions were redeemed before discontinuation. Each individual was matched according to year of birth, declared gender, and region of residence with three individuals from the general population who had not redeemed triptan prescriptions during the study period. Direct costs (prescription medicine costs, healthcare costs in the primary healthcare sector, costs of hospital admissions, and costs of outpatient visits), and indirect costs (earnings and public transfer (benefit) payments) were estimated from five years before to 11 years after the first triptan redemption.

Results: We identified 211,026 triptan discontinuers, with 82% (172,668) discontinuing after one, 14% (30,487) after two, and 4% (7,871) after three or more distinct triptans. On average, triptan discontinuation was associated with excess direct healthcare costs of EUR 9,554, EUR 10,942, and EUR 12,812, respectively, in the 16-year period from five years before to 11 years after the first triptan redemption. In the same period, triptan discontinuers had reduced indirect costs consisting of reduced earnings of EUR 27,964, EUR 35,920, and EUR 50,076, respectively, and greater public transfer payments of EUR 20,181, EUR 23,264, and EUR 26,459, respectively. Indirect healthcare costs constituted 83%, 84% and 86%, respectively, of the total cost of illness among triptan discontinuers (Figure 1). The combination of lower earnings and higher public transfer payments compared with those of their matched controls reflected a detachment of triptan discontinuers from the labour market.



Conclusion: Our study highlights the significant economic burden to individuals and society associated with migraine and discontinuation of triptan treatment. The excess indirect costs outweigh the direct costs by a factor of 5–6, indicating a significant impact on the labour market and public transfer payments. The high excess costs suggest a high unmet healthcare need for this patient population, who have presumably exhausted current treatment options.

Disclosure of Interest: MA reports receiving personal fees from AbbVie, Amgen, Eli Lilly, Lundbeck, Novartis, Pfizer and Teva Pharmaceuticals and reports serving as associate editor of Cephalalgia, associate editor of The Journal of Headache and Pain, and associate editor of Brain. JMH reports receiving personal fees from Pfizer. TFH reports no conflicts. DSH, USL and NH are employees of Pfizer Denmark. TJS is co-editor of the Journal of Headache and Pain, a director and trustee of Lifting The Burden, and reports receiving personal fees from Eli Lilly and Pfizer

IHC23-PO-138

International availability of headache medications – an ongoing global survey of the International Headache Society

Francesca Puledda[1,2], Irene de Boer[3], David Garcia-Azorin[4], Roberta Messina[5], Mohammad Al-Mahdi Al-Karagholi[6], Marcio Nattan Portes Souza[7], Olivia Begasse de Dhaem[8], Maria-Teresa Goicochea[9], Cristina Tassorelli[10,11] and Arne May[12]

[1]*Headache Group, Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[2]*NIHR King's Clinical Research Facility, King's College Hospital, London, United Kingdom*
[3]*Department of Neurology, Leiden University Medical Center, Leiden, Netherlands*
[4]*Headache Unit, Department of Neurology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[5]*Neuroimaging Research Unit and Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy*
[6]*Danish Headache Center, Department of Neurology, Rigshospitalet Glostrup, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*
[7]*Neurology Department, Universidade de São Paulo, São Paulo, Brazil*
[8]*Hartford HealthCare, University of Connecticut, Westport, Connecticut, USA*
[9]*Servicio de Dolor, Departamento de Neurología, Sección Cefaleas, Fleni, Buenos Aires, Argentina*
[10]*Headache Science & Neurorehabilitation Center, IRCCS C. Mondino Foundation, Pavia, Italy*
[11]*Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy*
[12]*University Clinic Hamburg Eppendorf, Dept. of Systems Neuroscience, Hamburg, Germany*

Objective: Availability of headache medication is highly variable in different countries around the world. We aimed to evaluate the differing access to main symptomatic and preventive headache medications across the globe.

Methods: A questionnaire was created by members of the International Headache Society (IHS) Junior Group and was sent to IHS members worldwide. These included neurologists, general practitioners and headache specialists, with a minimum of three years of experience in treating headache disorders. In this initial phase of the study, we accepted maximum one participant per country.

The questionnaire included a list of acute (simple analgesics, antiemetics, triptans, ditans, gepants, neuromodulation) and preventive (anti-hypertensives, anti-epileptics, antidepressants, supplements, neuromodulation, Onabotulinumtoxin A, CGRP monoclonal antibodies, gepants, greater occipital nerve blocks, dihydroergotamine, steroids, melatonin, lithium) treatments of three primary headaches, namely: migraine, tension-type headache, and cluster headache. For each treatment, participants were asked to comment on the availability, type of reimbursement and variability of access within different regions of their country.

Results: A total of eighty-four IHS members from an equal number of countries were contacted. Of these, sixty-six completed the questionnaire to date. The majority were neurologists (85%) or specialists in training (8%) working at an academic/university hospital (42%). Out of these participants, 41% were located in high-income economy countries and 12% were located in low income economy countries. The remainder were living in lower and upper-middle income countries. Data collection is currently ongoing.

With regards to common migraine treatments such as propranolol and topiramate, these were available in most

countries (respectively in 92% and 86% of responding countries). Sumatriptan was available in almost all countries studied (99%) whereas for other triptans availability was lower (i.e. eletriptan 44%). Novel migraine treatments such as rimegepant, erenumab and fremanezumab were only available in 14%, 50% and 45% of the responding countries. With regards to common cluster headache treatments, verapamil was available in 95% of responding countries. By contrast, invasive occipital nerve stimulation was only available in 38% of responding countries.

Conclusions: This ongoing survey shows that availability of headache medications, ranging from simple analgesics to novel therapies like anti-CGRP antibodies, varies greatly across the globe. International collaboration between headache specialists, global organizations like the IHS, local professional, patient organizations, pharmaceutical companies, political leaders, and stakeholders are necessary within the advocacy efforts for more equitable access to headache medications across the world.

Disclosure of Interest: None Declared

IHC23-PO-139

Vascular comorbidity and cognition in migraine

Burcu Polat[1], Alp Kagan Kale[2], Sevim Eyupoglu[3], Tugce Ozdemir Gultekin[4], Vugar Cafer[5], Ayse Irem Can[6], Aynur Ozge[7], Nermin Tepe[8], Elif Ertas[9], Ezgi Uluduz[10] and Derya Uluduz[11]

[1]Istanbul Medipol University, School of Medicine, Department of Neurology, Istanbul, Turkey
[2]Balıkesir University Faculty of Medicine, Department of Neurology, MD, Balikesir, Turkey
[3]Brain 360 Private Clinic, Istanbul, Turkey
[4]Baskent University, Department of Neurology, Istanbul Hospital, Istanbul, Turkey
[5]Medicana International Private Hospital, Department of Neurology, Istanbul, Turkey
[6]A.Ozge Private Clinic, Mersin, Turkey
[7]Mersin University School of Medicine, Department of Neurology, Mersin, Turkey
[8]Balıkesir University Faculty of Medicine, Deparment of Neurology, Balikesir, Turkey
[9]Selcuk University, Department of Biostatistics, Konya, Turkey
[10]Koc University, School of Medicine, graduate student, Istanbul, Turkey
[11]Department of Neurology Istanbul, Cerrahpasa Medical Faculty, Istanbul, Turkey

Objective: Cognitive dysfunction associated with migraine attacks affects patients' activities of daily living. It has significant clinical implications in terms of migraine-related disability and loss of labor force. Before and during a migraine attack, many patients complain of cognitive impairment along with pain. These include prolonged reaction time, attention deficit, difficulty in concentration, impaired visuospatial processing, episodic memory deficits and verbal learning difficulties. Sleep quality, comorbid depression and anxiety are effective in the deterioration of cognitive functions in migraine. The occurrence of cognitive dysfunctions and their interrelationships with psychological symptoms and vascular comorbidity are still a matter of debate in migraine patients. White matter hyperintensities, increased cortisol levels, deficiencies in nerve growth factors, neurotrophins, changes in amyloid plaque formation, infarct-like lesions, inflammation, cardiovascular disease, and changes in white and gray matter volume have been implicated. Nevertheless, the exact mechanisms have not been fully determined. The aim of this study was to characterize the cognitive and psychological profile in different migraine groups (migraine without aura, with aura and chronic, 3 groups) and to investigate the relationship with vascular comorbidities.

Methods: With a cross-sectional prospective design, 231 patients (48 of whom were male) aged 18–69 years with a definite diagnosis of migraine who were admitted to general neurology, headache and algology outpatient clinics from a total of 6 centers were included in the study. Demographic characteristics, headache characteristics, comorbidities, MoCA (Montreal Cognitive Assessment), Beck anxiety and depression scales, MigSCOG (Migraine Subjective Cognitive Impairment Scale), HIT-6 (Headache Impact Test) and MIDAS (Migraine Disability Assessment Test) scores were analyzed.

Results: 45 patients had chronic migraine and 78 patients had medication overuse headache. Anxiety and depression scores were significantly higher in the group with medication overuse headache ($<$0,001) and significant differences were not observed in MoCA subscores. When a comparative analysis was made between the groups, no significant differences were observed in the patient group with chronic migraine and medication overuse headache patients with normal scores in MoCA, while HIT-6, MIDAS, Beck Anxiety and Depression scale scores were significantly higher than epizodic migraine groups. Hypertension was present in 7.9%, diabetes in 5.2%, insulin resistance in 16.1%, and hyperlipidemia in 14.8% of the patients. There were no significant statistical differences or correlations between vascular risk factors and other parameters.

Conclusion: According to our results; patients with migraine regardless of vascular comorbidity have no impairment in general cognitive functions. In patients with medication overuse headache, changes related to behavioral scores are observed in the foreground. Few studies have investigated the relationship between migraine and the risk of cognitive impairment. Recent studies suggest that migraine may be a risk factor for dementia, especially vascular dementia and Alzheimer's disease. Some studies have also reported that migraine

does not seriously affect cognitive function, especially in young/middle-aged or older adults. While there is no clear evidence to support that migraine increases the risk of long-term or persistent cognitive dysfunction, the fact that it occurs during attacks and may persist in people with frequent to severe attacks should promote understanding of the mechanisms related to the pathophysiological processes underlying migraine.
Disclosure of Interest: None Declared

IHC23-PO-140

Identifying Common Medical Comorbidities in Medication Overuse Headache Patients

Ki Chang Oh, Young Bok Yung, Joong-Yang Cho, Young-gun Lee and Hong-Kyun Park

Inje University Ilsan Paik Hospital, Goyang, Korea, Republic of

Background: Medication overuse headache (MOH) is a debilitating form of headache disorder that occurs as a result of excessive use of medication for primary headache disorders. While psychiatric comorbidities such as depression and anxiety have been linked to MOH, little is known about the prevalence of other medical conditions that may impact the management of this condition. To shed light on the relationship between these medical comorbidities and MOH, we conducted a study to determine their frequencies and the time sequence of their onset in MOH patients.
Method: For this observational study, we prospectively enrolled patients with medication overuse headache (MOH) from June 2020 to March 2023. We collected information from patients on their medical history and the onset of various medical conditions including cardiovascular diseases such as hypertension and heart disease, endocrine disorders such as diabetes and hyperlipidemia, liver disease, kidney disease, gastric ulcer/gastroesophageal reflux disorders, fibromyalgia, cervical and lumbar radiculopathy, and depression.
Results: A total of 99 patients were enrolled, with 83% of them being female and a mean age of 45.3 ± 12.5 years. Cervical or lumbar radiculopathy was the most common medical comorbidity reported (15 patients, 15.2%), followed by depression (14 patients, 14.1%), hypertension (12 patients, 12.1%), hyperlipidemia (12 patients, 12.1%), fibromyalgia (11 patients, 11.1%), diabetes (6 patients, 6.1%), and heart disease (2 patients, 2.0%). There was no difference in the occurrence of these comorbidities before and after the medication overuse. However, of the patients with gastric ulcer/gastroesophageal reflux disorder ($n = 8$) and kidney disease ($n = 6$), 75.0% ($n = 6$) and 83.3% ($n = 5$) reported that these medical comorbidities developed after medication overuse, respectively.
Conclusion: The study found that medical comorbidities, including gastric ulcer/gastroesophageal reflux disorder and kidney disease, were reported to have developed after medication overuse in the majority of patients. These findings highlight the importance of monitoring and managing these conditions in patients with MOH. Clinicians should pay close attention to the potential development of these comorbidities in patients with MOH who use medication excessively.
Disclosure of Interest: None Declared

IHC23-PO-141

Understanding Pain Patterns in Medication Overuse Headache: Insights from Türkiye's Real-Life Experience

Nermin Tepe[1], Hayrunnisa Bolay[2,3], Merve Ceren Akgör[4], Doga Vurallı[2,3], Buse Cagla Arı[5], Sinan Eliaçık[6], Ayşın kısabay ak[7], Ozlem Uzunkaya[8], Nesrin Ergin[9], Ayşegül şeyma sarıtaş[7], Ruhsen Öcal[10], Fatma Gülhan Şahbaz[11], Tülin Gesoğlu Demir[8], Derya Uludüz[12], Ezgi Uluduz[13], Esra Acıman[14], Arife Çimen Atalay[15], Keriman Oguz[15], Taner Özbenli[16], Gülcan Göçmez Yılmaz[17], Nevra Öksüz[18], Hamit Genç[19], Muhammet Okay Örün[20], Ayşe İrem Can[21] and Aynur Özge[18]

[1]*Balıkesir university Department of Neurology, Balıkesir, Turkey*
[2]*Department of Neurology and Algology, Gazi University Faculty of Medicine, Ankara, Turkey*
[3]*Neuropsychiatry Center, Gazi University, Ankara, Turkey*
[4]*Department of Neurology, Gazi University Faculty of Medicine, Ankara, Turkey*
[5]*Bahcesehir University Medical Faculty, Neurology Department, İstanbul, Turkey*
[6]*Department of Neurology, Hitit University School of Medicine, Çorum, Turkey*
[7]*Department of Neurology, Celal Bayar University, Manisa, Turkey*
[8]*Harran Unıversity Faculty of Medicine, Department of Neurology, Urfa, Turkey*
[9]*Department of Neurology, Medical Faculty, Denizli, Turkey*
[10]*Department of Neurology, University of Health Sciences Antalya Training and Research Hospital, Antalya, Turkey*
[11]*Afyon State hospital, Department of Neurology, Afyon, Turkey*
[12]*Istanbul University, Cerrahpasa School of Medicine, İstanbul, Turkey*
[13]*Koç University school of medicine, graduate student, Istanbul, Turkey*
[14]*Department of Neurology, Faculty of Medicine, Bulent Ecevit University, Zonguldak, Turkey*
[15]*Kanuni Sultan Süleyman Education and Research Hospital Neurology Department, Istanbul, Turkey*
[16]*samsun medical park hospital, department of neurology, Samsun, Turkey*

[17]Mersin City Train, ng and Research Hospital, Mersin, Turkey
[18]Mersin University School of Medicine, Department of Neurology, Mersin, Turkey
[19]Gaziantep DR Ersin Arslan Education and Research Hospital Neurology Department, Gaziantep, Turkey
[20]Van Education and Research Hospital Neurology Departmen, Van, Turkey
[21]Private Clinic, Mersin, Turkey

Objective: The objective of this study was to gather extensive real-life data from across the country in order to understand the multifactorial pathogenesis of medication overuse headache (MOH).

Methods: In this prospective study, 908 patients diagnosed with migraine and MOH were enrolled by neurologists from 18 centers. The patients' demographic characteristics, comorbidities, changes in headache features, and treatment responses were evaluated.

Results: Among the 908 patients (89% with migraine without aura, 80.1% female), several headache features exhibited significant changes during the MOH process. These changes included laterality (50.6% to 4.6% unilateral), pain quality (pulsating 30% to 11%, dull 11.8% to 48.2%, stabbing 1.6% to 54%, burning 11.4% to 58%), and prolonged attack duration. However, the frequency of associated features such as photophobia, phonophobia, nausea, osmophobia, and autonomic findings were not significantly altered. The response to NSAIDs and triptans decreased (58% to 5% and 56.7% to 11.8%, respectively), while the response to opioids and ergotamine did not show significant alterations (refer to Table 1). The frequency of migraine and MOH was significantly higher in their first-degree relatives. Furthermore, 51% of the patients had never received any prophylactic medication. In 175 menopausal patients, the frequency and severity of headache attacks were not significantly changed compared to the premenopausal period, although analgesic intake was significantly increased (46.3%) (Table 1).

Conclusion: The medication overuse headache process is associated with significant changes in pain characteristics in migraine patients with no significant influence on associated symptom frequency. Understanding changed clinical symptoms, pain patterns, family history, and confounding factors will be helpful to recognize patients early in the transformation process and to manage MOH appropriately.

Table: Headache characteristics of 908 MOH patients

	Unchanged	Changed	
	n (%)	Before MOH n (%)	During MOH n (%)
Unilateral	302 **(47.5)**	302 **(50.6)**	29 (4.6)
Bilateral	322 **(47.2)**	48 (7.1)	311 **(45.8)**
Throbbing	441 **(59.0)**	224 (30.0)	82 (11.0)
Dull	225 **(40.0)**	66 (11.8)	271 **(48.2)**
Stabbing	143 **(44.5)**	5 (1.6)	165 **(54.1)**
Burning	73 (30.6)	27 (11.4)	138 **(58)**
Eye Tearing, Redness	142 **(58.4)**	54 (22.3)	47 (19.3)
Stuffy Nose, Runny Nose	118 **(61.7)**	34 (17.8)	39 (20.4)
4–12 H Attacks	145 (29.3)	130 **(59.3)**	56 (11.3)
12–24 H Attacks	130 (30.6)	129 (30.5)	165 (38.9)
>24 Lasting Attacks	154 (31.0)	83 (16.2)	273 **(53.5)**
Increase with physical activity	354 **(56.4)**	95 (15.1)	179 (28.5)
Progressed in severity	99 (15.5)	73 (11.5)	464 **(73)**
Phonophobia	448 **(60.8)**	147 (19.9)	141(19.1)
Photophobia	435 **(62.7)**	197 (28.5)	62 (8.9)
Osmophobia	175 **(68.1)**	92(31.1)	29 (9.8)
Nausea	375 **(54.0)**	220 (31.6)	100 (14.4)
Vomiting	168 (39.4)	159 (38.1)	100 (24.4)
Reduction with NSAID	267 (37.3)	413**(57.8)**	35 (4.9)
Reduction with Triptan	110 (31.5)	198 **(56.7)**	41 (11.8)
Reduction with Opioid	89 **(64.4)**	38 (27.2)	11 (8)
Reduction with Ergotamine	110 **(49.5)**	75 (37.1)	17 (8.4)
	Not Changed	Increased	Decreased
Attack frequency compared to pre-menopausal?	81 **(47.1)**	61 (35.5)	30 (17.4)
The severity of attacks compared to pre-menopausal?	79 **(45.1)**	66 (37.7)	30 (17.1)
Analgesic intake compared to pre-menopausal?	72 **(41.1)**	81 **(46.3)**	22 (12.6)

Disclosure of Interest: This study is important for neurologists about aware of medication overuse headaches.

IHC23-PO-142

Development of a Multi-country Migraine-Related Stigma Questionnaire for People Living With Migraine

Elizabeth Seng[1], Richard B. Lipton[1], Robert E. Shapiro[2], William Young[3], Kristina Fanning[4], Brett Dabruzzo[5], Michael Seminerio[6] and Dawn C. Buse[1]

[1]*Albert Einstein College of Medicine, Bronx, NY, USA*
[2]*The Larner College of Medicine, University of Vermont, Burlington, VT, USA*
[3]*Thomas Jefferson University, Philadelphia, PA, USA*
[4]*MIST Research, Wilmington, NC, USA*
[5]*AbbVie, Madison, NJ, USA*
[6]*AbbVie, Irvine, CA, USA*

Objective: To evaluate the validity and reliability of a stigma questionnaire for people living with migraine in 6 countries.

Methods: The Stigma Questionnaire for Migraine (SQM) was developed from survey items and responses created for inclusion in the Chronic Migraine Epidemiology and Outcomes – International (CaMEO-I) Study, a web-based survey study conducted simultaneously in Canada, France, Germany, Japan, the United Kingdom, and the United States. The items assessing stigma were developed by investigators based on a review of existing stigma literature, input from expert clinicians, and interviews with people living with migraine. Respondents meeting modified International Classification of Headache Disorders, 3rd edition, criteria for migraine were identified via a validated diagnostic questionnaire. The French, French Canadian, German, and Japanese surveys were translated from English into each language and then reviewed by the investigator in each country and local speakers. Following survey administration, results were back-translated into English. In each country, cognitive debriefing was performed using the survey in their language with patient stakeholders who gave feedback and adjustments were made as needed to the content and wording of the survey. The SQM comprises 9 items assessing the frequency with which respondents experience examples of migraine-related stigma and related feelings. Response options range from "never" (1) to "very often" (5). The response of "does not apply to me" was scored as 0 and was not included in the number of questions answered. Items were summed and rescaled to have a range of 0 to 100 (based on maximum possible summed score of 45) and quartile SQM scores were calculated: 1st quartile: $\leq$8.33, 2nd quartile: 8.34–25.00, 3rd quartile: 25.01–47.22, and 4th quartile: $>$47.22. The SQM was tested by exploratory factor analysis to determine the factor structure, Cronbach's alpha to measure internal consistency, and Spearman-Brown coefficients to measure the reliability of the subgroups. Differential item functioning methods were used to determine if item bias existed among respondents across the 6 countries surveyed.

Results: Among 14,492 survey respondents (mean age (SD), 41.7 (14.3); female, 71.2%; mean monthly headache days (SD), 4.73 (5.6); 5.4%–9.5% respondents across the 6 countries had $\geq$15 monthly headache days), the median SQM score was 25.0 (interquartile range, 38.9). The exploratory factor analysis extracted 1 factor. The SQM demonstrated high internal consistency (Cronbach's alpha 0.907) and split-half reliability (Spearman-Brown coefficient 0.929). Across all countries, median monthly headache days and stigma across SQM quartiles were moderately correlated overall (**Table**). Moderate/severe disability scores (MIDAS), presence of anxiety and depression symptoms (PHQ-4), and each domain score for the Migraine-Specific Quality of Life questionnaire version 2.1 and SQM scores across quartiles had strong correlations overall.

Abstract number: IHC23-PO-142

Table. Spearman Rho Correlations for the SQM Score Quartiles and Outcome Measures Across All Countries (N = 14,492)

	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	Total	Spearman Rho (across quartile)	P value
Median MHDs	2.0	2.7	3.3	4.0	3.0	0.242	<0.001
Percent moderate/severe MIDAS	18.5%	33.7%	50.0%	68.3%	41.7%	0.376	<0.001
Percent with PHQ anxiety symptoms	20.1%	28.0%	39.6%	65.3%	37.4%	0.333	<0.001
Percent with PHQ depression symptoms	17.4%	27.1%	38.9%	65.7%	36.4%	0.359	<0.001
Median MSQ-RFR score	77.1	68.6	60.0	42.9	62.9	−0.496	<0.001
Median MSQ-RFP score	90.0	80.0	70.0	55.0	75.0	−0.510	<0.001
Median MSQ-EF score	86.7	80.0	60.0	40.0	66.7	−0.586	<0.001

EF, Emotional Function; MHD, monthly headache day; MIDAS, Migraine Disability Assessment; MSQ, Migraine-Specific Quality of Life questionnaire version 2.1; PHQ, Patient Health Questionnaire; RFP, Role Function-Preventive; RFR, Role Function-Restrictive.
Quartile scores were calculated: 1st quartile: $\leq$8.33, 2nd quartile: 8.34–25.00, 3rd quartile: 25.01–47.22, and 4th quartile: $>$47.22.

Conclusion: The SQM shows face validity and appears to be a reliable tool across 4 languages and 6 countries to assess migraine-related stigma in people living with migraine.

Disclosure of Interest: Allergan (prior to its acquisition by AbbVie) Disclosures: Elizabeth Seng, PhD, has consulted for Click Therapeutics and GlaxoSmithKline and has served on an advisory board for AbbVie and Theranica. Richard B. Lipton, MD, has received research support from the National Headache Foundation, the National Institutes of Health, and the US Food and Drug Administration. He serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie/Allergan, Amgen, Biohaven, Dr. Reddy's Laboratories (Promius), electroCore, Eli Lilly, GlaxoSmithKline, Lundbeck, Merck, Novartis, Teva, Vector, and Vedanta Research. He receives royalties from Wolff's Headache, 8th edition (Oxford University Press, 2009), and Informa. He holds stock/options in Biohaven and Manistee. Robert E. Shapiro, MD, PhD, has received financial and/or authorship compensation for research consulting from AbbVie, Eli Lilly, Lundbeck, and Theranica. William Young, MD, has nothing to disclose. Kristina Fanning, PhD, is managing director of MIST Research, which has received research funding from AbbVie, Allay Lamp, GlaxoSmithKline, Juva Health, and NYC Langone Health via grants to the National Headache Foundation. Brett Dabruzzo, PharmD, and Michael Seminerio, PhD, are employees of AbbVie and may hold AbbVie stock. Dawn C. Buse, PhD, has received grant support and honoraria from AbbVie, Amgen, Biohaven, Eli Lilly and Company, Collegium, Lundbeck, and Teva and for work on the editorial board of Current Pain and Headache Reports.

Headache and gender

IHC23-PO-144

Side-effects of chronic CGRP blockade in middle age migraine sufferers: gender differences

Maria Nicolodi[1], Mariastella Pinnaro[2] and Leonardo Di Puccio-Sicuteri[3]

[1]*Foundation for Headache and Stress, Firenze, Italy*
[2]*Florence University, Florence, Italy*
[3]*Padua University, Padua, Italy*

Introduction: We showed a peak of calcitonin gene-related peptide (CGRP) during migraine (M) attacks. CGRP is involved in autonomic function, in NerveGrowthFactor and BrainDerived NeurotrophicFactor cascade, in immunity and cortisol/gonadal hormone systems. Gonadal hormones regulate pain, thus endorsing gender differences in pain. Aim: to observe gender-related side-effects following chronic CGRP mAbs administration

Methods: Perspective longitudinal real-world observation. Baseline Months 6, annually from 2018 to 2022. Volunteers: M without aura receiving CGRP mAbs for at least 3 years 594 (44.4 ± 4.5SD attacks/month10.5 ± 2.8SD) vs M without aura refusing treatments: 585 (44.3 ± 5.1SD attacks/month10.2 ± 2.6SD)

Treated Patients: GroupA 267 females, regular menses GroupB 249 menopause females; menopause symptoms 97%, GroupC 78 males. Untreated Participants GroupD1 262 females regular, menses GroupD2 247 menopause females; menopause symptoms 97% GroupD3 76 males. mAbs: Erenumab 70mg 82% Fremanezumab 225mg 8%

Parameters
Insulin
Insulin Resistance Test
Hormone Panel
Erectile Function: IIEF-5 Test
BMI
Genetic analysis gut microbiota
Cerebral MRI
Randt Memory Battery
Host-resistanceImmunodeficiency

Results: Asthenia 165 GroupA 61%, 130 GroupB, 52% 26 GroupD1 10%, 2 Group D3 2.6%, onset year 1 $p > 0.005$
Improved menopause symptoms 133 GroupB 53 4% onset year 1 $p > 0.005$
Precocious no familial menopause 42 GroupA 15% onset year 2 $p > 0.005$
Missed periods (no semiotic evidences) 73 GroupA 27% onset year 2 $p > 0.005$
LH blunting in males 7 GroupC 9% $p > 0.1$ onset year 2 $p > 0.01$
Erectile Dysfunction 4 GroupC 5% IIEF-5 score$>$1 onset year 2 $p > 0.01$
Insulin resistance amelioration in 30% positive patients GroupA, B 15% GroupC onset year 3 $p > 0.01$
BMI no decrease with dietary plan GroupA 45 17%, 21 GroupB 8.5%, 7 GroupC 9%, 8 D1 3%, 40 D2 16%, 6 D3 onset year 3 $p > 0.004$
Gut Flora decrease Lactobacillus, increase Escherichia Coli, Proteus 124 Group A 46%, 135 Group B 54%, 35 GroupC 49% onset year 2 $p > 0.005$
Cerebral MRI no changes 2018–2022 NS
Randt Memory Battery worsening 74 Group A 27% 63 Group B 27% 23 GroupC 29% onset year 3 $p > 0.005$
Herpes Zoster 16 Group A 6% 18Group B 7% onset year 3 $p > 0.001$
COVID-19 Pneumonia Group A, B, C vs GroupD1, D2, D3 1%NS
Opiate withdrawal management Group A, B vs Group D1, D2 onset month 6 $p > 0.06$ improvement

Conclusion: Relationships suggest use of mAbs in M associated with concomitant pathologies well managed

by CGRP blockade such as menopause symptoms, insulin resistance. Also, it seems that gonadal hormones type and levels likely have a role in determining proneness to several pro and cons in middle aged males and females M sufferers

Disclosure of Interest: None Declared

IHC23-PO-145

Features of headache in patients with chronic kidney disease

Sevara Khudayarova and Gulnara Rakhmatullaeva

Tashkent Medical Academy, Tashkent, Uzbekistan

Relevance: Headache in patients with chronic kidney disease is one of the most frequent clinical manifestations of this condition.

The aim of the study: To study the frequency and intensity of headache depending on gender characteristics in patients with CKD

Materials and methods of the study: 101 patients with CKD were examined.

Of these, 66 (65.3%) are men, and 35 (34.3%) are women. The average age of all patients was 46.2 ± 15.01 years, while the average age of men was 42.2 ± 12 years, the average age of women was 39.3 ± 11.5 years. In the predialysis stage C1-C4 ($n = 28$), 15 males (53.5%) and 13 females (46.6%) prevailed, while the average age in this group of patients was 56.1 ± 12.1. In the group of patients who receive hemodialysis ($n = 30$), gender gradation also showed a clear bias in favor of the stronger sex 18 (60%):12(40%); the average age was 53.1 ± 13.3. In group 3 ($n = 43$) there were similar data of men 23(53,4%); 20 (46,5%) women, average age 34.8 ± 9.3.

Results of the study: In the group of patients at the predialysis stage of CKD, 24 (85.7%) patients complained of headaches, and 13 (54.1%) of them were women and 13 (45.8%) men. The intensity of headache on the VAS in this group in women was 8 ± 2.1 ($P < 0.05$), in men 5.5 ± 1.7 ($P < 0.05$). In the group of patients undergoing hemodialysis, 22 (73.3%) complained of headaches. Of these, 12 (54.5%) were women, 10 (45.4%) were men. The assessment of pain on the VAS scale in women is 7 ± 1.8 ($P < 0.05$), in men 4.7 ± 2.6 ($P < 0.05$). In the group of patients after transplantation, headache was also one of the most frequent complaints of patients. At this stage, headache was detected in 30 (58.1%). Of these, 20 (66.6%) were women, 10 (33.3%) were men. Assessment of pain on the VAS scale in women is 5 ± 1.8 ($P < 0.05$), in men 3.8 ± 2.6 ($P < 0.05$)

Conclusions: According to the results of the study, CKD of various stages by gender characteristics is more common in men, but headache among them worries women more often. Also, in patients with kidney pathology, the threshold of sensitivity to headache is higher in women compared to men 7 ± 2.3:4.7 ± 1.8 ($P < 0.05$).

IHC23-PO-146

Prevalence and sex differences in non-headache symptoms and their association with headache characteristics in episodic migraine patients: a cross-sectional study

Samiran Chowdhury and Naresh Rajpal

VPIMS, Lucknow, India

To calculate female-to-male odds ratios for each non-headache symptom, a logistic regression with MMD as covariate was performed. A linear regression model was used to compare the total number of NHS between females and males, MMD as a covariate. The association between each NHS and the namely, monthly headache frequency [low: (2 to 8) versus high (9 to 14)], attack duration without treatment (<8 hours versus ≥8 hours) and attack severity assessed by visual analog scale (VAS) (<5 versus ≥5) were analyzed by a logistic regression model. p-values were adjusted for multiple testing with a Bonferroni correction. To find the relationship between total number of NHS and HIT 6 score, Pearson's correlation was done. The level of significance was set at <0.05

Objectives: To study non-headache symptoms (NHS) in episodic migraine (EM) patients stratified by sex and to find their association with various headache characteristics and headache related disability.

Methods: Consecutive patients with EM diagnosed by ICHD-3 criteria, aged 18 to 65 years seen in the outpatient department, were evaluated regarding the headache and NHS during the past one month using a questionnaire. Demographic details, family history, triggers, disease duration, headache characteristics, and attack-associated non-headache symptoms were recorded. Mean monthly migraine days (MMD), mean attack duration (MAD) and mean attack severity by VAS were estimated. The occurrence of twelve attack-related NHS such as visual aura, photophobia, phonophobia, osmophobia, nausea, vomiting, allodynia, motion sensitivity, neck pain, vertiginous sensation, mental slowing, and myofascial pain/myalgias in any of their attacks were documented. Patients were asked to specify their most bothersome symptom (MBS) amongst NHS. Three leading questions regarding disability were asked (are these non-headache symptoms equally disabling as headache itself? Are they more disabling than headache in some of the attacks? if yes, in what proportions of attacks?). Headache impact was quantified by Headache impact test 6. (HIT-6).

Results: One hundred twenty patients of EM were studied (96 F: 24M; mean age 30 ± 6.3) with a mean disease duration of 6 ± 3.6 years. 40% of the patient's 1st-degree relatives had a history of migraine-like headaches. Only 8% of patients were using preventive medication. The common triggers were menstruation (65% of females), bright light (48%), travel (45%), stress (44%), inadequate sleep (38%), loud noise (30%), and irregular eating habits (20%). The mean monthly headache days were 7.3 ± 3.2, the mean attack duration without treatment was 12.2 ± 8.9 hours, and the mean attack severity on VAS was 5.5 ± 1.7. NHS were photophobia (90%), phonophobia (77.5%), myofascial pain/myalgias (75%), allodynia (70.8%), vertiginous sensation (68.3%), nausea (64.2.3%), neck pain (60.8%), mental slowing (50.8%), motion sensitivity (40.8%), vomiting (34.2%), osmophobia (16.7%), and visual aura (9.2%). 66% of patients reported these NHS as equally disabling as the headache and 12% of patients reported them as more disabling than a headache in more than 50% of their attacks. Three common MBS were nausea, phonophobia and mental slowing. Female patients reported significantly more allodynia (OR:17.3; 95% CI: 2.9–103.1; $p = 0.024$), vertiginous sensation (OR:18.0; 95% CI: 3.1–104.1; $p = 0.012$) and myofascial pain/myalgias (OR:25.3; 95% CI: 4.0–161.6; $p = 0.012$). Females reported greater number of NHS compared to males (7.0 ± 0.3 vs 5.0 ± 0.1; $p < 0.001$). None of the NHS had a significant association with headache frequency, whereas patients with MAD$\geq$8 hours had significantly more phonophobia and allodynia. Patients with VAS $\geq$5 complained of significantly more, nausea, vomiting, photophobia, phonophobia and mental slowing. HIT 6 had a strong correlation with total number of NHS ($r = 0.678$; $p < 0.001$) and modest correlation with VAS ($r = 0.297$; $p = 0.001$).
Conclusion: About two-thirds of EM patients had atleast one equally disabling NHS during a migraine attack. Females reported more NHS. Patients with more prolonged and severe headache attacks complained of more NHS, whereas the headache frequency had no such association. NHS significantly correlated with disability. Our results suggest that the degree of neurogenic inflammation during a migraine attack rather than their repetitiveness may be related to these NHS symptoms. Treating a migraine attack early and effectively will be beneficial.
Disclosure of Interest: None Declared

IHC23-PO-147

Effect of smoking on the development of migraine in women: a nationwide cohort study

Seung Ae Kim[1], Kyungdo Han[2] and Mi Ji Lee[1,3]

[1]*Department of Neurology, Seoul National University Hospital, Seoul, Korea, Republic of*
[2]*Department of Statistics and Actuarial Science, Seoul, Korea, Republic of*
[3]*Seoul National University College of Medicine, Seoul, Korea, Republic of*

Background: Smoking has been suggested as a risk factor of migraine in several cross-sectional studies. However, there has been no longitudinal study regarding the effect of smoking on the risk of migraine. In this study, we aimed to investigate the effect of smoking on the incidence of migraine in women and effect modification of menopause.
Methods: Using a nationally representative National Health Insurance Service data, women aged $\geq$40 years who participated national breast cancer screening in 2009 were followed up until the end of 2018. Participants were classified based on their smoking status: non-smoker, ex-smoker, and current smoker. Information regarding the duration and amount of smoking were also collected. A Cox proportional hazard regression model was used to assess the independent effect of smoking on the risk of incident migraine. The model was adjusted for age, household income, body mass index, hypertension, diabetes mellitus, chronic kidney disease, dyslipidemia, alcohol assumption, regular physical activity, age at menarche, parity, breast feeding, and oral contraceptives and stratified by menopause (premenopause vs. postmenopause). The interaction between smoking and menopause was also investigated.
Results: A total of 1,827,129 women were included in the analysis. In both premenopausal and postmenopausal women, current smoking increased the risk of incident migraine compared to never smoking. However, the effect was greater in premenopausal women (adjusted HR 1.140 [95% CI 1.108–1.172]) than in postmenopausal women (adjusted HR 1.045 [95% CI 1.018–1.073]) (p for interaction $<$0.0001). The risk increased with increased amount of smoking in both premenopausal and postmenopausal, with greater association in premenopausal women (p for interaction $<$0.0001). Past smoking increased the risk of incident migraine only in premenopausal women (adjusted HR 1.055 [95% CI 1.011–1.100]).
Conclusion: Smoking increases the development of migraine attack in women, and its effect is influenced by menopausal factors. Interaction between smoking and estrogen may increase the vulnerability of migraine brain.

IHC23-PO-148

Chemogenetic Inhibition of the Posterior Thalamus: Effects on Migraine-like Phenotypes in Mice and Sex Differences

Huebner M.W.[1,2], Greenway A.M.[1,2,3], Dorricott N.O.[3], Waite J.S.[2,4], Tutt J.O.[3], Castonguay W.C.[1], Rea B.J.[2,4], Sowers L.P.[2,4] and Russo A.F.[1,2,5]

[1]*Dept. of Molecular Physiology and Biophysics, University of Iowa*
[2]*Center for the Prevention and Treatment of Visual Loss, Iowa VA Health Care System, Iowa City, Iowa*
[3]*Dept. of Biological Sciences, University of Bath*
[4]*Stead Family Dept. of Pediatrics, University of Iowa, Iowa*
[5]*Dept. of Neurology, University of Iowa, Iowa*

Purpose: The posterior thalamic region (PoT) is a brain region critical for sensory and pain processing. During a migraine attack, resting state functional magnetic resonance imaging studies show that signaling between the PoT and the cortical and subcortical regions is disrupted, highlighting this region as a potential therapeutic target in migraine. Previous work from our lab demonstrated that optogenetic activation of the PoT was sufficient to induce light aversion in mice. We sought to determine if the PoT is necessary for the development of migraine-like behaviors induced by calcitonin gene-related peptide (CGRP), including light aversion, touch hypersensitivity, and spontaneous pain.
Methods: Intraperitoneal injection of CGRP (0.1 mg/kg) was used to induce migraine like phenotypes in male and female C57BL/6J mice. The mice were previously injected with AAV vectors encoding Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) or control vectors encoding only mCherry reporters. We used the inhibitory DREADD hM4Di, which is a mutated G-protein coupled receptor that is no longer activated upon binding to acetylcholine and instead is activated by binding to derivatives of clozapine. Upon activation, the DREADD receptor inhibits neuronal transmission in that brain region allowing us to explore if said brain region is necessary for behavioral outputs. During inhibition, we performed a battery of tests to measure migraine-like behaviors beginning with touch hypersensitivity and grimace. Touch hypersensitivity of the hindpaw plantar regions was measured using von Frey filaments. Grimace was measured using an automated squint assay with facial tracking software.
Results: Our data demonstrate that DREADD inhibition of the PoT successfully rescued touch hypersensitivity and photophobia phenotypes induced by CGRP. The data also showed differences in off-target effects and rescues between sexes, with males showing stronger overall rescues. Several different designer ligands and dosages were used to minimize off-target effects.
Conclusion: We conclude that the PoT is necessary for CGRP-induced touch hypersensitivity and photophobia pain in mice, specifically males. These data suggest the PoT is part of a critical central network that could provide exciting targets for future brain modulation therapeutics for migraine.
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Disclosure of Interest: None Declared

IHC23-PO-149

Sex differences in the clinical utilities of Leeds Dependence Questionnaire and Severity of Dependence Scale in medication-overuse headache

Wei-Ta Chen[1,2,3], Yen-Feng Wang[1,2], Yi-Shiang Tzeng[1], Chia-Chun Yu[1], Yu-Hsiang Ling[1], Shih-Pin Chen[1,2], Kuan-Lin Lai[1,2] and Shuu-Jiun Wang[1,2]

[1]*Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*National Yang Ming Chiao Tung University, Taipei, Taiwan*
[3]*Ministry of Health and Welfare Keelung Hospital, Keelung, Taiwan*

Objective: The present study aimed to evaluate the diagnostic utilities of the Leeds Dependence Questionnaire (LDQ) and the Severity of Dependence Scale (SDS) in medication-overuse headache (MOH) in men and women and to characterize sex differences in dependence behaviors in MOH.
Methods: Consecutive patients with newly diagnosed chronic migraine (CM) with and without concomitant MOH were enrolled from the headache clinic of a tertiary medical center. Dependence behaviors were measured with the LDQ and the SDS. Migraine Associated Disability (MIDAS) and Hospital Anxiety and Depression Scale (HADS) were used to assess functional disabilities and psychological disturbances. The cut-off scores for a diagnosis of MOH were determined by using receiver operating characteristics (ROC) curves, and areas under the ROC curves (AUCs) were calculated. Comparisons between the sexes were made.
Results: In total, 1419 consecutive CM patients (1135F/284M, mean age 41.7 ± 13.9 years) were recruited, including 799 with MOH (56.3%). The number of days per month with acute medication use was positively correlated with the scores on the LDQ ($r = 0.641$, $p < 0.001$) and the SDS ($r = 0.618$, $p < 0.001$). Patients with MOH scored higher on the LDQ (12.8 ± 7.8 vs. 3.9 ± 5.0, $p < 0.001$) and the SDS (6.9 ± 3.9 vs. 2.3 ± 2.8, $p < 0.001$) than did

those without. The cut-off scores of the LDQ for MOH were determined at 7 for women (AUC = 83.9%) and 6 for men (AUC = 87.1%), and those for the SDS were 5 for women (AUC = 83.9%) and 4 for men (AUC = 82.7%). For patients with MOH, the LDQ (LDQ 13.2 ± 8.2 vs. 12.7 ± 7.7, p = 0.460) and SDS scores (6.5 ± 4.0 vs. 7.0 ± 3.9, p = 0.503) were comparable between women and men. However, the associations between the LDQ scores and the scores on the MIDAS (F: r = 0.288, p < 0.001; M: r = 0.131, p = 0.103) and the HADS (F: r = 0.277, p < 0.001; M: r = 0.095, p = 0.252) were stronger in women than in men, and the trends were similar for the SDS.

Conclusions: The severity of dependence behaviors is positively correlated with the frequency of acute medication use in CM patients. Both the LDQ and the SDS are useful in the detection of MOH, although the cut-off scores were lower in men then in women. There were sex differences in the associations between dependence behaviors and functional disabilities and symptoms of anxiety and depression. Further studies are needed to verify these findings and to clarify the underlying pathophysiology.

Disclosure of Interest: YF Wang has received honoraria as a speaker from Taiwan branches of Allergan/AbbVie, Chugai, Eli Lilly, Novartis, Pfizer, Sanofi, UCB, and Viatris, and Hava Bio-Pharma, and Orient EuroPharma. He has received research grants from the Taiwan Ministry of Science and Technology, and Taipei Veterans General Hospital. SJ Wang has served on the advisory boards of Daiichi-Sankyo, Eli Lilly and Novartis; has received honoraria as a moderator from Allergan/AbbVie, Pfizer, Eli Lilly, Biogen and Eisai and has been the PI in trials sponsored by Eli Lilly, Novartis, and Allergan/AbbVie. He has received research grants from the Taiwan Minister of Technology and Science (MOST), Brain Research Center, National Yang Ming Chiao Tung University from The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan, Taipei Veterans General Hospital, Taiwan Headache Society and Taiwan branches of Eli Lilly, Novartis, and Pfizer. WT Chen, YS Tzeng, CC Yu, YH Ling, SP Chen, and KL Lai reported no disclosures relevant to the manuscript.

IHC23-PO-150

Do men with migraine have the same effectiveness to galcanezumab in real-world experience? A large series of 180 men in Galca-Only Consortium.

Victor Obach[1], Rocio Alvarez-Escudero[2], Nurias Riesco[2] and David Garcia-Azorin[3]

[1]*Hospital Clinic, Barcelona, Spain*
[2]*Hospital de Asturias, Oviedo, Spain*
[3]*Hospital de Valladolid, Valladolid, Spain*

Objective: Due to the female sex predominance of migraine, men with migraine are usually underrepresented in clinical trials and real-world studies. We analyzed tolerability and effectiveness of galcanezumab in men patients from a large multicentric registry.

Methods: The "Galca-Only Consortium" is a multicenter prospective cohort study of consecutive patients with chronic migraine and high-frequency episodic migraine with prior failure to three or more migraine preventive drugs, treated with galcanezumab and followed up for 12 months. Patients were evaluated by headache experts and followed up quarterly. A series of variables were collected, including demographic variables, psychiatric comorbidities, data related to the migraine disease, and number of monthly headache days (MHD). Headache impact test 6 (HIT-6) test was also administered.

Response to treatment was assessed according to the 50% responder rate, defined as the proportion of patients who achieved a reduction of at least a 50% in the number of MHD, at 12 months, compared to the baseline. The proportion of patients who discontinued the treatment due to adverse effects was also assessed.

The statistical analysis compared the response to Galcanezumab and the demographic and other variables between male and female patients.

Results: In our registry of 1055 patients, 180 (17.1%) men were compared versus 877 women. Demographics are shown in the table. Men had fibromyalgia and other chronic pain syndromes less frequently.

At 12-month follow-up, the proportion of patients who achieved a 50% response was similar/different between men and women (50.6% vs. 49.6%, p = 0.6). The proportion of patients who discontinued the treatment due to inadequate tolerability was also similar (8.3% vs. 6.3%, p = 0.2).

Men had a SR50 of 50.6% similar to the 49.6% (p = 0.7) observed in women, with a similar discontinuation rate due to adverse events in 8.3% and 6.3% (p = 0.4), respectively. The overall galcanezumab retention rate favors men with a 72.5% compared to 66.1%in women (p = 0.03).

Conclusion: In the present study, men patients with migraine had a similar treatment response and to

Abstract number: IHC23-PO-150

Variables	Men n = 180	Women n = 877	P value
Age, mean (SD)	51.6 (11.6)	49.9 (12.1)	0.2
Migraine worsening, years [IQR]	8 [4–14]	8 [4–14]	0.1
Chronic migraine, n (%)	136 (75.6)	670 (76.6)	0.7
Monthly Headache Days at baseline [IQR]	20 [14–30]	20 [14–20]	0.6
HIT6 baseline [IQR]	68 [65–74]	69 [66–72]	0.2
Mood disorder	64 (35.6)	352 (40.1)	0.3
Fibromyalgia	5 (2.7)	116 (13.2)	0.001
Other chronic pain syndromes	28 (15.8)	218 (24.9)	0.02

Galcanezumab to women. There were no differences regarding the frequency of treatment discontinuations.
Disclosure of Interest: None Declared

IHC23-PO-151

Being female and having aura as predictors of more cranial autonomic symptoms during a migraine attack

Maria Dolores Villar-Martinez[1], David Moreno Ajona[2], Karthik Nagaraj[1] and Peter J Goadsby[1]

[1]*King's College London, London, United Kingdom*
[2]*Kings College London, London, United Kingdom*

Objective: Half of migraineurs present cranial autonomic symptoms, which are clinical signs usually associated with trigeminal autonomic cephalalgias (1, 2). Our objective was to determine clinical predictors of cranial autonomic symptoms with acute attacks of migraine.
Methods: We audited cases with a diagnosis of chronic migraine in a tertiary headache centre. The total number of cranial autonomic symptoms was set as the dependent variable in a generalized linear model using Poisson and negative binomial distributions, and log link function. As predictors, sex, the presence of aura, unilaterality of cranial autonomic symptoms, age at headache onset and pulsatility of the pain were examined.
Results: We audited three hundred and four cases. Both models significantly outperformed the null model, with slightly lower numbers for the negative binomial, according to Akaike and Bayesian Information Criteria (1216.93 and 1242.95 vs 1269.19 and 1295.21, respectively), and a higher likelihood-ratio chi-squared test for the Poisson model: 42.1 ($P < 0.001$) vs that using the negative binomial distribution: 13.7 ($P = 0.032$)[PJG1]. Female sex ($P = 0.029$), the presence of aura ($P < 0.001$) and unilaterality of cranial autonomic symptoms ($P < 0.001$) were related to the number of cranial autonomic symptoms the Poisson model. Aura symptoms ($P = 0.018$) and unilaterality of cranial autonomic symptoms ($P = 0.03$) were still significant when dispersion of data was considered. Age at headache onset and pulsatility, however, were not significant predictors.
Conclusion: Females with migraine and any type of aura may develop more evident clinical signs during an attack in the form of cranial autonomic symptoms, potentially complicating the differential diagnosis with the trigeminal autonomic cephalalgias. The cranial parasympathetic outflow pathway has important cerebrovascular protective effects (3), which is consistent with enhanced activation during aura. Females with aura could benefit more from therapies targeting the cranial autonomic pathway.
[PJG1]I understand this simply shows both models are better than the null model but does not directly support the use of either
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Headache pathophysiology – Basic science

IHC23-PO-152

Whole brain c-Fos expression patterns in a nitroglycerin-induced migraine model

Chunxiao Yang[1,2], Zihua Gong[2,2,4], Hao Wang[5] and Shengyuan Yu[2]

[1]*School of Medicine, Nankai University, Tianjin, China*
[2]*Department of Neurology, the First Medical Center, Chinese PLA General Hospital, Beijing, China*
[3]*Medical School of Chinese PLA, Beijing, China*
[4]*Department of Medical Oncology, Bethune International Peace Hospital, Shijiazhuang, China*
[5]*National Engineering Laboratory for Brain-inspired Intelligence Technology and Application, and School of Information Science and Technology, University of Science and Technology of China, Hefei, China*

Background: The exact mechanism of migraine attacks is unclear. Nitroglycerin (GTN) has been in use as the most established migraine model in both human and animal studies for more than two decades, using the pathways activated by GTN for deciphering migraine was proved to be effective and reliable. However, the traditional imaging methods of mechanically cut thin sections resulted in loss of information and inaccuracy of Fos-positive cell counts.
Methods: Here we performed whole-brain mapping of c-Fos expression in mice, with or without GTN, using a new ultrahigh-speed 3D imaging method with 1-μm resolution. Besides, we applied light-aversive test, von-frey test, and elevated plus maze test to investigate migraine-like behaviors induced by GTN.
Results: We found that in addition to the well-known areas activated by GTN including the supraoptic nucleus, subfornical organ, central amygdalar nucleus, and spinal nucleus of the trigeminal caudal part, the high sensitivity of new method helped reveal previously unknown activated areas, including medial habenula, lateral dorsal nucleus of thalamus, lateral posterior nucleus of the thalamus, etc. Behavioral tests showed reduced time in light, decreased mechanical withdrawal threshold, and reduced time in open arms in GTN mice.
Conclusions: Our findings confirm that GTN-induced mice model exhibits migraine-like symptoms, indicate the involvement of multiple subcortical areas in GTN-related behaviors, and establish new potential targets to study migraine pathophysiology and drug discovery.
Disclosure of Interest: None Declared

IHC23-PO-153

The trigeminal and dorsal root ganglia exhibit differences in calcitonin receptor, CGRP, and amylin expression

Tayla Rees[1], Zoe Tasma[1], Michael Garelja[2], Christopher Walker[1] and Debbie Hay[2]

[1]*The University of Auckland, Auckland, New Zealand*
[2]*The University of Otago, Dunedin, New Zealand*

Objective: The trigeminal ganglia (TG) and dorsal root ganglia (DRG) are anatomically important sites for pain, containing neuropeptides and receptors that modulate pain transmission. The neuropeptides calcitonin gene-related peptide (CGRP) and amylin have been linked to migraine and pain. They are potent agonists of the amylin 1 (AMY_1) receptor, a heterodimer of the calcitonin receptor (CTR) and receptor activity-modifying protein 1 (RAMP1). Co-expression of the CTR and CGRP has been reported in the TG, with little or no amylin observed. In the DRG, both peptides have been reported; however, their distribution relative to the CTR is unknown. This suggests that there may be differences in the relative abundance of each peptide between these two ganglia and which peptides might signal via CTR in each location. This study aimed to determine the relative distribution of the CTR with CGRP and amylin in the DRG and compare this to the TG.
Methods: Immunohistochemistry was performed with validated antibodies against CTR, CGRP, amylin and neural markers in mouse, rat, and human Cervical 1/2 DRG. Data were quantitatively compared to our prior TG data using the same conditions. This was supported by RNA-FISH to examine mRNA distribution.
Results: In the DRG, CGRP-like and amylin-like immunoreactivity (LI) and mRNA were present in distinct and overlapping neurons, indicating occasional co-expression of the peptides. CTR-LI was present in neurons which expressed CGRP or amylin alone, as well as neurons which expressed both peptides. Co-staining was uncommon with an A-fibre marker, NF200, indicating that CTR-LI, CGRP-LI, and amylin-LI were primarily in C-fibre neurons. There were significant differences in expression observed across species and sex.
Conclusions: CGRP and CTR expression patterns were similar between the ganglia. However, amylin expression and co-localisation with CTR were only observed in the upper cervical DRG. Distinct local agonists may activate CTR-based receptors, such as the AMY1 receptor, in C-fibre neurons in the DRG and TG. This highlights that local amylin may play a more important role in DRG-mediated pain responses than in the TG.
Disclosure of Interest: None Declared

IHC23-PO-154

Pyridin-2(1H)one derivatives: A new class of therapeutics for trigeminal pain

Pauline Murail[1], Amélie Descheemaeker[1], Gisela da Silva Borges[1], Nicolas Pinto-Pardo[1], Alexia Visseq[2], Fabrice Anizon[2], Pascale Moreau[2], Alain Artola[1] and Radhouane Dallel[1]

[1]*Université Clermont Auvergne, CHU Clermont-Ferrand, Inserm, Neuro-Dol, Clermont-Ferrand, France*
[2]*Université Clermont Auvergne, CNRS, SIGMA Clermont, Institut de Chimie de Clermont-Ferrand, Clermont-Ferrand, France*

Objective: Mechanical allodynia (MA), a frequent chronic pain symptom caused by normally innocuous stimuli, constitutes an unmet medical need, as treatments are not always effective and can be associated with important side effects. Recently, we found that a newly synthesized compound, the Pyridin-2(1H)one derivative 69 (**C69**), is effective in reducing pain hypersensitivity in an inflammatory pain model. C69 appears to inhibit p38α Mitogen-activated protein kinase, known to contribute to pain hypersensitivity. Here, we further assessed the antiallodynic potential of **C69** in rat multiple models of trigeminal pain.
Methods: We used Behavioral, in vivo electrophysiology and c-Fos immunoreactivity to examine the effect of the administration of **C69** (per os or intracisternally, IC) on, respectively, facial mechanical sensitivity and sensitization of medullary dorsal horn (MDH) neurons, in various models of trigeminal pain: inflammatory (formalin, Complete Freund Adjuvant, CFA), neuropathic (infraorbital nerve chronic constriction) and migraine (isosorbide dinitrate, ISDN) models.
Results: IC C69 dose-dependently attenuates MA in the facial CFA model. It also prevents formalin-induced facial MA and reverses neuropathic facial MA with long-lasting effects in both sexes. Importantly, per os **C69**, too, can reduce CFA and ISDN-induced facial MA. IC **C69** prevents CFA-induced c-Fos expression in the superficial laminae of ipsilateral MDH and inhibits responses to innocuous and noxious stimulations as well as the wind-up phenomenon of MDH wide dynamic range (WDR) neurons.
Conclusion: These data reveal that **C69**, a p38α MAPK inhibitor, has an antiallodynic potential in various models of trigeminal pain. **C69** exerts its therapeutic effects, at least in part, at the segmental level through presynaptic and postsynaptic actions. Hence, **C69** represents a novel class of analgesics for the treatment of trigeminal mechanical hypersensitivity.
Disclosure of Interest: None Declared

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Implication of peripheral and central delta opioid receptors in migraine-like headache in rats

Manon Dussol[1], Gisela da Silva Borges[1], Claudie Beaulieu[2], Philippe Luccarini[1], Louis Gendron[2] and Radhouane Dallel[1]

[1]*Université Clermont Auvergne, CHU Clermont-Ferrand, Inserm, Neuro-Dol, Clermont-Ferrand, France*
[2]*Département de Pharmacologie-Physiologie, Université de Sherbrooke, Sherbrooke, Canada*

Objective: Migraine is a highly incapacitating disorder, with available treatments lacking efficacy in many patients, thus highlighting the need for new treatments. The delta opioid receptor (DOP) has emerged as a very promising therapeutic target for migraine. In mice, DOP agonists inhibit the allodynia associated with migraine. However, species differences exist in the distribution of DOPs throughout the nervous system. Hence, we aimed at studying the distribution of DOPs within the trigeminal ganglia (TG) and the mechanisms of the antimigraine potential of a DOP agonist, SNC80, using a new rat model of migraine.
Methods: Using RNAscope (*in situ* hybridization), *in vivo* electrophysiology and behavioral analysis, we assessed, respectively, (i) DOP distribution in naïve rat TG, (ii) the effect of systemically applied SNC80 on the responses of wide dynamic range (WDR) neurons in the trigemino-cervical complex to innocuous/noxious mechanical and electrical stimuli, and (iii) the effect of this SNC80 on cutaneous mechanical hypersensitivity (CMH) in a rat model of migraine induced by isosorbide dinitrate (ISDN) and its site(s) of actions.
Results: We show that DOPs are expressed in all types of neurons within the rat TG, that is to say in large- and medium-size myelinated neurons, as well as in small non-peptidergic and peptidergic C-fibers, though less predominantly. Interestingly, systemic SNC80 administration inhibits the responses of WDR neurons to innocuous and noxious mechanical stimuli. Finally, behavioral testing shows that intracisternal and systemic SNC80 administration can respectively partially to completely prevent ISDN-induced CMH. The anti-allodynic effect of systemic administration was partially reversed by naloxone-methiodide, a peripherally-restricted opioid receptor antagonist.
Conclusion: Activation of DOPs appears to exhibit an antimigraine potential in rats. The present report also indicates that both peripheral and central delta opioid receptors regulate the migraine-like headache in rats.
Disclosure of Interest: None Declared

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Non-paralytic botulinum toxin A in orofacial pain and headache

Ana David-Pereira[1], Joseph Lloyd[1], Bazbek Davletov[2] and Anna P Andreou[1]

[1]*King's College London, London, United Kingdom*
[2]*University of Sheffield, Sheffield, United Kingdom*

Orofacial pain and headache disorders are highly prevalent types of pain, but their complex and diverse symptoms pose significant challenges in terms of classification, diagnosis, and treatment. Current management strategies lack effectiveness and are often associated with intolerable side effects. Therefore, there is a pressing need for innovative therapeutic approaches. Botulinum toxins (BoNT) have shown great potential for pain treatment, with successful use of type A (BoNT/A) in the clinical treatment of chronic migraine due to its long-lasting inhibition of sensory neuronal transmission. However, BoNT/A also has substantial paralytic effects on the neuromuscular junction, limiting the therapeutic dose that can be used, as well as having a considerable cosmetic outcome which may cause additional psychological distress to patients. To overcome these limitations, a new approach utilizing recombinant botulinum toxin-based molecules that retain their analgesic effects with minimal paralytic side effects. In this study, we investigate the efficacy of el-Bitox/A, a novel non-paralytic covalent BoNT/A molecule, in comparison to native BoNT/A, for the management of inflammatory facial pain models.

Using the orofacial pain assessment device (OPAD) as a measure of hyperalgesia, el-Bitox/A (20ng) efficacy was assessed in a model of carrageenan-induced temporomandibular joint (TMJ) inflammation and compared to BoNT/A (2.5U and 5U) and vehicle. Notably, none of the treatments independently altered the baseline values on the OPAD in naïve animals. However, both el-Bitox/A and BoNT/A were effective in reversing carrageenan-induced hyperalgesia, indicating their potential analgesic efficacy. We also monitored bodyweight as an indirect measure of facial paralysis. BoNT/A injections resulted in reduced jaw strength, leading to impaired food consumption and significant bodyweight loss. In contrast, el-Bitox/A and saline injections had no effect on bodyweight variation, further confirming the non-paralytic profile of el-Bitox/A. These findings suggest that el-Bitox/A has potential as an innovative treatment for inflammatory pain conditions. Future studies will aim to evaluate its therapeutic potential in trigeminal neuralgia models, further expanding our understanding of its efficacy and potential clinical applications.

Disclosure of Interest: B Davletov has received consultancy fees from Allergan. B Davletov is a founder of the Neuresta company. AP Andreou has received speaker fees for the participation in symposia sponsored by Allergan and fees for the participation in advisory boards for Allergan. The other authors don't have conflict of interest.

IHC23-PO-157

1 week of Nicotinamide Riboside Administration does not Mitigate Spreading Depression

Berkay Alpay[1], Elif Akaydın[1], Barışcan Çimen[1], Hayrunnisa Bolay[2] and Yıldırım Sara[1]

[1]*Hacettepe University, Ankara, Turkey*
[2]*Gazi University, Ankara, Turkey*

Objective: Spreading depression (SD) is the neurobiological substrate of migraine aura and is commonly employed as a disease model for preclinical migraine research. SD is characterized by an enormous and migrating wave of potassium efflux, which overloads the sodium-potassium ATPase pump (NaKATPase). NaKATPase activity is heavily dependent on ATP production, mainly through oxidative phosphorylation (OXPHOS). As a matter of fact, anoxia provokes SD due to ATP depletion and subsequent inadequate supply of ATP to NaKATPase, causing pump dysfunction. Nicotinamide riboside (NR) is a novel NAD+ booster that can increase the NAD/NADH ratio, which favors OXPHOS. We hypothesize that boosting OXPHOS augments NaKATPase activity and thus attenuates SD. Accordingly, in this study, we aimed to investigate if NR can inhibit migraine aura-correlated SD.

Methods: Male Wistar rats were allocated to two different treatment groups: control (CTRL) and NR. NR was administered perorally at a daily dose of 700 mg/kg in 0.9% saline (1 mg/mL). The CTRL group was given 0.9% saline. After 1 week of drug or vehicle administration, spreading depression (SD) parameters were quantified with in vivo electrophysiology. SD amplitudes, durations, thresholds, frequency, velocity, and propagation failure were evaluated.

Results: NR did not change SD amplitudes, durations, thresholds, and frequency. It modestly increased propagation failure and decreased velocity; however, no statistically significant difference was found between the two groups.

Conclusion: 1 week of NR administration did not alleviate spreading depression.

IHC23-PO-158

Differential interaction of β-arrestin with the CGRP and AMY_1 receptors

Tyla Alexander[1,2], Michael Garelja[1,2] and Debbie Hay[1,2]

[1]*University of Otago, Dunedin, New Zealand*
[2]*Maurice Wilkins Centre for Molecular Biodiscovery, Auckland, New Zealand*

Objective: Calcitonin gene-related peptide (CGRP) is important in migraine pathogenesis. This has led to the development of drugs to target CGRP and the CGRP receptor. There are two different classes of drugs that act at the CGRP receptor; small molecule antagonists (such as rimegepant) or monoclonal antibodies (erenumab). The CGRP receptor is composed of the calcitonin receptor-like receptor (CLR), and receptor activity-modifying protein 1 (RAMP1). However, there is a second CGRP-responsive receptor, the AMY_1 receptor, composed of the calcitonin receptor (CTR) and RAMP1. As this receptor may contribute to the actions of CGRP, it is important to understand how its pharmacology, signalling, and regulatory behaviour compares to that of the canonical CGRP receptor, CLR:RAMP1. Recently, it was shown that the CGRP and AMY_1 receptors are differentially regulated; the CGRP receptor readily internalised whereas the AMY_1 receptor did not. This study aimed to further examine these differences by investigating the interactions of both receptors with the key regulatory protein, β-arrestin, and to determine whether rimegepant and erenumab can antagonise this interaction.
Methods: A bioluminescent resonance energy transfer (BRET) β-arrestin translocation assay was used. β-arrestin was fused with nano-luciferase (BRET donor) and citrine (BRET acceptor) was anchored to the plasma membrane. Cells were transfected with receptor and the BRET constructs, and then stimulated with relevant peptides in the absence or presence of antagonist. The BRET signal was measured, and antagonism quantified.
Results: The CGRP receptor robustly translocated β-arrestin in an agonist-dependent manner, whereas only very weak translocation was evident for the AMY_1 receptor. Accordingly, antagonism could only be quantified with the CGRP receptor. Rimegepant and erenumab both antagonised the translocation of β-arrestin to the CGRP receptor.
Conclusion: These findings support prior data that the AMY_1 receptor is regulated differently to the CGRP receptor. Both rimegepant and erenumab antagonised β-arrestin translocation to the CGRP receptor. It is now important to evaluate this antagonism in comparison to other signalling pathways because bias in pathway antagonism has been observed with other gepants.

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IHC23-PO-159

Sex-dependent modulation of the trigeminovascular system, a role for the Hypothalamic-Pituitary-Gonadal-axis

Eloisa Rubio-Beltran[1], Alejandro Labastida-Ramirez[1], Kevin O'Byrne[2] and Philip R. Holland[1]

[1]*Headache Group. Wolfson Center for Age Related Diseases. King's College London, London, United Kingdom*
[2]*Department of Women and Children's Health, School of Life Course Sciences. King's College London, London, United Kingdom*

Objective: Before puberty, the prevalence of migraine is similar between males and females. Interestingly, after menarche, a sharp increase in incidence is observed in women. This phenomenon points to an interaction between the trigeminovascular system and the Hypothalamic-Pituitary-Gonadal (HPG)-axis. Kisspeptin is a hypothalamic neuropeptide that plays a major role in the regulation of the HPG-axis and puberty onset. Therefore, the aim of the present study was to evaluate the role of kisspeptin in the modulation of the trigeminovascular system, and to assess whether these responses are sex-specific.
Methods: In vivo electrophysiological recordings of spontaneous and dural-evoked nociceptive neuronal responses in the trigeminocervical complex were performed in both male and female rats after kisspeptin administration. Females were further stratified into rising or falling levels of estrogen by vaginal cytology. Durovascular nociceptive-evoked neuronal responses were recorded for 90 minutes and the responses compared between groups.
Results: There was no significant difference in any parameters at baseline (males, 100 ± 2.5; females: rising estrogen 100 ± 1.8, falling estrogen 100 ± 1.5; $p > 0.05$). Following kisspeptin administration, there was a significant increase in dural-evoked responses in the female group with falling levels of estrogen, but no change in male rats or females with rising estrogen levels (males, 86 ± 8.3; females: rising estrogen, 88 ± 16.1; falling estrogen, 201 ± 8.3; $p < 0.05$). Similarly, spontaneous neuronal responses in females in falling levels of estrogen significantly increased after kisspeptin administration when compared to females in rising levels of estrogen (rising estrogen, 87 ± 17.3; falling estrogen 211 ± 60.7; $p < 0.05$).
Conclusion: Our data highlight that kisspeptin can modulate trigeminal nociception in a sex- and estrous

cycle-dependent manner. This is in agreement with the female-predominant prevalence of migraine, as well as with the higher frequency of migraine attacks observed in patients during falling-estrogen states. Modulation of the HPG-axis may be a promising therapeutic option for the treatment of migraine.

IHC23-PO-160

An Innovative Model for CGRP Release: Preserving the Structural Integrity of the Trigeminal System

Kristian Agmund Haanes[1,2], Isabella Mai Christiansen[1] and Lars Edvinsson[1]

[1]*Rigshospitalet, Glostrup, Denmark*
[2]*University of Copenhagen, Copenhagen, Denmark*

Objective: Currently, it is believed that migraine attacks originate in the hypothalamus, followed by a succession of events that activate the trigeminal nucleus caudalis (TNC) and then the trigeminal ganglion (TG). Calcitonin gene-related peptide (CGRP) secretion from the trigeminal system is regarded as essential to migraine pathophysiology, as demonstrated by the efficacy of anti-migraine drugs that target CGRP signaling. This research intended to investigate the direction of communication between the TG and TNC, as well as the roles of transient receptor potential vanilloid 1 (TRPV1) and dopamine receptors. This is particularly important as TRPV1, can be activated by a variety of physical and chemical stimuli, including capsaicin and cannabinoids.
Methods: We adapted the traditional hemiskull-based CGRP release model into a novel model, preserving the fiber-rich connection between TG and TNC. A 3D-printed custom chamber enabled the separation of TG and TNC tissues while preserving their physical connection. This allowed for the examination of CGRP release levels in response to the application of various compounds to TNC or TG, and collect samples independently, establishing directionality.
Results: The application of 1 μM capsaicin to the TNC significantly increased CGRP release from the TG. In addition, 60 mM K+ also significantly stimulated CGRP release from the TG when added to the TNC. In contrast, applying 1 μM capsaicin or 60 mM KCl to the TG did not result in a significant release of CGRP from the TNC. We were further interested in potential modulation of CGRP release by dopamine. However, we found that dopamine induced a delayed CGRP release per se from the TNC. Notably, the D2-specific agonist quinpirole also induced the release of CGRP directly from the TNC, indicating the specific involvement of this receptor. Further, the TRPV1 antagonist AMG9810 (30 μM) inhibited the dopamine-induced release of CGRP, indicating the involvement of TRPV1.
Conclusion: When stimulating the TNC and sampling from the TG, we observed directional CGRP release, indicating that the trigeminovascular system predominantly exhibits anti-dromic (outwards) CGRP release. In addition, the delayed CGRP release induced by dopamine in the TNC and the participation of TRPV1 and dopamine receptors could suggest a potential connection with the hypothalamus. The nature of the agonist activating TRPV1, needs further investigation, but the most likely candidate being endogenous cannabinoids.
Disclosure of Interest: Presentations focusing on CGRP in migraine have been conducted at events sponsored by Teva. Research support has been provided by the Novo Nordisk Foundation, the International Headache Federation, the Lundbeck Foundation, and Innovation Fund Denmark.

IHC23-PO-161

Effect of TRP channels on CGRP release in the trigeminovascular system: potential key players in migraine pathophysiology

Philip Reducha and Kristian Haanes

Rigshospitalet Glostrup, Copenhagen, Denmark

Objective: Migraine is a common disease, but the pathophysiology is not yet resolved. The abundant release of calcitonin gene-related peptide (CGRP) in the trigeminovascular system (TGVS) have been implicated as a driver of the debilitating symptoms. However, little is understood as to how this release is provoked. Transient receptor potential (TRP) channels are a family of cation channels that have been suggested to be implicated in the release process. The TRPV1 channel is a heat sensitive channel, while the TRPM8 is a cold sensitive channel, and the two channels have been suggested to be able to inhibit one another. The TRPA1 channel is a reactive oxygen species sensitive channel and have also been suggested to interact with the TRPV1 channel. Meanwhile, the TRPM3 channel is a hormone sensitive channel, which is interesting in the context of menstrual migraine. When activated, these channels can cause different sensations, notably the sensation of pain. The TRPV1, TRPA1, TRPM8 and recently the TRPM3 are likely candidates in causing migraine symptoms by triggering CGRP release in the TGVS when activated. The aim of this study was to investigate whether using specific agonists of these channels would cause CGRP release in the trigeminal ganglion (TG) and dura mater, and whether there are some interactions between the channels.

Methods: Hemiskulls with intact dura mater and dissected trigeminal ganglions from male Sprague-Dawley rats and an enzyme like immunoassay (ELISA) kit were used to assess CGRP release content. Capsaicin (100 nM), JT010 (1 μM), WS-12 (2 μM) and CIM0216 (100 μM) was used as specific agonists of the TRPV1, TRPA1, TRPM8 and TRPM3 channels, respectively.
Results: Capsaicin caused significant CGRP release when compared to baseline values in both TG (54.5 ± 17.4 pg/ml vs. 126.5 ± 42.9 pg/ml, $p = 0.02$, $n = 6$) and dura mater (21.3 ± 8.7 pg/ml vs. 85.9 ± 12.6 pg/ml, $p = 0.02$, $n = 7$). Similarly, CIM0216 also caused significant CGRP release in both TG (25 ± 4.9 pg/ml vs. 92.3 ± 18.9 pg/ml, $p < 0.001$, $n = 6$) and dura mater (21.8 ± 6.5 pg/ml vs. 61.2 ± 12.7 pg/ml, $p = 0.02$, $n = 7$). In contrast, JT010 and WS-12 failed to cause any CGRP release. Interestingly, when JT010 was dissolved alongside capsaicin, it significantly reduced CGRP release content compared to the TG samples that were stimulated with capsaicin alone (62 ± 7.8 pg/ml vs. 127.4 ± 28 pg/ml, $p = 0.02$, $n = 5$). This was similarly observed with WS-12, however not significantly (52.3 ± 12 pg/ml vs. 87.6 ± 23.1 pg/ml, $p = 0.06$, $n = 7$). These data suggest that both the TRPV1 and TRPM3 channels are potential candidates in the pathophysiology of migraine by causing CGRP release. The TRPM8 and TRPA1 failed to cause CGRP release in the TG and dura mater, at least with the concentrations of the agonists applied. However, they seem to have an inhibitory effect on the TRPV1 channel, by a potential cross talk mechanism.
Conclusion: In conclusion, this study reveals that TRPV1 and TRPM3 channels could play a role in migraine pathophysiology by causing CGRP release in the trigeminal ganglion and dura mater. Conversely, TRPA1 and TRPM8 channels do not directly contribute but exhibit inhibitory effects on TRPV1 channel-mediated CGRP release, suggesting a potential cross talk mechanism. These findings advance our understanding of migraine mechanisms and may guide the development of targeted therapeutic strategies.

IHC23-PO-162

Evaluating the Efficacy of Trametinib Treatment in a Rodent Model of Complete Freund's Adjuvant-Induced Dural Inflammation

Mette Nyholm Jensen, Jesper Peter Bömers, Lars Edvinsson and Kristian Agmund Haanes

Rigshospitalet, Glostrup, Denmark

Objective: In our previously established CFA-induced dural inflammation model, periorbital allodynia and increased CGRP positive fibers in the trigeminal ganglion were observed, while fremanezumab did not mitigate allodynia, suggesting this model could represent other aspects of migraine. The current study aimed to investigate the therapeutic potential of Trametinib, a mitogen-activated protein kinase kinase (MEK) inhibitor, in the same model, assessing the effects on mechanical allodynia and light sensitivity in male Sprague-Dawley rats.
Methods: Rats were randomly assigned to two experimental groups ($n = 8$ each): vehicle and Trametinib treatment. Dural inflammation was induced with CFA, followed by intraperitoneal administration of Trametinib (1 mg/kg initial dose, 0.5 mg/kg daily thereafter). Behavioral tests, including electronic von Frey (day 4 and 6) and Light/Dark box (day 5), were conducted.
Results: Trametinib treatment led to increased mechanical allodynia in the treated group compared to the vehicle group on day 4 (mean: 82.6 ± 7.4 g vs. 116.6 ± 8.1 g, $p < 0.001$) and day 6 (mean: 59.2 ± 5.9 g vs. 107.3 ± 5.8 g, $p < 0.0001$), indicating higher sensitivity in the treated group. No significant differences were observed in light sensitivity (Light/Dark box test) or general behavior between the groups.
Conclusion: Trametinib treatment demonstrated mixed outcomes on CFA-induced dural inflammation in rodents, as it increased mechanical allodynia but did not significantly impact light sensitivity and general behavior. Future studies will include comprehensive molecular analyses to better understand the underlying mechanisms of Trametinib's effects in this model, potentially providing insight into alternative therapeutic strategies for migraine and other neuroinflammatory conditions associated with dural inflammation.

IHC23-PO-163

Chronic administration of lamotrigine or acetyl salicylic acid increases cortical spreading depolarization threshold in mice

Gurdal Sahin[1,2], Buket Donmez-Demir[3], Sena Uzun[1,2] and Hulya Karatas[3,4]

[1]*SkåNeuro Neurology Clinic, Lund, Sweden*
[2]*Department of Clinical Sciences of Malmö and Lund, Lund University, Lund, Sweden*
[3]*Hacettepe University, Institute of Neurological Sciences and Psychiatry, Ankara, Turkey*
[4]*Neuroscience and Neurotechnology Center of Excellence (NÖROM), Ankara, Turkey*

Background: Migraine is a chronic neurological disorder that is the second cause of disability worldwide. Treatment options used in the prophylactic treatment of migraine with aura are limited. In clinical practice, we still use

antidepressants, calcium antagonists, antihypertensives, beta-blockers, and antiepileptics as the prophylactic treatment of migraine, with modest efficacy. Lamotrigine (LMT) has been shown to be effective in migraine with aura according to small case series. Moreover, there are anecdotal reports claiming that acetylsalicylic acid (ASA) could also be used in the prophylaxis of migraine with aura. However, there is still an unmet need to study the preclinical effects of these treatments either separately or in a combination protocol which may help to decrease their individual side effects. Cortical spreading depolarization (CSD) is regarded as the electrophysiological correlate of migraine aura and an established method to investigate the effects of anti-migraine pharmaceuticals. In this study, our aim is to elucidate the impact of chronic administration of LMT and ASA individually or in combination on the generation, propagation, and electrophysiologic characteristics of CSD.

Methods: Adult Swiss albino female mice were divided into five groups of six animals, each randomly. To study the effect of combined drug therapy on migraine, we administered LMT (150 ul, 10 mg/kg in saline), ASA (150 ul, 30 mg/kg in saline), LMT (75 ul, 10 mg/kg lamotrigine) plus ASA (75 ul, 30 mg/kg) together, natrium valproate (VPA)(150 ul, 200 mg/kg in saline) and saline intraperitoneally (ip) for 28 days. Saline was used as a sham to eliminate the possible effects of ip vehicle injection on the results, and VPA was used as a positive control. CSDs were induced by topical potassium chloride (KCl) application over the dura and recorded electrophysiologically with two Ag-AgCl2-coated pellet electrodes placed over the thinned parietal cranium. To evaluate the CSD threshold, cotton balls soaked with increasing KCl concentrations (0.05, 0.075, 0.1, 0.125, 0.15, and 0.175 M) were placed over the dura through the burr hole opened at the frontal region with 5-minute intervals.

Results: CSD threshold was increased significantly in VPA, LMT, and ASA injection groups compared to the saline injection group ($p = 0.0043$; Kruskal-Wallis test). There was no significant difference between the CSD threshold results of drug-injected experimental groups ($p > 0.05$; Kruskal-Wallis test). CSD threshold of lower doses of LMT and ASA combination group did not change compared to the saline group which may indicate that LMT and ASA have no synergistic effects in this setting. Electrophysiologic characteristics and the propagation of CSDs after a month of drug injections did not change among groups.

Conclusion: LMT or ASA could be regarded as a treatment choice in the prophylactic treatment of migraine with aura. Chronic administration of low-dose lamotrigine and acetylsalicylic acid does not change the cortical spreading depolarization threshold in mice. Therefore, lower doses of LMT and ASA combination therapy may not be effective in migraine.

Disclosure of Interest: None Declared

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Characterization of a Minimally Invasive Method to Induce Cortical Spreading Depolarization

Beyza Turken[1], Kadir Oguzhan Soylu[1], Muge Yemisci[1,2,3] and Hulya Karatas[1,2]

[1]*Institue of Neurological Sciences and Psychiatry, Hacettepe University, Ankara, Turkey*
[2]*Neuroscience and Neurotechnology Center of Excellence (NÖROM), Ankara, Turkey*
[3]*Hacettepe University, Faculty of Medicine, Department of Neurology, Ankara, Turkey*

Objective: Cortical spreading depolarization (CSD) is a neuronal and glial depolarization wave that spreads through the cortex disturbing ion homeostasis and hemodynamics in the brain. CSD takes place in the pathophysiology of different neurological conditions including ischemic stroke, traumatic brain injury, and subarachnoid hemorrhage, and is considered to be the underlying cause of migraine aura. Different methods are used to induce CSD in experimental rodent studies, but conventional methods require opening a burr-hole on the skull. This invasive procedure itself may cause brain injury and lead to spontaneous CSDs and neuroinflammation. In this study, our aim is to compare the threshold and electrophysiological characteristics of CSDs induced by potassium chloride application on dura mater via burr-hole or thinned skull in mice.

Methods: Female and male adult Swiss albino ($n = 14$) and C57Bl6 ($n = 16$) mice were used for the experiments. Mice were anesthetized with urethane ($n = 26$) or isoflurane ($n = 4$). CSDs were induced by topical potassium chloride (KCl) soaked cotton ball application. To evaluate the CSD threshold, cotton balls soaked with increasing KCl concentrations (0.05, 0.075, 0.1, 0.25, 0.5, 0.75, 1 M) were used. In the conventional method, a 2–3 mm diameter burr hole was opened with a drill on the frontal bone, and KCl-soaked cotton balls were placed on the intact dura at 5-minute intervals. In the minimally invasive approach, an area of the same size and location as the burr-hole was thinned on the frontal skull. The thickness of the cortical bone was standardized such that only the internal compact bone layer was left under a stereomicroscope. KCl-soaked cotton balls were placed on the thinned area. CSD waves were recorded electrophysiologically with an Ag-AgCl2-coated pellet electrode placed over the parietal cranium. Mann-Whitney U test is used for statistical analyses, and invasive and minimally invasive CSD induction methods, gender effect, anesthesia agents, Swiss albino, and C57BL6 strains were compared according to the CSD threshold and electrophysiological properties of CSD waves.

Results: Half-maximum duration of CSD waves did not differ in all burr-hole groups compared to all intact skull groups. The amplitude of CSD waves was significantly increased in the intact skull groups compared to burr-hole groups independent of gender effect, anesthesia agents, and strains ($p = 0.03$). However, the CSD threshold was significantly different according to the induction method; the median value of the threshold concentration was 0.1 M KCl in the burr-hole groups and 0.25 M KCl in the intact skull groups ($p < 0.001$). CSD wave threshold and electrophysiological characteristics were not different in female and male, Swiss albino and C57Bl6 mice. Anesthetic agents also had no effect on CSD properties and threshold levels.
Conclusion: This study showed that a minimally invasive method by only thinning the skull may be sufficient to induce CSD and study its electrophysiological characteristics. This method has advantages over the invasive burr-hole approach regarding the prevention of disrupting cranium integrity and exposing dura mater which may lead to unwanted trauma and neuroinflammation. Thus, it can be used to study drug screening or other pathophysiological studies in which CSD takes place. However, for CSD threshold studies, burr-hole or other methods including electrical or optogenetic induction methods should be preferred.
Disclosure of Interest: None Declared

IHC23-PO-165

Modeling Familial hemiplegic migraine type 3 with patient-derived induced pluripotent stem cells

Tao Wang[1,2], Zhao Dong[1] and Shengyuan Yu[1]

[1]*Department of Neurology, Chinese PLA General Hospital, Beijing, China*
[2]*Medical School of Chinese PLA, Beijing, China*

Objective: Familial hemiplegic migraine type 3 (FHM3) is a severe form of migraine with aura caused by mutations in the SCN1A gene encoding the voltage-gated sodium channel Nav1.1. Effects of FHM3 mutations on Nav1.1 channels functioning in heterologous expression systems is variable and data from mouse cannot translate to human. Therefore, patient-specific models are needed for investigating the pathology.
Methods: We identified a Chinese FHM3 family and generated induced pluripotent stem cells (iPSC) from two FHM3 patients. FHM3 iPSCs and a human control iPSC was differentiated to forebrain GABAergic interneurons (GINs). Functionality of dierentiated GINs was examined by whole-cell patch-clamp recordings and Multielectrode array (MEA) recordings. Bulk RNA sequencing analysis was performed on FHM3 and control lines after 65 days of differentiation to detect the changes in transcriptome profile.
Results: All FHM3 patients in the family had typical clinical manifestations of hemiplegic migraine and a novel mutation, F1774C in SCN1A, was identified. FHM3 and human control iPSCs differentiate into MGE-like cells and then into GINs. Electrophysiologic recordings showed significantly lower sodium current density and decreased neural firing in FHM3 GINs compared with control. Consistent with electrophysiologic analysis, MEA recordings showed lower weighted mean firing rate in FHM3 GINs. Transcriptome analysis revealed specific dysregulations of genes for binding, catalytic activity, transporter activity and signal transducer activity in FHM3 GINs versus control.
Conclusion: We have for the first time investigated FHM3 pathophysiological mechanisms using human iPSC-based models. Our results indicate a functional decline in FHM3 GINs and patient-specific neurons are useful for modelling FHM3.
Disclosure of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this abstract.

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Annexin-A1 in the spinal trigeminal nucleus caudalis exerts anti-nociceptive effect in a mouse model of medication overuse headache

Zihua Gong[1,2,3], Chunxiao Yang[1,4], Shengyuan Yu[1,2] and Zhao Dong[1,2]

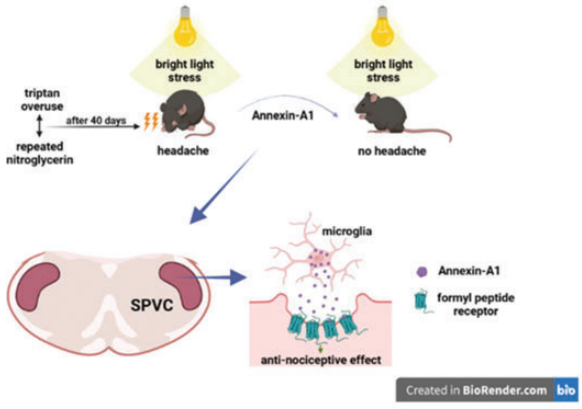
[1]*Department of Neurology, the First Medical Center, Chinese PLA General Hospital, Beijing, China*
[2]*Medical School of Chinese PLA, Beijing, China*
[3]*Department of Medical Oncology, 980th Hospital of PLA Joint Logistical Support Force (Bethune International Peace Hospital), Shijiazhuang, China*
[4]*School of Medicine, Nankai University, Tianjin, China*

Objective: Medication overuse headache (MOH) is a serious worldwide health issue with an incomplete understanding of its pathophysiology. The interaction between the headache attacks and medication overuse makes it difficult to understand the complex pathophysiology of MOH. We aimed to develop a preclinical MOH model incorporating these two key factors to explore the pathogenesis at the spinal trigeminal nucleus caudalis (SPVC) level.
Methods: An MOH mouse model was constructed by overusing rizatriptan benzoate (RIZ) in a glyceryl trinitrate (GTN) induced chronic migraine mouse model. The basal and acute (1h after bright light stress) mechanical

threshold was measured using the von Frey test to evaluate the cutaneous allodynia and latent sensitization. C-Fos immunofluorescent staining was performed to detect the excitability of the SPVC. Finally, RNA-Seq was used to explore the differentially expressed genes (DEGs) in SPVC. Quantitative RT-PCR, western blot, immunostaining, and pharmacological studies were used for further validation.

Results: RIZ overuse aggravated GTN-induced cutaneous allodynia and caused a prolonged state of latent sensitization accompanied by neural hyperactivity of the SPVC. RNA-Seq analysis identified 20 overlapped DEGs among four experiment groups. We further confirmed that Annexin-A1 (ANXA1) in the SPVC was significantly upregulated in GTN+RIZ mice. Microinjection of ANXA1-derived peptides Ac2-26 TFA into the lateral ventricle inhibited BLS-induced acute mechanical allodynia via the formyl peptide receptor in GTN+RIZ mice.

Conclusions: Our animal model successfully mimicked the clinical phenomenon of worsening of pre-existing headache by triptan overuse. We report for the first time that ANXA1 can centrally inhibit the nociceptive transmission associated with MOH and might become a potential therapeutic target.



Disclosure of Interest: None Declared

IHC23-PO-167

cGAS-STING pathway as a novel target in the context of spreading depolarization

Kadir Oguzhan Soylu[1], Onur Cagin Gurlek[1], Hulya Karatas[1,2] and Muge Yemisci[1,2,3]

[1]*Hacettepe University, Institute of Neurological Sciences and Psychiatry, Ankara, Turkey*
[2]*Neuroscience and Neurotechnology Center of Excellence (NÖROM), Ankara, Turkey*
[3]*Hacettepe University, Faculty of Medicine, Department of Neurology, Ankara, Turkey*

Objective: Spreading depolarizations (SDs) are slowly propagating waves of intense neuronal and glial depolarizations that have roles in ischemic stroke, traumatic brain injury and considered to be the electrophysiological correlate of migraine aura. Cyclic-GMP-AMP-synthase (cGAS)-Stimulator of interferon genes (STING) pathway is an innate immune system response that starts type I interferon signaling and is determined to be involved in several neuroinflammatory disorders. It is also implicated in the regulation of nociception. Recent data demonstrated that SD triggers parenchymal inflammation in the rodent brain. Our aim in this study is to investigate if cGAS-STING pathway takes part in SD induced parenchymal inflammatory response.

Methods: SDs were induced non-invasively by optogenetic stimulation in Thy1-ChR2-YFP genotype mice to determine cGAS-STING pathway activity after SD. One or six SDs were induced, and sham group was performed ($n = 3$/group). Naïve brains were also used as controls. Mice were sacrificed after 5 and 24 hours. Brain sections were immunohistochemically stained for cGAS-STING pathway proteins such as STING, cGAS, phospho-Interferon Regulatory Factor 3 and Interferon beta. Neurons were marked with NeuN and microglia with Iba1. Cerebral cortex regions of the sections were imaged with confocal microscope and three nonoverlapping images were taken from each. Positively stained cells were counted, and positive cell/total cell ratios were used for comparisons. We also evaluated SD susceptibility after cGAS-STING pathway inhibition. Mice were intraperitoneally injected with 20 mg/kg STING inhibitor C-176 (or its vehicle, $n = 4$/group) 4 hours prior to SD threshold experiments. SD thresholds were determined via topically applied gradually increasing potassium chloride (KCl) concentrations (0.0125–0.1M) on the dura until the first SD was detected as the typical DC potential shift in the electrophysiological recording. For statistical analyses Kruskal-Wallis H and Mann-Whitney U tests were used.

Results: Multiple SDs significantly increased the immunopositivity of cGAS-STING pathway proteins in cerebral cortex at 5 hours ($p < 0.001$) and 24 hours after SDs ($p < 0.001$) when compared to sham or naïve controls. Increase in immunopositivity was observed both in neurons and microglia. Single SD was also enough to determine an increase in immunopositivity ($p < 0.001$). Inhibiting STING with C-176 significantly decreased SD threshold compared to vehicle treatment ($p = 0.018$).

Conclusion: We showed that single or multiple SDs increase the expression of cGAS-STING pathway proteins in mouse cerebral cortex. This suggests cGAS-STING pathway activation after SDs. Notably, inhibiting this pathway increases SD susceptibility. Hence, further elucidation of the relationship between SD and cGAS-STING pathway might provide new pathophysiologic mechanisms and therapeutic targets for diseases where SDs occur.

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Disclosure of Interest: None Declared

IHC23-PO-168

Relevance of brainstem SD for breathing complications in FHM1 and FHM3 mouse mutants

Else Tolner, Nico Jansen, Maarten Schenke, Rob Voskuyl and Arn van den Maagdenberg

Leiden University Medical Center, Leiden, Netherlands

Familial Hemiplegic Migraine (FHM) mouse models display an enhanced susceptibility to experimentally induced cortical spreading depolarization (CSD), the correlate of the migraine aura. A severe consequence of the FHM type 1 (FHM1) S218L mutation is the risk for sudden death in association with epilepsy, for which we found brainstem SD and subsequent apnea to be a causative mechanism (1,2). While apnea during and following seizures is common, it can also occur in the absence of seizures, and may even cause sudden death. To this end, we now also studied mechanisms of fatal apnea in our FHM3 L263V knock-in (KI) mouse model, earlier described to display spontaneous events of cortical SD (3), and compared outcomes to the mechanisms leading to sudden death in FHM1 S218L mutant mice. Using direct-current and local field potential recordings in the brainstem and cortex of freely behaving heterozygous FHM3 mutant mice, we found that events of fatal apnea were caused by an apparent sudden and widespread brainstem depolarization that was not preceded by behavioural seizure activity. The lethal apnea in FHM3 mutant mice was rescued by sodium channel blockade. In comparison, events of lethal apnea in homozygous FHM1 S218L mutant mice were preceded by seizure-related brainstem SD, and could be prevented NMDA receptor antagonists. Our findings underscore the value of FHM mouse models for furthering insight in and developing therapeutic strategies for targeting SD-mechanisms and its consequences, including risk for (fatal) breathing complications.
Disclosure of Interest: None Declared

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IHC23-PO-169

Spontaneous spreading depolarizations in a novel mouse model of familial hemiplegic migraine type 2

Else Tolner, Nico Jansen, Maarten Schenke, Rob Voskuyl, Chelsey Linnenbank, Cor Breukel, Sandra van Heiningen and Arn van den Maagdenberg

Leiden University Medical Center, Leiden, Netherlands

The mechanisms of initiation of cortical spreading depolarization (SD) are understudied due to a paucity of disease models with spontaneously occurring events. We here present a novel mouse model of familial hemiplegic migraine type 2 (FHM2), expressing the missense T345A-mutated α2 subunit of the Na^+/K^+ adenosine triphosphatase (*Atp1a2*^{T345A}). Here we generated transgenic heterozygous and homozygous *Atp1a2*^{T345A} knock-in (KI) mice to study effects of the T345A mutation on brain function. We found that, in contrast to other models with an FHM2 mutation, also leading to loss of α2 Na^+, K^+ ATPase function but unlike in our model due to lack of protein expression, homozygous *Atp1a2*^{T345A} mice are viable. In fact, cortical and hippocampal α2 Na^+, K^+ ATPase protein expression in homozygous mice was comparable to that observed in wild type and heterozygous littermates. Notably, homozygous mutant mice had no apparent impairment of mobility or gross behaviour, but showed decreased survival with spontaneous death, we were able to identify as sudden apnea. Spontaneous cortical SD events occurred exclusively in the homozygous mice at remarkably regular intervals indicative of a diurnal rhythm and consistently showed propagation from the visual to the motor cortex. The events seemed to predominantly originate from the hippocampus. Despite observed hippocampal hyperexcitability, the spontaneous SDs in *Atp1a2*^{T345A} mice were only rarely associated with epileptiform behaviour and the mutant mice showed decreased seizure expression during kindling when compared to wildtype animals. The occurrence of spontaneous SDs in this FHM2 mouse model provides an excellent basis for studying mechanisms of SD initiation and developing selective therapies targeting SD initiation. This can benefit people suffering from migraine with aura but also other neurological disorders involving SD, such as stroke and certain epilepsy syndromes with the risk for lethal apnea.
Disclosure of Interest: None Declared

IHC23-PO-170

Stimulation of CGRP-expressing neurons in the medial cerebellar nucleus induces migraine-like sensory hypersensitivity in mice

Brandon Rea[1,2], Mengya Wang[3], William Castonguay[3], Thomas Duong[4], Michael Huebner[4], Harold Flinn[4], Jayme Waite[1,2], Agatha Greenway[4,5], Joseph Tutt[4,5], Nicholas Dorricott[4,5], Andrew Russo[2,4,6] and Levi Sowers[2,7]

[1]*Department of Pediatrics, University of Iowa, Iowa City, USA*
[2]*Center for the Prevention and Treatment of Visual Loss, Veterans Administration Health Center, Iowa City, USA*
[3]*Department of Neurology, University of Utah, Salt Lake City, USA*
[4]*Department of Molecular Physiology and Biophysics, University of Iowa, Iowa City, USA*
[5]*University of Bath, Bath, United Kingdom*
[6]*Department of Neurology, University of Iowa, Iowa City, USA*
[7]*University of Iowa, Iowa City, USA*

Objective: To better understand and treat migraine, identification of neuroanatomic contributors has been an integral component of ongoing studies. The cerebellum has become an auspicious region of interest regarding migraine. Notably, the cerebellum is a sensory integration center that communicates with migraine-related brain regions, is altered during migraine in human imaging studies and contains a high density of binding sites for calcitonin gene-related peptide (CGRP). CGRP injection centered on the deep cerebellar medial nucleus (MN) of mice induced migraine-like behaviors including light aversion, tactile hypersensitivity, and spontaneous squint. The objective of this study was to discern which cell types in the MN may contribute to these migraine-like phenotypes through selective optogenetic stimulation of different cell types within that nucleus.
Methods: To test if stimulation of the cerebellum is sufficient to induce migraine-like behaviors, we utilized an optogenetic approach to stimulate medial nucleus cell bodies and fiber projections in differing cell types. To stimulate all neuronal cell bodies, we used synapsin-driven channelrhodopsin (ChR2) expression in the medial nucleus. To stimulate CGRP-expressing neuronal cell bodies in the medial cerebellar nucleus (MN^{CGRP}) and fibers that project to the posterior thalamus (PoT) and zona incerta (ZI), we expressed Cre-dependent ChR2 in the medial nucleus of $Calca^{Cre/+}$ mice, which have Cre recombinase inserted into the α-CGRP encoding gene *Calca*.
Results: Optical stimulation of synapsin-driven ChR2, which targets all MN neurons, did not induce migraine-like behaviors. However, optical stimulation of MN^{CGRP} neurons in the medial nucleus of $Calca^{Cre/+}$ mice induced light aversive behavior and tactile hypersensitivity. No significant increase in spontaneous squint, anxiety-like behavior, or changes in gait were observed.
Conclusions: CGRP-expressing neurons in the medial nucleus of the cerebellum may contribute to migraine-like touch and light hypersensitivity.

IHC23-PO-171

Actions of an NF-kB inhibitor on the GTN-induced neuronal inhibition in the A11 hypothalamic nucleus

Joseph Lloyd[1], Ana Pereira[1], Ramla Abuukar Abdullahi[1], Martyn Jones[1,2] and Anna Andreou[1,3]

[1]*King's College London, London, United Kingdom*
[2]*Zenith NeuroTech Ltd., London, United Kingdom*
[3]*Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom*

Objective: Hypothalamc microinflammation may be involved in migraine and cluster headache initiation, given the hypothalamic increased activity that is observed before the onset of attacks or during the cluster headache bout periods. Previous work in our lab has shown a prominent activation of inflammatory and immune signalling pathways. Our objective was to investigate the role of the immune and inflammatory mediator NF-κB (nuclear factor kappa light chain enhancer of activated B cells) signalling pathway, in glyceryl trinitrate (GTN)-induced hypothalamic neuronal firing adaptations in models of migraine and cluster headache.
Methods: All procedures were performed under a UK Home Office licence in accordance with the 1986 Animal (Scientific Procedures) Act in anaesthetised Sprague Dawley rats (Charles River, 250–350g). Solutions of TPCA-1 (0.5 µl, 20 mM; IKK-2-inhibitor of the NF-kB pathway) and glyceryl trinitrate (GTN) (80 mg/kg, 0.5 mg/ml) were infused via cannulation of the carotid artery. A 7-barrel micro-iontophoresis electrode, filled with glutamate, dopamine and pontamine sky blue dye was placed within the A11 hypothalamic nucleus using stereotaxic coordinates. Glutamate-induced activity of the A11 was recorded using in vivo extracellular electrophysiological techniques, 5-sec pulses of glutamate were applied to cells at 1-min intervals. Dopamine was applied, over the course of 5 glutamate pulses, to confirm autoregulation of dopaminergic cells. GTN was infused over 20-min period followed by 90-min recording of glutamate-induced neuronal activity.
Following electrophysiology animals were perfused with 1% PFA and the tissue dissected and processed for histology. Brain and the trigeminal cervical complex tissue were

sectioned at 20 μm slices on a cryostat. Coronal sections of brain in containing the hypothalamic region were stained with antibody for P65 and DAPI and imaged on a confocal microscope.

Results: Following GTN infusion, glutamate-induced neuronal activity of dopaminergic cells in the A11 hypothalamic nucleus was reduced for the 90-min recording period, in agreement with previous observations of the spontaneous neuronal activity. This reduction was attenuated in animals pre-treated with the IKK inhibitor TPCA-1, but not in animals treated with vehicle control.

Intracarotid infusion of TPCA-1, as well as local hypothalamic microinjection of TPCA-1, was found to cause positive staining for P65, a component of the NF-kB complex, in the hypothalamus, including the A11 dopaminergic nucleus, which was not seen in tissue collected from animals treated with vehicle control. P65 was present in the cytosol and not in the nucleus.

Conclusion: Application of TPCA-1 appears to alter the dopaminergic hypothalamic response to GTN, by preventing internalization of the NF-kB dimer. This suggests that the NF-kB signalling pathway, which is involved in the initiation of inflammatory and immune responses, could be implicated in the initiation of cluster headache attacks driven by the hypothalamus.

Disclosure of Interest: J.O. Lloyd – Nothing to declare, A.D. Pereira – Nothing to declare, R.A. Abdullahi – Nothing to declare, M. Jones – founder and CEO of Zenith NeuroTech Ltd and consultant to Presidio Medical Inc. A.P. Andreou – Chair of the Headache SIG of the British Pain Society, Member of the Coordinating Panel on Neuroscience/Translational Neurology of the European academy of Neurology, Member of the Neuroscience Leadership Group of King's Health Partners, Speaker honoraria from AbbVie, Eli Lill, Research support to institution by: Brain Research UK, Medical Research Council, Medical Research Foundation, Rosetrees, Migraine Trust, Associate editor of Frontiers of Neurology, Editorial board of Journal of headache and pain, Journal of clinical medicine, Participation on a Data Safety Monitoring Board or Advisory Board Eli Lilly, AbbVie Clinical trials involvement, e.g. Principal investigator Eli Lilly, Teva, Board member of Neuresta

IHC23-PO-172

Capsaicin-induced mast cell degranulation in the pericranium does not alter the rate of mast cell degranulation in the adjacent dura mater in rats

Rita Santana dos Reis, Juliana Ramos de Andrade, Sandra Lopes de Souza and Marcelo Moraes Valença

Universidade Federal de Pernambuco, Recife, Brazil

Background: Pain is a biological protection mechanism moving away part of the body from a possible offending factor. In the head, we find two structures with a great richness of nociceptive innervation: the dura mater and the pericranium. Many studies were carried out with dura mater, as if it were the only site of the genesis of the primary headache, ignoring that the pericranium may be the first site where the individual would feel pain when activated. Another point to consider would be whether there would be communication between these two compartments – pericranium and dura mater.

Objective: To verify if there would be a functional communication between the pericranium, with the dura mater, we developed an animal model with rats to quantify the rate of mast cell degranulation induced by capsaicin in the pericranium by observing whether there was a concomitant alteration in the degranulation of mast cells in the adjacent dura mater.

Methods: The experiments were conducted in Wistar rats with authorization from the Ethics Committee on Animal Use (n°0084/2019). To verify the presence of mast cells in the pericranium (Experiment 1 – mechanical scalp remotion stimulation), we used male [n = 9] and female [n = 8] rats (80 days of age) that, after anesthesia, underwent mechanical stimulation, had their scalp removed and received 10 μl of 0.9% NaCl for 10 min. Experiment 2 – Capsaicin stimulation; male rats (n = 9) were used, and after anesthesia, the scalp was removed, and a longitudinal incision was made to separate the hemipericrania (right and left). On the left side, 10μl of 0.9% NaCl was pipetted, and on the right side, 10μl of capsaicin (10–6 M) for 5 min. After the 5 minutes, pieces of cotton soaked with the same amount of NaCl and capsaicin, respectively, were placed over the hemipericrania for another 5 minutes, totaling 10 minutes of stimulation. After that, the animals were euthanized, and the samples of the pericranium and the dura mater were fixed in 10% buffered formaldehyde. In Experiment 3, the control group (n = 5, male rats), without stimulation (no mechanical scalp remotion or capsaicin), the animals were anesthetized, decapitated, and fixed in 10% buffered formaldehyde. Scalp removal was performed only after fixation for histological analysis. In the histological preparation, the dura mater samples were fixed on slides stained with toluidine blue (0.1%), and the pericranium samples were deparaffinized and stained. The slides were photomicrographed (zoom 400x) to count granulated and degranulated mast cells. The data are presented as percentage or mean ± SD.

Results: Granulated and degranulated mast cells were found in the pericranium of male and female rats (Table 1). In the capsaicin-stimulated hemipericrania, there was a higher mast cell degranulation (%) (58 ± 5 [n = 9] vs. 76 ± 6 [n = 9]; p = 0.034). When the rate of degranulation of mast cells present in the adjacent dura mater was observed, there

was no significant difference between the pericranial side stimulated with capsaicin and the side stimulated with 0.9% NaCl (0.9% NaCl, 30 ± 8% [n = 9] vs. capsaicin, 23 ± 5% [n = 9]; p = 0.491). The mechanical stimulus over the pericranium caused greater degranulation of mast cells in relation to the pericranium of the control group (58 ± 5% [n = 9] vs. 27 ± 3% [n = 5]; p = 0.001).

Table 1. Individual quantitative count of granulated and degranulated mast cells in the pericranium.

	Female		Male	
Rat	granulated	degranulated	granulated	degranulated
1	2	17	9	21
2	4	40	17	23
3	0	58	14	39
4	3	35	36	48
5	15	76	28	60
6	1	46	27	11
7	24	73	20	37
8	5	13	13	8
9	–	–	19	30

Conclusion: We detected mast cells in both the pericranium and the dura mater of adult rats. Capsaicin was able to degranulate a higher rate of mast cells in the stimulated pericranium. However, a similar phenomenon was not observed in the adjacent dura mater on the same side of the stimulated pericranium. This experimental design suggests no functional communication between these two anatomical compartments. The pericranium may participate in the pathophysiological mechanism of some primary headaches mainly due to the presence of mast cells and their possible role in sterile inflammation. A disturbance of this mechanism, inherent to the pericranium, could be one of the triggers for a primary headache attack.

IHC23-PO-173

Inhibition of hypothalamic histamine reduces facial allodynia in murine models of migraine

Joseph Lloyd[1], Ana David Pereira[1], Ramla Abuukar Abdullahi[1], Martyn Jones[1] and Anna Andreou[1,2]

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

Objective: To investigate the role of hypothalamic histamine on animal behaviour involved in the nociceptive transmission and on cortical excitability relevant to migraine.

Methods: All procedures were performed under a UK home office licence in accordance with the 1986 Animal (scientific procedures) Act. HDC-Cre mice (Jackson Laboratory) had histidine decarboxylase (HDC) chemogenically inhibited with DREADD virus, injected into the tuberomammillary nucleus of the hypothalamus, according to stereotaxic coordinates, 3 weeks prior to behavioural testing. DREADD virus was subsequently activated with Clozapine N-oxide (CNO) on the day of testing.

Facial allodynia was assessed on freely moving, unanaesthetised animals using an orofacial pain assessment device (OPAD), which is testing animal willingness to touch face bars in return for a reward at normal temperature (33C) and at nociceptive temperatures (45 and 7°C). Facial allodynia was tested at baseline, following IP injection of CNO (inhibition of brain histamine) and at 30 minutes, 2 hours and 4 hours following IP injection of glyceryl trinitrate (GTN) (80 mg/kg, 0.5 mg/ml).

Following OPAD assessment, the cortical spreading depression (CSD) threshold was determined by applying electrical stimulation to the visual cortex and electrophysiological recordings of cortical steady-state potentials. Following, animals were perfused with 1% PFA and the tissue was dissected and processed for histology. The brain and the trigeminal cervical complex tissue were sectioned at 20 μm slices on a cryostat.

Results: Inhibition of HDC using the DREADD virus alone did not alter behavioural responses to noxious thermal stimuli. However, following GTN infusion naïve mice showed a reduction in response to noxious high (45°C) that was not seen in the HDC-Cre mice.

In these experimental groups, HDC-Cre animals were not found to have significantly different electrical thresholds for the induction of CSD following CNO than naïve animals.

Conclusion: In conclusion, inhibition of hypothalamic histamine appears to alter behavioural responses to noxious thermal stimuli during a model of migraine. This could suggest an attenuation of facial allodynia, indicating hypothalamic histamine as a potential driver of migraine pain. However, hypothalamic histamine does not appear to alter cortical excitability.

Disclosure of Interest: Disclosure of interest for Anna Andreou is listed below. All remaining authors have no interest to disclose. Leadership or Board position in other society, committee or advocacy group (voluntary or otherwise): 1. Chair of the Headache SIG of the British Pain Society 2. Member of the Coordinating Panel on Neuroscience/Translational Neurology of the European academy of Neurology 3. Member of the Neuroscience Leadership Group of King's Health Partners Membership of any professional bodies, special interest groups or mutual support organisations: 1. International Headache Society 2. British Association for the Study of Headache 3. British Pain Society 4. European

Academy of Neurology Personal fees (remuneration/honoraria/consultancy): 1. Speaker honoraria from AbbVie, Eli Lilly Participation on a Data Safety Monitoring Board or Advisory Board: 1. Eli Lilly 2. AbbVie Clinical trials involvement, e.g. Principal investigator 1. Eli Lilly 2. Teva Relationship with scientific journals, e.g. Editorial Board, reviewer 1. Associate Editor of Frontiers of Neurology, Editorial board of Journal of Headache and pain, Journal of clinical medicine Leadership or Board position in pharma and/or biotech companies 1. Board member of Neuresta

Headache pathophysiology – Imaging and neurophysiology

IHC23-PO-174

Clinical correlates of cerebrovascular reactivity in patients with migraine: a prospective CO2 targeting study

Soohyun Cho[1], Bo-yong Park[2] and Mi Ji Lee[3]

[1]*Uijeongbu Eulji Medical Center, Uijeongbu, Korea, Republic of*
[2]*Inha University, Incheon, Korea, Republic of*
[3]*Seoul National University Hospital, Seoul, Korea, Republic of*

Background: Reduced cerebrovascular reactivity (CVR) has been reported as associated with higher white matter hyperintensity burden in patients with migraine. We questioned whether the CVR has any impacts on clinical manifestation of migraine. In this study, we aimed to investigate clinical correlates of CVR using state-of-the-art methodology in patients with migraine without aura (MO) and those with migraine with aura (MA).
Methods: A total of 51 patients with episodic migraine (31 with MO and 20 with MA) aged 19–49 who had no vascular risk factors underwent 3T blood oxygenation level-dependent (BOLD) MRI with prospective end-tidal carbon dioxide (EtCO2) targeting. During the experiment, hypercapnia was induced with monitoring and targeting patients' EtCO2 while BOLD signal changes were simultaneously recorded. The CVR of each voxel was measured by changes in BOLD signals in response to EtCO2 increment. Average CVRs of whole brain, whole white matter and whole gray matter were calculated. The correlation between clinical factors (age, body mass index, disease duration, monthly migraine days, monthly days of acute medication use, and regular caffeine intake) and CVR was analyzed using Spearman's correlation coefficient.
Results: Patients included in this study had a median age of 35.0 (IQR, 27.0–41.0) years and median monthly headache days of 3.5 (IQR, 2.0–5.0). The median CVRs were not different between MO and MA in the whole brain ($p = 0.772$), whole white matter ($p = 0.685$), and whole gray matter ($p = 0.847$). In patients with MO, no correlations were observed between clinical factors and CVR in the whole brain, white matter, and gray matter. In patients with MA, monthly migraine days were negatively correlated with whole brain CVR as well as gray matter CVR (Spearman's rho $= -646$ and 610, $p = 0.002$ and 012, respectively). White matter CVR of patients with MA only correlated with age (rho $= -0.603$, $p = 0.005$).
Conclusions: In our study, CVR was not different between MA and MO. We found that lower CVR was associated with higher migraine frequencies only in patients with MA. Reduced vascular reservoir, particularly of gray matter, may play a role in generating migraine attacks in MA.
Disclosure of Interest: S. Cho: None Declared, M. J. Lee Conflict with: This study was supported by Samjin Pharmaceutical Co. and the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (No. 2020R1A2B5B01001826). The funders had no role in study design, data analysis, and interpretation of results.

IHC23-PO-175

Resting state EEG microstate dynamics altered in migraine patients with and without aura

Xiangyu Lei, Meng Wei, Liang Wang, Chenyu Liu, Qin Liu, Xiaoyu Wu, Qinfan Wang, Xinyue Sun, Guogang Luo and Yi Qi

Department of Neurology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

Objective: To evaluate EEG microstate differences between migraine with aura, migraine without aura, and healthy controls. **Background:** Previous research employing microstate analysis found unique microstate alterations in migraine without aura; however, it is uncertain how microstates appear in migraine with aura.
Methods: 30 participants each of migraine with aura (MA), migraine without aura (MO), and healthy controls (HC) were enrolled. EEG was recorded for all participants under resting-state. The microstate parameters of four widely recognized microstate classes A-D were calculated and compared across the three groups.
Results: The occurrence of microstate B in the MO group was significantly higher than in the HC ($P = 0.006$) and MA ($P = 0.016$) groups. While the contribution of microstate B was significantly increased in the MO group compared to the HC group ($P = 0.016$). Besides, the microstate A displayed longer duration in MA group compared to MO group ($P = 0.007$). Furthermore, the transition probability between microstate B and microstate D

was significantly increased in the MO group than in the HC group ($P = 0.009$ for B to D, $P = 0.007$ for D to B). Finally, the occurrence and contribution of microstate B were positively related to headache characteristics in the MO group but negatively in the MA group, whereas the duration of microstate A was positively related to the visual analogue scale in the MA group (all $P < 0.05$).

Conclusions: Migraine patients with and without aura have altered microstate dynamics, indicating that resting-state brain network disorders may play a role in migraine pathogenesis. Microstate parameters may have the potential to aid clinical management, which needs to be investigated further.

Disclosure of Interest: None Declared

IHC23-PO-176

Link between higher cortical dysfunctions during migraine aura and volume of hippocampus

Igor Petrušić[1], Mojsije Radović[2], Aleksandra Radojičić[2,3] and Marko Daković[1]

[1]*University of Belgrade, Faculty of Physical Chemistry, Laboratory for advanced analysis of neuroimages, Belgrade, Serbia*
[2]*University of Belgrade, Faculty of Medicine, Belgrade, Serbia*
[3]*Headache Center, Neurology Clinic, Clinical Center of Serbia, Belgrade, Serbia*

Objective: The role of the hippocampus and its subfields is insufficiently explored in people who have migraine with aura (MwA). Moreover, the heterogeneity of MwA patients prevents studies to investigate particular roles of specific brain regions in MwA pathophysiology. Therefore, choosing clinically homogenous MwA patients to explore the link between specific brain regions and specific MwA manifestations, such as higher cortical dysfunctions (HCDs), may overcome this limitation. This study used advanced structural neuroimaging techniques to compare subgroups of MwA patients (with and without HCDs), as well as to compare subgroups with healthy controls (HCs), regarding the volumes of hippocampal structures and its subfields.

Methods: Patients who have episodic migraine with typical aura were selected for this study. They were assigned to the MwA-HCD group if they reported HCDs (dysphasia, memory problems, etc.) during the aura phase or to the MwA-non-HCD group if they did not experience HCDs. Both subgroups were compared in between and to HCs to evaluate any specific changes in the hippocampus. Neuroimaging data derived from FreeSurfer-based segmentation of hippocampal subfields acquired from a 3 T magnetic resonance machine was used for comparisons.

Results: A total of 46 MwA patients (28 MwA-HCD group and 18 MwA-non-HCD group) and 31 HCs were studied. There were no significant differences in age and sex between groups ($p = 0.490$ and $p = 0.934$, respectively). The MwA-HCD group had significantly smaller volumes of the left (3328 vs. 3677 mm^3, $p < 0.001$) and right (3395 vs. 3748 mm^3, $p < 0.001$) hippocampus and all hippocampal subfields compared to the MwA-non-HCD group. Also, the MwA-HCD group had significantly smaller volumes of the left (3328 vs. 3541 mm^3, $p = 0.002$) and right (3395 vs. 3592 mm^3, $p = 0.015$) hippocampus compared to HCs. There was no significant difference between the MwA-non-HCD group and HCs relative to the hippocampal volumes.

Conclusion: Smaller volumes of the left and right hippocampus, as well as hippocampal subfields, might play an important role in the pathophysiology of HCDs during MwA attacks. Further functional neuroimaging studies are needed to explain the results of this study.

Disclosure of Interest: None Declared

IHC23-PO-177

Dynamic changes in glymphatic function in reversible cerebral vasoconstriction syndrome

Shih-Pin Chen[1,2,5], Chia-Hung Wu[1,6], Yu Kuo[1,6,7], Yu-Hsiang Ling[1,2], Yen-Feng Wang[1,2,3], Jong-Ling Fuh[1,2,3], Jiing-Feng Lirng[1,6], Hsiu-Mei Wu[1,6] and Shuu-Jiun Wang[1,2,3]

[1]*School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[2]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[5]*Division of Translational Research, Department of Medical Research, Taipei, Taiwan*
[6]*Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan*
[7]*Department of Nuclear Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*

The pathophysiology of the reversible cerebral vasoconstriction syndrome (RCVS) remains enigmatic. The role of glymphatics, a system critically important in brain homeostasis and neurovascular regulation, has not been explored in RCVS. In this study, we aimed to investigate the dynamic changes in glymphatic function and their potential clinical correlates in patients with RCVS. We evaluated the glymphatic function in RCVS patients by calculating the diffusion-tensor imaging along the perivascular space

(DTI-ALPS) index under a 3-tesla MRI. Clinical and vascular (transcranial color-coded duplex sonography) investigations were conducted. RCVS subjects were prospectively recruited from the headache center or emergency department of Taipei Veterans General Hospital, Taipei, Taiwan, a 3135-bed state-run tertiary center between August 2020 and December 2022. Participants were separated into two groups based on disease onset to MRI interval (acute $\leq$ 30 days; remission $\geq$ 90 days). Those with serial DTIs were included in longitudinal analysis. The water diffusivity on DTI in different orientations were analyzed by VolumeViewer and the DTI-ALPS index was calculated. The time-trend, longitudinal, cross-sectional investigations of the DTI-ALPS index were conducted. Correlations between DTI-ALPS index and vascular and clinical parameters were performed. Bonferroni correction was applied to the vascular investigations ($q = 0.05/11$). A total of 153 RCVS patients were approached, and 140 patients (182 scans) were enrolled. A significantly lower DTI-ALPS index was found in RCVS patients in the acute stage compared to the remission stage in both cross-sectional and longitudinal analyses ($p < 0.001$). A continuously increasing trend in the DTI-ALPS index after disease onset was demonstrated. The DTI-ALPS index was negatively correlated with the resistance index of the internal carotid arteries (ICA) in all subjects and positively correlated with the middle cerebral artery flow velocity between 50 and 100 days. The DTI-ALPS had a significantly negative correlation with the scores of the six-item Headache Impact Test (HIT-6). Glymphatic function in patients with RCVS exhibited a unique dynamic evolution that was temporally coupled to different vascular indices and headache-related disabilities along the disease course. These findings may provide novel insights into the complex interactions between glymphatic transport, vasomotor control and pain modulation.

Disclosure of Interest: None Declared

IHC23-PO-178

Regional cerebral perfusion changes associated with nitroglycerin-triggered migraine headache assessed using pseudo-continuous arterial spin labelling

Nazia Karsan[1,2], Pyari Bose[1,2], Owen O'Daly[1], Fernando Zelaya[1] and Peter Goadsby[1,2,3]

[1]*King's College London, London, United Kingdom*
[2]*NIHR-King's Clinical Research Facility, London, United Kingdom*
[3]*University of California, Los Angeles, United Kingdom*

Objectives: Functional neuroimaging studies have shown consistent brain changes during spontaneous and triggered migraine headache. Repeated measures study designs for validation can be challenging, owing to potential radiation and isotope-related exposure risks using some imaging techniques. Arterial spin labelling (ASL) is a non-invasive magnetic resonance perfusion means of quantitatively measuring regional cerebral blood flow (CBF).

We set out to perform a repeated measures ASL imaging study in migraine patients during directly observed nitroglycerin (NTG)-provoked attacks to compare imaging outcomes with those already published in the literature using alternative methodologies.

Methods: Subjects ($n = 53$) with migraine with or without aura, in the absence of daily or continuous headache were recruited following screening and informed consent. All study visits took place in a dedicated Clinical Research Facility housing a monitoring area with clinical beds next to a 3Tesla MRI scanner. Each subject was initially invited to a visit during which open-label exposure to an intravenous 0.5mcg/kg/min NTG infusion took place, to ensure that patients who developed migraine symptoms and headache within a reasonable time frame to allow imaging could be identified and invited for further scanning visits. At subsequent imaging visits, each eligible subject was exposed to either NTG infusion or placebo in a double-blind randomised fashion. The timeline and phenotype to development of migraine symptoms was documented. Structural brain imaging was obtained at baseline, along with whole brain CBF maps using 3D pseudo-continuous ASL (3D pCASL) at baseline, during the premonitory phase, during moderate-severe migraine headache and following headache resolution with treatment.

All images were processed and analysed within FSL and SPM, using a voxel-wise general linear model, according to the consensus ASL guidelines. Whole brain CBF changes in the baseline and post-headache scans on both visits were four conditions analysed within a time by treatment within subject flexible factorial model in SPM. *Post-hoc* paired *t*-tests were used for exploratory analyses. A cluster forming threshold of $P < 0.005$ was employed; and only those clusters with family wise error-corrected (FWE) $P < 0.05$ (following multiple comparison correction based on cluster-extent) are reported. All brain regions of significance are presented with cluster size (k_E) and in Montreal Neurological Institute (MNI) space.

Results: Forty-four (83%) subjects developed delayed migraine-like headache following NTG exposure (range 20–278 minutes, median 107). Four subjects had aura symptoms whilst in the scanner. Imaging on the triggered visit was obtained from 25 subjects, with 21 completing the entire imaging protocol including a placebo visit.

One subject was removed from the analysis due to poor data quality. There were no significant results for an interaction between time and trigger on CBF within the four

conditions of the flexible factorial model ($n = 20$). *Post-hoc* paired *t*-tests revealed significant CBF increases during migraine headache on the NTG visit only ($n = 24$) in medial frontal gyrus and anterior cingulate cortex ($k_E = 1312$, peak CBF change at [18, 66, 0], $P = 0.009$), and CBF decreases in the middle temporal and occipital gyri ($k_E = 1568$, peak CBF change at [46, –74, –14], $P = 0.004$).

Further analysis revealed a similar cluster of increased CBF increased in size at the same statistical threshold in the subjects not taking preventive therapy only ($n = 16$), $k_E = 2330$, peak CBF change at [8, 58, 2], $P < 0.001$. In subjects without underlying aura ($n = 10$), there were significant CBF increases during migraine headache in the midbrain and pons ($k_E = 914$, peak CBF change at [10, –8, –8], $P = 0.024$). The posterior CBF reductions over middle and inferior occipital gyri and fusiform gyrus were only significant on subgroup analysis in the migraine with underlying aura group ($n = 14$) ($k_E = 799$, peak CBF change at [38, –86, –14], $P = 0.03$).

Conclusions: We identified significant regional CBF changes on ASL associated with NTG-triggered migraine headache, broadly consistent with other investigations. It is likely that the use of migraine prevention and underlying presence of aura alter functional imaging outcomes. Homogeneity of patient cohorts yields more significant results despite smaller sample sizes. The presence of posterior hypoperfusion in migraine with aura is a feasible imaging correlate of cortical spreading depression. Understanding the biological and treatment-related heterogeneity in migraine is vital to evaluate functional imaging outcomes.

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IHC23-PO-179

Mapping the aberrant brain functional connectivity in new daily persistent headache: a resting-state functional magnetic resonance imaging study

Wei Wang[1], Ziyu Yuan[1], Xueyan Zhang[2], Xiaoyan Bai[3,4], Hefei Tang[1], Yanliang Mei[1], Dong Qiu[1], Peng Zhang[1], Xue Zhang[3,4], Yaqing Zhang[1], Xueying Yu[1], Binbin Sui[3] and Yonggang Wang[1]

[1]*Headache Center, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China*
[2]*Department of Neurology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*
[3]*Tiantan Neuroimaging Center of Excellence, China National Clinical Research Center for Neurological Diseases, Beijing, China*
[4]*Department of Radiology, Beijing Tiantan Hospital, Capital Medical University, Beijing Neurosurgical Institute, Beijing, China*

Background and purpose: The pathogenesis of new daily persistent headache (NDPH) is not fully understood. We aim to map aberrant functional connectivity (FC) in patients with NDPH using resting-state functional magnetic resonance imaging (MRI).

Methods: Brain structural and functional MRI data were acquired from 29 patients with NDPH and 37 well-matched healthy controls (HCs) in this cross-sectional study. Region of interest (ROI) based analysis was used to compare FC between patients and HCs, with 116 brain regions in the automated anatomical labeling (AAL) atlas were defined as seeds. The correlations between aberrant FC and patients' clinical characteristics, and neuropsychological evaluation were also investigated.

Results: Compared with HCs, patients with NDPH showed increased FC in the left inferior occipital gyrus, right thalamus and decreased FC in right lingual gyrus, left superior occipital gyrus, right middle occipital gyrus, left inferior occipital gyrus, right inferior occipital gyrus, right fusiform gyrus, left postcentral gyrus, right postcentral gyrus, right thalamus and right superior temporal gyrus. There were no correlation between FC of these brain region and clinical characteristics, neuropsychological evaluation after Bonferroni correction ($p > 0.05/266$).

Conclusions: Patients with NDPH showed abnormal FC in multiple brain regions involved in perception and regulation of emotion and pain.

Keywords: Functional magnetic resonance imaging; New daily persistent headache; Functional connectivity; Emotion; Pain

Trial Registration Information

ClinicalTrials.gov Identifier: NCT05334927.

IHC23-PO-180

Normal glymphatic system function in patients with new daily persistent headache using diffusion tensor image analysis along the perivascular space

Wei Wang[1], Xue Zhang[2,3], Xueyan Zhang[4], Xiaoyan Bai[2,5], Ziyu Yuan[1], Peng Zhang[1], Zhiye Li[6], Hefei Tang[1], Yaqing Zhang[1], Xueying Yu[1], Yonggang Wang[1] and Binbin Sui[2]

[1]*Headache Center, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China*

[2]Tiantan Neuroimaging Center of Excellence, China National Clinical Research Center for Neurological Diseases, Beijing, China
[3]Department of Radiology, Beijing Tiantan Hospital, Capital Medical University, Beijing, Beijing, China
[4]Department of Neurology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China
[5]Department of Radiology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[6]Tiantan Neuroimaging Center of Excellence, China National Clinical Research Center for Neurological Disease, Beijing, China

Objectives: To investigate the glymphatic function in patients with new daily persistent headache (NDPH) using the diffusion tensor image analysis along the perivascular space (DTI-ALPS) method.
Background: NDPH, a rare and treatment-refractory primary headache disorder, is poorly understood. There is limited evidence to suggest that headaches are associated with glymphatic dysfunction. Thus far, no studies have evaluated glymphatic function in patients with NDPH.
Methods: In this cross-sectional study conducted in the Headache Center of Beijing Tiantan Hospital, patients with NDPH and healthy controls were enrolled. All participants underwent brain magnetic resonance imaging examinations. Clinical characteristics and neuropsychological evaluation were examined in patients with NDPH. ALPS indexes for both hemispheres were measured to determine the glymphatic system function in patients with NDPH and healthy controls.
Results: In total, 27 patients with NDPH (14 males, 13 females; age [mean ± standard deviation (SD)]: 36.6 ± 20.6) and 33 healthy controls (15 males, 18 females; age [mean ± SD]: 36.0 ± 10.8) were included in the analysis. No significant differences between groups were observed in the left ALPS index (1.583 ± 0.182 vs. 1.586 ± 0.175, mean difference = 0.003, 95% confidence interval [CI] of difference = −0.089 to 0.096, p = 0.942), or right ALPS index (1.578 ± 0.230 vs. 1.559 ± 0.206, mean difference = −0.027, 95% CI of difference = −0.132 to 0.094, p = 0.738). Additionally, ALPS indexes were not correlated with clinical characteristics or neuropsychiatric scores.
Conclusion: No glymphatic dysfunction was detected in patients with NDPH by means of the ALPS method. Additional studies with larger samples are needed to confirm these preliminary findings and improve the understanding of glymphatic function in NDPH.
Trial Registration Information
ClinicalTrials.gov Identifier: NCT05334927.

Keywords: diffusion tensor imaging, glymphatic system, magnetic resonance imaging, new daily persistent headache

IHC23-PO-181

Cerebral perfusion variance in new daily persistent headache and chronic migraine: an arterial spin-labeled MR imaging study

Wei Wang[1], Xiaoyan Bai[2,3], Xueyan Zhang[4], Zhiye Li[2,5], Xue Zhang[2,5], Ziyu Yuan[1], Hefei Tang[1], Yaqing Zhang[1], Xueying Yu[1], Peng Zhang[1], Yonggang Wang[1] and Binbin Sui[2]

[1]Headache Center, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[2]Tiantan Neuroimaging Center for Excellence, China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[3]Department of Radiology, Beijing Tiantan Hospital, Capital Medical University, Beijing, Beijing, China
[4]Department of Neurology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China
[5]Department of Radiology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Background and purpose: New daily persistent headache (NDPH) and chronic migraine (CM) are two diferent types of headaches that might involve vascular dysregulation. There is still a lack of clarity about altered brain perfusion in NDPH and CM. This study aimed to investigate the cerebral perfusion variances of NDPH and CM using multidelay pseudo-continuous arterial spin-labeled magnetic resonance imaging (pCASL-MRI).
Methods: Fifteen patients with NDPH, 18 patients with CM, and 15 age- and sex-matched healthy controls (HCs) were included. All participants underwent 3D multi-delay pCASL-MRI to obtain cerebral perfusion data, including arrival-time-corrected cerebral blood fow (CBF) and arterial cerebral blood volume (aCBV). The automated anatomical labeling atlas 3 (AAL3) was used to parcellate 170 brain regions. The CBF and aCBV values in each brain region were compared among the three groups. Correlation analyses between cerebral perfusion parameters and clinical variables were performed.
Results: Compared with HC participants, patients with NDPH were found to have decreased CBF and aCBV values in multiple regions in the right hemisphere, including the right posterior orbital gyrus (OFCpost.R), right middle occipital gyrus (MOG.R), and ventral anterior nucleus of right thalamus (tVA.R), while patients with CM showed increased CBF and aCBV values presenting in the ventral lateral nucleus of left thalamus (tVL.L) and right thalamus (tVL.R) compared with HCs (all $p < 0.05$). In patients with NDPH, after age and sex adjustment, the increased aCBV values of IFGorb. R were positively correlated with GAD-7 scores; and the increased CBF and aCBV values of tVA.R were positively correlated with disease duration.

Conclusion: The multi-delay pCASL technique can detect cerebral perfusion variation in patients with NDPH and CM. The cerebral perfusion changes may suggest diferent variations between NDPH and CM, which might provide hemodynamic evidence of these two types of primary headaches.
Keywords: New daily persistent headache, Chronic migraine, Perfusion, Magnetic resonance imaging, Arterial spin labeling
Trial Registration Information
ClinicalTrials.gov Identifier: NCT05334927.

IHC23-PO-182

Neurophysiological reappraisal of light-evoked blink reflex in migraine

Gianluca Avino, Gionata Strigaro, Federica Cattaneo, Antonio Meo, Bendetta Gori, Claudia Varrasi and Roberto Cantello

Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, and Azienda Ospedaliero-Universitaria "Maggiore della Carità, Novara, Italy

Introduction: Light stimulus is a key concept in migraine being involved in many aspects of the disorder. Light-evoked blink reflex (L-BR), is a brainstem reflex induced by light stimuli. Afferent visual pathway carries the impulses to lateral geniculate body and pretectum; the efferent muscular pathway originates from the facial nuclei in the pons. It consists of two distinct EMG bursts, referred to as R50 and R80 based on their typical onset latencies. Aim of this study was to evaluating the feasibility and reliability of L-BR to study pathophysiology of migraine in patients with (MA) and without aura (MO).
Material and Methods: We studied between migraine attacks 49 patients, 30 with MO and 19 with MA, compared to 23 HS matched for age and sex. Surface EMG electrodes (Ag–AgCl) were placed over the right orbicularis oculi muscle. Signal was amplified and band-pass filtered (1–1000 Hz). After dark adaptation, 80 white flashes were delivered by a xenon lamp. EMG responses were rectified and averaged to measure the onset/peak latency and area under the curve of R50 (AR1) and R80 (AR2) components. Finally was calculated R1 + R2 total area (AUC) Non parametric tests were used for statistical analysis.
Results: L-BR was reliably recorded in all subjects. The procedure was well tolerated. The presence of two distinct EMG bursts was variable (half of the cases in each group). Mean R50/R80 onset and peak latencies and AR1/AR2 were similar between MO, MA and HS ($p > 0.05$). AUC was significantly smaller (by approximately 50%) in patients with migraine than in controls, regardless of aura's presence ($p < 0.05$).
Discussion: To our knowledge, this is the first study of L-BR in migraine patients. The procedures used were easy to perform and well tolerated. The measurement of R1 and R2 latencies is reliable and reproducible. The AUC, is to be preferred to the measurement of individual responses, in consideration of their intrinsic variability.
Conclusions: In conclusion, L-BR suggests a possible deficit of activation of the subcortical circuits, as from an altered processing of the light stimulus, underlying neurobiological brainstem dysfunction involved in the pathophysiology of migraine.

IHC23-PO-183

Ultrasonographic assessment of periaqueductal gray matter in migraine

David García López, José Miguel Láinez Andrés, Rosario Gil Gimeno, Jessica García Ull and Francisco Gascón Giménez

Hospital Clinico Universitario, Valencia, Spain

Introduction: Periaqueductal gray matter (PAG) is at the center of a powerful descending antinociceptive neuronal network and has an important role in endogenous pain modulation. Ventrolateral PAG is involved in migraine pathophysiology, particularly in the modulation of trigeminovascular nociceptive response although the exact role is unknown. Iron accumulation in PAG may be a marker of progressive dysfunction and could be linked to migraine chronification.
The objective of our study is to investigate iron accumulation in PAG with transcranial sonography taking into account heavy metal-induced hyperechogenicity
Methods: Ongoing prospective registry of patients from outpatient clinics with diagnosis of episodic and chronic migraine and a control group without known migraine. We performed a qualitative assessment of PAG echogenicity through the transtemporal bone window following recommendations on a consensus on Transcranial Sonography of Brain Parenchyma in Movement Disorders. We excluded patients with other diseases that may induce echogenic changes in midbrain structures and those with a suboptimal temporal bone acoustic window.
Results: 42 subjects were evaluated. 4 were excluded due to suboptimal acoustic window and 38 were included: 11 non migraine (NM), 15 episodic migraine (EM) and 12 chronic migraine (CM). Sex distribution and mean age in each group: NM = 8 females, 34.29 ± 8.38 years; EM = 10 females, 39.47 ± 14.27 years; CM = 9 females, 39.67 ± 9.79 years. 5 patients in the EM group had a previous

history of chronic migraine. Monthly headache frequency was 3.41 ± 3.42 days in EM vs 22.29 ± 6.52 days in CM. According to preventive treatment, botulinum toxin was effective in 6 EM patients (100%) and 2 CM patients (28.57%) and anti-CGRP antibodies were effective in 3 EM (100%) and 0 CM patients (0%). PAG hyperechogenicity was detected in 18.18% of NM, 33.33% of EM (4 of which had previous CM), and 83.33% of CM. PAG hyperechogenicity was associated with headache frequency (16.65 days/month in hyperechogenic PAG vs 5.73 days/month in non hyperechogenic PAG), migraine duration (25.59 ± 14.05 vs 18.06 ± 12.13 years) and worse response to botulinum toxin and anti-CGRP antibodies (in 100% of patients without response to these treatments PAG was hyperechogenic)

Our study has several limitations such as a low number of patients included (ongoing study), a qualitative rather quantitative assessment and a lack of both a standardized measure procedure and a reliable comparator with other techniques such as MRI.

Conclusions: Taking into account our preliminary results, PAG hyperechogenicity seems to be more frequent in CM than EM and NM and related to more frequent headache attacks, longer migraine duration and worse response to some preventive treatments such as botulinum toxin and anti-CGRP antibodies. Transcranial sonography stands as a low-cost, non-invasive and easily available tool in migraine investigation but more studies are needed in order to reliably use this technique for PAG evaluation.

Disclosure of Interest: None Declared

IHC23-PO-184

Increased Iron Deposition in Nucleus Accumbens Associated with Disease Progression and Chronicity in Migraine

Kaiming Liu[1] and Xiaopei Xu[2]

[1]*Department of Neurology, The Second Affiliated Hospital, Zhejiang University School of Medicine, No 88 Jiefang Road, HangZhou, China*
[2]*Department of Radiology, The Second Affiliated Hospital, Zhejiang University School of Medicine, HangZhou, China*

Background: Migraine is one of the world's most prevalent and disabling diseases. Despite huge advances in neuroimaging research, more valuable neuroimaging markers are still urgently needed to provide important insights into the brain mechanisms that underlie migraine symptoms. We therefore aim to investigate the regional iron deposition in subcortical nuclei of migraineurs as compared to controls, and its association with migraine related pathophysiological assessments.

Methods: A total of 241 subjects underwent MRI and clinical variables including monthly migraine days, monthly migraine attacks, duration of migraine, intensity of migraine, 6-item Headache Impact Test (HIT-6), Migraine Disability Assessment (MIDAS), and Pittsburgh Sleep Quality Index (PSQI) were recorded. Quantitative susceptibility mapping was employed to quantify the regional iron content in subcortical regions. Associations between clinical variables and regional iron deposition were studied as well.

Results: Increased iron deposition in putamen, caudate, and nucleus accumbens (NAC) was observed in migraineurs than controls. Meanwhile, patients with chronic migraine (CM) had significantly higher volume of iron deposits compared to episodic migraine (EM) in multiple subcortical nuclei, especially in NAC. Volume of iron in NAC can be used to distinguish patients with CM from EM with a sensitivity of 85.45% and specificity of 71.53%.[1] As the most valuable neuroimaging markers in all of the subcortical nuclei, higher iron deposition in NAC was significantly associated with disease progression, and higher HIT-6, MIDAS, and PSQI.

Conclusion: These findings provide evidence that iron deposition in NAC may be a biomarker for migraine chronicity and migraine-related dysfunctions, thus may help to understand the underlying vascular and neural mechanisms of migraine.

Trial registration: China Headache Registry Study (CHRS), ClinicalTrials.gov ID: NCT04939922 (06/14/2021).

Keywords: Migraine, Iron Deposition, Nucleus Accumbens, Disease Progression, Chronicity

Disclosure of Interest: Vice President, Headache Group, Neurologist Branch, Chinese Medical Association. Vice President, Youth Committee of Headache and Sensory Disorders, Chinese Research Hospital Association, 2019-present.

IHC23-PO-185

Headache-Related Quality of Life Associates Differently with Emotional Processing in Migraine and Tension-Type Headache Patients – an fMRI Study

Dora Dobos[1,2], Kinga Gecse[1,2], Edina Szabo[3,2,5], Daniel Baksa[1,2], Natalia Kocsel[3], Attila Galambos[3], Gyongyi Kokonyei[1,2,3] and Gabriella Juhasz[1,2]

[1]*NAP3.0- SE Neuropsychopharmacology Research Group, Hungarian Brain Research Program, Semmelweis University, Budapest, Hungary*

[2]Department of Pharmacodynamics, Faculty of Pharmacy, Semmelweis University, Budapest, Hungary
[3]Institute of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary
[4]Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, USA
[5]Department of Anesthesia, Harvard Medical School, Boston, USA

Objective: Migraine and tension-type headache differ in terms of headache features and accompanying symptoms. Migraine sufferers perceive their episodes more debilitating and usually report a poorer quality of life as compared to tension-type headache patients. The aim of this study is to reveal if differences in neural mechanisms underlying emotional processing can contribute to the differences in the debilitating effects of these headaches. To investigate emotional processing, faces expressing different emotions were shown to the subjects, while their neural activity was measured.
Methods: 41 (37 females, M age = 28.59, SD = 1.052) subjects with episodic migraine without aura (MwoA) and 31 (21 females, M age = 27.06, SD = 0.983) tension-type headache (TTH) subjects were involved in the study. All of them were free of medication, as well as psychological and neurological conditions. Their headache-related disability was assessed with the Comprehensive Headache-related Quality of life Questionnaire (CHQQ). This questionnaire has three subscales measuring physical, mental, and social quality of life. In interictal phase, all subjects underwent an fMRI scanning while completing an implicit facial emotion processing task. Emotion-related activities in interaction with CHQQ 1) total and 2) subscale scores were compared between groups in SPM12. In all analyses, age and sex were used as covariates. An initial cluster-level threshold $p < 0.001$ was applied, but only clusters surviving family-wise error correction ($pFWE < 0.05$) were considered statistically significant. In SPSS28, between-group differences in CHQQ total and subscale scores were calculated with independent samples t-test, except for the social subscale scores which were compared with Mann–Whitney U test.
Results: Based on CHQQ scores, the headache-related life quality was significantly lower in the MwoA group (total: $t = -4.926$; $p < 0.001$, physical: $t = -5.346$, $p < 0.001$; mental: $t = -3.806$, $p < 0.001$; social: $U = 282.50$, $p < 0.001$). The groups did not react differently to emotional faces. However, when looking at happy faces, MwoA subjects showed significantly lower activation in their left posterior cingulate cortex in interaction with total CHQQ scores and in their right medial orbitofrontal cortex in interaction with CHQQ physical subscale scores.
Conclusion: In healthy individuals, the posterior cingulate cortex shows a high level of activity to happy stimuli. In the present study, the same was found in tension-type headache subjects having a good quality of life. In migraineurs, however, an opposite trend was observed: the posterior cingulate cortex was more active in those with poorer life quality. This may indicate an improper functioning of this brain region since, despite their appropriate reaction to an emotional stimulus, these migraineurs have reduced coping ability. This phenomenon may be explained by the default mode network (DMN) dysfunction in migraineurs. Both the posterior cingulate and orbitofrontal cortex are parts of the DMN associated with cognitive and emotional processes. Our results support the notion that alterations in DMN could contribute to the higher levels of headache-related disability of migraine sufferers. In contrast, the above network does not seem to be impaired in tension-type headache individuals during emotional processing. Further investigations are needed to reveal differences in the pathomechanism of these primary headache diseases.
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Disclosure of Interest: None Declared

IHC23-PO-186

Patterns of gray matter MRI morphometry longitudinal change in patients with chronic and episodic migraine

Álvaro Planchuelo-Gómez[1,2], Ginebra Marchante-Reillo[3], Álvaro Sierra[3], Yésica González-Osorio[3], Ángel L Guerrero[3,4], Carmen Martín-Martín[2], Margarita Rodríguez[5], Raúl Moro[5], Santiago Aja-Fernández[2], Rodrigo de Luis-García[2] and David García-Azorín[3,4]

[1]CUBRIC, Cardiff University, Cardiff, United Kingdom
[2]Imaging Processing Laboratory, Universidad de Valladolid, Valladolid, Spain
[3]Headache Unit, Hospital Clínico Universitario de Valladolid, Valladolid, Spain
[4]Department of Medicine, Universidad de Valladolid, Valladolid, Spain
[5]Department of Radiology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

Objective: To evaluate long-term longitudinal gray matter morphometry changes in patients with CM and EM.
Methods: High-resolution 3D brain T1-weighted Magnetic Resonance Imaging (MRI) data were acquired

twice in 48 patients with CM and 33 patients with EM at baseline. The time between both MRI acquisitions was at least three years. The longitudinal pipeline of FreeSurfer (version 6.0) was employed to segment the T1-weighted images and extract the mean values of the cortical curvature (CC) and thickness (CT), surface area (SA) and gray matter volume (GMV) of 68 cortical regions. Additional 14 subcortical regions and the bilateral cerebellum were considered to analyze GMV. Generalized Linear Mixed Models were employed to assess the longitudinal changes. All models were corrected by age and GMV comparisons were adjusted for intracranial volume. Statistical significance was considered at $p < 0.05$.

Results: Among the patients with initial CM, 24 (50%) reverted to EM (mean time between MRI acquisitions: 61.6 ± 10.6 months; mean age: 44.5 ± 8.7 years; 20 women) and 24 stayed with CM diagnosis (mean time between MRI acquisitions: 61.7 ± 8.3 months; mean age: 42.1 ± 8.1 years; 24 women). Among the patients with EM, 31 stayed as EM (mean time between MRI acquisitions: 62.5 ± 8.6 months; mean age: 43.1 ± 8.2 years; 25 women), and two became CM. These two patients were excluded from the analysis to avoid bias effects. CC and GMV presented equal longitudinal patterns for all clinical evolutions, with a longitudinal increase of CC and decrease of GMV. In contrast, the SA and CT patterns were different depending on the clinical evolution. The SA patterns were longitudinal decrease for the CM reverted to EM group, increase for the stable EM group, and both trends for the patients with stable CM. The CT patterns were longitudinal decrease in the stable CM group, increase in the group with CM reverted to EM, and both trends in the patients with stable EM. CC longitudinal increase was observed in temporal regions and the pericalcarine cortex for the group with EM at both timepoints, and the group with CM reverted to EM only presented increase in the left inferior temporal gyrus. Regarding GMV, the persistent CM group presented longitudinal decrease in 13 regions, including the cingulate gyrus, hippocampus, and cerebellum, while in the group with CM reverted to EM the longitudinal decrease was found only in the cerebellum. Patients with EM at both timepoints showed GMV decrease in the frontal cortex and the cingulate gyrus. The longitudinal SA decrease in the reverted group was appreciated in regions from the paracentral cortex, pars orbitalis, and precentral and postcentral gyri. The longitudinal SA increase in the stable EM group was observed in the insula, the lateral orbitofrontal cortex, and pars orbitalis, opercularis and triangularis. In patients with stable CM, SA longitudinally decreased in the caudal anterior cingulate gyrus and increased in the lateral orbitofrontal cortex. Longitudinal CT decrease in patients with CM at both timepoints was observed in the frontal and temporal poles, and cingulate and lingual gyri. The longitudinal increase in the CM reverted to EM group was found in 14 regions, including the paracentral, temporal and superior parietal cortex, cuneus, and the supramarginal and postcentral gyri. In the stable EM group, there was longitudinal CT decrease in the cingulate and postcentral gyri, and the inferior parietal cortex, while there was longitudinal increase in 11 regions, including the cuneus, diverse temporal gyri, occipital and parietal regions, and the paracentral and supramarginal cortex. These results are summarized in Table 1.

Table 1. Number of regions with statistically significant longitudinal gray matter changes.

Longitudinal change	Stable CM	CM reverted to EM	Stable EM
CC increase	3	1	5
CC decrease	0	0	0
GMV increase	0	0	0
GMV decrease	13	1	5
SA increase	2	0	6
SA decrease	1	6	0
CT increase	0	14	11
CT decrease	7	0	5

Conclusion: Different clinical evolutions were associated with specific longitudinal gray matter longitudinal changes. Patients with CM with persistent condition were mainly characterized by GMV and CT decrease, while patients with CM reverting to EM were distinguished by SA decrease and CT increase. Patients with EM at both timepoints presented longitudinally reduced GMV, increased SA, and distinct CT patterns.

Disclosure of Interest: None Declared

IHC23-PO-187

Inverse relationship between trait-anxiety and periaqueductal grey connectivity in migraineurs compared to tension-type headache patients

Kinga Gecse[1,2], Norbert Károlyi[1,2], Angéla Hammer[2,3], Csaba Sándor Aranyi[4], Miklós Emri[4], Gyorgy Bagdy[1,2] and Gabriella Juhasz[1,2]

[1]*Department of Pharmacodynamics, Semmelweis University, Budapest, Hungary*
[2]*NAP3.0-SE Neuropsychopharmacology Research Group, Hungarian Brain Research Program, Semmelweis University, Budapest, Hungary*
[3]*Institute of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary*
[4]*Division of Nuclear Medicine and Translational Imaging, Department of Medical Imaging, Faculty of Medicine, University of Debrecen, Debrecen, Hungary*

Objective: Tension-type headache and migraine are the most common neurological disorders in the world. Both types of headache are often comorbid with anxiety disorders. The comorbidity may affect specific regions such as the periaqueductal grey matter (PAG) which is important in negative emotion regulation and pain modulatory system. However, less is known about the neuronal differences between the relationship of anxiety with migraine and tension-type headaches. Our aim was to investigate the effect of trait-anxiety on PAG functional connectivity in migraine patients compared to tension-type headache patients.
Methods: Functional connectivity (FC) analysis with PAG as seed region was conducted involving 37 episodic migraine without aura and 30 tension-type headache patients. They were headache and medication free. Trait-anxiety was measured with trait version of State-Trait Anxiety Inventory (STAI-T). To investigate the differences between the relationship of trait-anxiety and PAG-FC in migraineurs compared to tension-type headache group, STAI-T scores were used as covariates in interaction with PAG-FC in two sample t-tests using the Statistical Parametric Mapping (SPM12) toolbox in MATLAB environment.
Results: Significant difference was found between migraine and tension-type headache group in the relationship of trait-anxiety and PAG-FC with superior frontal gyrus (left SFG: pFWE = 0.001, right SFG: pFWE = 0.016). Namely, increased trait-anxiety level was correlated with higher PAG-SFG connectivity in tension-type headache patients. However, increased trait-anxiety was correlated with decreased PAG-SFG connectivity in migraine patients.
Conclusions: Our results suggest that anxiety may contribute differently to migraine and tension headache pathomechanism. Previous studies showed that SFG activity is reduced in pain stimuli, but increases with higher trait-anxiety. In line with this, anxiety may be associated with decreased pain inhibition pathways in migraine patients. Meanwhile in tension-type patients, anxiety may be contributed to cortical hypersensitivity.
Funding: Development of scientific workshops of medical, health sciences and pharmaceutical educations (EFOP-3.6.3-VEKOP-16-2017-00009); ÚNKP-22-3-II-SE-27; 2017– 1.2.1-NKP-2017-00002, NAP2022-I-4/2022; TKP2021-EGA-25; OTKA (K143391); ERA PerMed (2019-2.1.7-ERA-NET-2020-00005).
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IHC23-PO-188

Cyclic change of endogenous pain inhibition in patients with migraine

Li-Ling Hope Pan[1], Shuu-Jiun Wang[1,2,3], Yen-Feng Wang[2,3], Shih-Pin Chen[1,2,5], Kuan-Lin Lai[2,3], Hung-Yu Liu[2,3] and Yu-Hsiang Ling[2,3]

[1]Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan
[2]Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
[3]College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan
[4]Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan
[5]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan

Objective: The cold pressor test is one of the most commonly used measurements for conditioned pain modulation (CPM), which can be depicted as the net effect of the endogenous pathways for pain inhibition. However, the CPM changes in patients with migraine were inconclusive, possibly due to the insufficient consideration of headache phases. Most studies controlled the last headache attack before the assessment; however, some failed to report the following attack. As a result, the changes during the pre-ictal phases may easily be overlooked. Therefore, we aimed to compare the capacity of CPM in patients with migraine during different headache phases. Healthy controls (HCs) were also included for the comparisons. We hypothesize that the CPM capacity is reduced in patients with migraine and fluctuates across headache phases.
Methods: This is part of a large integration study. We prospectively recruited patients with episodic migraine (EM) and they were cleared from any forms of prophylactics for three months prior to enrollment. Age-and-sex-matched HCs were also recruited. All the participants underwent the cold pressor tests where they were asked to immerse their right palm up to the wrist in cold water ($4 \pm 2^{\circ}C$) until it became unbearable. The pressure pain thresholds (PPT) were measured on the left thenar eminence muscle before and right after the immersion. The subjects rated the pain of the cold-water immersion upon removal of hands using an 11-point numeric rating scale (NRS) to re-ensure the strength of the condition stimuli. Those with termination NRS < 5 were excluded from further analysis. The change in PPT (CPM capacity) was calculated. The last and the next headache attacks were carefully documented. Independent t-tests, chi-squared tests, and one-way way analysis of variance were used to compare the differences. The

comparisons of the CPM effect between HC and EM and between different phases in EM were made using a one-way analysis of covariance (ANCOVA) controlling for pre-immersion PPT. The significant level was set at $p < 0.05$.

Results: Seventy-one EM (34.4 ± 8.2 yrs., 76% female) and 60 HC (33.2 ± 8.0 yrs., 68% female) finished all the tests and were included in the analysis. No significant differences were found in age ($p = 0.419$) and sex ($p = 0.348$) between groups. EM had 6.1 ± 4.5 monthly headache days on average and 16 of them were identified as inter-ictal, 11 pre-ictal, 23 ictal, and 21 post-ictal phases. No significant difference was found between HC and EM (Estimated Marginal Mean (EMM): 42.7 vs. 31.6 kPa, $p = 0.153$). However, a significantly different CPM effect (ANCOVA $p = 0.008$) was found between different phases in EM. Specifically, those in the pre-ictal phase showed the lowest CPM (EMM: 15.2 kPa) compared to those in the inter-ictal (EMM: 40.8 kPa, $p = 0.01$) and ictal (EMM: 43.0 kPa, $p = 0.006$) phases. In addition, those in the post-ictal phase also showed decreased CPM (EMM: 22.1 kPa) compared to those in the inter-ictal ($p = 0.033$) and ictal ($p = 0.019$) phases.

Conclusion: The current findings showed the cyclic change of CPM capacity in EM participants. While EM as a whole may show a comparable capacity to HCs, impaired pain inhibition was noted during the peri-ictal phases. Therefore, even without an obvious headache attack, the pain processing system is still affected and should be considered in clinical practice and research.

Disclosure of Interest: None Declared

IHC23-PO-189

Impaired dynamic cerebral autoregulation is associated with blood-brain barrier disruption in reversible cerebral vasoconstriction syndrome

Yu-Hsiang Ling[1,2], Nai-Fang Chi[1,2], Li-Ling Hope Pan[3], Yen-Feng Wang[1,2], Chia-Hung Wu[2,4], Jiing-Feng Lirng[2,4], Jong-Ling Fuh[1,2,3], Shuu-Jiun Wang[1,2,3] and Shih-Pin Chen[1,2,3,5,6]

[1]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan*
[5]*Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[6]*Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan*

Objectives: Reversible cerebral vasoconstriction syndrome (RCVS) is an enigmatic syndrome presumably related to dysregulation of cerebral vasculature. Half of the sufferers of reversible cerebral vasoconstriction syndrome (RCVS) exhibit imaging-proven blood-brain barrier (BBB) disruption, which is known to be associated with complications of RCVS. The pathogenesis of BBB disruption in RCVS remains unclear and mechanism-specific intervention is lacking. We speculate that cerebrovascular dysregulation might be associated with BBB disruption in RCVS. Therefore, we aimed to evaluate whether the dynamic cerebral autoregulation (dCA), which measures the instantaneous responses of cerebral blood flow (CBF) to changes in blood pressure (BP), is altered in patients with RCVS and could be associated with BBB disruption.

Methods: A cross-sectional study was conducted in the headache clinics of Taipei Veterans General Hospital. Fifty-eight patients with RCVS were approached, of whom 13 declined. Forty-five age- and sex-matched healthy controls (HCs) were recruited from the nearby neighborhood. dCA was evaluated by concomitant recording of CBF velocity and BP. The capacity of the dCA to damp the pulsatile systemic blood flow, i.e., phase shift and gain between the CBF and BP waveforms in the very low frequency (VLF) and low frequency (LF) bands were calculated by transfer function analysis. The mean flow correlation index (Mx) was also calculated. RCVS patients received 3-dimensional isotropic contrast-enhanced T2 fluid-attenuated inversion recovery imaging to visualize BBB disruption. The average value from bilateral dCA metrics in the HCs was calculated and was compared with metrics derived from both sides in RCVS separately since the vessels in RCVS may be asymmetrically involved and it was impractical to define a "lesion side" in RCVS. Independent sample t-tests were used to compare the differences between RCVS and HC or between RCVS with and without BBB disruption. The one-way analysis of variance with post-hoc Fisher's least significant difference test was used to compare the differences in continuous variables between HC, RCVS without BBB disruption, and RCVS with BBB disruption. Univariate logistic regression was conducted to determine the odds ratio (OR) of the BBB disruption related to dCA metrics and the clinical characteristics that showed differences between patients with or without BBB disruption ($p < 0.1$). Significant dCA metrics identified with univariate logistic regression models were included in the multivariable logistic regression after controlling for significant clinical features. The significant level was set at $p < 0.05$.

Results: Forty-five RCVS patients (42.0 ± 9.6 yrs., 64% female) and 45 HCs (41.4 ± 12.5 yrs., 64% female) completed the study. Nineteen of the RCVS patients had BBB disruption. Compared to HCs, RCVS patients had poorer dCA, indicated by higher gain in the VLF band (left: 1.6 ± 0.7, $p < 0.001$; right: 1.6 ± 0.7, $p = 0.001$; HC: 1.1 ± 0.4)

and higher Mx (left: 0.39 ± 0.20, $p = 0.031$; right: 0.40 ± 0.18, $p = 0.014$; HC: 0.31 ± 0.17). Moreover, RCVS with BBB disruption had worse dCA, as compared to those without BBB disruption, by having less phase shift in VLF and LF bands, and higher Mx. When taking BBB disruption into consideration, we found significant differences in dCA between HCs, RCVS without BBB disruption, and RCVS with BBB disruption. By having the smallest phase shift and largest Mx, RCVS with BBB disruption showed the worst dCA as compared to RCVS without BBB disruption and to HC. The RCVS groups (either with or without BBB disruption) had larger gain as compared to HCs, suggesting worse dCA in RCVS. Univariate logistic regression models demonstrated older age, the presence of a history of migraine, having less VLF phase shift (bilateral), having less LF phase shift (left only), as well as larger Mx (bilateral) increased the odds of BBB disruption. Multivariable models showed VLF phase shift on both sides remained to be associated with BBB disruption (left: $p = 0.025$, OR: 0.95 [0.91∼0.99], Nagelkerke R^2: 53.5%; right: $p = 0.028$, OR: 0.95 [0.91∼0.995], Nagelkerke R^2: 51.3%) after controlling age and history of migraine.

Conclusion: Dysfunctional dCA was observed in patients with RCVS, particularly in those with BBB disruption. These findings suggest that cerebral dysautoregulation plays a pivotal role in RCVS pathophysiology and may be relevant to complications associated with BBB disruption by the impaired capacity of damping excessive pulsatile flow related to blood pressure fluctuations.

Disclosure of Interest: None Declared

IHC23-PO-190

Signatures of Migraine Aura in High – Density – EEG

Franz Riederer[1], Johannes Beiersdorf[2,3], Clemens Lang[2,3], Agnes Pirker-Kees[2,3], Antonia Klein[1], Adrian Scutelnic[1], Kirsten Platho-Elwischger[2,3], Jens P Dreier[4] and Christoph Schankin[1]

[1]*Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland*
[2]*Department of Neurology, Clinic Hietzing, Vienna, Austria*
[3]*Karl Landsteiner Institute for Clinial Epilepsy Research and Cognitive Neurology, Vienna, Austria*
[4]*Department of Neurology and Experimental Neurology Charité — Universitätsmedizin Berlin, Berlin, Germany*

Background: Cortical spreading depolarization (CSD) is highly conserved among the species and has been recorded in the cortex of humans with severe neurological disorders such as hemispheric stroke, traumatic brain injury or subarachnoid hemorrhage. It is widely accepted that CSD is also the pathophysiologic correlate of human migraine aura, although this needs further substantiation. The aim of the present study was to investigate possible signatures of CSD during migraine aura in typical migraineurs using full band High-Density EEG (HD-EEG).

Methods: In this prospective study, patients with migraine with aura (MwA) were investigated during migraine aura (ictally) and interictally, defined as at least 48 hours away from the last headache and aura episode if possible. Recordings from age- and gender-matched healthy controls were taken from a normal database. Time compressed HD-EEG were analyzed for (a) slow potential changes below 0.05 Hz, (b) suppression of faster activity in the range of 0.5 Hz–45 Hz (c) spreading of these changes to neighboring regions during the aura phase, and (d) topographical changes in alpha-power spectral density (8–14 Hz).

Results: In one 45-year-old male patient, a total of 8 EEGs could be recorded during spontaneous visual aura, one in the headache phase, and 6 in the interictal phase. In a 22-year-old man, HD-EEG was acquired during a prolonged visual aura and interictally. In another 60-year-old male subject, one HD-EEG could be recorded in the late visual aura phase. In a total of 6 different subjects, HD-EEGs were performed in the interictal phase. During auras or interictally, no slow potentials could be recorded. In the patient with repeated HD-EEGs during aura, α-power was significantly decreased in parieto-occipito-tempal location on the contralateral side. The suppression of alpha-power lasted into the headache phase. In the subject with prolonged visual aura, alpha power was decreased in the contralateral occipital region and α-peak was at lower frequency (9Hz) as compared to the interictal recording (10Hz). The 60-ear-old-male patient with late right-sided visual aura showed no marked asymmetry of occipital alpha power. The interictal HD-EEGs in MwA did not differ significantly from age- and gender-matched healthy controls.

Discussion: No direct current (DC) shift could be detected over the intact scalp during migraine aura using the present HD-EEG setup. In this study, EEG-recordings were started not earlier than 12 min after aura onset. Most visual auras begin in the center of the visual field and move to the periphery, i.e., CSD moves from the occipital pole anteriorly in the primary visual cortex . In the depth of the visual cortex, detection of the DC shift is then even more difficult than closer to the skull. It is thus likely that DC-shifts were missed which are 30 times smaller in scalp EEG than in subdural measurements anyway . However, the decrease in alpha-power in the affected hemisphere seen during right-sided auras is consistent with CSD-induced spreading depression of spontaneous brain activity.

Disclosure of Interest: None Declared

IHC23-PO-191

Exploring the parameningeal μ-opioid receptor availability in episodic and chronic migraine

Dajung Kim[1,2], Manyoel Lim[1,2,3], Thiago Nascimento[1,2], Peter Scott[4], Robert Koeppe[4], Niko Kaciroti[5], Nouchine Hadjikhani[6] and Alexandre DaSilva[1,2]

[1]*Headache and Orofacial Pain Effort (H.O.P.E.) Laboratory, Department of Biologic and Materials Sciences & Prosthodontics, University of Michigan School of Dentistry, Ann Arbor, USA*
[2]*Michigan Neuroscience Institute, University of Michigan, Ann Arbor, USA*
[3]*Food Convergence Research Division, Korea Food Research Institute, Wanju, Korea, Republic of*
[4]*Department of Radiology, University of Michigan, Ann Arbor, USA*
[5]*Department of Biostatistics, University of Michigan, Ann Arbor, USA*
[6]*Department of Radiology, Harvard Medical School, Boston, USA*

Objective: The activation of μ-opioid receptors (μORs) in the meninges plays an essential role in the regulation of meningeal nociception and sensitization, which links to migraine pain. This study aims to investigate the potential role of μOR availability in the parameninges on migraine pain experience.
Methods: This study employed [11C] Carfentanil Positron Emission Tomography (PET) to measure μOR availability in the parameningeal area of patients with chronic migraine (during ictal phase only) (n = 7), episodic migraine (during both interictal and ictal phases) (n = 8) and healthy controls (n = 22). The PET session comprised both an early resting and late thermal pain threshold stimulation phase, with clinical information on migraine collected. The averaged μOR availability in the parameningeal area surrounding the whole brain was compared between the migraine and healthy control groups, as well as between the interictal and ictal phases. Additionally, we tested the relationship between the clinical features of migraine and μOR availability.
Results: We found significant differences in the μOR availability between healthy individuals and those with episodic or chronic migraine during migraine attacks in the early-resting phase ($F(2, 18.5) = 4.83$, $P = 0.021$). Subsequent post-hoc tests demonstrated that only chronic migraine had significantly lower μOR availability than healthy controls ($P = 0.012$). Additionally, we observed a significant association between higher migraine frequency and reduced μOR availability measured during migraine attacks. ($rho = -0.61$, $P = 0.017$). Moreover, individuals with episodic migraine displayed reduced μOR availability during the late thermal pain stimulation phase, but not during the early resting phase, when comparing the migraine attacks to interictal period (Wilcoxon $W = 3.0$, $P = 0.039$).
Conclusion: A decreasing level of μOR availability associated with migraine attacks and frequency indicates that the role of the parameningeal μOR system in the pathophysiology of migraine and could inform the development of novel therapeutic approaches and targets for the management of migraine.
Disclosure of Interest: This work was supported by grant grant numbers R01-NS94413 (Dr. DaSilva) and K23-NS062946 (Dr.DaSilva) from the National Institute of Neurological Disorders and Stroke. No other disclosures were reported.

IHC23-PO-192

Functional connectivity characterization of NDPH — a graph-theoretic analysis of MEG

Dong Qiu

Headache Center, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Background: New daily persistent headache (NDPH) is a rare but debilitating primary headache disorder that poses a significant burden on individuals and society. Despite its clinical importance, the underlying pathophysiological mechanisms of NDPH remain unclear. In this study, we aimed to investigate the characteristics of brain connectivity in patients with NDPH using resting state magnetoencephalogram (MEG) analysis.
Methods: Fifty-three patients with NDPH and 53 healthy controls were recruited for this study, and their structural and resting-state data were collected by MEG. MEG source localization was conducted using the dynamic statistical parametric mapping. Based on the oscillatory envelope correlation analysis method, FC values of each cortical region were calculated as edges, and the connectivity was statistically analyzed by two-sample T test. Graph theory analysis was used to analyze the small-world network and the clustering index. The connectivity differences among groups and the correlation between clinical characteristics and network characteristics were analyzed.
Results: We found that NDPH group had enhanced connectivity in all brain regions compared with HC group. Graph theory analysis showed that clustering coefficient, normalized clustering coefficient, shortest path length and normalized characteristic path length of NDPH patients were enhanced compared with HC. Additionally, small worldness correlated with poor sleep quality in patients with NDPH.

Conclusion: We show that network measures based on resting-state MEG data had notable features. The observed network alterations could serve as therapeutic eadout parameters for future translational studies in NDPH research.
Keywords: new daily persistent headache; magnetoencephalography; functional neuroimaging

IHC23-PO-193

Dysfunction of Cerebral Venous Outflow and Vascular Regulatory Mechanisms in Migraine Patients

Xiangqi Cao[1,2], Chong Ye[1], Yixin Zhao[1], Litao Ruan[1], Guogang Luo[1] and Meng Wei[1]

[1]*The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China*
[2]*Air Force Medical University, Xi'an, China*

Background and Objective: Recent studies suspected that cerebral venous insufficiency may be involved in migraine and its transformation to chronification, probably resulting from dysfunction of cerebral autoregulation mechanisms. This study aims to elucidate the correlation by assessing the morphology and hemodynamics of the intracranial and external venous systems in individuals with migraine.
Methods: Patients with migraine who met the diagnostic criteria of ICHD-3 in the Headache Clinic were selected as the subjects. Baseline patient data was collected via questionnaire and the impact of headaches on daily life was assessed using HIT-6 and MIDAS. MRV was used to observe intracranial venous sinus structure, while Doppler contrast-enhanced ultrasonography was used to observe jugular vein structure, cerebral circulation time (CCT), cerebral blood volume (CBV) and cerebral blood flow volume (CBF). Flash visual evoked potentials were used to evaluate cerebral perfusion pressure (CPP) and intracranial pressure (ICP). The structures and hemodynamic characteristics of intracranial venous sinus and jugular vein in patients with migraine were analyzed.
Results: This study included 59 patients with migraine (average age: 44.3 ± 11.9 years; 15.3% male). 42 patients (71.2%) reported experiencing migraine for more than 10 years, including 31 patients (52.5%) with paroxysmal migraine and 28 patients (47.5%) with chronic migraine. We performed comparisons between migraine patients and healthy controls and then between subgroups. The CCT1 (4.65 ± 0.89 s, $P < 0.001$), defined as the time interval between the points of the polynomials reaching 10% of the overall intensity increase, was significantly shorter in migraine patients compared to the general population (6.59 ± 0.18s). Migraine patients also had lower CBV (57.48 ± 11.11ml, $P < 0.001$) than the general population (74 ± 19mL) and higher CBF (804.21 ± 166 ml, $P = 0.001$) than that of healthy subjects (760 ± 159 mL/min) as measured using the same method. Among 46 patients who underwent MRV or DSA examination, 38 (82.6%, $P < 0.001$) had transverse/sigmoid sinus stenosis, which was higher in migraine patients than the general population (40.0%). Migraine patients had similar ICP (126 ± 38 mmH2O) and CPP (81.0 ± 12.4 mmHg), regardless of migraine type. The comparisons of CBV was of significant difference between the EM and CM groups ($P = 0.017$), while CCT1, CBF and intracranial venous sinus stenosis rate were not.
Conclusion: This study provides evidence that migraine patients have shorter CCT and CBV, higher CBF and elevated incidence of intracranial venous sinus stenosis than that of the normal population, suggesting that the possible intracranial venous outflow disturbance. The CBV was higher in the CM group than in the EM group, which demonstrated compromised cerebral vascular regulation function, and may contribute to migraine chronification. In conclusion, intracranial and external venous systems are likely to be involved in the attack and development of migraine, but the specific mechanism needs further study.
Disclosure of Interest: None Declared

IHC23-PO-194

Task-free fMRI to assess the thalamic connectivity integrity during nitroglycerin-induced migraine attacks.

Daniele Martinelli[1], Maria Magdalena Pocora[1,2], Roberto De Icco[1,2], Marta Allena[1], Ana Bacila[3], Grazia Sances[1], Anna Pichiecchio[2,3], Gloria Castellazzi[1] and Cristina Tassorelli[1,2]

[1]*Headache Science and Rehabilitation Center, IRCCS C. Mondino Foundation, Pavia, Italy*
[2]*Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy*
[3]*Neuroradiology Unit, IRCCS C. Mondino Foundation, Pavia, Italy*

Objectives: Task-free functional MRI (rs-fMRI) has been widely used to study the brain functional connectivity (FC) changes occurring in migraine, to better understand the underlying cyclical mechanisms. In this study, we used rs-fMRI to describe changes in the functional connectivity of the thalami with other brain areas occurring during a nitroglycerin-induced migraine-like attack.
Methods: Ten subjects with episodic migraine (EM, 4 female, 29.4 yo, 4 monthly migraine days) underwent 3T

MRI examinations consisting in four rs-fMRI repetitions during the subsequent phases of a nitroglycerin-induced migraine attack (baseline, prodrome, full-blown attack, recovery). Ten healthy controls (HC, 4 female, 26.9 yo) were enrolled for reference. A seed-based component analysis (SCA) choosing the left and right thalami was performed comparing the two groups (migraine vs HC) to detect disease-specific hallmarks. In addition, in the migraine group we performed a within group comparison between the pain-free baseline scan and the scans taken during the different phases of the attack to identify phase-specific alterations.

Results: In subjects with migraine, both thalami had a higher FC correlation with the homolateral supramarginal gyrus and the superior frontal gyrus, as well as a lower FC correlation with the superior temporal gyrus. The [left] thalamus showed reduced FC starting from the prodromal phase, when compared to the pain-free state, especially with the posterior cerebellum, the frontal gyri, and the cingulate cortex. The SCA analysis also showed that the thalami, the brainstem, the cingulate cortex, and the posterior part of the cerebellum exhibited an altered functional coupling with one another.

Discussion: The intervention of the thalamus occurs predominantly during the ictal phase of a migraine attack. It orchestrates the activity of several structures being a fundamental point of relay for sensory processing in migraine. Secondly, this study further highlights the involvement of the cerebellum – a multiple effector system integrator and a ruler of pain perception modulation – and the frontal/prefrontal cortex. The changes observed in these areas may explain the cognitive impairment associated with the migraine ictal phase.

Disclosure of Interest: Daniele Martinelli, Maria Magdalena Pocora, Ana Bacila, Anna Pichiecchio and Gloria Castellazzi, have nothing to report. Roberto De Icco received lecture honoraria from Eli-Lilly and Teva. Marta Allena received lecture honoraria from Eli-Lilly. Grazia Sances has served on the advisory boards or received lecture honoraria from Eli-Lilly, Novartis, TEVA, Lundbeck, and Pfizer. Cristina Tassorelli has served on the advisory boards of Abbvie, Dompé, Eli-Lilly, Lundbeck, Novartis, and Teva; received lecture honoraria from Abbvie, Eli-Lilly, Lundbeck, Novartis, and Teva; honoraria for consulting services from Medscape; received research funding from the EU Commission, the Italian Ministry of Health, the American Migraine Foundation, and Allergan; and serves on the editorial boards of Cephalalgia and the Journal of Headache and Pain.

IHC23-PO-195

Induction of Migraine Aura with Calcitonin Gene-Related Peptide: A REFORM Study.

Haidar Al-Khazali

Department of Neurology, Danish Headache Center, Glostrup, Denmark

Objective: To investigate whether intravenous infusion of calcitonin gene-related peptide (CGRP) can induce migraine aura.

Methods: In an open-label, single-arm, non-randomized trial, 34 participants with migraine aura received continuous intravenous infusion of 1.5μg/min of CGRP over 20 minutes on one experimental day. The primary endpoint was the incidence of aura during a 12-hour observational period after the start of infusion.

Results: During the 12-hour observational period, 24 of 34 (71%) developed migraine attacks after intravenous infusion of CGRP. In addition, intravenous infusion with CGRP induced aura attacks in 13 of 34 (38%) participants. Among participants who experienced migraine attacks with aura, the median number of aura attacks was 60 (IQR, 36 to 96) days per year compared to 8.6 (IQR, 5 to 60) days per year in participants who reported migraine attacks without aura ($P = 0.03$).

Conclusion: CGRP triggers migraine attacks with aura. Frequent aura sufferers were more likely to experience aura after CGRP infusion, indicating a potential role of CGRP in aura development. Further studies that rigorously evaluate the effect of CGRP-targeting antibodies on aura frequency are needed.

IHC23-PO-196

Pulvinar involvement in the migraine cycle: a task-free fMRI analysis during nitroglycerin-induced attacks

Maria Magdalena Pocora[1,2], Daniele Martinelli[2], Roberto De Icco[1,2], Marta Allena[2], Ana Bacila[3], Grazia Sances[2], Anna Pichiecchio[1,3], Gloria Castellazzi[2,4,5] and Cristina Tassorelli[1,2]

[1]*Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy*
[2]*Headache Science and Rehabilitation Center, IRCCS C. Mondino Foundation, Pavia, Italy*
[3]*Neuroradiology Unit, IRCCS C. Mondino Foundation, Pavia, Italy*
[4]*NMR Research Unit, Department of Neuroinflammation, UCL Queen Square Institute of Neurology, Faculty of Brain Sciences, Queen Square MS Center, London, United Kingdom*

[5]Department of Electrical, Computer and Biomedical Engineering, University of Pavia, Pavia, Italy

Objective: Resting state functional magnetic resonance imaging (rs-fMRI) studies have depicted cyclical functional connectivity changes during a migraine attack, within the framework of thalamo-cortical dysrhythmia. The pulvinar is a thalamic microstructure implicated in the integration of visual stimuli and possibly also in migraine pathophysiology, namely in photophobia. In this rs-fMRI study, we aimed to assess the relationship between pulvinar and the cortex during various phases of nitroglycerin-induced migraine attacks (NTG).
Methods: Ten episodic migraine patients (EM) and ten healthy controls (HS) underwent 3T MRI scans during subsequent phases of the NTG migraine attack (baseline, prodrome, full-blown attack, recovery). Nine subjects developed photophobia during the full-blown phase. A seed-based correlation analysis (SCA) investigated the relationship between the pulvinar and the cortex during the different phases of the attack in EM and at pre-specified time points in HS. We also performed a comparison between each scan and the baseline (pain-free) condition and tested whether there was a correlation between mean functional connectivity (FC) and anamnestic features.
Results: At baseline, EM presented an increased FC between the pulvinar and the contralateral posterior cerebellum, middle temporal gyrus and middle frontal gyrus when compared to HS. During the migraine attack, we observed a reduced FC in the superior and medial frontal gyri in all phases and in the inferior parietal lobule and middle temporal gyrus during the full-blown attack phase. No significant findings ($p > 0.05$) were observed when correlating the mean global FC of each phase with pain side.
Conclusions: The pulvinar plays part in the processing of multisensory information, mostly visual. This study suggests its involvement in migraine also, with disease specific alterations which encompass bilateral frontal, parietal and temporal areas, that are well known for their role in modulating visual perception, attention, and awareness. Since rs-fMRI investigates basal activity, the observed FC reductions, mainly occurring during the full-blown phase, may suggest a reduced mutual information with pulvinar regions, possibly representing a compensatory mechanism to excessive sensory stimulation.
Disclosure of Interest: The authors declared the following potential conflict of intereset with respect to the research, authorship and/or publication of this article: CT received honoraria for the participation in advisory boards or for lecturing for: Allergan, Dompé, Eli-Lilly, Novartis and Teva. CT has no ownership interest and does not own stocks of any pharmaceutical company. RDI received honoraria for lecturing from: Eli-Lilly and Teva. GS received honoraria for the participation in advisory boards or for lecturing from: Eli-Lilly, Novartis and Teva. The remaining authors have no conflicts of interest.

IHC23-PO-197

Non-vascular ATP-sensitive potassium channel activation does not trigger migraine attacks: A randomized clinical trial.

Lili Kokoti, Mohammad Al-Mahdi Al-Karagholi, Zixuan Alice Zhuang, Sarkhan Amirguliyev, Faisal Mohammad Amin and Messoud Ashina

Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark

Objective: To investigate the potential of NN414, a selective ATP-sensitive potassium (K_{ATP}) channel opener for the Kir6.2/SUR1 channel subtype, which is expressed in neurons and β-pancreatic cells, to induce migraine attacks or affect cerebral hemodynamics in individuals diagnosed with migraine without aura.
Methods: In a randomized, double-blind, placebo-controlled crossover study, 13 participants with migraine without aura were randomly allocated to receive NN414 and placebo, on two different days separated by at least 1 week. The primary endpoint was the difference in the incidence of migraine attacks after NN414 compared with placebo. The secondary endpoints were the difference in the area under the curve (AUC) for headache intensity scores (0–12 hours), for middle cerebral artery blood flow velocity (V_{MCA}) (0–140 minutes), for superficial temporal artery (STA) diameter (0–140 minutes), for heart rate (HR) (0–150 minutes) and for mean arterial pressure (MAP) (T0–150 minutes).
Results: Twelve participants completed the study, with 2 (16.6%) reporting migraine attacks after NN414 compared to 1 (8.3%) after placebo ($p = 0.53$). The AUC for headache intensity, V_{MCA}, STA diameter, HR and MAP did not differ significantly between NN414 and placebo ($p > 0.05$ for all comparisons).
Conclusion: NN414, a selective K_{ATP} channel opener for the Kir6.2/SUR1 subtype, did not induce migraine attacks or cause significant hemodynamic changes in individuals with migraine. Our results indicate that this channel subtype may not have a major role in migraine pathogenesis. We instead suggest that the Kir6.1/SUR2B subtype expressed in cerebral vasculature is potentially involved in the signalling pathways leading to migraine attacks and a possible novel therapeutic target.
Disclosure of Interest: Faisal Mohammad Amin has received personal fees from Pfizer, Teva, Lundbeck,

Novartis, Eli Lilly, outside of the submitted work. Messoud Ashina reports receiving personal fees from AbbVie, Amgen, Eli Lilly, Lundbeck, Novartis, Pfizer and Teva Pharmaceuticals outside of the submitted work. MA received institutional grants from Lundbeck Foundation, Novo Nordisk Foundation, and Novartis. MA reports serving as associate editor of Cephalalgia, associate editor of The Journal of Headache and Pain, and associate editor of Brain

IHC23-PO-198

Differences in Cortical Thickness, Volume, and Surface Area in Participants with Migraine and Healthy Controls: A REFORM Study

Rune Häckert Christensen[1,2], Håkan Ashina[1,2,5], Haidar Muhsen Al-Khazali[1,2], Yixin Zhang[6], Daniel Tolnai[7], Amanda Holmen Poulsen[1], Alessandro Cagol[8,9], Nouchine Hadjikhani[10,11], Cristina Granziera[8,9], Faisal Mohammad Amin[1,2,5] and Messoud Ashina[1,2,12]

[1]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark*
[2]*Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*
[3]*Harvard Medical School, Boston, USA*
[4]*Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, USA*
[5]*Department of Brain and Spinal Cord Injury, Copenhagen University Hospital-Rigshospitalet, Copenhagen, Denmark*
[6]*Department of Neurology, The First Afliated Hospital of Chongqing Medical University, Chongqing, China*
[7]*Department of Radiology, Rigshospitalet Glostrup, Glostrup, Denmark*
[8]*Translational Imaging in Neurology (ThINk) Basel, Department of Biomedical Engineering, University Hospital Basel, Basel, Switzerland*
[9]*Neurologic Clinic and Policlinic, MS Center and Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel, University of Basel, Basel, Switzerland*
[10]*Gillberg Neuropsychiatry Centre, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*
[11]*Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Boston, USA*
[12]*Danish Knowledge Center on Headache Disorders, Glostrup, Denmark*

Objective: To identify robust cortical morphometry changes in a large cohort of participants with migraine and healthy controls.
Methods: Adult participants with migraine and age- and gender-matched healthy controls underwent a single magnetic resonance imaging (MRI) session with magnetization-prepared rapid acquisition gradient echo (MPRAGE) and fluid-attenuated inversion recovery (FLAIR). Cortical thickness, surface area, and volume were measured using FreeSurfer. General linear models were used to compare groups, with vertex-wise thresholds of $p < 0.0001$ and cluster-wise thresholds of $p < 0.05$, adjusted for age and gender.
Results: A total of 296 participants with migraine and 155 healthy controls were included. Chronic migraine was diagnosed in 180 participants and aura in 103. Participants with migraine had reduced cortical surface area in the left insula compared to controls ($p < .0001$). Participants with chronic migraine exhibited reduced surface area in the left insula ($p < .0001$) and increased surface area in the right caudal anterior cingulate cortex ($p < .0001$) compared to controls. Participants with a migraine attack during the scan displayed increased cortical thickness and volume in the right superior temporal gyrus, compared to controls ($p < .0001$ for both). No changes were observed in patients with aura or between migraine subtypes.
Conclusion: The identified cortical changes in migraine were limited to specific pain processing regions, including the insula and caudal anterior cingulate gyrus, and were most prominent in participants with chronic migraine. These findings suggest persistent cortical changes associated with migraine.
Disclosure of Interest: The study was funded by the Lundbeck Foundation Professor Grant (R310-2018–3711). Funding sources had no influence on study design, patient inclusion, or data interpretation. H.A. reports personal fees from Teva, outside of the submitted work. A.C. is supported by the Horizon 2020 Eurostar program (grant E!113682). C.G. is supported by: The University Hospital Basel (USB), as the employer of Cristina Granziera has received the following fees, which were used exclusively for research support: (i) advisory board and consultancy fees from Actelion, Novartis, Sanofi-Genzyme, Jannsen, and F. Hoffmann-La Roche; (ii) speaker fees from Biogen, F. Hoffmann-La Roche, Novartis, Jannsen, and Genzyme-Sanofi; (iii) research support by F. Hoffmann-La Roche. F.M.A. has received personal fees from Pfizer, Teva, Lundbeck, Novartis, Eli Lilly, outside of the submitted work. M.A. is a consultant, speaker, or scientific advisor for AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva and a primary investigator for ongoing AbbVie/Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva trials. Messoud Ashina has no ownership interest and does not own stocks of any

pharmaceutical company. Messoud Ashina serves as associate editor of Cephalalgia, associate editor of the Journal of Headache and Pain, and associate editor of Brain. R.C., H.M.A., Y.Z., D.T., A.P., and N.H. report no relevant conflicts of interest.

IHC23-PO-199

Cortical Inflammation in Migraine Measured with Quantitative Magnetic Resonance Imaging: A REFORM Study

Rune Häckert Christensen[1,2], Håkan Ashina[1,2,5], Haidar Muhsen Al-Khazali[1,2], Mario Ocampo-Pineda[6], Reza Rahmanzadeh[6,7], Nouchine Hadjikhani[8,9], Cristina Granziera[6,7], Faisal Mohammad Amin[1,2,5] and Messoud Ashina[1,2,10]

[1]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark*
[2]*Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*
[3]*Harvard Medical School, Boston, USA*
[4]*Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, USA*
[5]*Department of Brain and Spinal Cord Injury, Copenhagen University Hospital-Rigshospitalet, Copenhagen, Denmark*
[6]*Translational Imaging in Neurology (ThINk) Basel, Department of Biomedical Engineering, University Hospital Basel, University of Basel, Basel, Switzerland*
[7]*Neurologic Clinic and Policlinic, MS Center and Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel, University of Basel, Basel, Switzerland*
[8]*Gillberg Neuropsychiatry Centre, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*
[9]*Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Boston, USA*
[10]*Danish Knowledge Center on Headache Disorders, Glostrup, Denmark*

Objective: To investigate cortical inflammation using a novel quantitative, multimodal magnetic resonance imaging (MRI) technique in adult participants with migraine compared to age- and gender-matched healthy controls.
Methods: Participants underwent a single MRI session. T2 mapping was used to measure the water content of tissues, while T1 mapping was used to measure the distribution of water protons. The apparent diffusion coefficient (ADC) was used to measure the magnitude of diffusion of water molecules. Cortical quantitative T2 (qT2), quantitative T1 (qT1), and ADC values, considered surrogate markers of neuroinflammation, were measured in the cortical ribbon and compared between participants with migraine (with and without aura) and healthy controls. A general linear model was used with a vertex-wise threshold of $p < 0.05$ and a cluster-wise threshold of $p < 0.05$, adjusted for age and gender.
Results: A total of 296 participants with migraine and 155 age and gender matched healthy controls were included in the analysis. Of the participants with migraine, 103 had aura and 180 had chronic migraine. Participants with migraine had increased qT2 in the left occipital cortex compared to healthy controls ($p < .0001$). In participants with migraine with aura, the increased qT2 was more widespread and located bilaterally in the occipital cortices compared to healthy controls (left, $p < .0001$; right, $p = .004$). Exploratory analysis revealed higher ADC values within the qT2 clusters in participants with migraine with aura than in controls ($p = .01$). No significant differences were observed in qT1 values between the two groups.
Conclusion: Cortical inflammation is more prevalent in migraine with aura than in migraine without aura. The increased qT2 values in the occipital cortices of participants with migraine with aura are likely extracellular edema, as suggested by the concomitant ADC increase. These results support the importance of cortical inflammation in migraine pathogenesis, particularly in migraine with aura.
Disclosure of Interest: The study was funded by the Lundbeck Foundation Professor Grant (R310-2018–3711). Funding sources had no influence on study design, patient inclusion, or data interpretation. H.A. reports personal fees from Teva, outside of the submitted work. C.G. is supported by: The University Hospital Basel (USB), as the employer of Cristina Granziera has received the following fees, which were used exclusively for research support: (i) advisory board and consultancy fees from Actelion, Novartis, Sanofi-Genzyme, Jannsen, and F. Hoffmann-La Roche; (ii) speaker fees from Biogen, F. Hoffmann-La Roche, Novartis, Jannsen, and Genzyme-Sanofi; (iii) research support by F. Hoffmann-La Roche. F.M.A. has received personal fees from Pfizer, Teva, Lundbeck, Novartis, Eli Lilly, outside of the submitted work. M.A. is a consultant, speaker, or scientific advisor for AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva and a primary investigator for ongoing AbbVie/Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva trials. Messoud Ashina has no ownership interest and does not own stocks of any pharmaceutical company. Messoud Ashina serves as associate editor of Cephalalgia, associate editor of the Journal of Headache and Pain, and associate editor of Brain. R.C., H.M.A., M.O-P., R.R., and N.H. report no relevant conflicts of interest.

IHC23-PO-200

White Matter Hyperintensities and Etiology Differences in Stroke in Women with and without Migraine: A Relationship Investigation

A.E. Wilms[1]*, N. van der Weerd[1], T.W. van Harten[2], K.M. Linstra[1,3], H.J.A. van Os[1], I. de Boer[1], M.C. Kruit[2], A. MaassenVanDenBrink[3], M.J.H. Wermer[1] and G.M. Terwindt[1]

[1]*Department of Neurology, Leiden University Medical Center, Leiden, Netherlands*
[2]*Department of Radiology, Leiden University Medical Center, Leiden, Netherlands*
[3]*Department of Internal Medicine, Erasmus Medical Center, Rotterdam, Netherlands*

Objective: Migraine increases the risk of white matter hyperintensities (WMH) and ischemic stroke. It is unclear whether there is an additive effect on WMH volume in patients with a history of both migraine and ischemic stroke. We evaluated WMH volumes in women who had experienced a stroke, both with and without a history of migraine.

Methods: We enrolled middle-aged women with a history of migraine, ischemic stroke, or both, along with age-matched female control participants without neurological diseases. We classified the etiology of stroke based on the TOAST-criteria. We used our in-house developed semi-automated segmentation software in MeVisLab (version 3.4.1) to evaluate WMH volume on 3D fluid-attenuated inversion recovery (FLAIR) images. Cerebellar WMH were scored as present or absent. Differences between groups were assessed using (non-parametric) tests.

Results: A total of 186 women were included: migraine with aura (MA) (n = 38), stroke (n = 55), migraine and stroke (n = 55), controls (n = 38). Age and BMI were similarly distributed in all groups. Patients with ischemic stroke more often had a history of smoking compared with patients with stroke and migraine, migraine only, and controls (74% vs. 46%, 41% and 43% respectively, p = .005). Women with stroke (with and without migraine) more frequently reported hypertension and use of cholesterol-lowering drugs than those in the migraine and control groups (see Table 1). Women with both stroke and migraine more often had a stroke of undetermined origin according to the TOAST classification (49% vs. 27%, p = 0.020). Periventricular WMH volumes were higher in women with stroke (median [IQR]: 0.49 [0.27–0.95]) and stroke with migraine (0.55 [0.34–1.03]) than in those with migraine alone (0.42 [0.22–0.57]) or the control group (0.29 [0.17–0.65]), but no difference in deep WMH volume was found (Table 1). Importantly, there was no additional effect in WMH volume for those with a history of migraine and stroke compared to those with stroke alone.

Conclusion: No additive effect of migraine on WMH volume was observed in female stroke patients. Women with migraine had different stroke etiology, with smoking

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Table 1. Cohort characteristics and white matter hyperintensities (WMH) volume per group.

	Stroke N = 55	Stroke + migraine N = 55	Migraine N = 38	Control N = 38	P-value
Smoking, n (%)[a]	37 (74%)	22 (46%)	12 (41%)	15 (43%)	0.005
Hypertension, n (%)[b]	30 (54%)	35 (64%)	12 (32%)	8 (21%)	<0.001
Hypercholesterolemia, n (%)[c]	42 (76%)	43 (78%)	7 (18%)	2 (5%)	<0.001
TOAST classification, n (%)					
LAA	16 (29%)	10 (19%)			n.s.
CE	4 (7%)	4 (8%)			n.s.
SVD	11 (20%)	10 (19%)	–	–	n.s.
Other cause	9 (16%)	3 (6%)			n.s.
Undetermined	15 (27%)	26 (49%)			0.020
Migraine diagnosis, n (%)					
Migraine with aura	–	28 (51%)	38 (100%)	–	
Migraine without aura	27 (49%)	0 (0%)			
Periventricular WMH volume in mL, median (IQR)	0.49 (0.27–0.95)	0.55 (0.34–1.03)	0.42 (0.22–0.57)	0.29 (0.17–0.65)	0.009
Deep WMH volume in mL, median (IQR)	0.08 (0.01–0.30)	0.07 (0.02–0.35)	0.03 (0.01–0.15)	0.04 (0.01–0.10)	0.107
Cerebellar WMH, n (%)	9 (18%)	10 (21%)	4 (11%)	1 (3%)	0.070

[a]Smoking was defined as current smoker or ever smoked (n = 24 missing).
[b]Hypertension was defined as use of anti-hypertensive medication and/or reported history of hypertension by patient.
[c]Hypercholesterolemia was defined as use of cholesterol lowering drugs and/or reported history of hypercholesterolemia by patient.

being a more frequent risk factor in women with ischemic stroke without a prior history of migraine. Physicians should inquire about migraine history in non-smoking women with ischemic stroke.

IHC23-PO-201

Visual Evoked Potential Changes Related to Photophobia Severity in Migraine-Associated Photophobia

Tuba Erdogan Soyukibar[1], Elif Ilgaz Aydinlar[1], Kubra Canbaloglu[2], Mehmet Ergen[2] and Pinar Yalinay Dikmen[1]

[1]*Acibadem University School of Medicine, Department of Neurology, Istanbul, Turkey*
[2]*Acibadem University School of Medicine, Department of Physiology, Istanbul, Turkey*

Objective: Ictal and interictal photophobia is a common migraine-associated symptom and can negatively impact patients' quality of life. It is thought that electrophysiological responses may vary in patients with migraine accompanied by photophobia. This study aimed to define an objective parameter for migraine-associated photophobia severity in response to pattern reversal visual evoked potential (PRVEP) with varying luminance.
Methods: This prospective study included a total of 44 patients, consisting of 24 patients with episodic migraine (EM) (mean $\pm$ SD age: 34.42 $\pm$ 10.46 years; 70.8% were female) and 20 patients with chronic migraine (CM) (mean $\pm$ SD age: 31.80 $\pm$ 9.17 years; 95% were female), along with 20 healthy controls as a control group (CG) (mean $\pm$ SD age: 34.8 $\pm$ 11.58 years; 75% were female). The EM and CM groups completed the 12-item Utah Photophobia Symptom Scale (UPSIS-12) to evaluate ictal and interictal migraine-associated photophobia. For further evaluation, the patient was asked to indicate the degree of photophobia on a 4-point Likert scale. The impact of migraine on daily life was assessed by the Migraine Disability Assessment Scale (MIDAS) and the Headache Impact Test-6 (HIT-6). The severity of the headache was graded with a 10-point Visual Analog Scale (VAS). Cutaneous allodynia was graded with a 4-point Likert scale and assessed with the Allodynia Symptom Checklist (ASC-12). The patient's photophobia was graded as severe (UPSIS-12 $\geq$30) and mild (UPSIS-12 $<$ 30). PRVEP was recorded from the Oz electrode with reference to Fz during a headache-free period in EM patients. Due to the rarity of the interictal period in chronic migraine patients, those patients were asked to come to the PRVEP recording when they were headache-free or their headaches were not severe in intensity. Two variants of checkerboard stimuli with white square luminance as low (LL:45 cd/m2) and high (HL:85 cd/m2) were presented monocularly with 1 Hz reversal. PRVEP responses were recorded in 3 intermittent blocks of 100 epochs with a 2-minute rest period between blocks. The latency of N75, P100, and N145 and the peak-to-peak amplitude of N75-P100 were measured.
Results: Twenty-four patients (12 EM, 12 CM) had severe UPSIS-12 scores, and 20 (8 EM,12 CM) had mild UPSIS-12 scores. In all groups (CG, EM, CM), N75 and P100 latency shortened significantly when switching from low to high luminance ($p = 0.001$). Post-hoc tests revealed that a shorter latency of the N75 was noteworthy in the CM group (CM vs CG; $p = 0.01$ and CM vs EM; $p = 0.001$). P100 latency at both low and high luminance values was shorter in patients with severe UPSIS-12 scores than in patients with mild UPSIS-12 scores ($p = 0.024$). N75 latency was shorter in higher luminance stimulation in the group with severe UPSIS-12 scores than in the other group ($p = 0.01$).
Conclusion: Our findings suggest that shorter N75 latency with increasing luminance and luminance-independent shorter P100 latency are associated with severe UPSIS-12 scores. Additionally, CM patients had a shorter N75 latency with increasing luminance compared to CG and EM patients. These findings are promising for its use as a biomarker for migraine-associated photophobia.
Disclosure of Interest: None Declared

IHC23-PO-202

Enhanced synchronizability of structural connectomes in female chronic migraine is related to increased inter-hemispheric connectivity

Sebastián Risau-Gusman[1,2], Rodrigo de Luis-García[3], Álvaro Planchuelo-Gómez[3,4], Santiago Aja-Fernández[3], Tomás Hüttebräucker[1], Ángel L. Guerrero[3,5] and David García-Azorín[3,5]

[1]*Bariloche Atomic Center, Bariloche, Argentina*
[2]*CONICET, Bariloche, Argentina*
[3]*Universidad de Valladolid, Valladolid, Spain*
[4]*Cardiff University Brain Research Imaging Centre, Cardiff, United Kingdom*
[5]*Headache Unit, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*

Objective: To investigate the role of synchronizability of structural connectomes in episodic migraine (EM) and chronic migraine (CM).
Methods: High-resolution 3D brain T1-weighted Magnetic Resonance Imaging (MRI) and diffusion MRI data were acquired in 57 female EM patients, 61 female CM patients and 34 female healthy controls (HC).

Structural connectomes were built from anatomically-constrained tractography by jointly processing the T1-weighted and diffusion MRI data. 84x84 connectivity matrices were obtained, corresponding to connections between the 84 cortical and subcortical regions from the Desikan-Killiany atlas. Connectivity strength was estimated through the number of tractography streamlines connecting any two regions from the atlas, and weaker connections were pruned for more robust results.
Two synchronizability measures (λ_2 and R) were employed, following the Master Stability Function formalism from Physics. Synchronizability was evaluated for the whole brain and single hemisphere connections. Intra- and inter-hemispheric connectivity was also evaluated using the number of streamlines. Pairwise statistical comparisons were performed using Student's T test, and statistical significance was considered at $p < 0.05$.
Results: No statistically significant differences were found between the ages of the three groups.
Significantly increased whole-brain synchronizability was found in CM compared to HC (both larger λ_2 and R).
When only intrahemispheric connections were investigated, no statistically significant differences in synchronizability were found, indicating that interhemispheric connections are likely driving the detected differences.
To further investigate this, inter-hemispheric and intra-hemispheric streamline count was compared between the three groups. A significantly higher inter-hemispheric streamline count was found in CM compared to HC ($p < 0.01$), whereas no differences were found in intra-hemispheric streamline count. Three regions were mostly responsible for these differences: left superior frontal cortex, right precentral cortex, and right caudate.
Conclusion: Structural connectomes of chronic migraine patients are more synchronizable than those of healthy controls. Inter-hemispheric connections seem to be responsible for this difference.
Disclosure of Interest: None Declared

IHC23-PO-203

Quality assessment of neuroimaging criteria for idiopathic intracranial hypertension at a single tertiary headache center

Areeba Nisar[1], Prabath Mondel[2], Neelu Jain[2], Kiran Talekar[2], Scott Faro[2], Reid Gooch[2] and Hsiangkuo Yuan[1]

[1]*Jefferson Headache Center, Philadelphia, USA*
[2]*Thomas Jefferson University, Philadelphia, USA*

Objective: The current Friedman diagnostic criteria of idiopathic intracranial hypertension (IIH) recommend 4 distinct neuroimaging features, namely empty sella, posterior globe flattening, distention of the perioptic subarachnoid space, and transverse venous sinus stenosis. However, the operational definition and cut-off values for these imaging criteria were unclear, causing potential variation in clinical interpretation. A standardized neuroimaging criteria may reduce inter-rater variability but remain to be validated. In this study, we standardized neuroimaging criteria and evaluated their clinical utility.
Methods: Electronic medical records and brain images from patients who received venous manometry for refractory idiopathic intracranial hypertension between 1/2022-12/2022 at Thomas Jefferson University were screened and reviewed (IRB# 22D.519). Brain MRI and MRV were both required; subjects with prior brain or spine surgery or those with secondary causes of elevated intracranial hypertension were excluded. A standardized neuroimaging criteria (preferred sequence) were utilized: pituitary height $<$4.8mm (sagittal T1), posterior globe flattening or protrusion at the optic nerve head (axial T2 thin-cut), distention of the optic nerve sheath diameter $\geq$5.5mm (coronal T2 thin-cut fat-saturated), and transverse sinus of either side $\geq$50% stenosis (axial and coronal 2D time-of-flight with reconstruction). MRI/MRV were compared before and after the standardization of neuroimaging techniques and interpretation.
Results: We identified 20 subjects who received venous manometry, where 16 (93.7% female) had both brain MRI/MRV. Among them, 12 (75%) were Caucasian, and 4 (25%) were African American. Table 1 shows the quality assessment before and after standardization. Although IIH was mentioned in the report, most were not properly justified or described per criteria. In addition, we identified that the majority of images lacked fat saturation in the axial T2 sequences. Coronal sequences were only available in 9 patients, with only 2 patients having orbital T2 fat-saturated images for assessing perioptic subarachnoid space. In MRV sequences, 9/16 had axial 2D TOF, and 14/16 had coronal 2D TOF images. Overall, 13 met the IIH imaging criteria except for 3 cases, which we were unable to interpret due to poor image quality.
Conclusion: Our study demonstrated discrepancies in brain MRI/MRV findings before and after standardization. A lack of proper MRI sequences may also reduce interpretation reliability.
Quality assessment upon standardization
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	Pre-standardization	Post-standardization
IIH mentioned in MRI Report	10 (1 missing report)	–
Stenosis mentioned in MRV Report	12 (1 missing report)	–
Sella herniation (pituitary height <4.8 mm)	7 (mentioned but none measured)	16
Posterior globe flattening/optic nerve protrusion	3/1	12/6
Distention of the optic nerve sheath diameter ≥ 5.5 mm	1	13
Transverse sinus of either side $\geq 50\%$ stenosis	0	14

Migraine acute therapy

IHC23-PO-204

Music Medicine as a Component of Acute Migraine Attack Management in The Emergency Room: A Randomized Controlled Open-Label Trial

Artemio RoxasJr.[1] and Pearl Angeli Diamante[2]

[1]*The Medical City Hospital, Pasig City, Philippines*
[2]*The Medical City, Paranaque City, Philippines*

Objective: To identify if music medicine in addition to medical therapy will reduce the severity and duration of an acute attack of moderate to severe migraine compared to medical management alone.
Methods: An open label randomized controlled trial was conducted at the ER of a tertiary hospital in the Philippines from July 2017 to June 2018. Patients who presented at the ER with acute moderate to severe headache fulfilling the ICH-3 criteria for migraine were included. They were randomized to medical therapy or to medical therapy with music medicine. A decrease in the severity of the headache after one hour of medical treatment was the primary outcome.
Results: One hundred eighty-three adult migraneurs were included without difference between group in age, gender, and occupation. There was a statistically significant reduction ($p = 0.037$) in pain severity after one hour in 82 of 87 patients given medical treatment with music medicine (94%) compared to 73 of 86 in the medical therapy alone (85%). There were more headache-free patients at one hour in the music group (55% versus 42%, $p = 0.05$).
Conclusion: There is decreased duration and severity of pain when music medicine is added to conventional medical therapy in treating patients with an acute migraine. This is the first randomized trial done in the acute ER setting.
Disclosure of Interest: The paper has been published in the Annal of Headache Medicine Journal in 2020. We would like to share our study to all as we feel not everyone is aware on the benefit of music in acute migraine, considering this is a randomzied study.

IHC23-PO-205

Most bothersome symptom in migraine and probable migraine: a population-based study

Ki Moon Jang, Woo Seo Ha, Hye Jeong Lee, Soomi Cho, Kyung Min Kim and Min Kyung Chu

Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of

Background: The most bothersome symptoms (MBS) is recommended as a co-primary endpoint in clinical trials for the acute treatment of migraine. Probable migraine (PM) is a subtype of migraine fulfilling all but one criterion for migraine. However, information on MBS in PM is currently limited. We aimed to investigate MBS in PM in comparison with that in migraine.
Materials and Methods: This study used data from a nationwide study in Korea. MBS was assessed by requesting the participants to select one of the four typical accompanying symptoms of migraine. Responses to acute treatment were evaluated using the migraine Treatment Optimization Questionnaire-6.
Results: Nausea was the most common MBS, followed by phonophobia and vomiting in migraine (nausea, 61.8% [105/170]; phonophobia, 25.3% [43/170]; vomiting, 10.0% [17/170]; photophobia, 2.9% [5/170]), and PM (nausea, 81.7% [277/339]; phonophobia, 10.0% [34/339]; vomiting, 5.6% [16/339]; and photophobia, 2.7% [9/339]). Vomiting (adjusted odds ratio [AOR] = 6.513; 95% confidence interval [CI], 1.763–24.057) and phonophobia (AOR = 0.437; 95% CI, 0.206–0.929) were significantly associated with severe headache intensity in participants with migraine. Nausea was significantly associated with >3 headache days per 30 days (AOR = 0.441; 95% CI, 0.210–0.927). We observed no significant association between MBS and clinical characteristics in participants with PM. Acute treatment response was not significantly different according to the MBS for either migraine or PM.
Conclusions: MBS in PM revealed a different pattern than that in migraine. Our findings support the suitability of MBS as a co-primary endpoint for acute treatment in PM as well as migraine.

IHC23-PO-206

The efficacy and safety of lasmiditan in the acute treatment of hemiplegic migraine patients: A case series at a tertiary headache center

Daisuke Danno, Kumiko Ishizaki, Shoji Kikui and Takao Takeshima

Headache Center and Department of Neurology, Tominaga Hospital, Osaka, Japan

Objective: Hemiplegic migraine (HM) is a rare subtype of migraine with aura that is characterized by motor weakness related to headache attacks. HM is classified into a dominantly inherited familial subform (familial hemiplegic migraine [FHM]) and a sporadic subform without a family history (sporadic hemiplegic migraine [SHM]). HM is a disabling headache disorder. However, while weakness typically lasts for less than 72 h, it can sometimes last for several weeks. Headache characteristics are identical to those of typical migraine with aura, but it can last for more than three days and reach a severe intensity. Triptan use for HM is contraindicated because of the potential risk of enhancing ischemic stroke. Recently, the selective serotonin 1F (5-HT1F) receptor agonist lasmiditan was approved for the acute treatment of migraine. Lasmiditan has a low affinity for serotonin 1B (5-HT1B) receptors and does not cause vasoconstriction. Patients with contraindications to triptan, including HM, are therefore candidates for lasmiditan; however, the efficacy of lasmiditan for HM has not yet been reported. In the present study, we retrospectively investigated the efficacy and safety of lasmiditan in patients with HM.
Methods: In this retrospective study, we reviewed the medical notes of HM patients who were treated with lasmiditan at Tominaga Hospital Headache Center in Japan between June 2022 and April 2023. The proportion of attacks treated with lasmiditan that reached a pain-free condition or achieved pain relief at 2 and 24 h post-dose was evaluated. Nausea/vomiting and photophobia/phonophobia at 2 h post-dose, patients' Global Impression of Change (PGIC) at 24 h post-dose, and adverse effects (AEs) were also evaluated.
Results: We investigated 14 patients with HM (10 females, 4 males) with an average age of 37.1 years old. Twelve patients were diagnosed with SHM, and two were diagnosed with FHM. In total, 71 headache attacks were treated, and the number of treated attacks ranged from 1 to 10 per patient. Forty-four attacks were treated with 100 mg, and 27 were treated with 50 mg. Seventeen attacks were treated in combination with non-steroidal anti-inflammatory drugs, acetaminophen, or antiemetics. A total of 45.1% (32/71) and 26.8% (19/71) of patients reached a pain-free condition and achieved pain relief at 2 h, respectively, and 54.9% (39/71) and 35.2% (25/71) also reached a pain-free condition and achieved pain relief at 24 h, respectively. Nausea/vomiting and photophobia/phonophobia symptoms disappeared in 24.6% (15/61) and 25.4% (18/71) of patients, respectively. In terms of the PGIC, 23 and 31 of 71 patients were rated as very much improved and much improved, respectively. AEs were reported in all patients, including dizziness, nausea and somnolence; however, no serious AEs were reported.
Conclusions: In this study, we reported the efficacy and safety of lasmiditan in patients with HM for the first time. Lasmiditan is thought to be generally effective and tolerated as an acute treatment in HM. Our findings will support the treatment of patients with HM and the physicians treating these patients.
Disclosure of Interest: The authors received lecture fees from: Eli Lilly Japan, Daiichi Sankyo Co., Ltd., Amgen K.K., and Otsuka Pharmaceutical Co., Ltd.

IHC23-PO-207

Rimegepant for the Acute Treatment of Migraine in Adults From China

Shengyuan Yu[1], Aihong Guo[2], Mingjie Zhang[1], Zhen Wang[3], Jianguang Liu[4], Ge Tan[5], Qian Yang[6], Yu Liu[7], Qian Zhao[8] and Zhihong Lu[9]

[1]*Chinese PLA General Hospital, Beijing, China*
[2]*Yan'an University Xianyang Hospital, Xianyang, Shaanxi Province, China*
[3]*Changsha Central Hospital, Changsha, Hunan Province, China*
[4]*Wuhan Third Hospital, Wuhan, Hubei Province, China*
[5]*The First Affiliated Hospital of Chongqing Medical University, Chongqing, China*
[6]*Shanxi Provincial Hospital, Xi'an, Shanxi Province, China*
[7]*Pfizer Inc, Beijing, China*
[8]*Pfizer Inc, Chengdu, China*
[9]*Pfizer (China) Research and Development Ltd, Shanghai, China*

Objective: To evaluate the efficacy and safety of rimegepant, an oral small molecule calcitonin gene-related peptide receptor antagonist, for the acute treatment of migraine in adults from China.
Methods: This is a subgroup analysis of Chinese patients from a double-blind, randomized, placebo-controlled, phase 3 trial in Chinese and Korean adults with migraine (NCT04574362). Subjects received rimegepant 75 mg or placebo for a single migraine attack of moderate or severe intensity. Coprimary endpoints were pain freedom and freedom from the most bothersome symptom (MBS) at 2 hours post-dose.
Results: Rimegepant (n = 537) was superior to placebo (n = 537) for the co-primary endpoints of pain freedom

(18.2% vs 10.6%, P = .0004) and freedom from the MBS (48.0% vs 31.8%, P < .0001), as well as all key secondary endpoints (Table). The incidence of treatment-emergent adverse events (AEs) was similar in the rimegepant (15.2%) and placebo (16.4%) groups. No drug-related serious AEs were reported in rimegepant-treated subjects.

Conclusions: Rimegepant 75 mg demonstrated rapid and sustained efficacy, with safety and tolerability similar to placebo, for the acute treatment of migraine in adults from China.

N (%) of Subjects Meeting Coprimary and Key Secondary Endpoints

	Rimegepant 75 mg n=537	Placebo n=537	*P*-value
Coprimary			
Pain freedom at 2 hr	98 (18.2)	57 (10.6)	.0004
Freedom from the most bothersome symptom at 2 hr	258 (48.0)	171 (31.8)	<.0001
Key secondary			
Pain relief at 2 hr	351 (65.4)	256 (47.7)	<.0001
Normal functioning at 2 hr	176 (38.5)	110 (23.8)	<.0001
Sustained pain freedom from 2-48 hr	78 (14.5)	39 (7.3)	<.0001
Sustained pain freedom from 2-24 hr	82 (15.3)	43 (8.0)	<.0001
Rescue medication within 24 hr	28 (5.2)	75 (14.0)	<.0001

Disclosure of Interest: This study was sponsored by Biohaven which was acquired by Pfizer in October 2022. Zhihong Lu, Yu Liu, and Qian Zhao are employees of Pfizer. The remaining authors declare no conflicts of interest. Medical writing support was provided by Matt Soulsby, PhD, CMPP, of Engage Scientific Solutions and was funded by Pfizer.

IHC23-PO-208

Efficacy and Safety of Timolol Eye Drops in the Treatment of Acute MigraineA Systematic Review and Meta-Analysis

Carla Vianca Bartolome

Angeles university foundation medical center, Angeles city, Philippines

Background: Migraine is characterized by recurrent headache episodes. Pharmacologic therapy has focused on targeting migraine-associated genes and areas of the brain that exhibit increased activity during an attack. Some drugs under the beta blocker category are being studied and recommended. Timolol is a part of the treatment regimen for infantile hemangiomas, hypertension, myocardial infarction, and atrial fibrillation. However, data on the effect of topically administered Timolol in the abortive treatment of migraines is still lacking.

Objective: The study aimed to determine the effectiveness and safety of timolol eyedrops in the alleviation of acute migraine attacks.

Methods: An electronic search was performed via a systematic review of English journals by utilizing PubMed, Cochrane CENTRAL, and clinicaltrials.gov. Randomized clinical trials using Timolol eye drops to treat migraine were included. Study selection and data collection were performed by two reviewers independently. Quality and Bias assessments were determined by using the Cochrane risk-of-bias tool. The primary outcome was the achievement of a significant reduction in migraine headaches. The pool estimates were calculated.

Results: Three RCTs with a total of 613 subjects met the eligibility criteria set in this study. Overall, Timolol eye drops is 2.86 times (95%CI 0.75–11.00, P = 0.002) more efficacious as compared with placebo in the treatment of acute migraine based on headache pain reduction score. The only reported adverse effect is a mild stinging/burning sensation in the eye shortly after the administration of eye drops.

Conclusion: Timolol demonstrated a good efficacy and safety profile for the treatment of acute migraine based on three recently conducted randomized controlled trials. Most of the studies had small sample sizes; hence, it is recommended for more trials with similar objectives to be conducted in the future to enable more robust analysis of the effect of timolol in migraine treatment and management.

IHC23-PO-209

The first real word use experience of Rimegepant in a Chinese migraine patient: a case report

Wenyan Kang[1,2] and Peijian Huang[2]

[1]*Departerment of Neurology, Ruijin Hospital Affiliated Shanghai Jiaotong University School of Medicine, Shanghai, China*

[2]*Departerment of Neurology, Ruijin-Hainan Hospital Shanghai Affiliated Jiaotong University School of Medicine(Hainan Boao Research Hospital), Qionghai, China*

Objective: To present the first clinical case of the effectiveness and safety of Rimegepant in a Chinese migraine patient who has been poorly responsive to multiple therapies

Methods: A 37-year-old woman presented with 25 years history of migraine. In the past 3 months before visiting our hospital on Jan 11th 2023, the highest frequency of attacks could reach 3–4 times a week, and the attacks were often accompanied by nausea, photophobia or phonophobia. She had tried most of the migraine therapies, including nonsteroidal anti-inflammatory drugs (NSAIDs), combination analgesic, ergotamine, triptans, flunarizine, traditional Chinese medicine, acupuncture etc, which are either ineffective or intolerable. She was prescribed with Rimegepant to treat migraine as needed (PRN) and asked to report pain intensity (measured by a 4-point scale), most bothersome symptoms (MBS, nausea, phonophobia,

or photophobia) and function ability (measured by a four-point functional disability scale) at the onset of the treated attack and at 0.5, 1, 2, 24 and 48 hours postdose for 3 Rimegepant treated migraine attacks. Following 3 months, migraine events, tablet utilization, and other pain medication intake days were required to be recorded in patient diary.
Results: In general, for the 3 attacks, the patient achieved pain freedom, freedom from MBS and function normally within 2 hours postdose and the effect last for 48 hours without relapse and no other rescue medicines were taken within the 48 hours. The shortest time to achieve freedom from MBS and function normally is within 0.5 hour and achieve pain freedom is within 1 hour postdose. The monthly migraine days (MMD) were 5, 4 and 2 and Rimegepant intake days were 3, 4 and 1 in months 1–3 respectively. The patient took NSAIDs for the other 2 migraine days in the first month and 1 migraine day in the third month. No obvious adverse events were reported by the patient.
Conclusion: This case provides preliminary real world evidence that Rimegepant may be effective and safe for acute treatment of Chinese migraine patients and has showed a trend to reduce MMD by PRN use.
Disclosure of Interest: None Declared

IHC23-PO-210

Association between Triptan Use and Cardiovascular Disease and All-Cause Mortality among Patients with Migraine: A Systematic Review and Meta-analysis

Jing Jie Yu[1], Joshua E. Levine[1], Wei-Hsuan Lo-Ciganic[1], Yulia Orlova[2], Haesuk Park[1], Steven M. Smith[1], Yi Guo[2] and Seonkyeong Yang[1]

[1]*College of Pharmacy, University of Florida, Gainesville, USA*
[2]*College of Medicine, University of Florida, Gainesville, USA*

Objective: Triptans are contraindicated in patients with certain established cardiovascular diseases (CVD) due to their vasoconstrictive effects. Evidence regarding triptan-attributable CVD events is lacking among highly selected participants in clinical trials. We conducted a systematic review and meta-analysis to assess the association between triptan use and CVD risk among patients with migraine in real-world clinical settings.
Methods: We systematically searched observational studies that evaluated associations between triptans and

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Author, year	Data source	Study design	Study population[1]	Exposure[2]	Effect size measure	Adjusted effect size (95% CI) for outcomes included in the meta-analysis
Velentgas, 2004	Ingenix Research Database in the United States	Retrospective cohort	Patients with migraine (triptan users n = 50,383; nonusers n = 80,028)	Triptan use vs. non-use	Risk ratio	Coronary artery disease MI: 0.80 (0.58–1.11) Unstable angina: 0.72 (0.55–0.94) Stroke: 0.90 (0.64–1.26) Transient ischemic attack: 0.98 (0.66–1.45) All-cause mortality: 0.64 (0.45–0.89)
Wammes-van der Heijden, 2006	Pharmo record linkage system in Netherlands	Nested case-control	Patients with migraine (cases n = 188; controls n = 689)	Triptan use vs. non-use	Odds ratio	Coronary artery disease: 0.96 (0.49–1.90)
Becker, 2007	General Practice Research Database in the United Kingdom	Nested case-control	Patients with migraine (cases n = 200; controls n = 737)	Triptan use vs. non-use	Odds ratio	Stroke: 2.51 (1.10–5.71) Transient ischemic attack: 3.32 (0.61–18.0) All-cause death: 0.52 (0.18–1.52)
Lugardon, 2007	National Health Insurance System in France	Nested case-control	Patients with migraine (cases n = 155; controls n = 620)	Triptan use vs. non-use	Odds ratio	Coronary artery disease: 1.14 (0.58–2.25)
Ghanshan, 2020	Kaiser Permanente Southern California Health System in the United States	Retrospective cohort	Patients with migraine (triptan users n = 56,473; nonusers n = 56,473)	Triptan use vs. non-use	Hazard ratio	Coronary artery disease: 0.95 (0.84–1.08) All-cause death: 0.93 (0.81–1.08)
Li, 2022	Truven Health Analytics MarketScan in the United States	Retrospective cohort	Patients with migraine (triptan users n = 436,642; nonusers n = 1,168,212)	Triptan use vs. non-use	Hazard ratio	Coronary artery disease: 0.81 (0.74–0.89)

[1]Each study has a different operational definition of patients with migraine. [2]We included the highest defined daily dose and recent triptan use in the quantitative analysis, if multiple categories are available for triptan exposure status.

CVD events or all-cause death in MEDLINE, EMBASE, SCOPUS, Web of Science, and Cochrane Library databases up to November 2022. Two independent reviewers conducted study selection. For the included studies reporting adjusted risk ratios (RRs), hazard ratios (HRs), or odds ratios (ORs), we considered RR and HR comparable and converted OR to RR. We used random-effect models to estimate pooled RRs with 95% confidence intervals (95%CI) and assessed heterogeneity using I-squared statistic (I^2).

Results: Of 953 articles retrieved, the meta-analysis included 3 nested case-control and 3 cohort studies: 4 examining triptan-associated risk of coronary artery disease (CAD); 2 examining risk of stroke and transient ischemic attack (TIA); and 3 examining all-cause death. Pooled RRs showed no association between risks of stroke (1.40 [95%CI = 0.52−3.78], $I^2 = 80\%$), TIA (1.35 [0.47−3.86], $I^2 = 47\%$) and all-cause death (0.77 [0.56−1.07], $I^2 = 57\%$) among triptan users compared to nonusers in migraine patients. There was a decreased risk of CAD (0.85 [0.77 − 0.94], $I^2 = 25\%$) in triptan users compared to nonusers in migraine patients.

Conclusion: This meta-analysis showed that triptan use was not associated with stroke, TIA, or all-cause death risk but was associated with a decreased CAD risk in migraine patients. However, the findings are limited by the small number of studies that existed with high heterogeneity and potential residual confounding by triptans' contraindication. Future studies are warranted to provide evidence on triptan use and CVD risk in those with high CVD risk profiles.

Disclosure of Interest: None Declared

IHC23-PO-211

Efficacy of Electro Myogram (EMG) Biofeedback Training forMigraine Headache in Comparison with Pharmacological

Sagar Lavania[1], Amrit Pattojoshi[2] and Samayak Jain[3]

[1]*Sarojini Naidu Medical College, Agra, India*
[2]*Hi Tech Medical College, Bhubhaneshwar, India*
[3]*hapud Medical College, Meeruth, India*

Objective: Biofeedback has shown significant outcome with regard to headache especially to migraine and tension type headache. Current study was designed to know the efficacy of biofeedback along with pharmacotherapy in the management of migraine

Aim: To compare the efficacy of adjunctive EMG Biofeedback Training in controlling migraine headache with that of pharmacological treatment alone

Method: Current study was a case controlled, hospital based, prospective intervention study. The sample thus collected was grouped into two groups. Treatment for group one consisted of EMG biofeedback + pharmacological (n = 10) and for group two consisted of pharmacological alone (n = 10). Scales applied on both the groups were- Migraine severity Scale, Headache Impact Test, Hamilton Rating Scale for Depression & Hamilton Anxiety Rating Scale. Patients in the experimental group received 10 successful sessions of EMG biofeedback. Rating was done prospectively for two months.

Results: The baseline and post treatment evaluation did not show difference in terms of migraine severity, impact on daily living, co morbid conditions of depression and anxiety. However in the factor of tiredness and irritability (subcategory of headache impact test) the findings show a mean difference in both the group ($p = 0.05$). The experimental group got low score on items of tiredness (8.70 ± 1.49) and irritability (8.50 ± 1.96) comparing to the control group for these two items (tiredness 9.90 ± 1.10 and irritability 10.10 ± 1.45).

Conclusion: The study conveys the message of incorporating biofeedback training along with pharmacotherapy in the management of headache in the long run.

Disclosure of Interest: None Declared

IHC23-PO-212

Tackling opioid overuse for migraine in the Emergency Department: the multicentric Virtual Headache Training Program (VHTP)

Marcio Nattan Souza[1], Felipe Reinaldo Santos[1], Evelyn Pacheco[2], Marcelo Calderaro[3], João José Carvalho[4], Daniel Bezerra[5], Gustavo Kuster[6], Renand Domingues[6], Saulo Ribeiro[7] and José Luiz Carneiro Junior[2]

[1]*Universidade de São Paulo, São Paulo, Brazil*
[2]*United Health Group Brasil, São Paulo, Brazil*
[3]*Hospital Samaritano, São Paulo, Brazil*
[4]*Faculdade de Medicina Unichristus, Fortaleza, Brazil*
[5]*Americas Serviços Médicos, Rio de Janeiro, Brazil*
[6]*Hospital Samaritano Paulista, São Paulo, Brazil*
[7]*Américas Serviços Médicos, Rio de Janeiro, Brazil*

Introduction: Headache is one of the most common causes of visits to the Emergency Department (ED) worldwide, and migraine is the most common identifiable diagnosis in this context. Most guidelines consider analgesics, non-steroid anti-inflammatories, triptans, gepants, and lasmiditan as first-line treatment for the migraine attack. The use of opioids for migraine attacks is associated with CGRP overexpression, increased risk of migraine

chronification, and opioid addiction. Therefore, there is a consensus that opioids should be avoided for treating migraine attacks in most cases. Nevertheless, it is still common practice worldwide in the ED setting to prescribe opioids for migraine attacks.
Objective: To evaluate the impact of a virtual headache training program (VHTP) for physicians working at the ED of 17 Brazilian hospitals in reducing opioid prescriptions for patients with migraine and other headache disorders.
Method: We evaluated data from all visits to the ED that received a final diagnosis of migraine (CID G43) or unspecified headache (CID R51). The training consisted of an asynchronous virtual program of 90 minutes aimed at reviewing the clinical presentation of primary headaches, the alarm signs for secondary headaches, and an evidence-based treatment protocol for primary headaches. Data were collected for twelve months before and six months after the intervention. The primary endpoint was the reduction in the rate of opioid prescription.
Results: we evaluated 34.963 ED visits pre-VHTP intervention and 23.074 visits after, from 17 hospitals. The rate of opioid use per visit reduced from 17,06% (15,54%–18,68%) in the pre-VHTP period to 12.76% (9,80–15,94%). The reduction was progressive throughout the months, and the difference between the last month evaluated after intervention and the corresponding period in the previous year was 45,9% (from 18,14% to 9,80%). All the participant hospitals presented a reduction in opioids prescription after the intervention.
Conclusions: The Virtual Headache Training Program successfully improved headache treatment, reducing the opioid prescription in 17 hospitals by 45,9%.
Limitations: These are preliminary data from a short period of observation.
Disclosure of Interest: Marcio Nattan Portes Souza has received honorary for educational activities in the last 2 years from: Allergan-Abbvie, TEVA, Lilly, Libbs, Pfizer, Sanofi, and Lundbeck.

IHC23-PO-213

Evaluation of the efficacy and safety of intravenous levetiracetam in acute migraine attacks: a double-blind randomized clinical trial

Nooshin Yamani

Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of

Background: The genetic and pathophysiological relationship between migraine and epilepsy that has been proven in previous studies has led researchers to use anti-epileptic drugs in the treatment of migraine. The effects of Levetiracetam as an anti-epileptic drug in the prevention of migraine attacks have been studied before. However, sufficient studies have not been conducted to investigate the effect of this drug in improving acute migraine attacks, which are often very severe and debilitating based on patients' experiences.
Methods: The present study is a randomized clinical trial study (RCTs) that was conducted on 100 patients with migraine who referred to the neurology clinic of Valiasr Hospital in Zanjan in 2011. Eligible patients were randomly divided into two groups, one group received 1000 mg of Levetiracetam as a solution in 50 ml of normal saline through intravenous infusion for 15 minutes as a single dose, the second group received standard treatment in the form of receiving normal serum. Intravenous saline and ketorolac (30 mg) were administered. Then the two groups were compared in terms of headache severity, recurrence of headache attack 24 hours after treatment, time interval between the onset of the attack and drug administration, the time taken for complete recovery of headache and side effects (nausea, vomiting, blurred vision, photophobia and phonophobia). SPSS26 software was also used for data analysis.
Results: The results of the analysis of variance test for repeated measures showed that at all time points after the intervention, the mean severity of migraine headaches in the injectable Levetiracetam group was lower than that in the ketorolac group ($P < 0.001$). The mean time taken for complete recovery of headache in patients receiving injectable Levetiracetam was significantly shorter than patients receiving ketorolac (P-Value < 0.001). Also, the average time interval between the onset of attack and drug administration in patients receiving injectable Levetiracetam was significantly longer than in patients receiving ketorolac (P-Value $= 0.038$). The incidence of side effects of photophobia and phonophobia in patients treated with injectable Levetiracetam was significantly lower than that of patients treated with ketorolac (P-Value < 0.001). However, there was no statistically significant difference between the two groups in the recurrence of headache 24 hours after treatment ($P > 0.05$).
Disclosure of Interest: None Declared

IHC23-PO-214

Evaluation of the efficacy and safety of intravenous levetiracetam in acute migraine attacks: a double-blind randomized clinical trial

Nooshin Yamani

Zanjan University of Medical Sciences, Zanjan, Iran, Islamic Republic of

Background: The genetic and pathophysiological relationship between migraine and epilepsy that has been proven in previous studies has led researchers to use anti-epileptic drugs in the treatment of migraine. The effects of Levetiracetam as an anti-epileptic drug in the prevention of migraine attacks have been studied before. However, sufficient studies have not been conducted to investigate the effect of this drug in improving acute migraine attacks.
Methods: The present study is a randomized clinical trial study (RCTs) that was conducted on 100 patients with migraine who referred to the emerging ward of Valiasr Hospital in Zanjan in 2022. Eligible patients were randomly divided into two groups, one group received 1000 mg of Levetiracetam as a solution in 50 ml of normal saline through intravenous infusion for 15 minutes as a single dose, the second group received Intravenous saline and ketorolac (30 mg) as a standardgroup. Then two groups were compared in terms of headache severity, recurrence of headache attack 24 hours after treatment, time interval between the onset of the attack and drug administration, the time taken for complete recovery of headache and side effects (nausea, vomiting, blurred vision, photophobia and phonophobia). SPSS26 software was used for data analysis.
Results: The results of the analysis of variance test for repeated measures showed that at all time points after the intervention, the mean severity of migraine headaches in the injectable Levetiracetam group was lower than that in the ketorolac group ($P < 0.001$). The mean time taken for complete recovery of headache in patients receiving injectable Levetiracetam was significantly shorter than patients receiving ketorolac (P-Value < 0.001). Also, the average time interval between the onset of attack and drug administration in patients receiving injectable levetiracetam was significantly longer than in patients receiving ketorolac (P-Value $= 0.038$). The incidence of side effects of photophobia and phonophobia in patients treated with injectable Levetiracetam was significantly lower than that of patients treated with ketorolac (P-Value < 0.001). However, there was no statistically significant difference between the two groups in the recurrence of headache 24 hours after treatment ($P > 0.05$).
Disclosure of Interest: None Declared

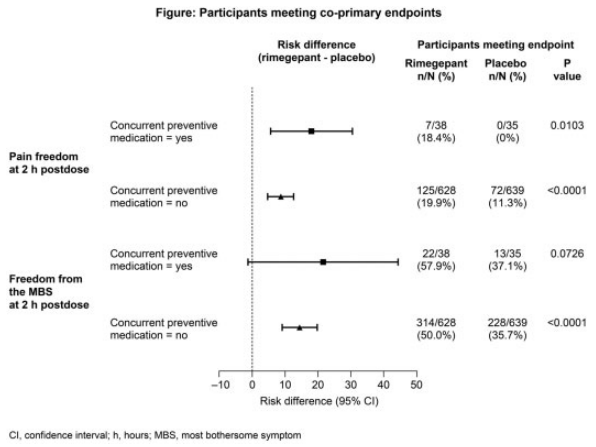
IHC23-PO-215

Efficacy of Rimegepant for the Acute Treatment of Migraine in Chinese and Korean Adults Receiving Concurrent Preventive Medication

Shengyuan Yu[1], Zhihong Lu[2], Yu Liu[3], Yunjun Zou[4] and Yanhui Sun[5]

[1]*Chinese PLA General Hospital, Beijing, China*
[2]*Pfizer (China) Research and Development Ltd, Shanghai, China*
[3]*Pfizer Inc, Beijing, China*
[4]*Pfizer Inc, Shanghai, China*
[5]*Pfizer CRDC, Shanghai, China*

Objective: To investigate the efficacy of rimegepant, an orally administered small molecule calcitonin gene-related peptide receptor antagonist, for the acute treatment of migraine in a subgroup of Chinese and Korean adults receiving concurrent preventive medication.
Methods: These subgroup analyses were from a phase 3, double-blind study conducted in China and Korea (NCT04574362) of single-dose rimegepant 75 mg or placebo for the acute treatment of moderate or severe migraine. Eligibility criteria included 2–8 moderate or severe migraine attacks per month. Co-primary endpoints at 2 hours (h) postdose were pain freedom and freedom from the most bothersome symptom (MBS), analyzed using Cochran-Mantel-Haenszel tests. Subgroup analyses were based on concurrent preventive medication use (yes/no).
Results: Of the 1340 participants analyzed (rimegepant $n = 666$, placebo $n = 674$), 81.2% were female, 80.1% were from China, 19.9% were from Korea, and 5.4% (rimegepant $n = 38$, placebo $n = 35$) were taking concurrent preventive medication. In the small subgroup taking preventive medication, response rates for pain freedom at 2 h were greater for rimegepant than placebo (18.4% vs 0%, respectively; $P = 0.0103$); for freedom from the MBS at 2 h the difference between rimegepant and placebo (57.9% vs 37.1%; $P = 0.0726$) showed similar trends but did not reach statistical significance (Figure). In the larger subgroup not taking preventive medication, response rates for pain freedom at 2 h (19.9% vs 11.3%; $P < 0.0001$) and freedom from the MBS at 2 h (50.0% vs 35.7%; $P < 0.0001$) were greater with rimegepant than placebo (Figure). Rimegepant was well tolerated.
Conclusion: Among participants who were taking concurrent preventive medication, more experienced pain freedom at 2 h after taking rimegepant 75 mg for the acute treatment of migraine compared with placebo. Rimegepant was effective compared with placebo in participants who were not taking concurrent preventive medication. The subgroup taking preventive medication was small so findings should be interpreted cautiously. Funded by Pfizer.



Disclosure of Interest: This study was sponsored by Biohaven which was acquired by Pfizer in October 2022. Medical writing support was provided by Kim Russell, PhD, of Engage Scientific Solutions and was funded by Pfizer. Shengyuan Yu declares no conflicts of interest. Zhihong Lu, Yu Liu, Yunjun Zou, and Yanhui Sun are employees of Pfizer and may hold stock/stock options.

IHC23-PO-216

Interim Results of a Long-Term Safety Study of 75 mg Rimegepant Administered as Needed in Acute Treatment of Migraine Among Chinese Adults

Shengyuan Yu[1], Liheng Ma[2], Qi Zhong[2] and Hua Zhu[2]

[1]*Chinese PLA General Hospital, Beijing, China*
[2]*Pfizer R&D, Shanghai, China*

Objective: This is a pre-planned interim analysis of a multicenter, open-label study (NCT05371652). The primary objective was to evaluate the long-term safety of rimegepant 75 mg orally disintegrating tablet (ODT) administered as needed (PRN) in Chinese patients to treat acute migraine. Secondary objectives were to evaluate the change of number of migraine days and severity of migraine attacks.
Methods: After 30-day observation period (OP), eligible patients with $\geq$6 qualified migraine days could take rimegepant PRN (maximum of 1 tablet per day), at the onset of mild to severe migraine attack. The long-term treatment phase of the study was 52 weeks. This interim analysis describes data from the first 12 weeks.
Results: Between May 19 2022 and Feb 17 2023, 276 patients were screened, 187 enrolled and 186 treated (female 151, 81.2%). A total of 137 (73.7%) patients had treatment emergent adverse events (TEAEs) and 16 (8.6%) patients had drug related TEAEs. Most abnormal laboratory parameters were of Grade 1–2. One patient (0.5%) had a serious TEAE (brain injury) that led to treatment and study discontinuation and death. This was considered to be unrelated to the drug (car accident as pedestrian). Mean reduction from the OP in the number of migraine days per 4 weeks was observed as early as the first 4 weeks (–1.8 days, [95% CI, –2.3 to –1.2]), and continued throughout the 12 weeks with an overall mean reduction of –2.6 (95% CI, –3.1 to –2.0) days for migraine attacks of any intensity and –2.8 (95% CI, –3.4 to –2.2) days for migraine attacks of moderate to severe pain intensity. Overall, 20.4% of patients had $\geq$50% reduction and 41.4% of patients had $\geq$30% reduction in migraine days per 4 weeks for migraine attacks of any intensity during the 12 weeks. For migraine attacks of moderate to severe pain intensity, 29.3% and 51.6% patients had $\geq$50% and $\geq$30% reductions, respectively.
Conclusions: Rimegepant 75mg ODT (PRN) showed a favorable safety profile and was well tolerated in Chinese patients during long-term treatment. Reduction in the number of monthly migraine days and severity of migraine attacks was observed as early as the first 4 weeks and continued throughout 12 weeks.
Disclosure of Interest: Shengyuan Yu declares no conflicts of interest. Liheng Ma, Qi Zhong, Hua Zhu are employees of Pfizer and may hold stock/stock options.

IHC23-PO-217

Prediction of Pharmacokinetics of Repeat Dosing of Dihydroergotamine Mesylate Via Precision Olfactory Delivery (INP104) for the Acute Treatment of Migraine

Sheena Aurora[1], Jennifer Robblee[2], Paul G. Mathew[3,2,5], Robert E. Vann[1], Sutapa Ray[1] and John Hoekman[1]

[1]*Impel Pharmaceuticals, Seattle, WA, USA*
[2]*Barrow Neurological Institute, Phoenix, AZ, USA*
[3]*Harvard Medical School, Boston, MA, USA*
[4]*Mass General Brigham Health, Foxborough, MA, USA*
[5]*Harvard Vanguard Medical Associates, Braintree, MA, USA*

Objective: INP104 (TRUDHESA®) is approved by the Food and Drug Administration for the acute treatment of migraine with or without aura in the United States (US) and has demonstrated clinical efficacy and safety. The approved dose of INP104 is 1.45 mg and can be repeated if needed a minimum of 1 hour after the first dose. No more than 2 doses within a 24-hour period or 3 doses within 7 days is recommended. The aim of this study was to predict the pharmacokinetics (PK) of repeat dosing of INP104, dihydroergotamine mesylate (DHE) delivered

Abstract number: IHC23-PO-217

Table

	Geometric Mean C_{max} (pg/mL)		Geometric Mean AUC (hr*pg/mL)	
	First Dose	Last Dose	First Dose	Last Dose
INP104 1.45 mg				
Two doses 1 hour apart	1097.6	1739.5	5597.2	11194.8[a]
One dose daily for 3 days	1097.6	1180.6	4638.7	5518.7[b]
One dose every 2 days for 5 days	1097.6	1127.3	5320.9	5596.0[c]
Three doses daily for 5 days	1097.6	1510.0	3173.9	5590.9[d]
IV DHE 1.0 mg				
Three doses daily for 5 days	12508.0	12912.1	4989.7	7493.2[d]

[a]AUC_{inf} for both doses together; [b]$AUC_{0–24h}$; [c]$AUC_{0–48h}$; [d]$AUC_{0–8h}$.

to the upper nasal space by Precision Olfactory Delivery (POD®), and compare it to the predicted PK of repeat dosing of intravenous (IV) DHE.

Methods: STOP 101 was a phase 1, open-label, randomized, crossover study in healthy participants that investigated the PK of a single dose of INP104 compared to IV DHE (Shrewsbury SB, et al 2019). A total of 34 participants received both IV DHE and INP104 and had complete plasma concentration vs time profiles that were included in this analysis. Repeat-dose PK was predicted using the Phoenix WinNonlin nonparametric superposition tool. Based on the approved US prescribing information, the following schedules were simulated for 1.45 mg INP104: two doses 1 hour apart, one dose daily for 3 days, one dose every 2 days for 5 days. Based on the Raskin protocol, 1.45 mg INP104 and 1.0 mg IV DHE (bolus) for three doses daily for 5 days were also simulated. Individual profiles for plasma concentration vs time were simulated. Non-compartmental methods were used to derive secondary exposure parameters including maximum plasma concentration (C_{max}) and area under the curve over one dosing interval (AUC_{tau}). Descriptive statistics were used to summarize derived exposure parameters.

Results: Exposure parameters are detailed in the **Table**. There was limited accumulation of DHE exposure with any of the repeat dosing regimens tested. Simulating two doses of INP104 1 hour apart resulted in peak DHE exposure that was 59% higher on average compared to a single dose. Peak DHE exposure was 38% higher and total DHE exposure was 77% higher on average compared with a single dose when simulating three INP104 doses daily for 5 days based on the Raskin protocol. Steady state was reached within the first 2 days of INP104 dosing. Simulations of three IV DHE doses daily for 5 days also showed limited accumulation; peak DHE exposure was 3% higher and total DHE exposure was 50% higher on average compared with a single dose. Comparing simulations of INP104 and IV DHE administered as three doses daily for 5 days, total exposures were similar between INP104 and IV DHE dosing regimens across the 5-day dosing period; however, peak exposures were approximately 10x lower from INP104 dosing.

Conclusions: Simulations of repeat dosing of INP104 indicate that giving two doses 1 hour apart will produce higher exposures compared with a single dose, but there is limited accumulation with any other repeat dosing regimen. For a three times daily dosing schedule based on the Raskin protocol, total DHE exposure from INP104 dosing is predicted to be generally similar to the established IV dosing regimen. However, peak concentrations from INP104 dosing were substantially lower than IV administration, suggesting that INP104 might offer the potential to minimize systemic side effects associated with high peak plasma concentrations. The data provide valuable information on INP104 dosing protocols that can help guide physicians in utilizing INP104 in the clinic. Clinical relevance remains to be determined.

Disclosure of Interest: Jennifer Robblee has received grant support from the Barrow Neurological Foundation and investigator support from AbbVie and Eli Lilly. She participated in a paid advisory board for AbbVie and is a speaker for Impel Pharmaceuticals. She also has a paid editorial relationship with MedLink® Neurology and Neurodiem™. A family member has partial ownership of the Scottsdale Providence Recovery Center. Paul G. Mathew served as an uncompensated consultant and not in his capacity as a member of the HMS/BWH Faculty. He has served as a consultant for AbbVie/Allergan, Amgen, Biohaven, ElectroCore, Eli Lilly, Impel Pharmaceuticals, Revance, Satsuma, Supernus, Takeda, Teva, and Theranica. Sheena K. Aurora, Robert E. Vann, Sutapa Ray, and John Hoekman are full-time employees of Impel Pharmaceuticals and are stockholders in Impel Pharmaceuticals.

IHC23-PO-218

The efficacy and safety of metoclopramide in relieving acute migraine attacks compared with other anti-migraine drugs: a systematic review and network meta-analysis of randomized controlled trials

Hanaa Abdelmonem[1], Hebatallah Mohamed Abdelhay[2], Gehad Taha Abdelwadoud[3], Amira Naser Mohammed Alhosini[1], Ahmed Eissa Ahmed[1], Samaher Walied Mohamed[4], Nada Mostafa Al-dardery[3], Mohamed Abd-ElGawad[1] and Mohamed Abdelmonem Kamel[1]

[1]*MBBCh, Faculty of Medicine Fayoum University, Fayoum, Egypt*
[2]*Oncology and Radiotherapy Resident at Fayoum University Hospital, Fayoum, Egypt*
[3]*Faculty of medicine, Fayoum University, Fayoum, Egypt*
[4]*Family Medicine Resident at Fayoum University Hospital, Fayoum, Egypt*

Objective: Many drugs are prescribed in relieving acute migraine attacks, we aim to compare metoclopramide with other antimigraine drugs.

Methods: We searched online databases like PubMed, Cochrane Library, Scopus, and Web of Science until May 2022 for RCTs that compared metoclopramide alone with placebo or active drugs. The main outcomes were the mean change in headache score and complete headache relief. The secondary outcomes were the need for rescue medications, side effects, nausea, and recurrence rates. We qualitatively reviewed the outcomes. Then, we performed network meta-analyses (NMAs) when it was possible. which were done by the Frequentist method using the Meta-Insight online software.

Results: Sixteen studies were included with a total of 1934 patients: 826 received metoclopramide, 302 received placebo, and 806 received other active drugs. In NMA of headache change after 30 minutes or one hour, metoclopramide effect came after granisetron, ketorolac, chlorpromazine, and Dexketoprofen trometamol. Only granisetron's effect was significantly higher than metoclopramide's effect, which was only significantly higher than placebo and sumatriptan. In headache-free symptoms, only prochlorperazine was non-significantly higher than metoclopramide, which was higher than other medications and showed significant higher effects only with valproate and placebo. In rescue medication, metoclopramide's effect was only non-significantly lower than that of prochlorperazine and chlorpromazine, while its effect was higher than that of other drugs and showed higher significant effects only for placebo and valproate. In terms of recurrence rate, studies showed no significant difference between metoclopramide and other drugs. Metoclopramide significantly decreased nausea than placebo. Regarding side effects, metoclopramide showed a lower incidence of mild side effects than pethidine and chlorpromazine and a higher incidence of mild side effects than placebo, dexamethasone, and ketorolac. The reported extrapyramidal symptoms with metoclopramide were dystonia or akathisia.

Conclusion: A dose of 10 mg of IV metoclopramide is effective in relieving migraine attacks with minimal side effects. Compared to other active drugs, it only showed a significant lower effect compared with granisetron in headache change, while it showed significant higher effects only with valproate and placebo in both rescue medication need and headache free symptoms. Also, it significantly decreased headache scores more than placebo and sumatriptan. However, more studies are needed to support our results.

Figure (1): Network meta-analysis of headache changes from 30 minutes to one hour.

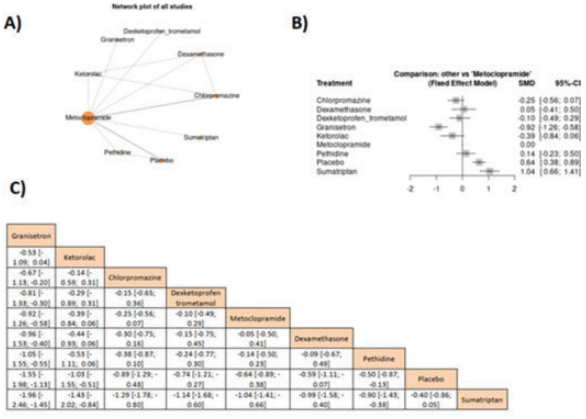


Figure (2): Network meta-analysis of headache free symptoms from 45 minutes to two hours.

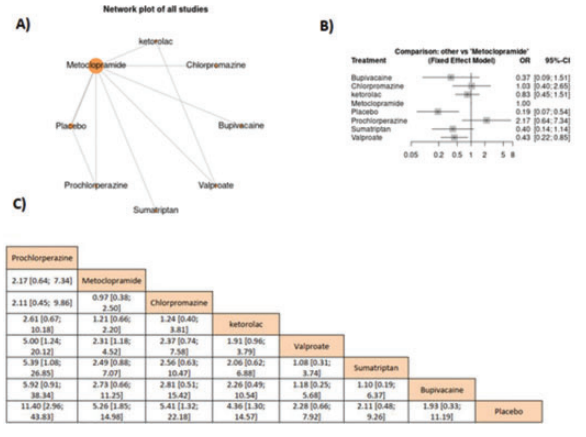
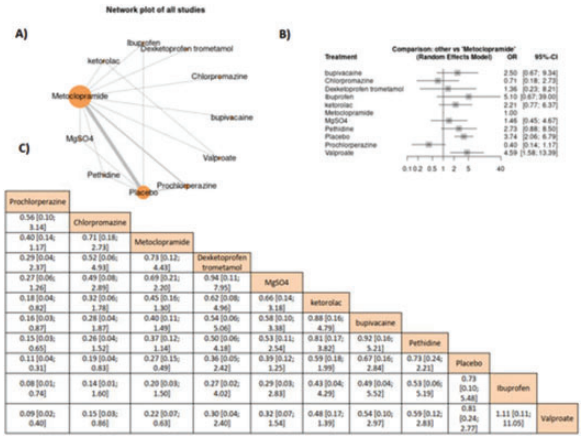


Figure (3): Network meta-analysis of rescue medication need from 30 minutes to one hour.



Disclosure of Interest: None Declared

Migraine preventive therapy

IHC23-PO-219

Early Effect of CGRP Monoclonal Antibodies in Migraine with Medication Overuse: A Single-Center Retrospective Study

Yasuo Ito, Takashi Mitsufuji, Mariko Okada, Shugo Fujita, Ryu Yokoyama, Hitoshi Kawasaki and Toshimasa Yamamoto

Department of Neurology, Saitama Medical University, Saitama, Japan

Objective: Calcitonin gene-related peptide (CGRP) – (receptor) monoclonal antibody (mAb) have been reported to reduce the frequency of medication overuse (MO) in patients with migraine. The purpose of this study was to determine whether CGRP-mAb are early effective for medication overuse headache (MOH) in Japan.
Methods: We retrospectively reviewed all 34 patients with MOH who received preventive treatment with CGRP-mAb from June 2021 to October 2022. The International Classification of Headache Disorders, 3rd Edition (ICHD-3) was used to diagnose MOH. This study was conducted at single center (Department of Neurology, Saitama Medical University). Patients were recruited from this specialized headache outpatient centers.
Results: 69 migraine patients were newly introduced CGRP-mAb, and MOH patients were 34 (49.3%), and average age was 44 ± 15.5 years old (mean ± SD). The study population included 24 women (70.6%). The types of CGRP-mAb were galcanezumab (GAL) in 16 cases (47.0%), fremanezumab (FRE) in 10 cases (29.4%), and erenumab (ERE) in 8 cases (23.5%). The mean disease duration was 19.6 ± 13.1 years. The types of migraine diagnosis were chronic migraine (CM) in 28 cases (82.4%) and migraine with aura (MWA) in 11 cases (32.4%). The mean number of headache days (MHD) in the month before administration of the CGRP-mAb were 22 ± 7.7 days, and one month after administration they were 16.9 ± 9.1 days. MHD change were –5.7 days (22.7%) and significantly improvement ($p < 0.05$).
Conclusion: CGRP-mAb have been suggested as a preventive medicine for MOH patients. It is necessary to investigate the long-term efficacy of CGRP-mAb for MOH in the near future.
Disclosure of Interest: Declaration of conflicting interests Yasuo Ito received personal consultancy fees from Daiichi Sankyo Company, Limited, Otsuka Pharmaceutical Co., Ltd during the conduct of the present study. Toshimasa Yamamoto received personal consultancy fees from Daiichi Sankyo Company, Limited, Eli Lilly Japan K.K., Otsuka Pharmaceutical Co., Ltd and Amgen Astellas BioPharma K.K., during the conduct of the present study. The other authors declare no conflicts of interest in association with the present study.

IHC23-PO-220

Efficacy and safety of Fremanezumab in the preventive treatment of high-frequency episodic and chronic migraine: Russian real-life study

Larisa Dobrynina, Maksim Afanasev, Anastasia Belopasova, Maria Gubanova and Ekaterina Baydina

Research Center of Neurology, Moscow, Russian Federation

Objective: To assess the effectiveness and safety of Fremanezumab, a monoclonal antibody to CGRP, in patients with high-frequency episodic migraine (HFEM) and chronic migraine (CM) in real-life study.
Material and Methods: In total, sixty patients (mean age 35.5 ± 8.96 years, women 85%) with HFEM and CM with and without aura regardless the previous treatment were enrolled in this study. All patients received a single subcutaneous injection of Fremanezumab, 675 mg, with a following assessment in 3 months. Changes in the number of days with headaches per month as well as oits intensity, impact on disability (HIT-6 scale, MIDAS), anxiety and depression (HADS) were taken into account.
Results: Globally, 76.7% of patients noted more than double decrease in the number of days with headache per month by the end of the third month after Fremanezumab injection, the headache intensity decreased from 8 ± 1.2 to 5 ± 2 ($p = 0.00000$). 15% of patients have not demonstrated sufficient improvement (reduction in number of days with headache less than on 30%) to treatment with

Fremanezumab. Patients showed a significant improvement in the quality of life, as well as a decrease in social disadaptation and disability, which is reflected in a decrease in the scores scored on the MIDAS scales – from 69 [45,129] to 35 [20, 80] points ($p = 0.00000$) and HIT-6 from 65 ± 6 to 57 ± 8 points ($p = 0.00000$). The manifestation of comorbid states significantly decreased (according to the results of HADS) compared to the baseline level: anxiety decreased from 7 ± 4 to 3 ± 3 points ($p = 0.00000$) and depression — from 6 ± 4 to 3 ± 3 points ($p = 0.00000$). Only 3 out of 60 patients (5%) reported few adverse events, such as redness and itching localized around the site of injection. No patient discontinued treatment due to adverse events.

Conclusion: This real-world study has demonstrated higher efficacy and safety of Fremanezumab in treatment of EM and CM comparing with results reported in randomized clinical trials. A single administration of Fremanezumab, 675 mg, provided effective prevention of migraine, a decrease in comorbid anxiety and depression, and an improvement in the quality of life during 3 months of follow-up.

Disclosure of Interest: None Declared

IHC23-PO-221

Oral synthetic medications vs monoclonal antibodies targeting the calcitonin gene-related peptide for the treatment of migraine. A systematic review and indirect comparison.

Theodoros Mavridis[1,2], Savvas Christophilos[2], Christina Deligianni[3], Anna Andreou[4,5] and Dimos D. Mitsikostas[2]

[1]*Connolly Hospital Blanchardstown – RCSI, Dublin, Ireland*
[2]*1st Department of Neurology, Eginition Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece*
[3]*Department of Neurology, Athens Naval Hospital, Athens, Greece*
[4]*Headache Centre, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom*
[5]*Headache Research-Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*

Background: Inhibitors of the calcitonin gene-related peptide (CGRP) pathway, in the form of orally administered synthetic small molecules, so-called gepants, or in the form of monoclonal antibodies (anti-CGRP mAbs), have shown positive results in the prophylaxis of episodic (EM) and chronic migraine (CM) and are currently used. However, their comparative appropriateness has not been examined. This systematic review aimed to indirectly compare gepants and anti-CGRP mAbs through analysis of the number needed to treat (NNT), the number needed to harm (NNH), and the likelihood of help or harm (LHH).

Methods: We performed a PRISMA search on PubMedand Clinical trials.gov for phase-3 placebo-controlled studies testing the gepants, atogepant and rimegepant, and the anti-CGRP mAbs eptinezumab, erenumab, fremanezumab, and galcanezumab in the prophylaxis of EM and CM, from 01–06-2000 to 01–07-2022. The Cochrane Revised Risk of Bias tool was used to assess the risk of bias. We considered the 50% responder rate (the proportion of participants with $\geq$50% monthly migraine days reduction from baseline) a positive outcome and the proportion of participants who discontinued treatment because of an adverse event (DEA) as a negative outcome. The number needed to treat (NNT), the number needed to harm (NNH), and the likelihood to help or harm (LHH) were calculated as 1/(absolute risk difference) and as NNH/NNT for every single study, respectively.

Results: We included six studies with gepants and three with anti-CGRP mAbs. All studies had a low risk of bias and included participants with EM, but in one study, rimegepant was tested in participants with either EM or CM. In addition, historical results of a previous identical analysis for anti-CGRP mAbs, including phase-3 trials for EM published up to 31–5-2020, were included in the analysis (12 studies), along with six trials with topiramate, one trial with propranolol and one pooled analysis data with onabotulinumtoxinA. All treatments tested were more likely to be beneficial than harmful (likelihood to help versus harm > 1), but not topiramate 200 mg daily to prevent EM. Both gepants and anti-CGRP mAbs in all tested doses had higher LHH values than propranolol or topiramate for EM and onabotulinumtoxinA or topiramate for CM prophylaxis. Among all treatments, fremanezumab had the highest LHH ratio in EM and galcanezumab in CM.

Conclusion: CGRP pathway inhibitors performed favorably vs. traditional treatments for migraine prophylaxis. In the absence of direct treatment comparisons, these results, together with patients' medical history and preferences, may help decision-making in practice.

Disclosure of Interest: None Declared

IHC23-PO-222

Predictors of galcanezumab response in a real-world study of Korean patients with migraine

Seung Ae Kim[1], Mi Ji Lee[1] and Hyemin Jang[2]

[1]*Seoul National University, Seoul, Korea, Republic of*
[2]*Samsung Medical Center, Seoul, Korea, Republic of*

Predictors of the efficacy of monoclonal antibodies targeting calcitonin gene-related peptide (CGRP) or its receptor (anti-CGRP(-R) mAb) have been rarely investigated in Asians. We aimed to assess factors associated with galcanezumab response in a real-world study of Korean patients with migraine. We prospectively recruited and followed up patients with migraine who received monthly galcanezumab treatment in a single university hospital from June 2020 to October 2021. We defined the treatment response with $\geq$ 50% reduction in moderate/severe headache days in the 3rd month of treatment compared to baseline. Responders and non-responders were compared in terms of demographics, disease characteristics and severity, and previous response to migraine prophylactic treatments. Potential predictors of anti-CGRP(-R) mAb response were tested by using the univariable and multivariable logistic regression analyses. Among 104 patients (81.7% female; mean age 42.0 $\pm$ 13.02; 76.9% chronic migraine; and 45.5% medication overuse headache) included, 58 (55.7%) were responders. Non-responders had more chronic migraine, medication overuse headache, monthly headache days, days with acute medication, and daily persistent headaches. The multivariable logistic analysis showed chronic migraine (OR 0.05 [95% CI 0.00–0.82], $p = 0.036$) and the number of previously failed preventive medication classes (OR 0.55 [95% CI 0.33–0.92], $p = 0.024$] were independently associated with treatment response. Chronic migraine and multiple failures from preventive medication are associated with poor galcanezumab response. Further studies are needed to investigate if earlier treatment before disease chronification or multiple failures may lead to a greater therapeutic gain from anti-CGRP(-R) mAb treatment.

IHC23-PO-223

The Effectiveness of Agomelatine on the Severity and Frequency of Attacks in Migraine Without Aura; a Randomized Controlled Trial.

Mahdi Shafiee Sabet

Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of

Objective: Migraine is a common headache disorder that affects the general health of more than one billion people worldwide and reduces their quality of life. Although the etiology of migraine is not fully known, and many patients are underdiagnosed and untreated, research efforts have greatly expanded, necessitating the administration of preventive medications to prevent acute attacks and headaches caused by overuse medication. Several guidelines on acute and maintenance treatment of migraine headaches have been developed and have recommended different medications with variable effectiveness. The documents have noted treatments are not effective enough or are not tolerated, in some patients and it seems that there is still no general consensus on the "selective" medication. Therefore, considering the usefulness of agomelatine, which is a class of melatonin antagonist drugs, in other diseases such as depression, as well as the results of case-control studies and the need for clinical trials, this study was conducted to determine the effectiveness of agomelatine on the severity and frequency of migraine attacks without aura, number of headache days per month, and also MIDAS (Migraine Disability Assessment).

Methods: The study was conducted as a parallel randomized controlled trial with two groups of intervention and control. At first, 400 patients were evaluated and eligible persons were subjected to the study successively after filling out informed consent, and were randomly assigned to the intervention group treated with agomlatine25 mg per day or in the control group receiving placebo with the same shape, color and size. Only major researcher (M Sh S), was aware of the type of medications. The prescribing physician and the data collector and analyzer were not aware of the allocation of the patient group, in other words, study was designed triple blinded. At first, the severity of headaches, frequency of attacks, number of headache days per month and MIDAS of each patient were measured by interview and available tools. Three months later post-test interviews were conducted with 49 patients in each group. Data were analyzed using SPSS software and descriptive and inferential statistics.

Results: Demographic data of the two groups were not significantly different ($p > 0.05$). There was no significant difference ($t = -0.39$, $df = 111$, $p = 0.695$) in the mean number of migraine attacks per month between the control (6.05 $\pm$ 1.4) and the intervention group (6.16 $\pm$ 1.62) before the intervention, and also regarding the number of headache days per month, there was no significant difference ($t = -1.81$, $df = 111$, $p = 0.072$) between the control (10.97 $\pm$ 2.86) and the intervention group (12.07 $\pm$ 3.58).

At the end of intervention, independent t-test showed a significant difference between the two groups, regarding the number of attacks ($t = 2.657$, $df = 97$, $p = 0.009$), and the number of headache days ($t = 2.27$, $df = 97$, $p = 0.025$), in the previous month.

Independent t-test showed a significant difference between the two groups in terms of changing the severity of headaches ($t = 4.41$, $df = 96$, $p < 0.001$) and MIDAS ($t = 5.56$, $df = 96$, $p < 0.001$), after the intervention.

Paired T-test for the intervention group, before and after the intervention, showed a significant difference in all four variables including frequency of attacks ($t = 8.42$, $df = 48$, $p < 0.001$), number of headache days per month ($t = 8.17$, $df = 48$, $p < 0.001$), the severity of headaches ($t = 8.26$,

df = 48, $p < 0.001$), as well as MIDAS ($t = 8.48$, df = 48, $p < 0.001$).

Conclusion: Agomelatine can be used as a preventive treatment in migraine without aura. It is suggested that the effectiveness of Agomelatonin on migraine attacks without aura be compared with other drugs, as well as on migraine attacks with aura.

IHC23-PO-224

The short-term effects of CGRP monoclonal antibodies on bone turnover: a prospective cohort study

Jason Ray[1,2,3], Shoshana Sztal-Mazer[2], Josephine Baker[2], Manjit Matharu[4] and Elspeth Hutton[1,2]

[1]*Monash University, Melbourne, Australia*
[2]*Alfred Health, Melbourne, Australia*
[3]*Austin Health, Melbourne, Australia*
[4]*University College London, London, United Kingdom*

Objective: Calcitonin gene-related peptide monoclonal antibodies (CGRP mAb) are an effective treatment of migraine however may have possible off-target effects. Pre-clinical studies implicate CGRP in several aspects of bone turnover and homeostasis. The aim of this study is to assess the impact of CGRP inhibition on markers of bone turnover.

Methods: Between June 2021 and July 2022, a multicentre prospective cohort study was undertaken with eligible patients undergoing paired testing of the validated bone turnover markers procollagen type I N-terminal propeptide (P1NP) and serum C-terminal telopeptide of type I collagen (CTX) prior to and at least three months following administration of a CGRP mAb.

Results: A total of 45 patients with a mean age of 41.8 (SD 11.9) were included in the final analysis, all of whom received a ligand-targeting CGRP mAb. Administration of a CGRP mAb was associated with a statistically significant increase in P1NP from 44.5 microg/L to 51.5 microg/L ($p = 0.004$), but no significant change in CTX.

Conclusion: In otherwise homeostatic conditions, short-term administration of a CGRP mAb is associated with increased P1NP, a bone formation marker but not with increased CTX, a bone resorption marker. Further study is required to validate these findings over longer time periods, in a larger cohort, and in pre-existing states of increased calcium stress and bone-turnover.

Disclosure of Interest: Dr. Ray has received funding from the Pharmaceutical Society of Australia and the Limbic supported by unrestricted educational grants from Viatris and Novartis respectively. Prof. Matharu serves on the advisory board for Allergan, Novartis, Eli Lilly, Autonomic Technologies Inc and TEVA and has received payment for the development of educational presentations from Allergan, electroCore, Eli Lilly, Novartis and TEVA. Dr. Hutton has served on advisory boards for Sanofi-Genzyme, Novartis, Teva, Eli Lilly, Allergan, Lundbeck, been involved in clinical trials sponsored by Novartis, Teva, Xalud, Cerecin, and has received payment for educational presentations from Allergan, Teva, Eli Lilly and Novartis.

IHC23-PO-225

The short-term effects of CGRP monoclonal antibodies on bone turnover: a prospective cohort study

Jason Ray[1,2,3], Shoshana Sztal-Mazer[2], Josephine Baker[2], Manjit Matharu[4] and Elspeth Hutton[1,2]

[1]*Monash University, Melbourne, Australia*
[2]*Alfred Health, Melbourne, Australia*
[3]*Austin Health, Melbourne, Australia*
[4]*University College London, London, United Kingdom*

Objective: Calcitonin gene-related peptide monoclonal antibodies (CGRP mAb) are an effective treatment of migraine however may have possible off-target effects. Pre-clinical studies implicate CGRP in several aspects of bone turnover and homeostasis. The aim of this study is to assess the impact of CGRP inhibition on markers of bone turnover.

Methods: Between June 2021 and July 2022, a multicentre prospective cohort study was undertaken with eligible patients undergoing paired testing of the validated bone turnover markers procollagen type I N-terminal propeptide (P1NP) and serum C-terminal telopeptide of type I collagen (CTX) prior to and at least three months following administration of a CGRP mAb.

Results: A total of 45 patients with a mean age of 41.8 (SD 11.9) were included in the final analysis, all of whom received a ligand-targeting CGRP mAb. Administration of a CGRP mAb was associated with a statistically significant increase in P1NP from 44.5 microg/L to 51.5 microg/L ($p = 0.004$), but no significant change in CTX.

Conclusion: In otherwise homeostatic conditions, short-term administration of a CGRP mAb is associated with increased P1NP, a bone formation marker but not with increased CTX, a bone resorption marker. Further study is required to validate these findings over longer time periods, in a larger cohort, and in pre-existing states of increased calcium stress and bone-turnover.

Disclosure of Interest: Dr. Ray has received funding from the Pharmaceutical Society of Australia and the Limbic supported by unrestricted educational grants

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IHC23-PO-226

Effect of Erenumab on Absenteeism and Presenteeism in Patients with Episodic and Chronic Migraine in Actual Clinical Practice in Japan: A Retrospective Observational Study

Yasutaka Sadamoto

Takanoko Hospital, Matsuyama, Japan

Background and Purpose: Migraine is a chronic neurological disorder that recurs paroxysmally and is highly prevalent among people 11–49 years of age. Thus, it has a significant impact on the overall productivity of society. In Japan, migraines were estimated to cause an annual economic loss of approximately 21.3 billion US$/year in Japan (2021), drawing attention to the effects of migraine on absenteeism and presenteeism.

We conducted a retrospective study to investigate the effects of erenumab treatment on absenteeism and presenteeism in patients with episodic migraine (EM) and chronic migraine (CM) in actual clinical practice in Japan. We examined changes in the Migraine Disability Assessment Scale (MIDAS) total score (items 1 and 2) from three months before treatment to the first six months of treatment with erenumab.

Patients and Methods: Of the 167 patients at our hospital who received at least one dose of erenumab 70 mg subcutaneous injection from August 12, 2021, to December 31, 2022, 75 patients (53 EM, 22 CM) who continued to visit our hospital at least six times within 4–5 weeks and whose headache diary and MIDAS were confirmed from 3 months prior to 6 months after treatment initiation were included in this retrospective observational study. The primary endpoint was the MIDAS score. The secondary endpoints were mean changes from baseline of monthly migraine day (MMD).

Results: MIDAS showed significant improvement in both the EM and CM groups at the first and second evaluation compared with baseline ($p < 0.001$) (Fig.1 Left). Absenteeism was evaluated using Item 1 of the MIDAS (absenteeism score) and presenteeism using Item 2 (presenteeism score). The presenteeism score decreased significantly from 11.25 (standard deviation (SD), 10.48) and 30.55 (SD, 20.37) days in the EM and CM groups at baseline to 2.17 (SD, 3.49) and 7.86 (SD, 9.17) days at the first evaluation, and 1.68 (SD, 2.81) and 4.23 (SD, 5.39) days at the second evaluation, respectively ($p < 0.001$) (Fig.1 Right).

The mean change from baseline to the secondary endpoint of MMD was significantly lower in both the EM and CM groups at the first month of treatment than that at baseline (EM, $p < 0.01$) (CM, $p = 0.01$).

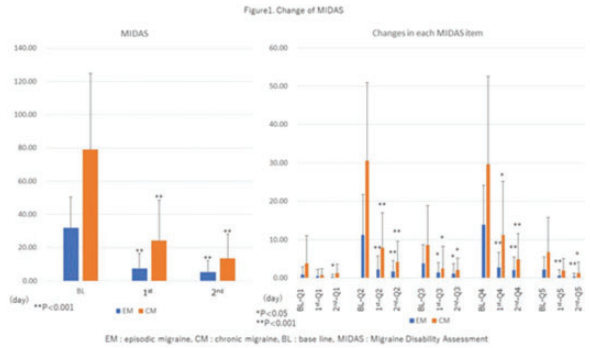
No serious adverse events (AEs) were observed during erenumab treatment.

Discussion: To assess patient perception of treatment efficacy, assessment measures of patient-reported migraine impact are essential. The MIDAS focuses on a single indicator (disability) and evaluates its impact as a static measure by scoring the number of days of lost work/study, housework, family, and social activities limited by headaches in the past three months in response to five questions. The MIDAS is a direct and intuitive way to evaluate absenteeism and presenteeism.

It has been demonstrated that presenteeism while working with an illness leads to more lost working time than absenteeism. In the present study, erenumab consistently and significantly improved presenteeism in both the EM and CM groups. Patients with migraines are often of working age, and erenumab should be more widely and continuously used in patients who need it to prevent economic losses at both an individual and societal level.

Among the AEs, constipation was observed in 22.67% of the patients; pruritus (12.00%) and redness (1.33%) were observed as injection site reactions. Constipation was mild in all cases and was observed after the first administration. All cases of constipation were relieved after 1 or 2 months and a temporary increase in laxative dose. Injection site reactions were often mildly pruritic and occurred for one or two days after the second dose but resolved with the application of external agents in all cases. No patients discontinued erenumab treatment due to AEs, including constipation.

Conclusion: Erenumab was found to be effective for improving presenteeism in patients with migraines in actual clinical practice in Japan. No serious AEs were observed during this study.



IHC23-PO-227

Preventive effect of greater occipital nerve block on patients with episodic migraine: A randomized double-blind placebo-controlled clinical trial

Ghaemeh Nabaei

Shariati Hospital, Tehran, Iran, Islamic Republic of

Objective: Greater occipital nerve (GON) block with local anesthetics and steroids has been used to treat several types of headaches. Since the data regarding the efficacy of GON block in episodic migraines are rare, we aimed to examine the efficacy of this method in the prophylaxis of episodic migraines without aura and compare different injectable drug regimens.
Methods: In a randomized, double-blind placebo-controlled trial, adult patients suffering from episodic migraines without aura were randomized to one of the following: triamcinolone, lidocaine, triamcinolone plus lidocaine, and saline. Patients were assessed at baseline, one week, two weeks, and four weeks after the injection for severity and duration of headaches and side effects.
Results: Fifty-five patients completed the study. Repeated measures ANOVA indicated that the severity and duration decreased significantly after the greater occipital block ($P < 0.001$, P ¼ 0.001 respectively) in all four groups. However, there was no difference between groups at any study time points ($P > 0.05$). In paired sample T-test, only groups 2 and 3 with lidocaine as a part of the injection showed a significant decrease in frequency compared to the baseline (P ¼ 0.002, P ¼ 0.019). Three patients reported side effects with a possible association with triamcinolone.
Conclusion: Greater occipital block with a local anesthetic significantly decreases the number of attacks in episodic migraine, whereas no injection was superior to the placebo in regards to the duration and severity of the headaches.
Disclosure of Interest: None Declared

IHC23-PO-228

Comparison of responders and non-responders to CGRPmAb in patients with chronic migraine in Japan: a single-center retrospective observational study

Keiko Ihara[1], Seiya Ohtani[1,2], Narumi Watanabe[1], Nobuyuki Takahashi[1], Naoki Miyazaki[3], Kei Ishizuchi[1], Satoko Hori[2], Ryo Takemura[3], Jin Nakahara[1] and Tsubasa Takizawa[1]

[1]*Department of Neurology, Keio University School of Medicine, Tokyo, Japan*
[2]*Division of Drug Informatics, Keio University Faculty of Pharmacy, Tokyo, Japan*
[3]*Biostatistics Unit, Clinical and Translational Research Center, Keio University Hospital, Tokyo, Japan*

Objective: Anti-calcitonin gene-related peptide monoclonal antibodies (CGRPmAbs) have dramatically changed the preventive treatment options for patients with migraine. However, they are more expensive than traditional prophylactic drugs and cause minor adverse effects such as injection site reaction. It is essential to optimize the use of CGRPmAb by acknowledging the difference between responders and non-responders. There have been several reports on responder analysis but only a few reports have been published from Asian countries. Since Asian patients with migraine have unique characteristics, we aimed to investigate the clinical characteristics of patients with chronic migraine in Japan who responded well to CGRPmAb based on real-world data.
Methods: We retrospectively analysed patients with chronic migraine who visited Keio University Hospital, Tokyo, Japan, between August 2021 and August 2022, and started on one of three CGRPmAbs (erenumab, galcanezumab, and fremanezumab) and continued it for more than 3 months. The patients' demographic data and basic migraine characteristics, such as pain quality, monthly migraine days (MMD), monthly headache days, and the number of prior treatment failures were reviewed from the charts. We defined responders as patients whose MMDs decreased by more than 50% after 3 months of treatment and other patients as non-responders. We compared the demographic data and baseline migraine characteristics between the two groups.
Results: In total, 43 patients were considered eligible for the responder analysis (galcanezumab: 28 (65%), fremanezumab: 9 (21%), and erenumab: 6 (14%)). After 3 months of treatment, 20 (43%) patients achieved $\geq$50% reduction in MMDs. Comparisons between $\geq$50% responders and non-responders revealed that the number of prior treatment failures was significantly lower ($p = 0.0383$), and the

duration of headache was significantly shorter ($p = 0.0477$), in responders than in non-responders.

Conclusion: Patients with chronic migraine who responded well to CGRPmAbs had experienced fewer prior treatment failures and shorter-duration headaches.

Disclosure of Interest: TT is a consultant/advisor and/or served as advisory board for Eli Lilly, Otsuka, Amgen, Pfizer, and Teijin. TT received speaker honoraria from Eli Lilly, Daiichi Sankyo, Otsuka, Amgen, Kowa, Kyowa Kirin, Eisai, UCB Japan, Takeda, and Santen Pharmaceutical, and research funding from Eli Lilly and Tsumura outside the submitted work. JN received honoraria and research scholarships from Amgen and Daiichi Sankyo.

IHC23-PO-229

Eptinezumab demonstrated efficacy regardless of prior preventive migraine treatment failure: Post hoc DELIVER analyses

Patricia Pozo-Rosich[1,2], Messoud Ashina[3,4], Stewart J. Tepper[5], Sidsel Jensen[6], Line Pickering Boserup[6], Mette Krog Josiassen[6] and Bjorn Sperling[6]

[1]*Headache Unit and Research Group, Vall d'Hebron University Hospital and Research Institute, Barcelona, Spain*
[2]*Universitat Autonoma de Barcelona, Barcelona, Spain*
[3]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital– Rigshospitalet, Copenhagen, Denmark*
[4]*Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*
[5]*Dartmouth Hitchcock Medical Center, Lebanon, USA*
[6]*Lundbeck A/S, Copenhagen, Denmark*

Objective: This post hoc analysis evaluated the efficacy of eptinezumab vs placebo across 24 weeks of treatment in the placebo-controlled period of the DELIVER study in subgroups defined by prior treatment failure.

Methods: DELIVER (NCT04418765) randomized adults with migraine to eptinezumab 100 mg, 300 mg, or placebo intravenous infusion every 12 weeks. Eligible patients needed documented evidence of 2–4 prior preventive treatment failures within the past 10 years. This post hoc analysis summarized the changes from baseline in monthly migraine days (MMDs) and percent of patients with ≥50% reduction from baseline in MMDs (≥50% migraine responder rate [MRR]) in subgroups of patients with prior treatment failure on topiramate, beta blockers (metoprolol, propranolol), amitriptyline, and/or flunarizine; subgroups are not mutually exclusive.

Results: The full analysis set included 890 patients: 633 previously failed topiramate, 538 failed beta blockers, 508 failed amitriptyline, and 333 failed flunarizine; within each subgroup, most patients had 2 prior treatment failures (51–56%). Across Weeks 1–12 in all subgroups, patients treated with eptinezumab experienced greater reductions from baseline in MMDs than those receiving placebo, with larger reductions observed over Weeks 13–24 (Table). Similarly, ≥50% MRRs were higher with eptinezumab than with placebo and increased following a second infusion.

Conclusions: Eptinezumab demonstrated greater reductions in MMDs compared with placebo across all subgroups of prior preventive treatment failure, with evidence to suggest that a second dose provides additional benefit.

Table. Change from baseline in monthly migraine days by prior failure subgroup. Values are LS-means (standard error).

	Eptinezumab 100 mg	Eptinezumab 300 mg	Placebo
Topiramate			
Weeks 1–12	−4.8 (0.44)	−5.5 (0.43)	−2.3 (0.43)
Weeks 13–24	−5.4 (0.47)	−6.2 (0.45)	−2.4 (0.46)
Beta blockers			
Weeks 1–12	−4.5 (0.55)	−5.0 (0.56)	−1.6 (0.54)
Weeks 13–24	−5.0 (0.57)	−5.9 (0.58)	−2.0 (0.56)
Amitriptyline			
Weeks 1–12	−4.7 (0.51)	−5.0 (0.48)	−1.8 (0.50)
Weeks 13–24	−5.6 (0.54)	−6.0 (0.51)	−2.2 (0.53)
Flunarizine			
Weeks 1–12	−5.0 (0.73)	−5.5 (0.76)	−2.4 (0.78)
Weeks 13–24	−5.6 (0.75)	−6.0 (0.78)	−2.6 (0.79)

IHC23-PO-230

Three one-year cycles of treatment with CGRP-targeting monoclonal antibodies: a real-life study in a cohort of chronic migraine patients

Gloria Vaghi[1,2], Roberto De Icco[1,2], Michele Corrado[1,2], Francescantonio Cammarota[1,2], Federico Bighiani[1,2], Carla Brancaccio[2], Elena Guaschino[2], Natascia Ghiotto[2], Cristina Tassorelli[1,2] and Grazia Sances[2]

[1]*Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy*
[2]*Headache Science & Neurorehabilitation Center, IRCCS Mondino Foundation, Pavia, Italy*

Objectives: In Italy, antibodies targeting CGRP pathway (mAbs) are subsidized for 1-year cycles separated by a mandatory interruption period of at least 1 month. Few data is available regarding mAbs effectiveness during consecutive one-year cycles and related suspensions. Our primary aim was to evaluate mAbs effectiveness across 3 consecutive 1-year cycles (C1, C2 and C3) and associated suspension periods.

Methods: We evaluated 46 patients with chronic migraine (CM) (69.5% females, age: 51.8 ± 10.3 years, Medication Overuse Headache 89.1%). All patients were treated with erenumab or galcanezumab and were responders to mAbs. They completed three 1-year cycles (T0 to $T1_{end}$ for C1, S1 to $T2_{end}$ for C2, and S2 to $T3_{end}$ for C3), separated by a suspension period of at least 3 months (S1 and S2). Co-primary outcomes were: changes in monthly migraine days (MMDs): i) during each cycles compared to baseline (calculated in the 3 months prior to each cycle) and ii) during the suspension periods. As secondary outcome we considered changes in migraine-related disability (assessed using MIDAS questionnaire) at the same timepoints.

Results: MMDs showed an early, stable and similar improvement during the three consecutive cycles (C1: T0 22.4 ± 5.2 vs. $T1_{end}$ 6.8 ± 4.0; C2: S1 18.3 ± 6.1 vs. $T2_{end}$ 8.0 ± 4.5; C3: S2 14.4 ± 5.8 vs. $T3_{end}$: 7.8 ± 4.4, factor TIME $p < 0.001$, factor GROUP $p = 0.303$). MMDs were comparable at the end of each cycle ($p = 1.000$) and worsened during the suspension periods (S1 vs. $T1_{end}$ $p < 0.0001$; S2 vs. $T2_{end}$ $p < 0.0001$). Notably, MMDs remained lower compared to T0 value both during S1 and S2 (S1 $p = 0.0167$, S2 $p < 0.0001$). MIDAS scores behaved accordingly (C1: T0 70.7 ± 53.3vs. $T1_{end}$ 16.3 ± 20.6, $p < 0.0001$, C2: S1 57.8 ± 37.2 vs. $T2_{end}$ 22.0 ± 18.3, $p < 0.0001$; C3: S2 41.9 ± 28.9 vs. $T3_{end}$: 15.5 ± 14.6, $p = 0.006$).

Conclusion: In our population of CM patients, mAbs induced an early and sustained reduction in MMDs during each 1-year cycle. Though MMDs significantly worsened during suspension periods, they were lower compared to pretreatment levels. At the end of all cycles MMDs reached comparable values suggesting a floor effect.

Disclosure of Interest: GV, MC, FC, FB, CB, EG, NG, RDI have no conflicts of interest. CT has received personal fees from AbbVie, Allergan, Biohaven, Eli Lilly, Lundbeck, Novartis and Teva. CT has received research funding from the European Commission, the Italian Ministry of Health and MigraineResearch Foundation GS received personal fees as speaker or Advisory Board from: Eli-Lilly, Novartis, TEVA, Lundbeck, Pfizer RDI received honoraria for scientific presentations from Eli-Lilly, and Teva NG received personal fees as speaker from Eli Lilly EG received personal fees as speaker from Lundbeck and Novartis.

IHC23-PO-231

Real-world effectiveness of Anti-CGRP Monoclonal antibodies compared to OnabotulinumtoxinA. The RAMO study: early results.

Danilo Antonio Montisano[1], Riccardo Giossi[2], Mattia Canella[1], Claudia Altamura[3], Fabrizio Vernieri[3], Carlo Ferrarese[4] and Licia Grazzi[1]

[1]Headache Center;IRCCS Istituto Neurologico C.Besta, Milan, Italy
[2]Chemical Clinical Analyses Unit, ASST Ospedale Metropolitano Niguarda, Milan, Italy
[3]Headache Unit, Campus Bio-Medico, Rome, Italy
[4]4Neurological Clinic, MilanoBicocca University, Milan, Italy

Objective: Chronic migraine (CM) is a disabling condition with huge impact on the quality of life. OnabotulinumtoxinA (BoNT-A) is an effective treatment for CM. Recently, monoclonal antibodies (mAbs) against calcitonin gene related peptide (anti-CGRP) pathways have been approved. Our aim is to compare effectiveness and safety of anti-CGRP mAbs and BoNT-A after 6 and 12 months of treatment.

Methods: We retrospectively collected patients' data from IRCCS Neurologic Institute C. Besta and Bio-Medic Campus University, with a diagnosis of CM, who received anti-CGRP mAbs or BoNT-A, at least 6 months follow-up, age 18–65, ≥2 preventive treatment failures, baseline MIDAS ≥11. Exclusion criteria: serious psychiatric diseases, received BoNT-A before anti-CGRP mAbs treatment (for mAbs arm). Study outcomes included difference from baseline in monthly migraine days (MHD), number of monthly acute medications (MAM), MIDAS, and treatment discontinuation due to adverse events (AE). Data are presented as mean (sd) and count (%). Wilcoxon rank-sum and Fisher's exact tests were used for the analyses (significance at $p < 0.05$).

Results: At the time of this interim analysis we screened 122 patients with 92 included (25 mAbs and 67 BoNT-A). Population: mean age 51.1 (8.6) y, 87.9% female, 98.9% medication overuse (non-significant differences between arms). At baseline the BoNT-A arm had significantly higher mean MHD (23.0 [6.3] vs 17.4 [32.2]; $p = 0.0003$), MAM (24.1 [13.7] vs 16.5 [2.8]; $p = 0.0107$), and MIDAS (93.0 [66.8] vs 55.6 [36.8]; $p = 0.0123$) compared to mAbs arm. MHD reduction was significantly greater in the mAbs arm (–12.4 [4.8] vs –9.0 [8.8]; $p = 0.0403$) at 6 months compared to BoNT-A. Nonsignificant differences were observed for other outcomes and time-points. Discontinuation due to AE: 1(4.8%) patient mAbs arm, 3 (4.5%) patients BoNT-A arm.

Conclusion: Our preliminary results show a comparable effectiveness and safety of the two treatments, with

significantly higher efficacy of mAbs at 6 months, suggesting a possible more rapid onset of effectiveness.
Disclosure of Interest: None Declared

IHC23-PO-232

Treatment outcome of switching between monoclonal antibodies targeting calcitonin gene-related peptide in patients with migraine

Michelle Youn[1], Mi Ji Lee[1,2] and Manho Kim[1,2]

[1]*Department of Neurology, Seoul National University Hospital, Seoul, Korea, Republic of*
[2]*Seoul National University College of Medicine, Seoul, Korea, Republic of*

Background: Monoclonal antibodies targeting calcitonin gene-related peptide (CGRP) or its receptor (anti-CGRP (-R) mAb) have been widely used for patients with difficult-to-treat migraine. In patients in whom the anti-CGRP(-R) mAb are ineffective, switching between anti-CGRP(-R) mAbs can be the next option. However, treatment outcomes of the antibody switching are limited and only available regarding switching from anti-CGRP-R mAb (erenumab) to anti-CGRP mAb (galcanezumab or fremanezumab). We aimed to assess the treatment outcome of switching between anti-CGRP mAbs (galcanezumab to fremanezumab).
Methods: From a prospective headache clinic registry, we identified patients with migraine who received galcanezumab for $\geq$3 months and switched to fremanezumab for another $\geq$3 months in a single university hospital from June 2020 to April 2023. We defined the treatment response as $\geq$50% reduction in moderate/severe headache days in the 3rd month of treatment compared to baseline from galcanezumab and fremanezumab, respectively. Treatment response of switching to fremanezumab was compared between initial treatment response from galcanezumab.
Results: We identified 22 patients (81.8% female; mean age 45.55 $\pm$ 13.26; 68.2% chronic migraine; and 45.5% medication overuse headache) included, 7 (31.8%) were initially responders to galcanezumab. After switching to fremanezumab, 8 (36.4%) patients showed treatment response. Treatment response was 33.3% in initial responders and 41.7% in non-responders to galcanezumab ($p > 0.999$).
Conclusion: We report the first data of antibody switching from galcanezumab to fremanezumab. Switching between anti-CGRP mAbs (galcanezumab to fremanezumab) yielded comparable treatment outcome than switching from anti-CGRP-R mAb (erenumab) to anti-CGRP mAb (galcanezumab or fremanezumab) which has been previously reported. Treatment response to fremanezumab seems to be independent of prior treatment response to galcanezumab. Our study results suggest that switching to another anti-CGRP mAb can be considered when an anti-CGRP mAb is ineffective or intolerable.

IHC23-PO-233

Preventive treatment of migraine with (100%) aura with lamotrigine

Sena Uzun[1,2], Ulf Frejvall[2], Gülsen Özkaya-Sahin[3] and Gürdal Sahin[1,2]

[1]*Lund University, Lund, Sweden*
[2]*Skaneuro Neurology Clinic, Lund, Sweden*
[3]*Region Skane, Lund, Sweden*

Objective: To propose a preventive treatment with lamotrigine (LMT) in patients with "migraine with 100% aura" by evaluating the real-world effectiveness.
Methods: We conducted a retrospective analysis of patients with "migraine with 100% aura" based on published case-series and clinical experience accumulated from our clinic over the years. "Migraine with 100% aura" refers to the presence of aura with every migraine attack or aura being the most bothersome symptom. The primary outcome was the change from baseline in the frequency of monthly aura at a minimum of 50% after LMT prophylaxis. Patients who experienced a reduction less than 25% were classified as non-responders and more than 75% were classified as super-responders. Moreover, we have depicted average dose and safety profile of LMT based on data from patient journals.
Results: Out of 79 patients, 78 had visual impairments, 13 had motor weaknesses, 44 had sensorial symptoms and 27 had language difficulties as aura symptom during migraine attacks. In addition, 9 patients experienced extreme photosensitivity. The average dose of LMT was 148.8 mg $\pm$ 8.4 (SEM) and average time to reach maximum dosage was 22.8 $\pm$ 3.2 months. Mean duration of LMT treatment has been detected as 58.6 $\pm$ 4.9 months.
Efficacy analysis with enough data was possible in 75 patients (51 female, 24 male). Among these patients, 81.3% were super-responders, 9.4% were responders and 9.3% were non-responders. Overall, the monthly aura days (MAD) was decreased from 6.9 $\pm$ 0.9 days to 1.2 $\pm$ 0.4 days with 83% improvement rate. Twenty-eight patients had adverse events (AE) and 7 dropped out of the study due to AEs. Some of the most common AE include skin changes, dizziness, tiredness, arthralgia, psychological and metabolic disturbances. There was a significant inverse correlation between the occurrence of AE and time to reach maintenance dose ($p < 0,05$).

Conclusion: The results from this study indicate that LMT is an effective prophylactic treatment of aura in patients with migraine with 100% aura and should be considered as a prescribed treatment due to its high efficacy and low-side effect profile.
Disclosure of Interest: None Declared

IHC23-PO-234

Treatment efficacy of switching CGRP monoclonal antibody therapies for chronic migraine in Australia: a multicentre retrospective cohort study

Shuli Cheng[1,2], Bronwyn Jenkins[3], Nicole Limberg[4], Lucie Aldous[5] and Elspeth Hutton[1,2]

[1]*Alfred Health, Melbourne, Australia*
[2]*Monash University, Melbourne, Australia*
[3]*Royal North Shore Hospital, Sydney, Australia*
[4]*Migraine Specialist Brisbane, Brisbane, Australia*
[5]*Royal Hobart Hospital, Hobart, Australia*

Objectives: To determine the treatment response when switching from one class of calcitonin gene related peptide receptor monoclonal antibody (CGRP-receptor mAb) to another class of calcitonin gene related peptide monoclonal antibody (CGRP-ligand mAb) in patients with chronic migraine in the real world setting in Australia
Methods: Patients were prescribed erenumab (CGRP-receptor mAb) in the setting of either a product familiarisation program or private pay access in 3 headache centres in Australia in 2018 which was discontinued in 2020. In 2021, galcanezumab and fremanezumab (CGRP-ligand mAb) were made available on the national Pharmaceutical Benefits Scheme. We retrospectively analysed the treatment effectiveness to CGRP-ligand mAb in this cohort with chronic migraine and compared this to their treatment response to erenumab.
Results: We analysed 170 patients with chronic migraine treated with erenumab in our original cohort. Out of the 170, we had 86 patients who switched to either galcanezumab or fremanezumab. The average age was 48 years old (rage 18–73), female n = 77 (90%), baseline monthly migraine days, mean 18.7 (SD 7.6), monthly migraine days at 3 months on erenumab was 9.4 (SD 7.6), monthly migraine days at 3 months on CGRP-ligand mAb was 8.7 (SD 8.2). Out of the 36 patients who were non-responders to erenumab, 24 patients (67%) had a 50% treatment response rate when switched to a CGRP-ligand mAb. 14% of patients who tried both CGRP-receptor mAb and CGRP-ligand mAb did not have a 50% response rate to either agents. Only 72% of erenumab responders then had a similar 50% responder rate to the next CGRP-ligand mAb.
Conclusion: Our analysis support that a relevant proportion of erenumab non responders might benefit from a treatment switch to a CGRP-ligand mAb. We measured a treatment resistance rate of 14%. A response to the first CGRP-receptor mAb did not guarantee a response to the next CGRP-ligand mAb.
Disclosure of Interest: None Declared

IHC23-PO-235

Impact of pandemic on Botox™ treatment and treatment effect in patients with chronic migraine

Shuli Cheng[1], Valentina Favoni[2], Alicia Alpuente[3], Paula Cavanzo[4], Gudrun Gossrau[5] and Ian Finkelstein[6]

[1]*Alfred Health, Melbourne, Australia*
[2]*IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy*
[3]*Vall d'Hebron University Hospital, Barcelona, Spain*
[4]*Dali Medical Centre, Compensar Complimentary Plan, Bogota, Colombia*
[5]*University Hospital Carl Gustav Carus, Dresden, Germany*
[6]*Toronto Headache and Pain Clinic, Toronto, Canada*

Objectives: We studied the impact of the pandemic on 1) Botox™ treatment and treatment effect in patients with chronic migraine, 2) migraine comorbidities, at 1.5 years into the pandemic, in headache clinics in different countries.
Methods: We carried out a multicentre survey of patients with chronic migraine being managed in headache clinics from July to October 2021. We collected information including demographics, comorbidities, current medications, acute medications use, monthly headache and migraine days (MHD), MHD 2 years ago in 2019, Depression, anxiety, stress 21 scale (DASS21) scores, Headache Impact Test 6 (HIT6), pandemic and Botox™ related questions. The primary outcome measured was change in MHD in 2021 compared to 2019.
Results: We collected data from 49 patients in 5 different countries. The baseline characteristics were average age of 46 years old, 80% female gender. The DASS21 score was 21.8 (0–66), HIT6 score 59 (40–71), monthly acute medication use was 6.6 (0–30), current preventive with Botox™ in 47 out of the 49 patients. The 2021 MHD was 11.3 (1–30) and the 2019 MHD was 18 (3–30), with the change in MHD –6.7. All patients were affected by the pandemic in many aspects including work, family, social, travel restrictions. 15/45 said their migraines worsened with the pandemic. 39/45 did not have a change in the effect of Botox™ treatment in the current restrictions.
Conclusions: Headache and migraine control improved by –6.7 days per month compared to 2 years ago.

Headache centres had minimised disruptions to patients receiving Botox™ for their migraine treatment. The Botox™ treatment effect remained stable in the pandemic.
Disclosure of Interest: None Declared

IHC23-PO-236

OnabotulinumtoxinA (Botox) for Chronic Migraine during pregnancy; experience from Hull (UK) Headache clinic over 11 years

Rafiullah Khan[1], Modar Khalil[1], Alina Buture[1], Ho-Tin Wong[1] and Fayyaz Ahmed[1,2]

[1]*Hull University Teaching Hospitals NHS Trust, Hull, United Kingdom*
[2]*Hull York Medical School, Hull, United Kingdom*

Introduction: Migraines are common in women of reproductive age and its control may deteriorate although 50–75% see improvement during pregnancy. There is limited evidence demonstrating safety and efficacy of the oral preventive agents in pregnancy with only amitriptyline and low dose propranolol deemed suitable for use. OnabotulinumtoxinA has been the established treatment for chronic migraine (CM) in the UK where three or more oral preventive agents have failed. Its use in pregnancy has not been fully evaluated.
We previously reported a mean 3.5 years (3 months – 7 years) follow up of a cohort of 45 patients exposed to OnabotulinumtoxinA for CM treatment during pregnancy.
Aim: We report pregnancy outcomes on 102 patients with CM exposed to OnabotulinumtoxinA during pregnancy.
Methods: Female patients of reproductive age group attending Hull headache clinic who received OnabotulinumtoxinA treatment for CM were given advice on contraception because of the unknown impact of the toxin on pregnancy. On reporting pregnancy, they are appraised on the risk/benefit of treatment continuation. All patients are consented to access their medical records and pregnancy outcome and those who wished to continued were asked to sign a disclaimer.
Pregnancy outcome data were collected on all patients for the gestational age, mode of delivery, birth weight, congenital malformation and any other unexpected outcome.
Results: 102 patients reported pregnancy while on treatment with OnabotulinumtoxinA (8–16 weeks). 60 patients received treatment in the first trimester while 41 received treatment few weeks before conception. 76 patients wished to continue with further treatment at three monthly interval while 26 decided to stop. All patients were followed up every 3 months. Those on treatment (N = 76) continued to show a good response and 20/26 who stopped relapsed 3–6 months following the last treatment and 6 remained in remission. 17 restarted treatment after pregnancy and 3 chose to take oral prophylaxis. Patients received an average of 4 cycles at pregnancy (range 1–12)
Of the 76 patients that continued treatment there was 1 miscarriage. Remaining 75 were full term deliveries of which there were 8 forceps and 6 caesarean. No fetal malformation were reported. Of the 26 who stopped treatment all had full term deliveries of which there was 2 forceps and 2 caesarean and no fetal malformation.
The patient with miscarriage continued treatment and got pregnant twice with normal full term deliveries. One patient got pregnant thrice and 2 patients conceived twice while on OnabotulinumtoxinA treatment.
Conclusion: Based on our experience with 102 patients with CM over the last 11 years, OnabotulinumtoxinA is a safe treatment option during pregnancy although there is need for a larger data before it is considered a safe established option.
Disclosure of Interest: Fayyaz Ahmed has received honorarium from Novartis, Electrocore, ENeura, Abbvie, Eli Lilly, Pfizer, Teva and Lundbeck for being on their advisory board. Rafi Khan – Nil Alina Buture – Nil Modar Khalil – Nil Ho Tin Wong – Nil

IHC23-PO-237

Efficacy of three calcitonin gene-related peptide monoclonal antibodies in patients with migraine: a 12-month single-center observational real-world study

Keisuke Suzuki, Shiho Suzuki, Tomohiko Shiina, Muneto Tatsumoto, Hiroaki Fujita, Yasuo Haruyama and Koichi Hirata

Dokkyo Medical University, Tochigi, Japan

Background: Real-world data on the effectiveness of calcitonin gene-related peptide monoclonal antibodies (CGRP mAb) in migraine patients with various clinical backgrounds and comorbid conditions are needed.
Methods: We performed a retrospective, observational, single-center, real-world study with an observation period of up to 12 months after CGRP mAb administration. A total of 228 patients with episodic or chronic migraine (age, 45.9 ± 13.2 years; 184F; 45 erenumab; 60 galcanezumab; 123 fremanezumab) who were at least treated with CGRP mAbs for 3 months were finally included in this study. The number of monthly migraine days (MMD) was assessed by headache diary, and the clinical factors related to ≥50% MMD reduction were evaluated. The effect of three different CGRP mAbs on MMD reduction was also assessed.

Results: In the total cohort, after CGRP mAb treatment, mean MMDs decreased by 5.7 ± 4.6, 7.2 ± 4.8, 8.3 ± 4.7, and 9.5 ± 5.0 at 1, 3, 6 and 12 months, respectively. The $\geq$50% MMD reduction rates at 1, 3, 6 and 12 months were 36.0%, 48.2%, 61.0% and 73.7%, respectively. Overall, the $\geq$50% and $\geq$75% response rates increased gradually over 12 months. In the logistic regression analysis, the presence of osmophobia, fewer baseline MMDs and a lower number of previous prophylactics used were related to $\geq$50% responders at 3 months. At 6 and 12 months, the presence of osmophobia and fewer baseline MMDs contributed to $\geq$50% responders. There was no difference in MMD reduction over 12 months among 3 different CGRP mAbs (erenumab, galcanezumab and fremanezumab). Adverse reactions were observed in 28 (12.3%) patients, with injection site reactions being the most common ($n = 22$) though generally mild in severity.

Conclusion: This real-world study confirmed the efficacy and safety of 3 different CGRP mAbs for prophylactic treatment of patients with migraine. The gradual increase in the rate of responders over 12 months has important clinical implications, and the relationship between osmophobia and CGRP mAb efficacy requires further study.

Disclosure of Interest: K Suzuki received lecture fees from Eli Lilly Japan, Daiichi Sankyo, Amgen and Otsuka Pharmaceutical Co., Ltd., during the conduct of the study. S Suzuki received lecture fees from Eli Lilly Japan, Daiichi Sankyo, Amgen and Otsuka Pharmaceutical Co., Ltd., during the conduct of the study. T Shiina received lecture fees from Eli Lilly Japan, Daiichi Sankyo, Amgen and Otsuka Pharmaceutical Co., Ltd., during the conduct of the study. M Tatsumoto received lecture fees from Eli Lilly Japan, Daiichi Sankyo, Amgen and Otsuka Pharmaceutical Co., Ltd., during the conduct of the study. H Fujita and Y Haruyama have nothing to disclose. K Hirata received lecture fees from Eli Lilly Japan, Daiichi Sankyo, Amgen, Sawai Pharmaceutical Co., Ltd. and Otsuka Pharmaceutical Co., Ltd. during the conduct of the study.

IHC23-PO-238

Real-world data on erenumab interruption in migraine patients in Germany: the SPECTRE study

Charly Gaul[1], Hartmut Goebel[2], Mirja Koch[3] and Cordula Weiss[4]

[1]*Headache Center Frankfurt, Frankfurt, Germany*
[2]*Schmerzklinik Kiel, Kiel, Germany*
[3]*Novartis AG, Basel, Switzerland*
[4]*Novartis Pharma GmbH, Nuremberg, Germany*

Objective: Erenumab is a CGRP-receptor antibody developed for the prevention of migraine. International guidelines on the use of monoclonal antibodies for migraine prevention suggest pausing the treatment after 12 to 18 months. Our clinical study APOLLON provides data on the impact of treatment discontinuation yet evidence from routine clinical practice is limited. The SPECTRE study aimed to analyze real-world evidence on treatment patterns including treatment interruption.

Methods: This non-interventional study was conducted at 105 sites in Germany and enrolled 571 adult migraine patients receiving erenumab treatment (70 mg/140 mg) for not more than 3 months before study start. Patients were allowed to interrupt treatment (drug holiday) at any time. Throughout the study and during drug holidays monthly migraine days (MMD) were reported using a headache diary.

Results: The final analysis includes data from 571 migraine patients, predominantly female with chronic migraine, who were treated with erenumab for 12–24 months. Most patients (68.5%) started on the lower dose of 70 mg. In total, 118 patients took at least one drug holiday after approximately 11 months (37–633 days) on treatment with the main reason reported by patients being good effectiveness (42.4%), indicating a wish to reduce treatment dependency. The duration of the drug holiday varied between 3 and 447 days (mean 75.2 days). After the drug holiday, 78.0% of patients restarted treatment with erenumab and most returned to their previous dose (70.3%). In the 4 weeks prior to the treatment interruption, patients had an average of 1.3 MMD which remained improved to 1.0 MMD during the drug holiday and improved to 0.9 MMD within 12 weeks after treatment resumption.

Conclusion: The SPECTRE study provided real-world insights into the motivation for and impact of treatment interruption of the migraine patient population in Germany. Overall, the observations align with results from our clinical trial APOLLON where patients who took a drug holiday mostly returned to the previous dose afterwards and reported a return to the same average MMDs as before the treatment interruption within 2 months after resuming treatment.

Disclosure of Interest: Dr. Charly Gaul received honoraria for consulting and lectures within the past three years from Allergan Pharma, Lilly, Novartis Pharma, Hormosan Pharma, Grünenthal, Sanofi-Aventis, Weber & Weber, Lundbeck, Perfood, and TEVA. His research is supported by a grant of the German Research Foundation (DFG). He does not hold any stocks of pharmaceutical companies. He is honorary secretary of the German Migraine and Headache Society. H. Göbel received honoraria for consulting and lectures from Allergan, Almirall, Astra Zeneca, Bayer Vital, Berlin-Chemie, Bionorica, Bristol-Myers-Squibb, Elli Lilly, Fujisawa, GlaxoSmithKline, Grünenthal, Hermal, Hormosan, Ipsen-Pharma, Janssen-Cilag, Johnson&Johnson, Krewel-Meuselbach, Klosterfrau,

Lichtwer, Menarini Pharma, Merz Pharmaceuticals, Minster Pharmaceuticals, MSD, Novartis Pharma, Pfizer, Pharmacia, Sandoz, Schaper und Brümmer, Schwarz-Pharma, Teva, Weber&Weber, Smith Kline Beecham. Dr. Mirja Koch is an employee of Novartis AG. Dr. Cordula Weiss is an employees of Novartis Pharma GmbH. Funding: This study is supported by Novartis Pharma GmbH, Nuremberg, Germany. Erenumab is co-developed by Amgen and Novartis.

IHC23-PO-239

Safety concerns of treatment with anti-CGRP monoclonal antibodies in patients with migraine

Britt W.H. van der Arend[1,2], Nancy van Veelen[1], Joëlle E.T. de Ruijter[1], Michael H. Olsen[3,4], Antoinette Maassen van den Brink[2] and Gisela M. Terwindt[1]

[1]*Leiden University Medical Center, Leiden, Netherlands*
[2]*Erasmus MC, Rotterdam, Netherlands*
[3]*Holbæk Hospital, Holbæk, Denmark*
[4]*University of Southern Denmark, Odense, Denmark*

Background: Anti-CGRP (receptor) antibodies are a new class of drugs for the treatment of migraine, but their long-term safety profile is still being studied. In particular, the cerebro- and cardiovascular safety of these drugs requires further investigation.
Methods: In this follow-up study, we monitored 227 patients with migraine treated with either erenumab (n = 114) or fremanezumab (n = 113) for at least 12 months. Electrocardiogram and clinical laboratory values were collected at the start of treatment and thereafter approximately every three months. Abnormalities in heart rhythm, heart rate, electrical axis, conduction intervals, P-wave morphology, QRS complex morphology, and ST-T segment changes were identified. All adverse events were reported.
Results: During the follow-up period, 4.8% (11/227) of the patients developed cardiovascular events (n = 4) or an abnormal ECG (n = 7). Among them, 2.6% (6/227) discontinued treatment due to severe hypertension (n = 1), negative ST-T segments in V1-V3 (n = 1) or cardio- or cerebrovascular events of different etiologies, such as cerebellar stroke (n = 1), spontaneous coronary artery dissection (SCAD) (n = 1), thoracic pain with peripheral oedema (n = 1) or pericarditis (n = 1). There were no clinically significant changes in liver and kidney function, lipid, electrolyte, or glucose serum levels over time.
Conclusion: While we cannot establish a definitive causal relationship, our study underscores the importance of monitoring cardiovascular risk in patients undergoing anti-CGRP (receptor) antibody treatment for migraines. Based on our prior research1, we recommend regular blood pressure monitoring. Routine blood tests and ECG monitoring may not be required unless the patient experiences symptomatic complaints.
Disclosure of Interest: None Declared

Reference

1. de Vries Lentsch S, van der Arend BWH, Maassen VanDenBrink A, Terwindt GM. Blood Pressure in Patients With Migraine Treated With Monoclonal Anti-CGRP (Receptor) Antibodies: A Prospective Follow-up Study. *Neurology*. 2022 Oct 25; 99(17): e1897–e1904.

IHC23-PO-240

Dietary Pattern Analysis: A Comparison Between Episodic and Chronic Migraine

Fahimeh Martami[1], Sakineh Shab-Bidar[2], Kathleen Holton[1] and Mansoureh Togha[3]

[1]*American university, Washington DC, USA*
[2]*Tehran university of medical sciences, Tehran, Iran, Islamic Republic of*
[3]*Tehran University of medical sciences, Tehran, Iran, Islamic Republic of*
*Corresponding Author

Objective: Little is known about the potential differences between migraine subtypes regarding dietary patterns. We aimed to investigate the association between posteriori dietary patterns by principal component analysis (PCA) and migraine characteristics with a special focus on episodic (EM) and chronic (CM) migraine comparison.
Methods: Patients of both sexes, aged between 18–60, diagnosed with episodic and chronic migraine were enrolled in this cross-sectional study. Dietary intake was assessed using a 168 item semi-quantitative food frequency questionnaire (FFQ). Data regarding migraine-related outcomes including frequency, severity, disability, and medications were collected. Additionally, information about a wide range of covariates including sociodemographic, anthropometric, and lifestyle factors was gathered. Extraction of dietary patterns was performed via PCA.
Results: Ninety episodic migraine patients and 90 chronic migraine patients were included in the analysis. PCA extracted two major dietary patterns: "Western diet" and "Healthy diet". Patients in the highest tertile of the Western diet had significantly higher attack frequency than the first tertile (16.0 vs. 10.3, P = 0.003). Patients with CM had a significantly greater intake of refined grains, fast food/snacks, high-fat dairy and processed meat compared to EM. Moreover, a significant positive association

between the highest tertile of the Western diet and the chance of having CM compared to EM was detected in the regression model. This association increased and remained statistically significant in the fully adjusted model (OR = 4.6, 95% CI: 1.15, 18.52, P trend: 0.030).
Conclusion: Our findings suggest that high adherence to a western diet is positively associated with an increased frequency of migraine attacks. In addition, finding the higher risk of CM in the top tertile of the western diet compared to EM suggest that dietary pattern might play a role in migraine progression by increasing the number of attacks.
Disclosure of Interest: None Declared

IHC23-PO-241

Case Report of a Patient Who Developed Chillblains During Treatment with Erenumab and Galcanezumab, But Not During Subsequent Treatment with Rimegepant for Prevention of Chronic Migraine

Bradley Torphy, Melody Smith, Christopher Medrano, Brian Murphy, Jodi Straube, Megan Helle and Brent Rancher

Chicago Headache Center & Research Institute, Chicago, USA

Objective: To present a case report of a patient who developed chillblains during treatment with erenumab and galcanezumab, but not during subsequent treatment with rimegepant for prevention of chronic migraine.
Methods: Calcitonin gene-related peptide (CGRP) has been targeted in the acute and preventive treatment of migraine. There have been case reports of new or worsening Reynaud's Phenomenon (RP) during treatment with CGRP monoclonal antibodies (CGRP mAbs) and fewer case reports of RP during treatment wtih CGRP receptor antagonists (gepants). To our knowledge there is no prior evidence to implicate CGRP mAbs or gepants in the development of chillblains. Chillblains is a condition characterized by the development of swollen patches and blistering on peripheral extremities, which is often seen in patients with RP due to similar circulation pathology. This case reports the development of chillblains in a patient who received two different GCRP mAbs for prevention of chronic migraine. To our knowledge this is the first case of development and recurrence of chillblains with subsequent tolerance of an alternative treatment with a gepant. A 38 year-old female patient with chronic migraine was initially treated with erenumab 140 mg subcutaneous injection monthly. Treatment was changed to galcanezumab 120 mg subcutaneous injection monthly after the patient was diagnosed with Chillblains during the first winter of treatment with erenumab. When the patient again developed symptoms of chillblains while taking galcanezumab the following winter, migraine preventive treatment was changed to rimegepant 75 mg tablet every other day.
Results: This case involved the development of chillblains in the digits during the winter months during treatment with erenumab. When the patient was treated with galcanezumab, she again developed chillblains in the digits. Since discontinuation of mAbs, the patient has tolerated rimegepant well without recurrence of chillblains.
Conclusion: CGRP mAbs have recently been associated with development of RP in patients treated for migraine. This case reports new onset chillblains while on two different long-acting antibody therapies, but tolerance of a receptor antagonist without development or recurrence of chillblains. This report may help better elucidate the mechanism of microvascular complications of migraine therapy. The risk of chillblains and RP may be related to the pathway target point or the longer half-life of CGRP mAbs relative to gepants.
Disclosure of Interest: Bradley Torphy: Speaker for Abbvie, Amgen, Impel, Lilly, Lundbeck, Pfizer, and Teva, Impel. He consults for Abbvie, Amgen, Lilly, Neurolief, Teva, and Theranica. He has served as a principal investigator for Abbvie, Amgen, Lilly, Pfizer, Teva, and Theranica.

IHC23-PO-242

Effectiveness and safety of monthly versus quarterly fremanezumab for migraine prevention: a real-life study

Ilaria Cetta[1], Roberta Messina[1], Laura Zanandrea[1], Federica Genovese[1], Simone Guerrieri[1], Fabrizio Vernieri[2], Claudia Altamura[2], Sabina Cevoli[3], Valentina Favoni[3], Bruno Colombo[1] and Massimo Filippi[1]

[1]IRCCS San Raffaele Scientific Institute, Milan, Italy
[2]Fondazione Policlinico Campus Bio-Medico, Rome, Italy
[3]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Objective: Two dose regimens of fremanezumab are currently approved: subcutaneous administration of fremanezumab 225 mg monthly and 675 mg quarterly. Previous randomized controlled trials demonstrated that both regimens are effective and safe for migraine prevention. To date, a direct comparison between the two dosages in terms of effectiveness and safety is lacking in a real-life setting.
Methods: This is a multicentric study. Ninety-seven patients attending the Headache Clinic at San Raffaele Hospital in Milan, Headache and Neurosonology Unit of Campus Bio-Medico in Rome and the Headache Centre of

IRCCS Institute of Neurological Sciences in Bologna were prospectively enrolled. Forty-nine patients received monthly fremanezumab (Group A) for three months and 43 completed a six-month treatment period; 48 patients received quarterly fremanezumab (Group B) for three months and 38 received a second dose of fremaezumab 675mg after 3 months. Between-group differences in monthly headache (MHD) and migraine days (MMD), number of days (AMD) and pills (AMP) of acute medication intake, Headache Impact Test (HIT-6), Migraine Disability Assessment Test (MIDAS) and Numeric Rating Scale (NRS) scores were assessed after 3 (M3) and 6 (M6) months of treatment. Within-group and between-group differences in treatment efficacy over time were assessed using Wilcoxon and mixed-effect ANOVA tests. The presence of adverse events was also investigated.

Results: In Group A, 36 patients (74%) were women and the mean age was 55 years (range: 26–75) while the 81% of patients in Group B were females and 50 years was the mean age (range: 27–73). Thirty-three and 31 patients had chronic migraine in Group A and Group B, respectively. No statistically significant differences in demographic and clinical variables between the two groups at baseline, M3 and M6 were observed. After 3 and 6 months, both groups showed a significant reduction of MHD, MMD, AMD, AMP, HIT-6, NRS, and MIDAS scores, with no significant differences between the two groups (Group A vs Group B M3: $p < 0.01$; M6: $p < 0.01$ for all variables). One patient of Group A reported constipation after three months, which regressed at the follow-up visit. In Group B, one patient at M3 and one at M6 reported having a reaction at the injection site.

Conclusion: Our real-life findings confirm that monthly and quarterly fremanezumab are effective and safe for migraine prevention.

Disclosure of Interest: None Declared

IHC23-PO-243

Characteristics of medication overuse headache in patients over 60 years of age

Tae-Jin Song[1], Hong-Kyun Park[2], Min Kyung Chu[3], Sun-Young Oh[4], Jin-Ju Kang[4], Heui-Soo Moon[5], Mi Ji Lee[6], Mi-Kyoung Kang[7], Yooha Hong[7] and Soo-Jin Cho[7]

[1]*Department of Neurology, Ewha Womans University Seoul Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of*
[2]*Department of Neurology, Inje University Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea, Republic of*
[3]*Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of*
[4]*Department of Neurology, Chonbuk National University Hospital, Chonbuk National University School of Medicine, Jeonju, Korea, Republic of*
[5]*Department of Neurology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of*
[6]*Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*
[7]*Department of Neurology, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of*

Objective: Medication overuse headache (MOH) can affect people of all ages, mostly in middle age (30∼50 years). Meanwhile, in the relatively aged population, MOH can be particularly concerning as they may have a higher risk of adverse reactions to medication due to age-related changes in metabolism and organ function. Nevertheless, information on the characteristics, disabilities, and management of MOH in the relatively aged population remains uncertain. This study aimed to elucidate the clinical characteristics of MOH patients over 60 years of age in Korea.

Methods: The Registry for Load and Management of MEdicAtion OveruSE Headache (RELEASE), a cross-sectional prospective observational study including seven referral headache centers in Korea, started enrolling adult patients with MOH in April 2020. In this RELEASE registry, data included information on headache characteristics, burden on daily function, depression, anxiety, history of acute and preventive medications, and treatment strategies. For this study, we compared clinical characteristics by dividing into groups over 60 years old and under 60 years old. In addition, at the time of 3-month follow-up, it was confirmed whether there was a difference between the two groups (over 60 years old and under 60 years old) in headache day reduction of 50% or more and MOH day reduction of 9 days or more compared to those of baseline.

Results: A total of 309 patients (85.1% females; mean age, 45.2 ± 13.9 years) were enrolled by April 2023. Even though MOH patients with $\geq$60 years had relatively better quality of life scores and disability scale (MIDAS 68.8 ± 68.6 vs. 47.5 ± 44.9) than those of $<$60 years, overall headache days within last months, severe headache days within last month, headache days with acute medication within last month were more frequently noted in MOH patients with $\geq$60 years (Table 1). Regarding proportion of acute medication day – less than 9 days and proportion of 50% reduction of migraine days at 3 months follow up, there were no statistical difference between two groups.

Conclusions: MOH patients with $\geq$60 years showed different clinical characteristics from MOH patients with $<$60 years. MOH patients with $\geq$60 years may require

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Table 1. Characteristics of medication overuse headache in patients over 60 years of age

	Total (n = 309)	Less than 60 years (n = 55)	More than 60 years (n = 254)	p value
Presence of without headache days within last 1 month	154 (49.8)	137 (53.9)	17 (30.9)	0.002
Headache days within last month	25.5 ± 5.3	25.3 ± 5.3	27.0 ± 5.3	0.037
Severe headache days within last month	10.5 ± 7.7	10.1 ± 7.3	12.5 ± 9.4	0.078
Headache days with acute medication within last month	21.1 ± 7.4	20.2 ± 7.2	25.3 ± 6.8	0.001
Quality of life (MSQ a)	54.5 ± 24.3	52.4 ± 23.8	64.3 ± 24.3	0.001
Quality of life (MSQ b)	62.2 ± 24.6	60.8 ± 24.1	68.4 ± 25.7	0.038
Quality of life (MSQ c)	57.6 ± 30.0	56.3 ± 30.4	63.6 ± 27.4	0.105
Quality of life (MSQ total)	174.3 ± 70.8	169.5 ± 70.8	196.4 ± 67.3	0.011
Proportion of acute medication day – less than 9 days at 3 months after follow up (n = 242)	47 (19.4)	37 (18.4)	10 (24.4)	0.378
Proportion of 50% reduction of headache days at 3 months after follow up (n = 242)	61 (25.2)	47 (23.4)	14 (34.1)	0.148

different diagnostic procedures and treatment policies compared to those of relatively younger MOH patients.

Disclosure of Interest: None Declared

IHC23-PO-244

Real-world effectiveness after initiating fremanezumab treatment of 165 migraine patients in a regional headache center in Japan

Shoji Kikui, Daisuke Danno, Junichi Miyahara, Hanako Sugyama, Kuniko Ota, Kenji Murakata, Yoshihiro Kashiwaya and Takao Takeshima

Department of Neurology & Headache Center, Tominaga Hospital, Osaka, Japan

Objective: Fremanezumab is the second anti-calcitonin gene-related peptide monoclonal antibody approved in Japan in August 2021. Fremanezumab has demonstrated to be effective, safe, and tolerated in the prevention of both episodic migraine (EM) and chronic migraine (CM) in randomized, placebo-controlled trials. To the best of our knowledge, no real-world studies on fremanezumab have been published in any international journal from Japan. We evaluate the efficacy and safety of fremanezumab in patients with migraine in a real-world study in Japan.

Method: In Japan, fremanezumab can be used for patients with $\geq$ 4 migraine days per month and for those who have undergone treatment with at least one migraine-preventive drug (lomerizine, propranolol, or valproate) with ineffectiveness, intolerance, or strong concern about side effects. Eligible patients were given subcutaneous fremanezumab at the doses of 225 mg monthly or 675 mg quarterly, according to their preference. We retrospectively examined patients with migraine who received $\geq$3 times of 225 mg monthly or $\geq$ twice of 675 mg quarterly between September 2021 and August February 2022 at Tominaga Hospital. We assessed changes in global patient's impression (GPI), monthly migraine days (MMD), responder rate (RR), and acute medication intake days (AMD). We used the $\geq$ 50% RR to examine the positive and negative predictors. Approval for the examination was provided by the institutional ethics committee of Tominaga Hospital (Approval number: 120130). Informed consent was obtained from participants.

Results: The subjects were 165 migraine patients (M: F = 17:48, 45.5 ± 16.0 years old), of whom 53 had EM and 112 had CM. Sixty-seven patients had concomitant of medication overuse headache due (MOH). Subjectively, 25 cases (14.5%, EM:CM = 12:13) were markedly effective, and 30 cases (17.6%, EM:CM = 3:27) were ineffective. Fremanezumab was effective in both EM and CM, inducing at week 24 a significant reduction in MHD (–3.3, –8.3, $p < 0.01$), MMD (–2.4, –7.2, p 0.01), and AMD (–2.5, 6.7, $p < 0.01$). The $\geq$ 50%, $\geq$ 75% and 100% responder rates at week 24 were 48.5%, 18.2%, and 15.2% in EM and 45.5%,18.2%, and 5.1% in CM, respectively. Longer migraine hystory (17.9 y vs 21.5 y, $p < 0.05$), MOH at baseline (21.4% vs 41.1%, $p < 0.05$) and higher number of prior preventive treatments (1.7 vs 2.4, $p < 0.05$) emerged as a negative response predictor. Treatment-emergent adverse events were uncommon (4.8%) and mild.

Conclusion: remanezumab seems effective and safety in real-life study in Japan. Longer migraine hystory, MOH at baseline and higher number of prior preventive treatments emerges as a negative response predictor.

Disclosure of Interest: Kikui S and Danno D are on the speaker board for Lilly, Daiichisankyo, Amgen, Otsuka. Takeshima T is on the speaker board for Lilly, Daiichisankyo, Amgen, Otsuka, Eisai and on the editorial board for Japanese Headache Society and Japanese Society for Neurology.

IHC23-PO-245

Favorable Response to Combined Treatment with OnabotulinumtoxinA and Anti-CGRP Monoclonal Antibody in Chronic Migraine Resistant to Monotherapy

Heui-Soo Moon, Yong Beom Kim, Pil-Wook Chung, Bum Chun Suh, Won-Tae Yoon, Jang-Hyun Baek, Junsang Sunwoo, Sorae Lee, Sumin Kim and So-Ei Ann

Department of Neurology, Kangbuk Samsung Hospital, Sungkyunkwan University College of Medicine, Seoul, Korea, Republic of

Objective: OnabotulinumtoxinA(BTXA) and anti-calcitonin gene–related peptide monoclonal antibodies (CGRP mAbs) act through different physiological mechanisms and have synergistic effects within the trigeminovascular system. Our objective was to assess the effectiveness of combining a BTXA and CGRP mAbs in treatment-refractory patients with chronic migraine (CM) who failed to respond on adequate monotherapy.
Methods: We retrospectively analyzed the effectiveness of combination treatment in 23 patients with CM who showed less than 30% response rate to BTXA treatment (more than 2 cycles) and anti-CGRP mAb treatment (more than 3 monthly courses) respectively. Dual therapy was performed by adding BTXA to an already used anti-CGRP mAb for a more than 6 months (range 6–12 months). The prescribed mAb was galcanezumab for 19 patients and fremanezumab for 4 patients.
Results: The patients consisted of 3 males (13.0%) and 20 females (87.0%) with a mean age of 44.2 $\pm$ 13.0 (range: 21–67) years, 14 patients (60.9%) with medication overuse. Seventeen (73.9%) patients showed at least 30% reduction rate in monthly headache days, at least 50% reduction rate in 10 patients (43.5%), and at least 75% reduction rate in 2 patients (8.7%). In 2 patients who achieved a 75% reduction, one of the combination drugs was discontinued and the number of headache days increased again within 3 months. There were no cases of early withdrawal of the dual intervention due to safety/tolerability issues.
Conclusion: Combination therapy with BTXA and anti-CGRP mAbs is effective and can be a good preventive option for difficult-to-treat CM patients who have failed individual monotherapies. Our results emphasize individualized decisions and advocate combination therapy. Controlled trials are necessary to determine the true advantage in efficacy of this combination in difficult to treat migraineurs.
Disclosure of Interest: None Declared

IHC23-PO-246

A good response to anti-CGRP monoclonal antibodies is related not to strictly unilateral location of the pain but to the unilaterality of the pain at onset.

Hyoung Cheol Lee[1], Soohyun Cho[2] and Byung-Kun Kim[1]

[1]*Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Korea, Republic of*
[2]*Uijeongbu Eulji Medical Center, Eulji University School of Medicine, Uijeongbu, Korea, Republic of*

Background: The literature to date has shown that the response to botulinum toxin or anti-calcitonin gene-related peptide monoclonal antibodies (CGRPmAbs) is positively associated with unilateral migraine. However, no studies have precisely defined unilateral migraine.
Objectives: We explored for the evolution of pain location during the attacks that might distinguish migraine patients who benefit from CGRPmAbs.
Methods: We analyzed 321 patients with migraine who visited Nowon Eulji Medical Center and were prescribed CGRPmAbs for more than 3 months. We examined the unilaterality of the pain at onset, the unilaterality of the pain throughout the attack and the locations of the maximal pain intensity with semi-structured interview. The definition of response was a $\geq$75% reduction in monthly headache days (MHD) in the third month after treatment with a CGRPmAb compared to the month prior to treatment begin. Non-response was defined as $\leq$25% reduction in MHD.
Results: Among 321 patients, we identified 146 responder and 25 non-responders. Responders reported more often unilateral pain at onset (responders n = 86/146, 58.9% vs. non-responders n = 9/25, 36% p = 0.03). However, strict (90% or more of the time) unilaterality of established headaches were not different between the groups (responders n = 33/146, 22.6% vs. non-responders n = 5/25, 20% p = 0.77). The distribution of pain locations (anterior vs. posterior) of maximal intensity was not different between the groups (responders n = 79/146, 54.1.% vs. non-responders n = 13/25, 52% p = 0.12).
Conclusions: The chance of good outcome to CGRPmAbs may be related not to strictly unilateral location of the pain but to the unilaterality of the pain at onset. A detailed history of the evolution of the pain locations may help to achieve a more personized treatment in patients with migraine.
Disclosure of Interest: None Declared

IHC23-PO-247

Preclinical Assessment of MEDI0618, A Novel PAR2 Monoclonal Antibody for Treatment of CGRP-dependent and CGRP-independent Migraine-like Pain

Caroline Machado Kopruszinski[1], John Linley[2], Edita Navratilova[1], Guy Meno-Tetang[2], Tharani Chessell[2], Iain Chessell[2] and Frank Porreca[1]

[1]*University of Arizona, Tucson, USA*
[2]*Neuroscience, BioPharmaceutical R&D, AstraZeneca, Cambridge, United Kingdom*

Objective: Migraine pain is thought to require activation of meningeal nociceptors. PAR2 is a 7-transmembrane GPCR that is expressed in neurons as well as in mast cells (MC) and is activated by protease cleavage of a tethered ligand cleaved from its own extracellular domain. Increased migraine attacks are reported during seasons with high levels of airborne allergens suggesting MC involvement. Experimentally-induced MC degranulation, tryptases or PAR2 activators produce migraine-like pain in rodents. These observations suggest that PAR2 may be a novel target for migraine prevention. In spite of major pharmaceutical efforts, however, the discovery of novel potent antagonists to target PAR2 has been challenging. We have discovered and characterized MEDI0618, as a novel, fully humanized PAR2 monoclonal antibody with picomolar affinity and a PK profile in non-human primates that suggests suitability of clinical development.
The potential efficacy of MEDI0618 was explored in preclinical models of migraine-like pain. MEDI0618 was administered prior to inducing migraine-like pain with systemic nitroglycerin (NTG), or with supradural compound 48/80 (MC degranulator) or inflammatory mediator cocktail (IM). The effects of supradural IM were evaluated in the absence or presence of olcegepant (CGRP antagonist) in animals receiving prior treatment with MEDI0618. MEDI0618 was also evaluated against migraine-like pain induced by inhalational umbellulone (UMB), a TRPA1 agonist, in animals primed with restraint stress (RS).
Methods: All experiments were conducted in female C57BL/6J mice (8 weeks old). Periorbital sensitivity was determined by measuring the frequency of behavioral response to probing with von Frey filaments with increased responses interpreted as cutaneous allodynia (CA). MEDI0618 was administered subcutaneous (s.c.) 24 hr prior to (a) induction of latent sensitization by priming with three daily episodes of RS followed by challenge with a subthreshold exposure to UMB on day 16 after RS; (b) systemic administration of NTG; (c) supradural compound 48/80 or (d) IM. Olcegepant was given 30 min prior to supradural IM and in other cohorts, animals received a prior treatment with s.c. MEDI0618 (–24 hr).
Results: Systemic NTG or supradural administration of compound 48/80 or IM produced CA that were fully prevented by MEDI0618 pretreatment. Olcegepant only partially reduced IM-induced CA. In contrast, MEDI0618 fully blocked IM-induced CA regardless of whether the animals were treated with olcegepant. UMB elicited CA only in animals previously primed with RS and this effect was prevented by MEDI0618 pretreatment.
Conclusion: We report the preclinical evaluation of MEDI0618 as a novel, PAR2 monoclonal antibody for potential application in migraine prevention. Blockade of PAR2 receptors prevented periorbital allodynia in all preclinical migraine models evaluated. Additionally, while a small molecule CGRP receptor antagonist only partially blocked CA elicited by dural IM, MEDI0618 was fully effective, suggesting the potential for efficacy in CGRP-receptor independent migraine mechanisms. MEDI0618 may therefore represent a novel therapy for migraine prevention possibly with a broad efficacy profile that may capture both CGRP and non-CGRP mechanisms that can promote migraine pain.
Disclosure of Interest: Caroline M. Kopruszinski and Edita Navratilova declare that they have no personal, financial, or relational conflicts of interest with this abstract. John Linley, Guy Meno-Tetang, Tharani Chessell and Iain Chessell are employees of AstraZeneca. Frank Porreca has served as a consultant or received research funding from Voyager, SiteOne Therapeutics, Nektar, Amgen, Acadia, Blackthorn, Teva, Eli Lilly, Hoba, Allergan, Ipsen, and Proximagen and has served as a founder of Catalina Pharma, Scientific Advisory Board Regulonix, and Condor Pharma. RK is a stakeholder in Regulonix Holding Inc.

IHC23-PO-248

Protective Effect of Naringin Against Nitroglycerin-Induced Migraine Headaches via Downregulating Oxidative Stress and Inflammation

Ekta Yadav

SHUATS, Allahabad, India

Objective: Naringin (NN) is a natural flavanone glycoside distributed in citrus fruits and grapes having strong antioxidant and anti-inflammatory activity. Migraine is a recurrent neurovascular pain disorder that impacts not only health but also social and economic status of patients. Still, there is a lack of targeted, effective and well-tolerated treatment. Therefore, natural medicinal

formulations or bioactive phytoconstituents offer great potential to target migraine and it can be utilized as a novel therapeutic agent. The current study was envisaged to explore the propensity of NN against migraine pain induced by nitroglycerin (NG, 10 mg/kg, i.p.) in rat model.
Methods: NN was given for seven days consecutively by oral gavage to the rats at two dose levels and various behavioral parameters related to pain were determined after injecting NG. At the end of the experimentation, animals were sacrificed and subjected to perform brain immunohistochemical study.
Results: Various parameters such as walking status (locomotor behavior), sniffing and rearing time along with frequency (exploratory behavior) and total time spent by rats in light compartments were alleviated in NG alone group as compared to control group. In addition, an elevation in calcitonin gene-related peptide, C-Fos cell release stimulation in the trigeminal caudal nucleus and decreased level of antioxidant enzymes were also observed in NG alone group indicating the onset of the migraine-like condition. Whereas, animals administered with NN showed less severe status of behavioral as well as pathological measures as compared to NG alone group in a dose-dependent manner.
Conclusion: NN improved NG-triggered migraine pain in a rat model via modulating oxidative stress and inflammation level. Therefore, NN may be utilized as a potent agent to treat migraine-related pain and its associated behaviors.

IHC23-PO-249

The era of new migraine prophylaxes: the vascular safety profile of mAbs anti CGRP in the Elderly.

Giorgia Andrini[1], Davide Mascarella[1], Sabina Cevoli[2], Valentina Favoni[2] and Giulia Pierangeli[2]

[1]*University of Bologna, DIBINEM, Bologna, Italy*
[2]*Istituto delle scienze neurologiche, ISNB Bologna, Bologna, Italy*

Background and Objectives: The advent of monoclonal antibodies (mAbs) that specifically target CGRP (Calcitonin Gene Related Peptide) or its receptor have revolutionized both episodic (EM) and chronic migraine (CM) management, providing significant improvements over existing therapies with minimal side effects. Given the worldwide increase in life expectancy, older age migraine management is becoming a huge public health issue. Recent concerns have been raised on anti-CGRP mAbs potential effect on BP function, suggesting an association between hypertension and anti-CGRP mAbs. In this study we aimed to estimate the effects of anti-CGRP mAbs treatment on systolic (SBP) and diastolic Blood Pressure (DBP) in EM and CM patients $\geq$60 years of age.
Method: Multicenter, prospective analysis of all EM and CM patients aged $\geq$60 years who started a prophylaxis with Anti-CGRP mAbs. We evaluated systolic and diastolic BP at three (T3) and twelve (T12) months, and we assess the number of patients who started treatment with antihypertensive drugs during the follow-up period.
Results: 155 patients were included, 42.5% (66/155) had a known diagnosis of hypertension and 39.3% (61/155) were on ongoing antihypertensive therapy at baseline (T0). The mean SBP of the entire study population at baseline was 123.72 mmHg (95% CI), and the estimated fixed effects over time were +0.34 mmHg ($p = 0.897$) at three months, and no effect after twelve months. The mean DBP at T0 in the whole study population was 81.24 mmHg (95% CI, and the estimated fixed effects over time were +1.24 mmHg ($p = 0.490$) at T3, and no effect at T12. Mean changes in SBP and DBP across study visits were similar between erenumab, galcanezumab, fremanezumab groups, and no statistically significant estimated effect was observed. 10 out of 155 patients (6.54%) required an increase or initiation of anti-hypertensive therapy, of which 50% had a pre-existing diagnosis of hypertension and ongoing anti-hypertensive therapy that required an increase in dosage or addition of a new medication; at the 12-month blood pressure measurement, only 1 of the 10 patients had values above the normal range.
Conclusion: Selective blockade of calcitonin gene-related peptide or its receptor for migraine prevention in an over 60 population has a vascular safety profile over 12 weeks, with a lack of both statistically significant changes in systolic and diastolic BP, and significant dose increases in antihypertensive medications or initiation of new antihypertensive medication across study visits, providing evidence that mAbs anti CGRP did not have a significant impact on PB function. Further study of long-term safety of mAbs anti CGRP in elderly population is needed.
Disclosure of Interest: None Declared

IHC23-PO-250

Economic impact of stopping or reducing the injection frequency of botulinum toxin for chronic migraine treatment in Alberta, Canada.

Lawrence Richer[1], Khanh Vu[1], Karen Martins[1], Huong Luu[1], Phyong Uyen Nguyen[2], Kai On Wong[1], Alexis Guigue[2], Thiliane Rajapakse[1] and Scott Klarenbach[1]

[1]*University of Alberta, Edmonton, Canada*
[2]*University of Calgary, Calgary, Canada*

Background: While guidelines recommend OnabotulinumtoxinA (botulinum toxin) be administered every 3-months for chronic migraine (CM) treatment among adults, optimal treatment duration is not well known. Some jurisdictions outside Alberta recommend positive stopping criteria and/or inter-injection interval extension if symptom improvement criteria are met. Understanding healthcare resource use and costs in those who continue and stop/reduce treatment frequency in Alberta may be informative to decision-making.
Methods: A retrospective observational study using administrative data from Alberta, Canada (2012–2020) was performed. Adults who received $\geq$3 botulinum injections/year for CM (1-year pre-index) were grouped into those who continued this injection frequency (continued use) or received $\leq$2-injections (stopped/reduced use) over a 1-year post-index period. Healthcare resource and medication use were described; pre-post costs were assessed using generalized estimating equations.
Results: Among subjects who continued use (n = 3,336), pre-post healthcare resource and medication use, and costs were largely consistent. Among the stopped/reduced use cohort (n = 1,099), healthcare resource use, migraine medication use, and costs (total all-cause: adjusted cost ratio 0.86 [95% CI: 0.79, 0.99]; total migraine-related: 0.44 [0.40, 0.48]) were lower post- versus pre-index.
Conclusions: In a jurisdiction where patients and providers determined botulinum treatment decisions, most remained concordant with guideline-recommended injection frequency and had stable healthcare resource and medication use, and costs. Given the lower healthcare and medication use, and costs among those who stopped/reduced botulinum treatment, it is hypothesized that their CM symptoms were well controlled and that the decision to stop/reduce use may be in keeping with appropriate symptom management. Further studies are needed to inform optimal CM management.
Disclosure of Interest: Conflict of interest: The author (s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: KV, KM, HL, PUN, and SK are members of the Alberta Real World Evidence Consortium (KW and AG previous members), an academic entity that conducts research including investigator-initiated industry-funded studies. No other conflict of interest was declared. Source of Funding: This research study was funded by AbbVie to LR. The funders were given the opportunity to comment on the study design, analysis, interpretation of the data, and the abstract draft; however, all authors of this study had complete autonomy over the design and execution of the study, as well as the content and submission of the abstract.

IHC23-PO-251

Safety and tolerability of antiCGRP mAbs in real-life: a multicenter, prospective, observational study on 1635 migraine patients

Gabriella Egeo[1], Cinzia Aurilia[1], Bianca Orlando[1], Giulia Fiorentini[1,2], Paola Torelli[3], Cinzia Finocchi[4], Florindo d'Onofrio[5], Luigi d'Onofrio[6], Stefano Messina[7], Maurizio Zucco[8], Bruno Colombo[9], Angelo Ranieri[10], Antonio Salerno[11], Barbara Petolicchio[12], Alessandro Valenza[13], Steno Rinalduzzi[14], Francesco Zoroddu[15], Cecilia Camarda[16], Laura Borrello[17], Maria Albanese[18], Carlo Tomino[19], Stefania Proietti[20], Stefano Bonassi[2,21] and Piero Barbanti[1,2]

[1]*Headache and Pain Unit, IRCCS San Raffaele Roma, Rome, Italy*
[2]*San Raffaele University, Rome, Italy*
[3]*Neurology Unit, Department of Medicine and Surgery, Headache Center, University of Parma, Parma, Italy*
[4]*Neurology Unit, San Paolo Hospital, ASL 2 Savona, Savona, Italy*
[5]*Neurology Unit, San Giuseppe Moscati Hospital, Avellino, Avellino, Italy*
[6]*Campus Bio-Medico University Hospital, Rome, Rome, Italy*
[7]*Department of Neurology-Stroke Unit, Laboratory of Neuroscience, Istituto Auxologico Italiano, IRCCS, Milano, Milan, Italy*
[8]*Headache Center, Neurology Unit, San Camillo-Forlanini Hospital, Rome, Rome, Italy*
[9]*Headache Unit, Department of Neurology, Scientific Institute San Raffaele Hospital, Vita-Salute University, Milan, Milan, Italy*
[10]*Neurology Unit and Stroke-Unit, AORN A. Cardarelli, Napoli, Naple, Italy*
[11]*San Giovanni Addolorata Hospital, Rome, Rome, Italy*
[12]*Headache Center, Sandro Pertini Hospital, Rome, Rome, Italy*
[13]*Headache Center, UOC Neurology, Ospedale Belcolle, Viterbo, Italy, Viterbo, Italy*
[14]*Stroke Unit, S. Camillo de Lellis Hospital, Rieti, Rieti, Italy*
[15]*Pediatric Headache Center, Neurology Unit, University of Sassari, Sassari, Italy*
[16]*Department of Biomedicine, Neurosciences, and Advanced Diagnostics, University of Palermo, Palermo, Italy*
[17]*Headache Center, Hospital F. Spaziani Frosinone, Frosinone, Italy*
[18]*Neurology Unit, Headache Center, University Hospital of Rome "Tor Vergata", Rome, Rome, Italy*
[19]*IRCCS San Raffaele, Rome, Rome, Italy*
[20]*Clinical and Molecular Epidemiology, IRCCS San Raffaele Rome, Rome, Italy*
[21]*Clinical and Molecular Epidemiology, IRCCS San Raffaele Rome, Italy; Department of Human Sciences and Quality of Life Promotion, Rome, Italy*

Introduction: Monoclonal antibodies (mAbs) targeting the calcitonin gene-related peptide (CGRP) show a favorable efficacy/tolerability ratio. In randomized controlled trials (RCTs), treatment-emergent adverse events (TEAEs) occurred in 42%–55% of migraine patients with multiple prior therapeutic failures, while serious adverse events (SAEs) emerged very rarely (0.9%–2%).
We investigated safety and tolerability of anti-CGRP mAbs in a large population of migraine patients affected by high-frequency episodic migraine (HFEM: >8 days/month) or chronic migraine (CM).
Methods: Multicenter (n = 26), prospective, cohort, real-life study across 9 Italian regions. We enrolled all patients affected by HFEM or CM who had previously failed >3 preventive medications classes (according the rules of the Italian Medicines Agency) receiving >1 dose of erenumab (70 mg or 140 mg), galcanezumab (120 mg) or fremanezumab (225 mg monthly or 675 mg quarterly) from 01/02/2019 to 31/03/2023. Patients were asked to report the occurrence of any adverse event throughout the study using a paper-pencil diary.
Results: A total of 1635 patients had received >1 dose of erenumab (928 pts; 56.8%), fremanezumab (479 pts; 28.7%), galcanezumab (237; 14.5%). Sixty-three patients (3.8%) reported at least 1 TEAE. The most common were constipation (65%), injection site erythema (15.9%) and back pain (15.9%), followed by alopecia (4.7%), dyspepsia (3.2%), asthenia (3.2%), nausea (3.2%), amenorrhea (1.6%), and paresthesias (1.6%). TEAEs occurred more frequently in patients treated with erenumab (73%) compared to those receiving galcanezumab (15%) or fremanezumab (12%). SAEs events occurred in 3 patients (0.18%) treated with erenumab who discontinued the treatment. Two individuals affected by CM with medication overuse manifested non-ST segment elevation myocardial infarction which was considered unrelated to the treatments. A 58-year-old woman presented with an acute coronary syndrome (7 days after the fifth administration of erenumab 70 mg) while learning that her apartment was on fire. A 54-year-old, man with a positive family history for cardiovascular disorders, overweight, affected by hypercholesterolemia and hypertension, developed a myocardial infarction 10 days after the seventh administration of erenumab 140 mg. A 58-year-old man suffering from CM and medication overuse developed a treatment-related paralytic ileus 20 days after the injection of the first erenumab 70 mg dose.
Conclusion: AntiCGRP mAbs are overall safe and well tolerated in real-life in migraine patient with multiple therapeutic failures. The occurrence of TEAEs is lower than that reported in RCT. TEAEs are more common in patients treated with erenumab.
Disclosure of Interest: Gabriella Egeo received travel grants and honoraria from Eli-Lilly, Novartis, New Penta and Ecupharma Cinzia Aurilia received travel grants from FB-Health, Lusofarmaco, Almirall, Eli-Lilly Novartis and Teva; Giulia Fiorentini has no disclosures to declare. Bianca Orlando has no disclosures to declare. Paola Torelli received travel grants and honoraria from Allergan, Teva, Eli-Lilly and Novartis. Cinzia Finocchi received grants and honoraria from Novartis, Eli Lilly, TEVA, AIM group Florindo d'Onofrio received travel grant, honoraria as a speaker or for partecipating in advisory boards from Novartis, Teva, Neopharmed Gentili, Qbgroup srl, K link srl and Eli-Lilly Luigi d'Onofrio has no disclosures to declare. Stefano Messina has no disclosures to declare. Maurizio Zucco received travel grants and honoraria from Novartis. Bruno Colombo has received congress fee reimbursements from Teva and Novartis. Angelo Ranieri received speaker honoraria from Teva, Lilly. Antonio Salerno has no disclosures to declare. Barbara Petolicchio has no disclosures to declare. Alessandro Valenza has no disclosures to declare. Steno Rinalduzzi has no disclosures to declare. Francesco Zoreddu has no disclosures to declare Cecilia Camarda has no disclosures to declare. Laura Borrello received travel grants and honoraria from Eli-Lilly. Maria Albanese received travel grants and honoraria from Novartis, Teva, Eli-Lilly and Lundbeck. C. Tomino has no disclosures to declare. S. Proietti has no disclosures to declare. S. Bonassi has no disclosures to declare. Piero Barbanti received travel grants, honoraria for advisory boards, speaker panels or clinical investigation studies from Alder, Allergan, Angelini, Assosalute, Bayer, ElectroCore, Eli-Lilly, GSK, Lundbeck, Lusofarmaco, 1MED, MSD, New Penta, Noema Pharma, Novartis, Stx-Med, Teva, Visufarma, Zambon.

IHC23-PO-252

Real-life study of Eptinezumab in Asian Patients with migraine (REAP)

Yi Jing Zhao[1], Jonathan J.Y. Ong[2,3], Marianne Sheila[4], Keira Herr[4], Rohini Bose[4] and Yasmin Binte Idu Jion[1]

[1]*Department of Neurology, National Neuroscience Institute, Singapore, Singapore*
[2]*Division of Neurology, Department of Medicine, National University Hospital, Singapore, Singapore*
[3]*Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore*
[4]*Lundbeck Singapore, Singapore, Singapore*

Objective: To evaluate the real-world effectiveness of eptinezumab for migraine prevention in Asian patients (pts).
Methods: Observational, prospective multisite cohort study of adults with migraine (ICHD-3 2018 criteria) in

Singapore who were prescribed eptinezumab (100 mg intravenous infusion at baseline [BL] and at month 3 [M3]) and followed until month 6 [M6]. Primary endpoints: change from BL in monthly migraine days (MMDs) at M3 and M6. Secondary endpoints: responder rate (≥50% MMD reduction), migraine-related disability score (MIDAS) and acute medication use (days/month). Linear mixed models were used to analyse change from BL in MMDs, MIDAS, and acute medication use.

Results: Enrolled pts (completed = 29/30 [96.7%]) had a mean (SD) of 3.4 (2.9) prior medication treatment failures; 26/30 (86.7%) failed previous oral preventives and 21/30 (70.0%) received eptinezumab after failing ≥1 other calcitonin gene-related peptide monoclonal antibody treatments. Mean (SD) MMDs were 16.1 (7.1) at BL, 11.9 (7.0) at M3 and 11.4 (6.6) at M6. Mean MMD was significantly reduced from BL by 4.3 days (95% CI 2.1–6.4; p = 0.0002) at M3 and 4.9 days (95% CI 2.1–7.7; p = 0.0008) at M6. At M3 and M6, 6/30 (20.0%) and 8/29 (27.6%) pts were ≥50% responders. MIDAS score (BL: mean (SD) 62.6 (54.7)) was reduced by 14.4 (95% CI –2.6–31.4; p = 0.0943) at M3 and 24.6 (95% CI 2.8–46.4; p = 0.0275) at M6. Acute medication use (BL: mean (SD) 14.6 (8.1) days/month) was reduced by 3.3 days/month (95% CI 1.0–5.6; p = 0.0065) at M3 and 4.7 days/month (95% CI 1.7–7.7; p = 0.0029) at M6. Treatment-emergent adverse events (TEAEs) were reported in 16/30 (53.5%) pts, mostly mild/moderate in severity. No serious TEAEs led to treatment discontinuation.

Conclusion: In this small real-world study of hard-to-treat Asian pts with migraine, quarterly eptinezumab administration led to rapid and sustained reductions in MMDs, migraine-related disability, and acute medication use days over 6 months. The safety/tolerability of eptinezumab was similar to global studies, with no unexpected/serious safety issues.

Disclosure of Interest: Jonathan J.Y. Ong has served on advisory boards and received speaker honoraria from Lundbeck (Singapore), Pfizer (Singapore), AbbVie (Singapore), DKSH (Singapore), Teva (Singapore), and Novartis (Singapore). Yasmin Binte Idu Jion has served on advisory boards and received speaker honoraria from Lundbeck (Singapore), AbbVie (Singapore), DKSH (Singapore), Teva (Singapore), and Novartis (Singapore). Yi Jing Zhao has served on advisory boards and received speaker honoraria from Lundbeck (Singapore, Pfizer (Singapore), DKSH (Singapore, Teva (Singapore) and Novartis (Singapore). Keira Herr was an employee of Lundbeck Singapore at the time of the study. Marianne Sheila and Rohini Bose are employees of Lundbeck Singapore.

IHC23-PO-253

Vitamin D for chronic migraine: an evidence-based case report

Irma Savitri Madjid[1], Ramdinal Aviesena Zairinal[2], Henry Riyanto Sofyan[1] and Tiara Aninditha[1]

[1]*Department of Neurology, Faculty of Medicine, Universitas Indonesia/Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia*
[2]*Department of Neurology, Faculty of Medicine, Universitas Indonesia/Universitas Indonesia Hospital, Depok, Indonesia*

Background and clinical scenario: A 37-year-old man came to our neurology outpatient clinic with a headache that occurred almost everyday for the past 5 years, with headache phenotype consistent with chronic migraine. As a physician, we were interested whether there were any supplements, alongside prophylactic and abortive headache therapy, that could be given to the patient to alleviate the symptoms. Vitamin D has shown beneficial evidence in many neurological conditions. We aimed to synthesize information from previous systematic reviews to answer our clinical question of whether vitamin D supplementation on top of standard therapy, compared to standard therapy alone, was superior in decreasing frequency, intensity, duration of migraine attack in patients with chronic migraine.

Methods: We performed electronic search using vitamin D and migraine as keywords in PubMed, Cochrane, and Prospero systematic review database. We included meta-analyses and systematic reviews of interventions with adults suffering from migraine as the population, defined according to the International Classification of Headache Disorders-3 (ICHD-3) guidelines, without any limitations on existing comorbidities. Intervention of our interest was vitamin D of any dose, with or without control group. We looked at the studies that analyzed differences in frequency, intensity, duration of migraine attack. After title and abstract selection, risk of bias was assessed using the Risk of Bias in Systematic Reviews (ROBIS) tool by two independent reviewers, with third-reviewer consultation for indisputable matters.

Results: We found 2 systematic reviews that matched our clinical question, looking at vitamin D as the sole intervention. All systematic reviews only include interventional studies, with placebo or usual care as controls. Both studies showed that vitamin D was beneficial as supplemental pharmacotherapy for migraine, in terms of reducing headache days. All studies showed low risk of bias.

Discussion: In all systematic reviews, the duration of migraine history was not clearly specified, therefore not all participants might fit the definition of chronic migraine. The dose of vitamin D of trials included in each systematic

review also varied. Outcome measures were similar (headache days, severity, duration). Considering good validity (low risk of bias) of the assessed studies, we recommended giving vitamin D supplementation as a supportive treatment to mainly reduce headache days, alongside intensity, and duration of migraine attack.
Disclosure of Interest: None Declared

IHC23-PO-254

Effectiveness of Galcanezumab on sleep, migraine and multidimensional patient-reperted outcome measures: A real-world experience in Turkish patients with episodic migraine and chronic migraine

Elif Ilgaz Aydinlar, Tuba Erdogan Soyukibar and Pinar Yalinay Dikmen

Acibadem University School of Medicine, Department of Neurology, Istanbul, Turkey

Objective: This real-word study aimed to investigate the impact of galcanezumab on migraine outcome, sleep and multidimensional patient-reported outcomes measures (PROMs) in patients with episodic migraine (EM) and chronic migraine (CM).
Methods: A total of 54 patients (mean $\pm$ SD age: 38.3 $\pm$ 10.1 years; 90.7% were female) diagnosed with EM ($n = 24$) or CM ($n = 30$) who received galcanezumab injection series over a 3-month period were included in this single-center real-word prospective cohort study. Galcanezumab was administered at a loading dose (240 mg) at baseline visit, and then at 120 mg dose on a monthly basis during 1st to 3rd month visits. Migraine outcome was evaluated based on monthly headache days (MHDs), monthly migraine days (MMDs) and headache severity. The sleep was assessed by Pittsburgh Sleep Quality Index (PSQI), PROMs included Migraine Disability Assessment Scale (MIDAS), Headache Impact Test-6 (HIT-6), Allodynia Symptom Checklist (ASC-12), SF-36 Health-related Quality of Life (HRQoL), Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI).
Results: From baseline to 1st, 2nd and 3rd months, galcanezumab significantly improved median (IQR) MHDs, MMDs, headache severity ($p < 0.001$). Total PSQI scores were significantly decreased from baseline to 3rd month in subgroups of patients with low anxiety at baseline ($p = 0.002$) and none/minimal depression ($p = 0.003$) at baseline. Total PSQI score ($p < 0.001$), sleep latency ($p = 0.018$), sleep disturbances ($p = 0.015$) and daytime dysfunction ($p = 0.003$) in the overall population were also significantly decreased. PROMs were significantly improved from baseline to 1st, 2nd and 3rd months, including MIDAS ($p < 0.001$), HIT-6 ($p < 0.001$ for each), ACS-12 ($p = 0.005$, $p = 0.017$ and $p = 0.002$), BAI ($p < 0.001$ for each), BDI ($p = 0.048$, $p < 0.001$ and $p < 0.001$) and SF-36 HRQoL (p ranged 0.012 to <0.001).
Conclusion: Galcanezumab seems to be a promising and effective agent for migraine prophylaxis in real life setting of CM or EM, enabling rapid-onset improvements in migraine outcome, sleep problems especially in patients without comorbid depression and/or anxiety, and in multidimensional PROMs including HIT-6, MIDAS, MBSs, allodynia, HRQoL and negative emotional states.
Disclosure of Interest: Lilly has supported only the medical writing/statistical analysis of this study without being involved in any steps of its development (conception and design, analysis or interpretation of the results etc).

IHC23-PO-255

Fremanezumab Effectiveness and Tolerability in Clinical Routine: Interim Real-World-Data of the Observational FINESSE Study

Andreas Straube[1], Gregor Broessner[2], Charly Gaul[3], Xenia Hamann[4], Torsten Kraya[5,6] and Lars Neeb[7,8]

[1]*University Hospital LMU Munich, Department of Neurology, Munich, Germany*
[2]*Innsbruck Medical University, Department of Neurology, Innsbruck, Austria*
[3]*Headache Center Frankfurt, Frankfurt am Main, Germany*
[4]*Teva GmbH, Ulm, Germany*
[5]*Hospital Sankt Georg Leipzig gGmbH, Department of Neurology, Leipzig, Germany*
[6]*Headache Center Halle, Department of Neurology, University Hospital, Halle, Germany*
[7]*Helios Global Health, Berlin, Germany*
[8]*Charité Universitätsmedizin Berlin, Department of Neurology, Berlin, Germany*

Objective: To evaluate effectiveness and tolerability of fremanezumab administered in migraine patients as part of their routine disease management.
Methods: FINESSE is an ongoing prospective, non-interventional study in adults with episodic or chronic migraine (EM, CM). Observation period: 24 months. Primary endpoint: proportion of patients reaching $\geq$50% reduction in average number of monthly migraine days (MMD) during the 6-month period after the first dose of fremanezumab. Further measures: monthly average number of migraine days, MIDAS (Migraine Disability Assessment), HIT-6 (6-Item Headache Impact Test), acute medication use. Adverse events as reported in routine clinical practice.
Results: Of 826 patients (intention-to-treat analysis), 44 (53.8%) achieved a MMD reduction of $\geq$50% over

6 months [EM (N = 277): 58.4%, CM (N = 167): 47.4%)]. Number of MMD: 12.6 (Baseline, N = 926), 5.3 (Month 6, N = 712), 5.0 (Month 12, N = 484). MIDAS: 75.2 (Baseline, N = 545), 32.0 (Month 6, N = 500), 27.3 (Month 12, N = 296), HIT-6: 65.9 (Baseline, N = 581), 57.2 (Month 6, N = 510), 57.0 (Month 12, N = 303). Days with acute medication use: 9.6 (Baseline, N = 901), 3.7 (Month 6, N = 712), 3.7 (Month 12, N = 484). Of 1076 patients (safety analysis), 523 (48.6%) reported any adverse event. Injection site reactions: 186 (17.3%), COVID-19: 170 (15.8%), drug ineffective: 130 (12.1%), constipation: 31 (2.9%).

Conclusion: 53.8% of patients achieved the primary endpoint. Current results of the FINESSE study substantiate continuous MMD reduction, and sustained decrease in disability and acute medication use. Real-world-data on tolerability are in line with the expected favourable safety profile of fremanezumab demonstrated in the pivotal studies.

Disclosure of Interest: A. Straube is or was member of the following advisory boards: Novartis, Lilly, Sanofi, Allergan, TEVA, and speaker or member of speaker boards on behalf of Novartis, Lilly, Sanofi, Allergan, TEVA. He acted as consultant for Sanofi and TEVA, received grant support for research or education from Novartis and acted as an editorial board member for Lilly, Sanofi and Novartis. G. Broessner was or is member of the following advisory boards: Novartis, Lilly, TEVA, Grünenthal, and speaker or member of following speakers boards: Novartis, Lilly, TEVA, Grünenthal; Consultant: Novartis, Lilly, TEVA, Grünenthal; he received grant support for research or education from TEVA. C. Gaul is or was member of the following advisory boards: Abbvie, Lilly, Novartis Pharma, Hormosan Pharma, Sanofi-Aventis, Perfood, and TEVA, and speaker or member of the following speaker boards: Abbvie, Lilly, Novartis Pharma, Hormosan Pharma, Grünenthal, Sanofi-Aventis, Reckitt-Benckiser and TEVA. He acted as consultant for Weber & Weber, Lundbeck, and Perfood, and served in the following editorial boards: Acta Neurologica Scandinavia, Frontiers in Neurology, and Medizinischer Sachverständiger; Author royalties: Novartis Pharma; furthermore, he is honorary secretary of the German Migraine and Headache Society. X. Hamann is employee of TEVA GmbH. T. Kraya is or was member of the following advisory boards: Allergan, and speaker or member of the following speaker boards: Allergan, TEVA, Lilly, Hormosan. L. Neeb was member of the following advisory boards: TEVA, Lilly Novartis and Hormosan and speaker or member of the following speakers' boards: Lilly, TEVA, Novartis, Abbvie and Hormosan Pharma He received grant support for research from TEVA and Lilly. He served in the editorial boards of Journal of Headache and Pain and Frontiers in Neurology.

IHC23-PO-256

Real-life Experiences with Galcanezumab disclosed New Predictors for Response

Pinar Yalinay Dikmen[1], Betul Baykan[2], Derya Uluduz[3], Aynur Ozge[4], Elif Ilgaz Aydinlar[1], Burcu Polat[5], Necdet Karlı[6], Nermin Tepe[7], Nese Celebisoy[8], Hayal Ergin Toktas[9], Buket Niflioglu[10], Rahsan Karaci[11], Fusun Mayda Domac[11], Ezgi Uluduz[12], Tuba Erdogan Soyukibar[1], Nevra Oksuz[4] and Mustafa Ertas[13]

[1]*Acibadem University School of Medicine, Department of Neurology, Istanbul, Turkey*
[2]*EMAR Medical Center, Istanbul, Turkey*
[3]*Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey*
[4]*Mersin University, Faculty of Medicine, Mersin, Turkey*
[5]*Istanbul Medipol University, Istanbul, Turkey*
[6]*Bursa Uludag University, Faculty of Medicine, Bursa, Turkey*
[7]*Balikesir University, Faculty of Medicine, Balikesir, Turkey*
[8]*Ege University, Faculty of Medicine, Izmir, Turkey*
[9]*Icerenkoy Bayindir Hospital, Istanbul, Turkey*
[10]*Private Practice, Istanbul, Turkey*
[11]*UHS, Erenkoy Mental and Nervous diseases Training and Research Hospital, Istanbul, Turkey*
[12]*Koc University Medical School, Istanbul, Turkey*
[13]*Istanbul University, Istanbul Medical Faculty, Istanbul, Turkey*

Objective: This study aimed to investigate the efficacy, effectiveness, and safety of Galcanezumab in treating migraine in real-life setting, as well as identify predictors of treatment response.

Methods: We recruited 461 patients with migraine (80.9% females, 50.3% episodic form) in Turkey. Demographics, clinical features of migraine and Galcanezumab treatment experiences were recorded through a Google form after an interview.

Results: The mean age was 42.8(10.6; range = 18–77 years) and mean duration of migraine was 18.9(10.7) years. In our cohort, 88.9% (n = 410) reported that the Galcanezumab treatment was beneficial for them. The average time to benefit from the medication was 1.85 (2.2) months and average duration of treatment discontinuation was 6.6(3.8) months.

With Galcanezumab treatment, 71.2% of patients experienced a decrease in headache frequency, 68% reported a decrease in headache severity, and 68.9% experienced a decrease in analgesic use. The mean number of monthly headache days (MHD) before treatment was 14.7(8.1), while the number of MHD in the last month was reported as 4.8(6.0).

Treatment discontinuation occurred in 128 patients, with 8.9% (n = 41) discontinuing due to ineffectiveness,

1.7% (n = 8) discontinuing due to side effects, and the majority (17.1%) discontinuing due to economic reasons. Among these latter patients, 4.3% resumed treatment. The most common side effects were constipation (5.2%) and injection site reactions (3.9%).
The most bothersome symptoms during an attack were reported as photophobia (38.2%) and nausea (23.0%). After treatment, photophobia improved by 50–100% in 56.6% (n = 261) of patients, and nausea improved in 62.7% (n = 289). The rates of benefit from Galcanezumab were reported as 50–74% in 125 of patients, 75–99% in 209 patients, and 100% in 64 (13.9%) of patients. 59.1% reported improvement in their quality of life, and 35.4% reported improvement in their sleep quality.
Conclusion: Male gender, previous history with sleep disturbances, and ictal nausea were suggested as negative predictors of treatment response to Galcanezumab in patients with migraine in Turkey.
Disclosure of Interest: None Declared

IHC23-PO-257

Effect of CGRP antibodies on Headache associated vertigo

David Moreno Ajona[1,2], Stefania Maniataki[1], Fiona Greenwood[1], Konstantinos Christoforou[1] and Peter J Goadsby[1]

[1]NIHR King's Clinical Research Facility & SLaM Biomedical Research Centre, and Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom
[2]Neurology, Queen Elizabeth Hospital, London, United Kingdom

Objectives: Migraine with vestibular symptoms or vestibular migraine is a common disorder. Flunarizine is the only treatment with a positive randomised placebo-controlled study in this group of patients. A recent study including 28 patients suggested CGRP-pathway monoclonal antibodies could be useful in treating vertigo symptoms (1). Our objective was to establish if patients on CGRP monoclonal antibody treatment have change in vestibular symptoms, through a retrospective study.
Methods: An audit of consecutive patients attending the Headache Novel Therapies Clinic at King's College Hospital, London, UK, included patients on CGRP pathway monoclonal antibodies seen between January 2019 and March 2023. Patients fulfilling ICHD-3 criteria for vestibular migraine who were contacted as part of the Nurse Telephone Headache Clinic were asked about the effect of the treatment in headache and non-headache symptoms, including vertigo. To address the efficacy in terms of vertigo symptoms patients were asked if they had experienced an overall improvement or change in their vertigo using a scale of nil (0/3), mild (1/3), moderate (2/3) and significant (3/3), in line with previous work (1).
Descriptive statistics were used to stablish mean or median of scale variables and proportion of categoric variables. Chi-square test was used to stablish a potential relationship between the proportion of patients who noted a benefit in terms of headache and those who noted improvement of their vertigo. Subjective vertigo response was transformed to a dichotomous variable where any response (1-3/3) was considered positive (1) and nil was negative (0). A logistic regression model with a logit link function was subsequently conducted with vertigo efficacy as dependent variable and baseline headache and migraine days, duration of the headache disorder and presence of migraine associated symptoms, namely, photophobia, phonophobia, nausea and allodynia, as covariates.
Statistical significance was established at $P < 0.05$ (IBM SPSS Statistics for Mac, Version 28.0. Armonk, NY: IBM Corp).
Results: On analysis, 79 patients were identified as being on treatment with CGRP-antibodies and having headache with associated vertigo noted and 70 were contacted. Median age was 42 and 8 patients were male. Of note, allodynia was present in 52 patients (more than 65%). Twenty-one patients (30%) noted some benefit of their vertigo symptoms, 6/70 reported mild improvement, 4/70 reported moderate improvement and 11/70 reported significant improvement. All patients who experienced a response in terms of vertigo noted a subjective response in term of headaches, Chi-square 7.5 ($P = 0.006$). The logistic regression showed that baseline headache days was the only significant predictor of outcome (–0.414, $P = 0.041$).
Conclusion: There was a significant number of patients who noted a reduction in their vertigo symptoms alongside those that had a reduction in their head pain. CGRP pathway antibodies could be considered for the treatment of patients whose main complaint is vertigo although most patients did not experience a change in these symptoms. Placebo-controlled studies in this subgroup of patients addressing change in vertigo symptoms would clarify the utility of these drugs.
Disclosure of Interest: PJG reports, over the last 36 months, a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly and Company, Epalex, GlaxoSmithKline, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from

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IHC23-PO-258

A retrospective evaluation of the efficacy and tolerability of Galcanezumab

Mona Ghadri-Sani and Sarah Broadhurst

The Walton Centre NHS Trust, Liverpool, United Kingdom

Introduction: Galcanezumab (Emgality) is a Calcitonin Gene Related Peptide (CGRP) monoclonal antibody (MAB) approved by NICE for management of patients with migraine who have 4 or more headache days per month and have failed three previous preventative options. Galcanezumab binds to the CGRP ligand and prevents its binding to the receptor. At the Walton Centre we also recommend lifestyle to be addressed prior to starting this treatment.

Objective: To assess the effectiveness and tolerability of Galcanezumab in Migraine management at the Walton Centre NHS Trust.

Methods: Retrospective review of 72 Patient notes between May 2021 and May 2023 was undertaken. We looked at various parameters including patient demographics, number of previous preventatives, patient's self-reported headache diaries, side effects, discontinuation rates and reason.

Results: At the point of analysis, from 72 patients who were started on Galcanezumab, 57 (79%) remained on treatment (39 F/18 M) with a mean age of 46 years. Lifestyle measures had been addressed in all patients, including medication overuse. 9 patients had a secondary headache diagnosis.

Out of the 15 (11%) patients who discontinued treatment, 10 (67%) stopped due to inefficacy. 9 of these had previous Botox, 10 had at least one other CGRP MAB, 3 of which had tried both other CGRP MABs. 8 patients had tried both CGRP MABs and Botox. 2 patients had exacerbation of headaches, 1 had injection site reaction, 1 severe constipation and 1 anxiety, shortness of breath and chest pain. Out of these 15 patients, 5 went onto oral preventatives, 4 on Erenumab, 3 on Fremanezumab and 3 on Botox.

The mean number of preventatives tried prior to Galcanezumab was 7 (range: 3–21); 38% (22) of patients had previously had Botox and (40) 70% had another CGRP MAB. 6 (10.5%) patients had previously been treated with Botox, Fremanezumab and Erenumab, 13 had Botox and one other CGRP MAB and 3 had both other CGRP MABs. Overall, 31 patients had tried Fremanezumab, 23 Botox and 9 Erenumab.

We had no baseline diaries for 4 patients (7.7%) and no 6 month diaries for a further 3 patients (5.8%), 23 patients have been started on treatment in the last 3 months and so have not yet had their review to obtain 6 month diaries (44.2%).

In the 27 patients who remained on treatment and maintained headache diaries (from baseline to 6 months post treatment, 52%), there was 7 days mean reduction in severe headache days by 7 days/month and an increase of 3 days/month in clear days. The HIT6 reduced by an average of 9 per month.

Fig1: Demographic of patients currently on Galcanezumab 7 patients had a Trigmeminal Autonomic Cephalalgia (TAC) as well as migraine; 4 hemicrania patients showed and average increase of 1 clear day, 13 M/M days and reduction of 7 severe days and 7 points from their HIT-6 score. 3 cluster patients had increase of 9 clear days, 4 M/M days and reduction of 12 severe days. 1 IIH patients had an increase of 1 clear days, 21 M/M days and –22 severe days with 17 points reduction in the HIT-6.

Conclusion: Based on our data, Galcanezumab is well tolerated and effective in management of highly refractory migraine patients who have failed other CGRP MABs &/or Botox and those with co-existing TACs.

Abstract number: IHC23-PO-258
Fig 1

Diagnosis	No of Patients	Failed Botox	Failed CGRP MAB (name)	CGRP & Botox	Clear days	Mild/Moderate days	Severe days	HIT6
Episodic Migraine	3	1	0	0	No change	+8 days/month	−6 days/month	−17
Chronic Migraine	15	7	8 Ajovy 2 Aimovig	6	+6 days/month	+1 day/month	−5 days/month	−6
Chronic Migraine + TAC	7	3	5 Ajovy 1 Aimovig	3	+4 days/month	+4 days/month	−8 days/month	−3

IHC23-PO-259

Efficacy of Fremanezumab for Migraine Prevention in Asian Patients: Outcomes from Four Phase 3 Trials

Fumihiko Sakai[1], Miki Ishida[2], Byung-Kun Kim[3], Xiaoping Ning[4], Nobuyuki Koga[5], Verena Ramirez Campos[4], Lynda J. Krasenbaum[4] and Gabriela Kivelevitch[6]

[1]*Saitama International Headache Center, Saitama Neuropsychiatric Institute, Saitama, Japan*
[2]*Headquarters of Clinical Development, Otsuka Pharmaceutical Co., Ltd., Osaka, Japan*
[3]*Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Korea, Republic of*
[4]*Teva Branded Pharmaceutical Products R&D, Inc., West Chester, USA*
[5]*Medical Affairs, Otsuka Pharmaceutical Co., Ltd., Tokushima, Japan*
[6]*Teva Pharmaceuticals Industries Ltd., Tel Aviv, Israel*

Objective: To evaluate the efficacy of fremanezumab for migraine prevention in Asian patients with episodic (EM) or chronic migraine (CM).
Methods: Data from Asian patients from four different double-blind, randomized, Phase 3 trials are presented: HALO EM (NCT02629861) and CM (NCT02621931), and studies in Japanese (JP) and Korean (KOR) patients with EM (NCT03303092) and CM (NCT03303079). All patients received monthly (CM: 675/225/225 mg; EM: 225/225/225 mg) or quarterly (675 mg/placebo [PBO]/PBO) fremanezumab or matched PBO for 12 weeks. Endpoints: mean change (baseline [BL] to Week 12) in average monthly migraine days (MMD) and monthly headache days (MHD) of at least moderate severity, and the proportion of patients with ≥50% reduction in MMD or MHD (BL to Week 12).
Results: Compared with PBO, fremanezumab treatment resulted in reductions in MMD and MHD outcomes over 12 weeks in all trials (**Table**).
Conclusion: Data from four different Phase 3 trials evaluating the effectiveness of fremanezumab demonstrated that this treatment was consistently associated with reductions in MMD and MHD in Asian patients with CM and EM.

Table. Migraine Endpoints Over 12 Weeks

	Change from BL		≥50% reduction	
	MMD, mean (SE)	MHD, mean (SE)	MMD, %	MHD, %
HALO EM				
PBO, n = 25	−1.3 (1.36)	−0.1 (1.23)	12	24
Mthly, n = 25	−3.7 (1.34)	−2.0 (1.28)	40	32
Qtly, n = 27	−4.2 (1.43)	−2.4 (1.19)	41	41
HALO CM				
PBO, n = 40	−4.2 (1.13)	−2.8 (0.87)	15	8
Mthly, n = 41	−6.3 (1.14)	−5.9 (0.87)	28	29
Qtly, n = 40	−6.2 (1.11)	−5.7 (0.85)	27	30
JP&KOR EM				
PBO, n = 116	−1.0 (0.4)		11.2	
Mthly, n = 121	−4.0 (0.4)	NR	41.3	NR
Qtly, n = 117	−4.0 (0.4)		45.3	
JP&KOR CM				
PBO, n = 190	−2.8 (0.5)	−2.4 (0.4)		13.2
Mthly, n = 187	−4.9 (0.5)	−4.1 (0.4)	NR	29.0
Qtly, n = 189	−4.1 (0.5)	−4.1 (0.4)		29.1

N, number of patient included in the efficacy analysis; NR, not reported.

Disclosure of Interest: Nobuyuki Koga and Miki Ishida are full-time employees of Otsuka pharmaceutical Co., Ltd. Gabriela Kivelevitch is a Medical Director in Teva for International Markets.

IHC23-PO-260

Ultra-late response (>24 weeks) to antiCGRP mAbs: a multicenter, prospective, observational study

Cinzia Aurilia[1], Gabriella Egeo[1], Stefania Proietti[2], Sabina Cevoli[3], Bruno Colombo[4,5], Roberta Messina[4], Paola Torelli[6], Florindo D'Onofrio[7], Antonio Salerno[8], Marco Aguggia[9], Licia Grazzi[10], Michele Trimboli[11], Antonio Carnevale[12], Bruno Mercuri[8], Maurizio Zucco[13], Laura Di Clemente[13], Maria Albanese[14], Cinzia Finocchi[15], Francesco Bono[16], Fabio Frediani[17], Massimo Filippi[4,5], Valentina Favoni[3], Davide Bertuzzo[9], Paola Di Fiore[17], Bianca Orlando[1], Giulia Fiorentini[1], Stefano Bonassi[2,18] and Piero Barbanti[1,18]

[1]*Headache and Pain Unit, IRCCS San Raffaele Roma, Rome, Italy*
[2]*Clinical and Molecular Epidemiology, IRCCS San Raffaele Roma, Rome, Italy*
[3]*IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy*
[4]*Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy*
[5]*Vita-Salute San Raffaele University, Milan, Italy*
[6]*Unit of Neurology, Department of Medicine and Surgery, Headache Center, University of Parma, Parma, Italy*

[7]Headache Center Neurology Unit, San Giuseppe Moscati Hospital, Avellino, Italy
[8]Headache Center San Giovanni Addolorata Hospital, Rome, Italy
[9]Headache Center Cardinal Massaia, Asti, Italy
[10]Neuroalgology Unit, Headache Center Fondazione IRCCS Istituto Neurologico"Carlo Besta", Milan, Italy
[11]University Magna Graecia, Catanzaro, Italy
[12]Headache Center San Filippo Neri Hospital, Rome, Italy
[13]Headache Center San Camillo-Forlanini Hospital, Rome, Italy
[14]Regional Referral Headache Center Neurology Unit, University Hospital Tor Vergata, Rome, Italy
[15]Division of Neurology San Paolo Hospital ASL 2 Savonese, Savona, Italy
[16]Center for Headache and Intracranial Pressure Disorders, Neurology Unit, A.O.U. Mater Domini, Catanzaro, Italy
[17]Headache Center, ASST Santi Paolo Carlo, Milan, Italy
[18]San Raffaele University, Rome, Italy

Objective: Almost 60% of migraine patients treated with monoclonal antibodies (mAbs) targeting the calcitonin gene-related peptide (CGRP) pathway show a >50% reduction in monthly migraine days (MMD) at 12 weeks compared to baseline. However, approximately half of the patients not responding to anti-CGRP mAbs <12 weeks do respond <24 weeks (late responders). This study is aimed at verifying frequency and characteristics of patients responding to anti-CGRP mAbs only >24 weeks (ultra-late responders).

Methods: This is a multicenter (n = 16), prospective, observational, real-life study. We enrolled all consecutive adult patients affected by high-frequency episodic migraine (HFEM: >8 days/month) or chronic migraine (CM: >15 days/month), with >3 prior therapeutic failures and a MIDAS score >11 [according to the rules of the Italian Medicines Agency] treated with any anti-CGRP mAbs for >48 weeks. We defined ultra-late responders those patients achieving a >50% response only >24 weeks. Patients were asked to detail MMD during a 28-day run-in period and across the study using a paper-pencil headache diary.

Results: 572 migraine patients (HFEM/CM = 154/418; M/F = 140/432; mean age = 48.2 ± 10.6) completed >48 weeks of treatment with anti-CGRP mAbs (erenumab 527 pts; fremanezumab 40 pts; galcanezumab 5 pts). Three-hundred-forty-six out of 572 patients (60.5%) showed a >50% response rate <12 weeks (responders), while 86 (15%) not responding <12 weeks achieved a >50% response <24 weeks and were considered late responders. Ninety (64.3%) of the 140 subjects non-responding <24 weeks, became treatment responder <48 weeks: 42 of them (30%) responded at all subsequent time intervals (i.e., weeks 28, 32, 36, 40, 44, 48; ultra-late responders), whereas 48 patients (34.3%) only at some of them (fluctuating ultra-late responders). Fifty patients (35.7%) did not respond at any time interval <48 weeks. Ultra-late responders differed from responders for higher BMI (23.8 ± 4.2 vs 23.0 ± 3.1; p = 0.033), less common unilateral pain (46.7% vs 62.3%; p = 0.010), longer medication overuse duration (78.4 ± 110.7 vs 35.9 ± 81.7 months; p < 0.001), dopaminergic symptoms (78.9% vs 61.3%; p = 0.003), psychiatric comorbidities (44.4% vs 30.1%; p = 0.014), Numeric Rating Scale (7.3 ± 1.3 vs 7.7 ± 1.3; p = 0.017) and HIT-6 scores (63.7 ± 11.6 vs 66.9 ± 7.7; p = 0.002).

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Orlando, Giulia Fiorentini, Stefano Bonassi have no disclosures to declare.

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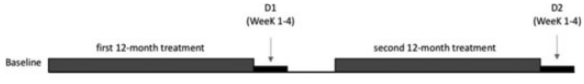
Effects of multiple treatment cycles with anti-CGRP monoclonal antibodies on migraine course: a multicenter, prospective, observational study

Cinzia Aurilia[1], Gabriella Egeo[1], Stefania Proietti[2], Paola Torelli[3], Sabina Cevoli[4], Florindo D'Onofrio[5], Antonio Carnevale[6], Bianca Orlando[1], Giulia Fiorentini[1], Stefano Bonassi[2,7] and Piero Barbanti[1,7]

[1]*Headache and Pain Unit, IRCCS San Raffaele Roma, Rome, Italy*
[2]*Clinical and Molecular Epidemiology, IRCCS San Raffaele Roma, Rome, Italy*
[3]*Unit of Neurology, Department of Medicine and Surgery, Headache Center, University of Parma, Italy, Parma, Italy*
[4]*IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy*
[5]*Headache Center Neurology Unit, San Giuseppe Moscati Hospital, Avellino, Italy*
[6]*Headache Center Neurology Unit, San Filippo Neri Hospital, Rome, Italy*
[7]*San Raffaele University, Rome, Italy*

Background: A single 12-month treatment cycle with monoclonal antibodies (mAbs) targeting the calcitonin gene-related peptide (CGRP) is not disease-modifying because cessation is associated with migraine worsening. In the present study, we evaluated the effect of a second 12-month treatment cycle with anti-CGRP mAbs on the course of high-frequency episodic migraine (HFEM: >8 days/month) or chronic migraine (CM: >15 days/month).

Methods: This is a multicenter (n = 5), prospective, real-life study on consecutive adult patients affected by HFEM or CM with >3 previous preventive medication failures, treated with two consecutive 12-month treatment cycles with anti-CGRP mAbs. The Italian Medicines Agency reduced the duration of the treatment discontinuation period from 3 to 1 month. Thus, we compared the changes in migraine features at D2 (first month of the second treatment discontinuation) with D1 (first month of first treatment cessation) as detailed below



Primary endpoint was the change in monthly migraine days (MMD) at D2 compared to D1. Secondary endpoints were variation in monthly headache days (MHD), monthly analgesic medications, Numerical Rating Scale (NRS) and HIT-6 scores at the same time intervals.

Results: Sixty-seven patients (HFEM/CM: 11/56; M/F: 19/48; mean age: 47.3 ± 11.6) completed two 12-month treatment cycles with anti-CGRP mAbs (erenumab: 58 pts; galcanezumab: 2 pts; fremanezumab: 7 pts). MMD, MHD, monthly analgesic intake, NRS and HIT-6 score were significantly reduced ($p < 0.001$) at 12 months (weeks 45–48), D1(weeks 1–4) and D2 (weeks 1–4) compared to baseline (table).

At D2, patients showed a significant reduction ($p < 0.001$) in MMD (10.1 ± 3.9 vs 12.6 ± 4.1), MHD (10.2 ± 4.0 vs 12.6 ± 4.1), monthly analgesic intake (9.7 ± 4.2 vs 12.0 ± 4.1), NRS score (6.0 ± 1.7 vs 6.6 ± 1.2), and HIT-6 score (57.6 ± 7.6 vs 60.8 ± 6.7) compared to D1.

	Baseline	12 months (weeks 45–48)	D1 (weeks 1–4)	D2 (week 1–4)
MMD	19.4 ± 6.1	5.6 ± 2.2	12.6 ± 4.1	10.1 ± 3.9*
MHD	20.3 ± 6.3	5.7 ± 2.4	12.6 ± 4.1	10.2 ± 4.0*
Monthly analgesic intake	20.5 ± 9.5	5.7 ± 4.2	12.0 ± 4.1	9.7 ± 4.2*
NRS	7.9 ± 0.9	4.3 ± 0.8	6.6 ± 1.2	6.0 ± 1.7*
HIT-6	68.2 ± 5.5	52.6 ± 8.8	60.8 ± 6.7	57.6 ± 7.6*

*$p > 0.001$.

Conclusion: The second anti-CGRP mAbs 12-month treatment cycle significantly reduces migraine MMD, MHD, monthly analgesic intake, NRS and HIT-6 score compared to the first 12-month treatment cycle, at least comparing the first months of treatment discontinuation. Prolonged or repetitive treatments with anti-CGRP mAbs could modify migraine course.

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IHC23-PO-262

CandeSpartan: Candesartan Spanish Response-prediction and Tolerability Study (NCT: 04138316)

Cristina Martínez-Badillo[1], Javier Camiña Muñiz[2], Ana Beatriz Gago-Veiga[3], Noemí Morollón Sánchez-Mateos[4], Vicente González-Quintanilla[5], Jesús Porta-Etessam[6], Andrea Recio García[1], Yésica González Osorio[1], Álvaro Sierra-Mencía[1], Ángel Luis Guerrero Peral[7] and David García-Azorín[7]

[1]*Headache Unit, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[2]*Hospital Universitari Son Espases, Palma de Mallorca, Spain*
[3]*Hospital Universitario de la Princesa, Madrid, Spain*
[4]*Hospital Universitario de la Santa Creu y Sant Pau, Barcelona, Spain*
[5]*Hospital Universitario Marques de Valdecilla, Santander, Spain*
[6]*Hospital Clínico San Carlos, Madrid, Spain*
[7]*Headache Unit, Department of Neurology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*

Objective: Candesartan has shown efficacy in the preventive treatment of migraine. To date, two randomized controlled trials that included n = 57 and n = 71 patients, among which 31,6% and 43,0% presented a 50% responder rate. In these studies, most patients had a low-frequency episodic migraine, with prior failure of 0–2 preventive drugs. Herein, we aim to report the effectiveness and tolerability of candesartan between weeks 8–12, compared to the baseline.
Methods: Observational, multicenter, prospective cohort study including adult patients with episodic and chronic migraine, according to The International Classification of Headache Disorders treated with candesartan. Patients were excluded if 1) they had previously failed to three or more preventive drugs, 2) received another drug with effectiveness as migraine preventive, 3) had history of another headache disorder, 4) had previously used candesartan, 5) had any severe disorder. The effectiveness was evaluated by estimating the 50%, 75% and 30% responder rates, calculated as percent reduction from baseline in the number of headache days, between weeks 8–12, compared with the baseline period. The frequency and type of treatment-emergent adverse events (TEAE) was evaluated.
Results: Eighty-six patients were included, 68 (79.1%) females, aged 40 [inter-quartile range (IQR) 26.1–49.9], 37 (43.0%) with chronic migraine, 48 (55.8%) with medication overuse headache and a median number of prior preventive treatments of 2 [IQR: 0.75–3]. At baseline patients had 14 [IQR: 10–24] headache days per month, 10 [IQR: 5–15] days of use of acute medication, and 5 [IQR: 0–8] days of triptan use. Between weeks 8–12, 29 (33.7%) patients had a ≥50% response, 15 (17.4%) patients had a ≥75% response, and 41 (47.7%) patients had a ≥30% response. The number of patients who experienced TEAE was 30 (34.9%), with lightheadedness (n = 17 (19.8%)), and asthenia (n = 14 (16.3%)) being the most frequently reported.
Conclusion: The present study provides Class II evidence on the effectiveness and tolerability of Candesartan in the treatment of migraine, including patients with chronic migraine, medication overuse and treatment-resistant migraine.
Disclosure of Interest: None Declared

IHC23-PO-263

Efficacy of Mindfulness added to treatment as usual in patients with Chronic Migraine and Medication Overuse Headache: a randomized clinical trial, early results.

Licia Grazzi[1], Domenico D'Amico[2], Danilo Antonio Montisano[1], Erika Guastafierro[3], Benedetta Del Corso[4] and Alberto Raggi[3]

[1]*Headache Center, Neuroalgology dpt – Neurological Institute Carlo Besta IRCCS Foundation, Milan, Italy*
[2]*Headache Center, Neuroalgology dpt – Neurological Institute Carlo Besta IRCCS Foundation, Milan, Japan*
[3]*Neurology, Public Health and Disability Unit – Neurological Institute Carlo Besta IRCCS Foundation, Milan, Italy*
[4]*Neuroscience Institute – National Research Council, Padova, Italy*

Objective: To assess the efficacy of a six-session mindfulness-based treatment added to treatment as usual (TaU) on headache frequency reduction and medication intake.
Methods: This is a phase-III single blind RCT single-center study, carried out at the third-level Italian headache center IRCCS "C.Besta". Patients were enrolled between November 2018 and December 2021, and followed-up for 12 months. 177 patients with Chronic Migraine and Medication Overuse Headache (CM and MOH) were randomized 1:1 to either TaU or mindfulness added to TaU (TaU+MIND). Exclusion criteria were: psychiatric comorbidities; pregnancy; secondary headaches; withdrawal from MOH at least twice in the previous two years; previous experience with mindfulness. TaU consisted of withdrawal from overused drugs, patients' education, and prescription of prophylaxis. Patients attending mindfulness sessions were taught to focus their attention on the present and enhance awareness of body sensations, which enabled tackling the pain-pill automatism, and were encouraged to engage in a 7–10 minute/day self-practice. The primary

endpoint was the achievement, at 12 months of ≥50% headache frequency reduction compared to baseline. Secondary endpoints included medication intake.
Results: Out or the 177 participants (median age 47.9 years [Q1-Q3: 40.1–54.2]; 19 [11.3%] males; median CM duration 14.6 years [Q1-Q3: 4.9–22.2]) 89 were randomized to TaU and 88 to TaU+MIND. Patients in the TaU+MIND group outperformed those in TaU for the primary endpoint, achievement of ≥50% headache frequency reduction (78.4% vs 48.3%; $p < 0.0001$). They also showed superiority in some secondary endpoints, namely headache frequency and medication intake.
Conclusion: These findings show that a six-week mindfulness-based treatment as add on to TaU is superior to TaU for the treatment of patient with CM and MOH.
Disclosure of Interest: None Declared

IHC23-PO-264

SYNCHRONIZE: Real-World Retrospective Safety Analysis in Patients with Chronic Migraine Treated with OnabotulinumtoxinA for More Than One Therapeutic Indication

Andrew Blumenfeld[1], Grace Forde[2], Kim Becker Ifantides[3], Ritu Singh[3], Katherine Sommer[3], Simona Battucci[4] and Christopher Rhyne[5]

[1]*Headache Center of Southern California, Carlsbad, USA*
[2]*Forde Headache and Pain Center, Lake Success, USA*
[3]*AbbVie, Irvine, USA*
[4]*AbbVie, Rome, Italy*
[5]*Diamond Headache Clinic, Chicago, USA*

Objective: Assess the real-world safety of onabotulinumtoxinA (onabotA) concomitant administration for the prevention of chronic migraine (CM) and ≥1 other therapeutic indications (TIs).
Methods: SYNCHRONIZE, a phase 4, retrospective chart review conducted at 10 US clinical sites, evaluated the safety of onabotA in adults treated for multiple TIs within a 3-month period. Data was collected for up to 24 months.
Results: Of 279 patients, in SYNCHRONIZE 183 (66%) received onabotA for prevention of CM and ≥1 concomitant TI (mean age 46.3 years; 83% female; 55% White). Commonly treated TIs in CM-treated patients were cervical dystonia (n = 121; 66%), oromandibular dystonia (n = 16; 9%), or blepharospasm (n = 9; 5%). Comorbidities included anxiety (n = 52; 28%), depression (n = 48; 26%), and insomnia (n = 28; 15%). 163 patients (89%) received treatment from the same provider for all TIs and most (n = 114; 62%) were treated for multiple TIs within 24 hours. 60 patients (33%) traveled ≥20 miles for onabotA treatment. Treatment-emergent adverse events (TEAEs) occurred in 23% (42/183) of patients within 6 months and were consistent up to 24 months (31%; 18/58). The most common TEAEs (neck pain [n = 12; 7%], migraine [n = 9; 5%], and headache [n = 9; 5%]) were related to the TIs treated and site of injection and were consistent with the onabotA label for approved TIs. The overall mean 3-month cumulative dose was 304U, 111 patients (61%) received ≥200 to <400U. There was no apparent trend between AEs and dosing intervals or cumulative 3-month dose. No patients were determined to have a lack of effect based on clinical objective measurement.
Conclusions: In this real-world study, onabotA demonstrated consistent safety, with no new signals in adults treated concomitantly for the prevention of CM and other TIs within a 3-month period. Most patients received injections within 24 hours. Some patients traveled a long distance to receive onabotA treatment, highlighting the potential burden of treating multiple TIs on separate days.
Disclosure of Interest: Andrew Blumenfeld has served on advisory boards for, consulted for, and/or been a speaker or contributing author for AbbVie, Alder, Amgen, Biohaven, Lilly, Lundbeck, Novartis, Pfizer, Teva, Theranica, and Zoscano. He has received grant support from AbbVie and Amgen. Kim Becker Ifantides, Ritu Singh, and Simona Battucci are employees of AbbVie and may hold AbbVie stock. Grace Forde has received personal compensation from AbbVie. Christopher Rhyne has no financial conflicts to disclose at this time.

IHC23-PO-265

Switching preventive migraine treatments during the COVID-19 pandemic: a 4-year Observational analysis

Luis Idrovo[1,2], Kanokrat Suwanlaong[1], Linford Fernandes[2], Fred Amores[2], Stefania Maniataki[1], Fiona Greenwood[1], Konstantinos Christoforou[1] and Peter J Goadsby[1]

[1]*NIHR King's Clinical Research Facility & SLaM Biomedical Research Centre, King's College Hospital and Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK, London, United Kingdom*
[2]*Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Objective: During COVID-19 access to onabotulinum toxin type A (BTX-A) for chronic migraine patients became restricted. Chronic migraine patients were switched to the novel anti-calcitonin gene-related peptide (CGRP) monoclonal antibody (MAB) therapies although they had been responding to BTX-A. Our objective was to analyse the outcome of switching to anti-CGRP

therapies and the effect of COVID-19 pandemic on our cohort of chronic migraine patients treated in BTX-A clinics.

Methods: We audited outcomes from consecutive chronic migraine patients referred from January 2019 until January 2023 to two headache services in the UK: Leeds Teaching Hospitals and King's College Hospital, London. We analysed demographic variables, tolerability, response rate of BTX-A, number of patients switched from BTX-A to anti-CGRP MABs before, during and post pandemic and reasons behind the decision to switch. We also analysed tolerability and response rates of patients on anti-CGRP therapy. We analysed the clinical characteristics of patients who switched back from anti-CGRP therapies to BTX-A.

Results: A total of 496 new patients with chronic migraine were referred to the BTX-A clinics during this period. There were 421 (84%) female, and the mean age was 45 ($\pm$13, SD) years. A total of 341 (69%) patients received BTX-A. In 2019, (pre-pandemic) 137 new patients had $\geq$ 2 BTX-A cycles by PREEMPT. Sixty-three (46%) had a $\geq$30% reduction of monthly headache days (MHD) and 51 (37%) stopped BTX-A: lack of efficacy 47 (92%), side effect 2 (4%), episodic migraine 2 (4%). There were 39 (29%) switched to anti-CGRP therapies from which 35 (89%) had at least a 30% reduction of HD and 4 (10%) stopped due to side effects in 1 and lack of efficacy in 3. During 2020–21 (pandemic), 132 new patients had BTX-A therapy, 57 (43)% had a $\geq$30% reduction of MHD and 81 stopped BTX-A: 72 (88%) due to lack of efficacy/personal preference, 2 (2%) side effects, and 7 (5%) due to clinic delays/pandemic. Sixty-six (50%) were switched to anti-CGRP therapies of which 45 (68%) had a $\geq$ 30% reduction of HD and 21 (32%) stopped anti-CGRP therapy: 16 due to lack of efficacy and 5 due to side effects. In 2022 (post pandemic), 72 had $\geq$ 2 BTX-A cycles. Fifty-three (73%) had a $\geq$30% reduction of MHD and 15 (21%) stopped BTX-A due to lack of efficacy. Fifteen were switched to anti-CGRP therapies of which 14 (93%) had a $\geq$30% reduction of MHD and 1 (7%) stopped due to side effects. During this 4-year period there were 121 (36%) that were switched from BTX-A to anti-CGRP MABs and 15 (4%) patients that switched back from Anti-CGRP to BTX-A. The clinical characteristics of those patients are shown in the table.

Conclusion: About one-third of our CM cohort referred to the BTX-A clinic switched to anti-CGRP therapy. During the COVID-19 pandemic more patients were switched to anti-CGRP treatment and most had a good response to the novel anti-CGRP therapies. Lack of response and not pandemic delays was the main reason for switching. Both treatments were well tolerated, and a small proportion of patients preferred to switch back from anti-CGRP treatment to BTX-A.

Disclosure of Interest: PJG reports, over the last 36 months, a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly and Company, Epalex, GlaxoSmithKline, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer, and for medicolegal advice in headache, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee. LI reports honoraria for consulting activities and/or serving on advisory boards from Allergan, Abbvie, Novartis and Eli Lilly. He also reports research support from Eli Lilly.

IHC23-PO-266

Anti-CGRP monoclonal antibodies: migraine prevention in patients with psychiatric comorbidities.

Francesca Schiano di Cola[1], Giulia Ceccardi[1], Salvatore Caratozzolo[2], Marco Bolchini[1], Michele Di Pasquale[1], Renata Rao[2] and Alessandro Padovani[1]

[1]*Università degli Studi di Brescia, Brescia, Italy*
[2]*ASST Spedali Civili Brescia, Brescia, Italy*

Objective: aim of the present study was to evaluate anti-CGRP monoclonal antibodies' (erenumab, galcanezumab and fremanezumab) efficacy in migraine patients affected by psychiatric comorbidities and compare their outcomes to those of patients not affected by psychiatric disorders.

Materials and Methods: this observational study was conducted at the Headache Centre – ASST Spedali Civili Brescia. All patients in monthly treatment with an anti-CGRP (either molecule or receptor) monoclonal antibody (mAb) with an available 6 months follow-up were included. Clinical and demographical characteristics were gathered at baseline (T0) for all patients, in particular the presence of psychiatric comorbidities. Data regarding efficacy outcome (monthly migraine days – MMDs, monthly headache days – MHDs, analgesics' consumption, pain intensity – Visual Analogue Scale score, migraine disability – MIDAS and HIT-6 scores) were collected following three (T3) and six (T6) months of treatment.

Results: one hundred and fifty patients were enrolled, of whom 129 female (86%). Mean age at T0 was 47.2 (10.1; range 23–67) years old, with a mean disease duration of 30.6 (10.1; range 5–59). Ninety-five patients (63.3%) had a

diagnosis of chronic migraine, and medication overuse was observed in 100 patients (66.7%). Seventy patients (46.7%) were on prophylactic treatment with galcanezumab, 49 patients (32.7%), with erenumab (all 140 mg), and 31 (20.7%) with fremanezumab. Thirty-six patients (24%) had a diagnosis of a psychiatric disorder (major depressive disorder, bipolar disorder type II, personality disorders and generalized anxiety disorder).

Among patients with psychiatric comorbidities a significant reduction, from baseline to T3 and T6, in terms of MHDs (20.6 ± 8.2 vs 10.3 ± 8.4 vs 11.7 ± 8.9; $p < 0.0001$), MMDs (13.4 ± 7.5 vs 2.7 ± 3.4 vs 5.02 ± 6.7; $p < 0.0001$), pain intensity (8 ± 2.1 vs 5.8 ± 2.2 vs 6.1 ± 1.6; $p < 0.0001$), analgesics consumption (24.8 ± 28.2 vs 8.17 ± 9.3 vs 10.19.39.4; $p = 0.01$), MIDAS (113.1 ± 75 vs 25 ± 23.8 vs 30.6 ± 31.1; $p < 0.0001$) and HIT6 scores (66.4 ± 6.3 vs 58.8 ± 9.7 vs 58.3 ± 12.2; $p < 0.001$).

Psychiatric comorbidities were significantly more frequent in the female population compared to males (27.1% vs 4.8%; $p = 0.02$). At baseline, psychiatric patients documented a higher frequency of MMDs compared to non-psychiatric patients (13.4 ± 7.5 vs 10.04 ± 6.1; $p = 0.007$) and a higher monthly analgesic consumption (24.8 ± 28.2 vs 17.2 ± 9.3; $p = 0.01$). Patients with psychiatric comorbidities also documented a higher migraine associated disability compared to non psychiatric patients, although not statistically significant (MIDAS score: 107.1 ± 75.2 vs 88.9 ± 66.1, $p = 0.14$; HIT-6 score: 66.06 ± 6.1 vs 64.5 ± 6.3, $p = 0.21$). Overall, at T3 72% of patients documented a $\geq$50% response – in terms of MHDs reduction compared to baseline, and 67.6% at T6.No significant differences at T3 were found, in migraine outcomes, in patients with psychiatric comorbidities versus those with none. At T6 psychiatric comorbidities were more frequent in non responders compared to those with a $\geq$30% response (52.8% vs 25.9%; $p = 0.003$). Moreover, a higher frequency of psychiatric comorbidities was found among patients who documented a 30–50% (25.9% vs 13.4%; $p = 0.01$) whereas their frequency was significantly lower when analyzing the 50–75% response group (16.7% vs 37.5%; $p = 0.01$). No differences were between super-responders (30.6% vs 36.6%; $p = 0.21$).

Conclusions: the present study on a real-world sample confirms the beneficial effect of anti-CGRP monoclonal antibodies. Their efficacy was high in all patients, including those with a psychiatric comorbidity, although these patients documented a lower response following six months of treatment. In particular, the present data documents a higher frequency of non- and partial- responders in patients with psychiatric comorbidities. Of notice, no differences were found in the $\geq$75% response group. Based on our data, we might conclude that the presence of a psychiatric comorbidity might affect response to anti-CGRP mAbs.

Further studies will have to confirm the present results in a larger patients cohort and with a longer follow-up.

IHC23-PO-267

Early clinical response in patients with migraine in treatment with anti-CGRP monoclonal antibodies: a possible "loading dose" effect?

Giulia Ceccardi, Francesca Schiano di Cola, Marco Bolchini, Michele Di Pasquale, Renata Rao and Alessandro Padovani

Neurology Unit and Headache Centre, Dipartimento di continuità di cura e fragilità, ASST Spedali Civili and Università degli studi di Brescia, Brescia, Italy

Objective: Aim of the present study was to evaluate the clinical response in terms of monthly headache days (MHDs) reduction following the first month of treatment (T1) in patients with migraine – episodic and chronic – in prophylactic treatment with anti-CGRP monoclononal antibodies. In particular, clinical outcome at T1 among the different anti-CGRP monoclonal antibodies was assessed.

Methods: This retrospective study was performed at the ASST Spedali Civili of Brescia, between January 2019 and November 2022. All patients had a diagnosis of migraine according to the International Classification of Headache Disorders III (ICHD-III), with a baseline frequency of at least 8 headache days per month. The primary endpoint was to evaluate the reduction of MHDs at T1 in all patients, regardless of the specific type of monoclonal antibody. A further analysis was conducted in order to compare the frequency of fast responders among (1) single different monoclonal antibodies, (2) monoclonal antibodies with different pharmacodynamics (CGRP-ligand vs CGRP-receptor, respectively galcanezumab and fremanezumab versus erenumab), (3) monoclonal antibodies with different administration patterns (loading dose at T0 versus equal dosing throughout the treatment cycle, respectively galcanezumab versus erenumab and fremanezumab).

Results: One hundred and fifty-seven patients were enrolled, of which 58 patients in treatment with galcanezumab (loading dose of 240 mg followed by monthly administration of 120 mg), 75 in erenumab (140 mg every four week) and 24 in fremanezumb (225 mg monthly). One hundred and eighteen patients (75.2%) had a diagnosis of chronic migraine (CM) and 39 (24.8%) of high frequency episodic migraine (HFEM). Considering all patients, a 45% MHDs reduction was found at T1 (52% in treatment with galcanezumab, 34% in treatment with fremanezumab and 43% in treatment with erenumab).

No significant differences were found when comparing the single monoclonal antibodies ($p = 0.100$). Similarly, no significant differences were found when comparing anti-CGRP ligand (galcanezumab and fremanezumab) versus anti-CRGP receptor (erenumab), both in the entire sample ($p = 0.215$) and when considering HFEM versus CM ($p = 0.261$). Concerning galcanezumab alone (loading dose) versus fremanezumab and erenumab (constant dosing), in the whole cohort, patients in treatment with galcanezumab – receiving, thus, the loading dose- documented a 52% MHDs reduction, whereas patients in the other treatment groups documented a 41% reduction. This difference was statistically significant ($p = 0.031$). Regarding patients with CM, a significant difference was found in patients treated with galcanezumab compared to those in treatment with fremanezumab or erenumab (54% MHDs reduction vs 43%; $p = 0.01$).
Moreover, although not statistically significant ($p = 0.211$), 74.2% of CM patients with medication overuse in treatment with galcanezumab reversed their overuse status compared to 61% of CM patients in treatment with erenumab and fremanezumab.
Conclusion: The present study confirms previous reports regarding the fast clinical response in migraine prevention obtained with anti-CGRP monoclonal antibodies. In particular, our data suggest a possible role of a baseline loading dose – as with galcanezumab – in improving treatment rapidity of action, in patients with CM. A similar trend, not statistically significant, was found in CM patients treated with galcanezumab regarding medication overuse. We recognise our data might be biased by the higher prevalence of chronic compared to episodic migraine patients. Further studies will be needed to confirm the present findings.

IHC23-PO-268

The role of needle length in improving the tolerability profile of BoNTA injections in chronic migraine patients.

Emmanouil V. Dermitzakis[1], Michail Vikelis[2], George Vlachos[2] and Andreas Argyriou[2]

[1]*Euromedica General Clinic, Thessaloniki, Greece*
[2]*Headache Clinic, Mediterraneo Hospital, Athens, Greece*

Background: To assess the role of needle length in improving the tolerability/safety profile of OnabotulinumtoxinA (BoNTA) for chronic migraine (CM) prophylaxis, with a specific focus on neck pain, based on patients' body habitus and other variables.
Methods: BoNTA was administered quarterly for two consecutive cycles, using the standard 0.5-inch 27 G needle at all pre-defined PREEMPT injection sites, except the left-hand side trapezius and paraspinal muscles, which were injected using longer needles of 1-inch 23 G at first and 1-inch 27 G at second infusion. Participants were interviewed at day 14 following each session for evidence of neck pain. The predictive significance of Body Mass Index (BMI) and other variables with neck pain was also examined.
Results: A total of 100 consecutive CM patients were evaluated, and each patient servedas her/his self-control. The incidence, duration and intensity of neck pain did not significantly differ using either 1-inch needle compared with standard 0.5-inch 27 G needle, although the incidence and characteristics of neck pain with the use of longer needles appeared slightly higher and more intense. BMI index and other tested variables remained unrelated to neck pain.
Conclusions: We were not able to identify significant differences or correlations in the incidence, characteristics and locationof neck pain with the use of different needle length to inject BoNTA, although the use of the longer1-inch needles likely increased the risk of this adverse event
Disclosure of Interest: None Declared

IHC23-PO-269

Real-world evidence of monoclonal antibodies for migraine treatment in Argentina: a retrospective analysis

Maria Vanesa Nagel, Gustavo Portuondo, Yasmin Bravo, Grandinetti Mariela, Daniela Calvo, Teresa Gutierrez, Natalia Larripa, Emilia Tajan, Santiago Crema, Lucas Bonamico and Maria Teresa Goicochea

FLENI, Buenos Aires, Argentina

Objective: To analyze the clinical characteristics and response to treatment with CGRP-monoclonal antibodies (CGRP-mAbs) in migraine patients.
Methods: Retrospective, descriptive study. We reviewed electronic medical records of patients evaluated in our headache service with EM (episodic migraine) or CM (chronic migraine) who received Erenumab (ERE) 70 or 140 mg or Fremanezumab (FRE) 225 mg monthlyas preventive treatment of migraine between July 2019 and March 2023. We included patients over 18 years old, with EM or CM diagnose who completed at least 3 months of treatment with CGRP-mAbs. We analyzed age, sex, prior migraine preventive medication, type and dose of mAbs, adverse effects (AEs). We assessed changes in headache days/month (HDM), use of analgesics, medication overuse (MO) in the month before treatment and

at 3, 6, 12 months after treatment. Response was defined as reduction in HDM ≥30% for CM and ≥ 50% for EM.
Results: Medical records of 89 patients were analyzed (82% women, 49 years average), including 94 CGRP-mAbs treatments (5 patients switched mAb). 81% of patients had CM. 94% had failed to ≥ 3 preventive drugs. 48 patients with CM (66,6%) had received onabotulinumtoxin A. 65% were treated with ERE and 35% with FRE.
17 patients with EM received 18 treatments with mAbs (14 ERE, 4 FRE), 39% of them responded at 3 months, 46% at 6 months and 57% at 12 months.
72 patients with CM were treated with mAbs (76 treatments) with a response of 57%, 53%, 53% at 3, 6 and 12 moths, respectively. 34 patients with CM completed 12 months of treatment, 27 of them change their diagnostic category from CM to EM (79%).19 patients (21%) treated reported AEs, none of them serious.
48 patients had MO before treatment: 22 completed 12-months follow-up, 21 of them without MO.
Conclusions: Our real-world data demonstrate that ERE and FRE are effective in patients with EM and CM who had failed to other preventives treatments. CGRP-mAbs treatment is also effective in patients with MO.
Both drugs showed good tolerance and compliance, with only 1% of discontinuation rate due to AEs.
Of note, most health insurance in Argentina do not cover these treatments.

IHC23-PO-270

Factors associated with calcitonin gene-related peptide (CGRP) monoclonal antibody (mAb) ever versus never use: Results of the OVERCOME (US) study

Sait Ashina[1], Gilwan Kim[2], E. Jolanda Muenzel[2], Dawn C. Buse[3], Armen Zakharyan[4], Anthony J. Zagar[2], Robert E. Shapiro[5], Robert A. Nicholson[2], Eric M. Pearlman[2] and Richard B. Lipton[6]

[1]*Department of Neurology and Department of Anesthesia, Critical Care and Pain Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA, USA*
[2]*Eli Lilly and Company, Indianapolis, IN, USA*
[3]*Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, USA*
[4]*TechData Service Company, LLC, King of Prussia, PA, USA*
[5]*Department of Neurological Sciences, Larner College of Medicine, University of Vermont, Burlington, VT, USA*
[6]*Department of Neurology, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY, USA*

Objective: In this study of systematically-sampled people with migraine, among those who ever used a preventive medication for migraine, we examined the patient characteristics and migraine treatment patterns of those who ever vs. never used a CGRP-targeted monoclonal antibody (mAb). We also examined factors associated with CGRP mAb use and patient-reported reasons for starting a CGRP mAb.
Methods: Data were obtained from the combined 2019 and 2020 baseline cohorts of the OVERCOME(US) study, a web survey conducted annually in a demographically representative US adult sample. Respondents who had migraine via a validated migraine diagnostic questionnaire based on the International Classification of Headache Disorders 3rd edition (ICHD-3) criteria and ever used a preventive medication were identified; they were further categorized as CGRP mAb ever or never users. Patient sociodemographic, clinical and migraine-related characteristics, and migraine treatment utilization were descriptively reported by CGRP mAb ever vs. never users. Patient reported outcomes included the Migraine Disability Assessment (MIDAS), Migraine Symptom Severity Scale (MSSS), and Migraine Treatment Optimization Questionnaire (mTOQ). Patient-reported reasons for starting a CGRP mAb were also captured. Machine learning techniques [Random Forest (RF, 1000 individual trees) and Least Absolute Shrinkage and Selection Operator (LASSO)] were used to identify variables to include in the logistic regression that examined the factors associated with CGRP mAb ever vs. never use.
Results: Among participants with migraine (n = 39,113), 26% (10,011) ever used a preventive medication. Of these, 81% (8,059/10,011) had never used a CGRP mAb, and 19% (1,952/10,011) had ever used a CGRP mAb. Of the total sample of 39,113, only 5% (1,952) had ever used a CGRP mAb. When descriptively compared to CGRP mAb ever users, CGRP mAb never users were numerically older [mean (standard deviation) = 42.7 (13.6) vs. 37.5 (12.0) years], more likely to be female (76.6% vs. 57.5%), to be White (71.7% vs. 60.6%), to have joint pain (42.5% vs. 30.5%) and psychiatric comorbidities (66.4% vs. 58.2%). In contrast, CGRP mAb ever users had higher rates of 2+ cardiovascular comorbidities (61.2% vs. 40.7%), a self-reported comorbidity that contraindicated triptan use (56.5% vs. 27.8%), and severe (9+) ictal cutaneous allodynia (41.4% vs. 25.9%) when compared to CGRP mAb never users. A higher proportion of CGRP mAb ever users reported currently using 2+ recommended non-CGRP mAb preventive medications (36.7% vs. 12.8%) and recommended non-CGRP mAb preventive and acute prescription (Rx) medications (56.0% vs. 32.0%). Of 60 sociodemographic, clinical, and migraine-related variables, 6 variables were identified by RF or LASSO as most strongly associated with CGRP mAb use. Currently taking an antidepressant for migraine (odds ratio [OR] = 2.25; 95% confidence interval [CI]:

1.94–2.62), currently taking anti-hypertensive medication for migraine (OR = 2.00; 95% CI: 1.71–2.34), currently taking 2+ recommended non-CGRP mAb preventive medications (OR = 1.31; 95% CI: 1.05–1.65) and having contraindication to triptans (OR = 2.12; 95% CI: 1.87–2.41) increased the likelihood of CGRP mAb use. Conversely, currently using 1 recommended non-CGRP mAb preventive medication (OR = 0.80; 95% CI: 0.67–0.96) was associated with decreased likelihood of CGRP mAb use. Number of years with migraine was a statistically significant factor but had a small effect size (OR = 0.99; 95% CI: 0.98–0.99). Top reasons for starting CGRP mAb were efficacy (61.0%), dosing/delivery (47.5%) and recommendation/request (43.3%).

Conclusion: CGRP mAb use was significantly associated with currently taking 2+ recommended non-CGRP mAb preventive medications, antidepressant or cardiovascular medications for migraine, and having contraindications to triptans. The most common reasons for starting a CGRP mAb were efficacy, dosing/delivery, and recommendation/request.

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Erenumab effect on brain network function in episodic migraine patients: a randomized, placebo-controlled, clinical trial

Roberta Messina[1], Marta Bartezaghi[2], Ilaria Cetta[1], Bruno Colombo[1], Licia Grazzi[3], Daniele Martinelli[4], Raffaele Ornello[5], Anna Pichiecchio[4], Debora Raimondi[2], Maria Assunta Rocca[1], Antonio Russo[6], Simona Sacco[5], Alessandra Splendiani[5], Cristina Tassorelli[4], Renato Turrini[2], Paola Valsasina[1] and Massimo Filippi[1]

[1]*IRCCS San Raffaele Scientific Institute, Milan, Italy*
[2]*Novartis Farma, Milan, Italy*
[3]*IRCCS Istituto Neurologico "Carlo Besta", Milan, Italy*
[4]*IRCCS Mondino Foundation, Pavia, Italy*
[5]*Department Biotechnological and Applied Clinical Sciences, l'Aquila, Italy*
[6]*University of Campania "Luigi Vanvitelli", Naples, Italy*

Objective: Monoclonal antibodies targeting the calcitonin gene-related peptide (CGRP) pathway, like erenumab, are believed to prevent migraine attacks via the block of CGRP activity in the periphery. In this study, we explored the effect of erenumab treatment on the functional connectivity (FC) of brain networks involved in migraine and investigated the persistence of such an effect following treatment discontinuation.

Methods: This was a randomized, double-blind, placebo-controlled, multicenter trial with a crossover design performed in adult episodic migraine patients with previous treatment failure. Patients were randomized (1:1) to 12 weeks of treatment with erenumab 140 mg or placebo, followed by a 12-week crossover. Clinical and safety outcomes were assessed every 4 weeks. Resting state (RS) FC changes of brain networks were investigated at baseline, week 12 and week 24 using a seed-based correlation approach.

Results: Sixty-one patients were enrolled and randomized to treatment. In each treatment sequence, 27 patients were included in the analyses. We observed a carry-over effect of erenumab treatment on clinical and MRI variables during the placebo treatment and therefore data analysis was performed as a parallel comparison of erenumab vs placebo for the first 12 weeks of treatment. From baseline to week 12, compared to placebo, patients receiving erenumab showed RS FC changes within the cerebellar, thalamic and periaqueductal gray matter networks, significantly associated with clinical improvement. Compared to non-responders, patients achieving a 50% reduction in migraine attack frequency had distinct patterns of thalamic and visual network RS FC. Brain RS FC changes tended to revert when erenumab was stopped. A lower baseline RS FC of the pontine network identified patients

responding to erenumab. No safety concerns emerged during the study.
Conclusion: Erenumab modulates RS FC of networks involved in migraine pathophysiology. In line with clinical response, erenumab-induced brain RS FC changes tend to revert when treatment is stopped.
Disclosure of Interest: This study has been funded by Novartis Pharma.

IHC23-PO-272

What's a migraine day? variety in definition of a migraine day across phase III trials with monoclonal antibodies targeting the CGRP pathway

Jan Versijpt

UZ Brussel, Brussels, Belgium

Objective: In most preventive migraine trials with monoclonal antibodies targeting the CGRP pathway the reduction in monthly migraine days compared to baseline is used as a primary endpoint. Therefore a uniform definition of a migraine day across trials would be preferred in order to be able to indirectly compare treatment outcomes. The present study aimed at exploring the variation in the definition of a migraine trial used across trials.
Methods: The definition of a migraine day of 18 phase III randomised placebo-controlled trials with monoclonal antibodies targeting the CGRP pathway were compared.
Results: Across these 18 trials in episodic, chronic and difficult-to-treat migraine 10 different definitions were found. Trials with the four monoclonal antibodies available (erenumab, fremanezumab, galcanezumab and eptinezumab) all used different definitions but even within one group of trials with the same monoclonal antibody up to 3 different definitions were used. Within the respective subgroups of trials in episodic, chronic and difficult-to-treat migraine using the same monoclonal antibody consistent definitions were used for all 4 monoclonal antibodies available. Differences in the definition of a migraine day were found in the minimal duration of a headache episode (ranging from 30 minutes to 4 hours), the in- or exclusion of a probable migraine day and the in- or exclusion of a headache episode treated with a (migraine-specific or general) painkiller.
Conclusions: Variations in the used definition of a migraine day renders trials with monoclonal antibodies targeting the CGRP pathway not fully comparable. There is an urgent need for a uniform definition of a migraine day used in clinical research.
Disclosure of Interest: None Declared

IHC23-PO-273

Long term (1-year) effectiveness, safety and tolerability of fremanezumab in migraine: a real-life, prospective, cohort, multicenter study.

Gabriella Egeo[1], Cinzia Aurilia[1], Bianca Orlando[1], Giulia Fiorentini[1], Florindo D'Onofrio[2], Maria Albanese[3], Roberta Messina[4], Paola Di Fiore[5], Maurizio Zucco[6], Massimo Filippi[4], Marco Bartolini[7], Francesco Bono[8], Licia Grazzi[9], Pietro Querzani[10], Laura Borrello[11], Alberto Doretti[12], Annalisa Gai[13], Stefania Proietti[14], Stefano Bonassi[14,15], Fabrizio Vernieri[16], Paola Torelli[17] and Piero Barbanti[1,15]

[1]*Headache and Pain Unit, IRCCS San Raffaele Roma, Rome, Italy*
[2]*Neurology Unit, San Giuseppe Moscati Hospital, Avellino, Italy*
[3]*Regional Referral Headache Center, Neurology Unit, University Hospital Tor Vergata, Rome, Italy*
[4]*Headache Unit, Department of Neurology, Scientific Institute San Raffaele Hospital, Vita-Salute University, Milan, Italy*
[5]*Headache Center, ASST Santi Paolo Carlo, Milan, Italy*
[6]*Headache Center, Neurlogy Unit, San Camillo-Forlanini Hospital, Rome, Italy*
[7]*Neurological Clinic, Marche Polytechnic University, Ancona, Italy*
[8]*Center for Headache and Intracranial Pressure Disorders, Neurology Unit, A.O.U. Mater Domini, Catanzaro, Italy*
[9]*Neuroalgology Unit, Headache Center Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milan, Italy*
[10]*Ravenna Hospital, Headache Center, Ravenna, Italy*
[11]*Frosinone Hospital, Headache Center, Frosinone, Italy*
[12]*Department of Neurology-Stroke Unit, Laboratory of Neuroscience, Istituto Auxologico Italiano, IRCCS, Milan, Italy*
[13]*Cardinal Massaia Hospital, Headache Center, Asti, Italy*
[14]*Clinical and Molecular Epidemiology, IRCCS San Raffaele Roma, Rome, Italy*
[15]*San Raffaele University, Rome, Italy*
[16]*Headache and Neurosonology Unit, Campus Bio-Medico University Hospital, Rome, Italy*
[17]*Neurology Unit, Department of Medicine and Surgery, Headache Center, University of Parma, Parma, Italy*

Background: Fremanezumab demonstrated to be effective, safe and well tolerated in the long-term preventive treatment of migraine in a randomized trial. The present study is aimed to assess the long-term effectiveness, safety, and tolerability of fremanezumab in real-life patients affected by high-frequency episodic (HFEM: 8–14 days/month) or CM.
Methods: This is a prospective, cohort, real-life study at 9 headache centers on consecutive patients affected by HFEM or CM with at least 3 prior preventive treatment failures who were prescribed subcutaneous

fremanezumab (225 mg monthly/675 mg quarterly) for ≥ 48 weeks. Primary endpoint was the change in monthly migraine days (MMD) in HFEM and monthly headache days (MHD) in CM at weeks 45–48 compared to baseline. Secondary endpoints encompassed variation in monthly analgesic intake (MAI), Numerical Rating Scale (NRS), Headache Impact Test-6 (HIT-6) and Migraine Disability Assessment Scale (MIDAS scores, and >50%, >75% and 100% responder rates at the same time intervals.

Results: 470 migraine patients had received >1 subcutaneous fremanezumab dose and were considered for safety analysis, while 54 patients completed 48 weeks of treatment and were included also in the effectiveness analysis. Fremanezumab was effective in both HFEM and CM, inducing at week 48 a significant ($p < 0.001$) reduction in MMD (–6.8 ± 3.9), MHD (–14.3 ± 7.3), MAI (–7.4 ± 3.7, 15.0 ± 11.4), NRS (–2.8 ± 2.6, –2.5 ± 2.6) and HIT-6 (–10.0 ± 6.8, –11.6 ± 11.3). The >50%, >75% and 100% responder rates at week 48 were 72.2%, 38.9% and 16.7% in HFEM and 86.1%, 55.6 and 5.6% in CM. Treatment emergent adverse events [PB1] occurred in 12.9% of the patients (7/54). The most common were injection site erythema (3.7%) and asthenia (3.7%), followed by constipation (1.9%), amenorrhea (1.9%) and nausea (1.9%). No patient discontinued fremanezumab for any reason.

Conclusions: Long-term (48-week) treatment with fremanezumab provides sustained effectiveness, safety, and tolerability in real-life patients with HFEM or CM with prior therapeutic failures. Fremanezumab seems more effective in real-life than in randomized control studies [PB1]nessun evento avverso in 12 mesi su 40 pz è un record del mondo. Ricontrollare bene

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IHC23-PO-274

Comparative Efficacy, Quality of Life, and Safety/Tolerability of Atogepant and Rimegepant in Migraine Prevention: A Matching-Adjusted Indirect Comparison

Cristina Tassorelli[1], Kateryna Onishchenko[2], Molly Duan[3], Matthew Hemstock[4], Corey Voller[5], Pranav Gandhi[6] and Laure Dupont-Benjamin[7]

[1]*Headache Science & Neurorehabilitation Centre, C. Mondino Foundation and University of Pavia, Pavia, Italy*
[2]*AbbVie, London, United Kingdom*
[3]*AbbVie, North Chicago, IL, USA*
[4]*Lumanity, Sheffield, United Kingdom*
[5]*Lumanity, London, United Kingdom*
[6]*AbbVie, Madison, NJ, USA*
[7]*AbbVie, Courbevoie, France*

Objective: To evaluate the relative efficacy, quality of life, safety, and tolerability of atogepant compared with rimegepant for the prevention of episodic migraine using a matching-adjusted indirect comparison (MAIC) analysis.

Methods: Data were pooled from two phase 3 atogepant trials (PROGRESS and ADVANCE) and one phase 2/3 rimegepant trial (BHV3000-305). Participants receiving atogepant 60 mg once daily (QD) and rimegepant orally disintegrating tablet 75 mg once every other day (QOD) were included in this analysis. Patients receiving placebo were also included to allow for an anchored comparison. Since inclusion/exclusion criteria based on monthly migraine days (MMDs) and monthly headache days (MHDs) varied across trials, this analysis only included patients who met the BHV3000-305 inclusion/exclusion criteria of ≥6 MMDs and ≤18 MHDs at baseline. To make an adjusted comparison between pooled atogepant and rimegepant trial populations, an anchored MAIC was

conducted utilizing patient level data from the atogepant studies. Within the MAIC, propensity score weights were derived for patients in the atogepant studies to match patients in BHV3000-305 based on identified treatment effect modifiers. To estimate the relative treatment effect between atogepant and rimegepant, a Bucher comparison was performed utilizing the aggregated data for the reweighted atogepant trial sample versus the observed effects in BHV3000-305 using placebo as an anchor between the studies; confidence intervals (CIs) for the indirect estimate were derived. The efficacy assessment of interest was change in MMDs, which was assessed for atogepant across weeks 1–12 relative to rimegepant across weeks 1–12. In a scenario analysis, the change in MMDs for atogepant across weeks 9–12 was compared relative to rimegepant across weeks 9–12. The change from baseline in Migraine-Specific Quality of Life Questionnaire v2.1 (MSQv2.1) Role Function−Restrictive (RFR) domain score was assessed at week 12 and safety/tolerability outcomes were evaluated across the 12 weeks.

Results: The pooled atogepant 60 mg QD analysis group included 252 patients and the rimegepant 75 mg QOD group included 348 patients for the efficacy endpoints. After weighting, average baseline characteristics of atogepant-treated patients were balanced with those of rimegepant-treated patients. Across weeks 1–12, atogepant 60 mg QD demonstrated a statistically significant greater reduction in mean MMDs vs rimegepant 75 mg QOD (mean difference [MD] [95% CI]: −1.65 [−2.49, −0.81]; $P < 0.001$; **Table**). In the scenario analysis, atogepant 60 mg QD demonstrated statistically significant greater reduction in mean MMDs across weeks 9–12 (MD [95% CI]: −1.5 [−2.55, −0.43]; $P < 0.01$) vs rimegepant 75 mg QOD thus confirming the findings of the base case. Atogepant 60 mg QD demonstrated a significantly higher MSQ v2.1 RFR domain score (MD [95% CI]: 7.36 [1.88, 12.82]; $P < 0.01$) vs rimegepant 75 mg QOD. While patients treated with atogepant 60 mg QD had similar odds of experiencing a treatment-emergent adverse event (odds ratio [OR] [95% CI]: 0.91 [0.56, 1.45]; $P = 0.7366$) and numerically higher odds of discontinuing treatment due to any reason (OR [95% CI]: 1.43 [0.69, 3.06]; $P = 0.3284$) vs rimegepant 75 mg QOD, neither difference was statistically significant.

Conclusion: In this MAIC analysis, atogepant 60 mg QD demonstrated significant improvements in both efficacy and quality of life endpoints compared with rimegepant 75 mg QOD. Both atogepant and rimegepant demonstrated similar safety and tolerability profiles.

Disclosure of Interest: Allergan (prior to its acquisition by AbbVie) Cristina Tassorelli, MD, PhD, has participated in advisory boards for AbbVie, Dompé, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva. She has lectured at symposia sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva. She is principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva. She has received research grants from the European Commission, the Italian Ministry of Health, the Migraine Research Foundation, and the Italian Multiple Sclerosis Foundation. She serves as an associate editor for Cephalalgia and The Journal of Headache and Pain. Matthew Hemstock and Corey Voller are employees of Lumanity, which was reimbursed by AbbVie as a consultancy for time spent planning, reviewing, and reporting the statistical analyses. Molly Duan, Kateryna Onishchenko,

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Table. Comparison of Efficacy, Quality of Life Endpoints, and Safety/Tolerability Among Atogepant-Treated and Rimegepant-Treated Participants

	Atogepant 60 mg QD	n	Rimegepant 75 mg QOD	n	Relative Treatment Effect
Change from baseline in MMDs, mean (95% CI) – atogepant 60 mg QD weeks 1–12 vs rimegepant 75 mg QOD weeks 1–12	−2.45 (−3.19, −1.72)	252	−0.8 (−1.3, −0.3)	348	−1.65 (−2.49, −0.81)
Change in MMDs, mean (95% CI) – atogepant 60 mg QD weeks 9–12 vs rimegepant 75 mg QOD weeks 9–12	−2.30 (−3.18, −1.43)	252	−0.8 (−1.5, −0.2)	348	−1.50 (−2.55, −0.43)
MSQ v2.1 RFR score, mean (95% CI)	10.86 (6.32, 15.40)	230	3.5 (0.2, 6.7)	269	7.36, (1.88, 12.82)
All-cause discontinuation, OR (95% CI)	1.25 (0.68, 2.30)	259	0.87 (0.58, 1.30)	370	1.43 (0.69, 3.06)
Treatment-emergent adverse events, OR (95% CI)	0.92 (0.64, 1.32)	259	1.00 (0.74, 1.36)	370	0.91 (0.56, 1.45)

MMD, monthly migraine day; MSQv2.1, Migraine-Specific Quality of Life Questionnaire version 2.1; OR, odds ratio; QD, once daily; QOD, once every other day; RFR, Role Function-Restrictive.

Pranav Gandhi, and Laure Dupont-Benjamin are employees of AbbVie and may hold AbbVie stock.

IHC23-PO-275

6-month Real-World Effectiveness of Fremanezumab in Patients with Migraine who switched from another mAb targeting the CGRP pathway (subgroup analysis from FINESSE)

Andreas Straube[1], Gregor Broessner[2], Charly Gaul[3], Xenia Hamann[4], Joachim Hipp[4], Torsten Kraya[5,6] and Lars Neeb[7,8]

[1]*Department of Neurology, University Hospital LMU, Munich, Germany*
[2]*Innsbruck Medical University, Department of Neurology, Innsbruck, Austria*
[3]*Headache Center Frankfurt, Frankfurt am Main, Germany*
[4]*Teva GmbH, Ulm, Germany*
[5]*Hospital Sankt Georg Leipzig gGmbH, Department of Neurology, Leipzig, Germany*
[6]*Headache Center Halle, Department of Neurology, University Hospital, Halle/Saale, Germany*
[7]*Helios Global Health, Berlin, Germany*
[8]*Charité Universitätsmedizin Berlin, Department of Neurology, Berlin, Germany*

Objective: To evaluate effectiveness and tolerability of fremanezumab administered in migraine patients who switched from a previous anti-CGRP pathway mAb as part of their routine disease management.
Methods: FINESSE is an ongoing prospective, non-interventional study in adults with episodic or chronic migraine (EM, CM). Observation period: 24 months. Primary endpoint: proportion of patients reaching $\geq$50% reduction in average number of monthly migraine days (MMD) during the 6-month period after the first dose of fremanezumab. Further measures: monthly average number of migraine days, MIDAS (Migraine Disability Assessment), HIT-6 (6-Item Headache Impact Test), acute medication use. In this subgroup analysis, 6-month-data in patients who experienced poor effectiveness or tolerability with a prior anti-CGRP pathway mAb and therefore switched to fremanezumab are presented.
Results: Of 140 patients (47.6 $\pm$ 11.5 years, 84.7% female) 54 (38.6%) achieved a MMD reduction of $\geq$50% over 6 months (EM: 44.3%, CM: 31.2%). Number of MMD decreased from 13.3 $\pm$ 6.42 at baseline, by 6.1 $\pm$ 5.47 (month 6). Acute migraine medication was used on 9.5 $\pm$ 4.92 days/month at baseline and decreased to 5.0 $\pm$ 3.86 days/month (month 6). MIDAS: 71.1 $\pm$ 57.1 (Baseline, N = 68), 43.7 $\pm$ 44.4 (Month 6, N = 48), HIT-6: 65.8 $\pm$ 4.8 (Baseline, N = 78), 59.6 $\pm$ 7.9 (Month 6, N = 55).
Conclusion: In this interim analysis of the FINESSE non-interventional study, about 38.6% of anti-CGRP pathway mAb-non-responder benefit ($\geq$50% response) from switching to fremanezumab. These results suggest that switching to fremanezumab may be a promising option for patients experiencing inadequate efficacy or poor tolerability with prior other anti-CGRP pathway mAb use.
Disclosure of Interest: Competing interests: The authors declare that they have had or are having the following economic or personal ties to the pharmaceutical industry, consulting firms, payers, or healthcare providers: A. Straube is or was member of the following advisory boards: Novartis, Lilly, Sanofi, Allergan, TEVA, and speaker or member of speaker boards on behalf of Novartis, Lilly, Sanofi, Allergan, TEVA. He acted as consultant for Sanofi and TEVA, received grant support for research or education from Novartis and acted as an editorial board member for Lilly, Sanofi and Novartis. G. Broessner was or is member of the following advisory boards: Novartis, Lilly, TEVA, Grünenthal, and speaker or member of following speakers boards: Novartis, Lilly, TEVA, Grünenthal; Consultant: Novartis, Lilly, TEVA, Grünenthal; he received grant support for research or education from TEVA. C. Gaul is or was member of the following advisory Boards: Abbvie, Lilly, Novartis Pharma, Hormosan Pharma, Sanofi-Aventis, Perfood, and TEVA, and speaker or member of the following speaker boards: Abbvie, Lilly, Novartis Pharma, Hormosan Pharma, Grünenthal, Sanofi-Aventis, Reckitt-Benckiser and TEVA. He acted as consultant for Weber & Weber, Lundbeck, and Perfood, and served in the following editorial boards: Acta Neurologica Scandinavia, Frontiers in Neurology, and Medizinischer Sachverständiger; Author royalties: Novartis Pharma; furthermore, he is honorary secretary of the German Migraine and Headache Society. J. Hipp and X. Hamann are employees of TEVA GmbH. T. Kraya is or was member of the following advisory Boards: Allergan, and speaker or member of the following speaker boards: Allergan, TEVA, Lilly, Hormosan. L. Neeb was member of the following advisory boards: TEVA, Lilly Novartis and Hormosan and speaker or member of the following speakers' boards: Lilly, TEVA, Novartis, Abbvie and Hormosan Pharma He received grant support for research from TEVA and Lilly. He served in the editorial boards of Journal of Headache and Pain and Frontiers in Neurology.

IHC23-PO-276

Enhancing Prophylaxis: Erenumab to Fremanezumab Transition in Migraine

Nina Vashchenko[1], Alikhan Uzhakhov[1,2], Daria Korobkova[1], Julia Azimova[1] and Kirill Skorobogatykh[1]

[1]*University Headache Clinic, Moscow, Russian Federation*
[2]*Darmed University Clinic, Astana, Kazakhstan*

Objective: Treatment with anti-CGRP monoclonal antibodies is effective in preventing migraine, but not all patients achieve the desired result. However, it is possible that these patients may benefit from switching from anti-CGRP receptor medications to medications that target the protein itself.
Methods: The single-centre prospective study included 103 patients with migraine who started preventive treatment with erenumab 70 mg monthly between April 2021 and May 2022. Patients completed an electronic headache diary before and during treatment. The efficacy of erenumab was assessed after 3 months. A positive response was defined as a 50% reduction in headache days. Patients who did not achieve a positive response could switch to another monoclonal antibody, fremanezumab 225mg if they desired. The efficacy of fremanezumab was assessed using the same criteria after 3 months.
Results: Of the 103 patients included in the study, 3 discontinued treatment after the first month, one because of side effects (constipation) and two because they moved to another city.
One hundred patients were included in the final analysis. We included 12 men and 88 women with migraine (mean age 41.74 ± 10.73 years). Thirty-four had episodic migraine, and 66 had chronic migraine. Fourteen patients had migraine with aura, and 41 patients had medication-overuse headache.
Sixty-four patients had a positive response to erenumab therapy: the mean number of headache days before treatment was 18.64 days and 7.28 days after 3 months. Of the 36 patients who did not respond to erenumab (the mean number of headache days before treatment was 19.76 days and 15.48 days at 3 months), 27 patients switched to fremanezumab (the rest preferred other prophylaxis options). Of the 27 patients who switched, 21 (77.8%) had a positive response after 3 months of fremanezumab therapy and continued the treatment.
Conclusions: Switching from erenumab to fremanezumab may benefit migraine patients who have not achieved the desired effect. Larger studies are needed to confirm the results and to define the predictors of who might benefit from switching.

Disclosure of Interest: Dr Kirill Skorobogatykh reports receiving speaker fees and fees for serving as a principal investigator from Eli Lilly, Lundbeck, Novartis and Teva. Dr Julia Azimova reports having received speaker fees from Novartis and Teva. Other authors report no conflict of interest.

IHC23-PO-277

Daith ear piercing, vagus nerve stimulation and changes in migraine symptoms

Chris Blatchley[1] and Arnold Wilkins[2]

[1]*London Migraine Clinic, London, United Kingdom*
[2]*Essex University, Colchester, United Kingdom*

Objectives: We report on the change in migraine symptoms after Daith ear piercing.
Background: Reports of unexpected improvement in migraines were reported soon after the first cosmetic Daith piercings were performed in 1992, and has increased in popularity since then. By chance, the piercing passes through the area innervated by the auricular branch of the vagus nerve (ABVN). Electrical stimulation of the vagus nerve is an established treatment for migraine and epilepsy recognised by NICE in the UK. We hypothesize that the piercing stimulates the ABVN by mechanical/inflammatory irritation.
Design: Electronic questionnaires assessing qualitative/quantitative changes in migraine frequency/severity were completed by participants before, during, and after the piercing.
Setting: A national chain of piercing studios in seven locations throughout the UK collaborated.
Participants: Between 1/8/22 and 14/11/22 a consecutive series of 133 participants sought a piercing for their migraines, of whom 119 consented to be contacted later by email. A follow-up questionnaire was sent on 15/01/23, 2–4 months after the piercing. 90 of the 119(76%) participants completed the questionnaire: 84 female and 6 male, 19–69 years old (mean 43). The median duration of migraine was in the range 11–20 years; 82/91(91%) had a medical diagnosis of migraine; 58% had migraine with aura.
Intervention: Experienced piercers inserted 100% titanium jewellery through the crus helix cartilage immediately above the auditory meatus, an area innervated by the ABVN.
Main Outcome at 2–4 Month Follow-up: The average incidence of migraine days for the whole group was reduced by 50% from 6.3 to 3.2 per month ($p < .0001$) with no serious side effects.
Detailed Outcomes: Qualitatively, 65/90(72%) reported that their migraines had "stopped" (13%) or

the frequency was "much better" (59%). The frequency was "a little better" in 14/90 (16%), and 11/90 (12%) reported "no change" (9%) or "worse" (3%).
Quantitatively, for the group of 65 whose migraines had "stopped" or were "much better": (1) the average incidence of migraine days was reduced by 69% from 5.5 to 1.7 per month, $p < .0001$; (2) the average monthly number of days off work/in bed was reduced by 73% from 3.1 to 0.8, $p < .0002$; (3) the average number of completely symptom-free days per month was increased by 71% from 9.8 to 16.7, $p < .0001$. Corresponding analyses for the remaining 25 who reported little or no improvement showed no significant change.
There was a negligible correlation ($r = 0.03$) between initial expectation and later reported outcome.
67/90 (74%) reported the effect "not wearing off" or "improving"; 5/90 (6%) reported "never had an effect"; 18/90 (20%) reported a reducing effect
Complications: 3/90 patients (3.4%) reported infection that required medical attention but not removal of the piercing. Separately, prior to follow-up, 2 had had the piercing removed because of infection, which then resolved.
Conclusion: The study continues, eventually to follow up 1,000 participants over 12 months. Daith piercing is readily available and costs little. Given that more than 50% of our large sample report a maintained reduction in headaches, Daith piercing merits further exploration as a migraine treatment.
Further information on this research is available at www.migraine-research.org
Disclosure of Interest: None Declared

IHC23-PO-278

Real-world experience of Galcanezumab in 101 patients with migraine and fibromyalgia. (Galca-Only Consortium)

Rocio Alvarez-Escudero[1], Víctor Obach[2], Nuria Riesco[3], Alba Bravo[4], Marta Ruibal[5], Ane Minguez[5], Fernando Velasco[6], Izaro Kortazar[7], Amaya Echeverria[7], Elisa Cuadrado[8], Sonsoles Aranceta[9], Santiago Fernandez-Fernandez[2], Neus Fabregat[2], Teresa Marco[2], Juna Carlos Garcia-Monco[10], Aintzine Ruisanchez[11] and David Garcia-Azorin[12]

[1]*Hospital de Asturias, Oviedo, Spain*
[2]*Hospital Clinic, Barcelona, Spain*
[3]*Hospital Asturias, Oviedo, Spain*
[4]*Hopital Reina Sofia, Tudela, Spain*
[5]*Hospital de Donosti, San Sebastian, Spain*
[6]*Hopsital Cruces, Bilbao, Spain*
[7]*Hospital Txagorritxu, Alava, Spain*
[8]*Hospital del MAr, Barcelona, Spain*
[9]*Hospital Tauli, Sabadell, Spain*
[10]*Hospital de Basurto, Bilbao, Spain*
[11]*Hospital Galdakao, Bilbao, Spain*
[12]*Hospital de Valladolid, Valladolid, Spain*

Objective: Fibromyalgia is a frequent comorbidity of migraine. Due to its painful nature, patients with fibromyalgia were excluded from most of the randomized clinical trials that assessed the efficacy of monoclonal antibodies against the calcitonin gene-related peptide (CGRP), and data regarding routine clinical practice is scarce. We analyzed tolerability and effectiveness of galcanezumab in patients with migraine and fibromyalgia.
Methods: The "Galca-Only Consortium" is a multicenter ambispective cohort study. All consecutive patients with chronic migraine or high-frequency episodic migraine with prior failure to three or more migraine preventive drugs, treated with galcanezumab were included. Patients were systematically assessed by headache experts and followed up quarterly for 12 months. A series of variables were gathered, related to patients' demographics, comorbidities, migraine diagnosis and situation and migraine burden. Response to treatment was according to the 50% responder rate, defined as the proportion of patients with who achieved a reduction of at least 50% in the number of headache days per month, compared to the baseline period. Tolerability was assessed as the proportion of patients who discontinued the treatment due to inadequate tolerability. Data of follow-up at 12 months are presented.
In the present sub-analysis, patients with a diagnosis of fibromyalgia were compared with patients with no prior history of fibromyalgia. One center of the Galca-Only Consortiun was enable to register fibromyalgia as comorbidity and therefore their 175 patients with migraine were excluded from the present study.
Results: During the study period, 101 patients with fibromyalgia were included in our 880 patients' registry. Demographics are shown in table 1. Patients with fibromyalgia were more frequently female, had chronic migraine more frequently and had a higher frequency of monthly headache days per month.
At 12 month follow up, the proportion of patients who achieved a 50% response was 32.7% in fibromyalgia and 52.1% in non-fibromyalgia group ($p = 0.001$). The proportion of patients who continued treatment at 12-months was 62.4% among patients with fibromyalgia, and 73% among patients with no fibromyalgia history. Discontinuation of galcanezumab due to adverse events was 28.3% and 13–9% ($p = 0.01$), respectively.
Conclusion: Migraine patients with fibromyalgia had a great migraine burden. Despite this, one third of them had a good response to galcanezumab.

	Fibromyalgia n = 101	Non-Fibromyalgia n = 779	P value
Age, mean (SD)	50.6 (11.0)	49.4 (12.3)	0.1
Female, n (%)	97 (96.0)	637 (81.8)	0.001
Migraine worsening, years [IQR]	8 [4–15]	8 [4–14]	0.2
Chronic migraine, n (%)	86 (85.0)	562 (72.1)	0.001
Mood disorders, n (%)	70 (69.3)	276 (35.4)	0.001
Monthly headache days, baseline [IQR]	27 [20–30]	20 [13–30]	0.001
HIT6 baseline [IQR]	72 [67–74]	68 [65–72]	0.2

Disclosure of Interest: None Declared

IHC23-PO-279

What is the optimal MAB use ratio per 100.000 inhabitants in centers with Headache Unit or monografic headache clinic? Estimation from the Galca-Only and Frema-Only consortium

victor Obach[1], Alberto Andres Lopez[2], Alberto Lozanp[3], Alexandra Figueroa[4], Almudena Layos[5], Ana Echavarria Iñiguez[6], Antonio Sabchez Soblechero[3], Beartiz Alavarez-Mariño[7], Fernando Iglesias[6], Laura Rubio[8], Manuel Peinado[9], Maria Recio[10], Raquel Portillo[10], Sendo Gil Luque[6], Yesica Gonzalez-Osorio[11], Sonsoles Aranzeta[12], Elisa Cuadrdo[13], Neus s Fabregat[14], Teresa Marco[15], Santiago Fernandez Fernandez[14], Ana Rizo[14], Nuria Pola[15], Nagore Urduri[16], Ane Minguez[17], Marta Ruibal[17], Alba Bravo[18], Rocio Alvarez[19], Nuria Riesco[19], Fernando Velasco[20], Aintzine Ruizanchez[21], Izaro Kortazar[22], Amaya Echeberria[22], Maria Martin Bujante[23], Juna Carlos Garcia-Monco[24] and David Garcia-Azorin[11]

[1]*Barcelona, Barcelona, Spain*
[2]*Hospital de Albacete, Albacete, Spain*
[3]*Hospital Gregorio Marañon, Madrid, Spain*
[4]*Hospital Infanta Elena, Madrid, Spain*
[5]*Hospital Albacete, Albacete, Spain*
[6]*Hospital de Burgos, Burgos, Spain*
[7]*Hospital Rey Juan Carlos, Madrid, Spain*
[8]*Hospital de Villahba, Madrid, Spain*
[9]*Hospital de Castellon, Castellon, Spain*
[10]*Hospital Reina Sofia, Cordoba, Spain*
[11]*Hospital de Valladolid, Valladolid, Spain*
[12]*Hospital Tauli, Sabadell, Spain*
[13]*Hsopital del Mar, Barcelona, Spain*
[14]*Hospital Clinic, Barcelona, Spain*
[15]*Hsopital Clinic, Barcelona, Spain*
[16]*Hospital Urduriz, Bilbao, Spain*
[17]*Hospital Donosti, San Sebastian, Spain*
[18]*Hospital Reina Sofia, Tudela, Spain*
[19]*Hospital de Astudias, Oviedo, Spain*
[20]*Hospital de Cruces, Bilbao, Spain*
[21]*Hospital Galdakoa, Bilbao, Spain*
[22]*Hospital Txagorritzu, Alava, Spain*
[23]*Hospital Navarra, Pamplona, Spain*
[24]*Hospital de Basurto, Bilbao, Spain*

Objective: Anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAB) for migraine profylaxis have been approved in 2019 in Spain and therefore expertise and logistics in its use have been established.
We analyze the experience in 20 centers participating in 2 large multicentric registries.
Methods: Pharmaco-therapeutic Commissions of 20 centers with Headache Units or monografic headache consults, approved Galcanezumab (GalcaOnly) or Fremanezumab (FremaOnly) use in 2020 as the first line mAB option treatment of high frequency (>7 attacks per month, refractory to three or more oral migraine preventive treatments) or chronic migraineurs refractory to at least two oral migraine preventives and onabotulinumtoxinA), according to the Spanish health regulation. In Spain, the healthcare system is public and universally covers all inhabitants, with the mABs being free of charge when the patients met the aforementioned requirements.
Herein, consecutive patients treated with mABs were interviewed for demographics and monthly headache days (MHDs) and were included in this two registries, GalcaOnly Consortium and FremaOnly Consortium.
The novo patients with mAB initiation from January to March 2023 were recorded in 20 centers covering 6.361.500 reference population. The ratio of monthly mAB initiation per 100.000 inhabitants was calculated from each center.
Results: A total of 546 de novo mABs were prescribed in 3 month-period in the 20 centers resulting a ratio of mAB per month per 100–000 inhabitant of 2.86
Three centers have a ratio of more than 5 prescription per month per 100.000 inhabitants.
Conclusion: The optimal MABs prescription ratio per 100.000 inhabitants is unkown and depends on many variables but 2.8/months/100000 inhabitants targed is feasable in many centers.
Disclosure of Interest: None Declared

IHC23-PO-280

Persist-spain: peristence of anti-CGRP monoclonal antibodies as migraine preventive treatment after one year

Samuel Díaz Insa[1], Mariano Huerta[2], Robert Belvis[3], Jaime Rodríguez Vico[4], Candela Nieves[1], Albert Muñoz[5], Noemí Morollón[3], Alex Jaimes[4], Marina Olivier[1], Sergio Campoy[2] and Andrea Gómez García[4]

[1]Headache Unit. Neurology. Hospital Universitari i Politècnic La Fe, València, Spain
[2]Headache Unit. Neurology. Hospital de Viladecans, Viladecans, Spain
[3]Headache Unit. Neurology. Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain
[4]Headache Unit. Neurology. Hospital Universitario Fundación Jimenez Díaz, Madrid, Spain
[5]Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Spain

Objective: We are used to evaluate the efficay of new preventive treatments for migraine in terms of reduction in monthly migraine days (MMD), 50% of reduction in MMD, different Patient Related Outcomes (PRO) and more efficay and safety measures at 3 or 6 months of treatment. Now, antiCGRP MAbs are available in clinical practice from more than 2–3 years in our country and we are increasing its use and our experience with them. The aim of the present study is to evaluate the persistence of antiCGRP MAbs use after one year of being initiated.
Methods: Several Spanish hospitals were invited to share their data in terms of persistence of antiCGRP MAbs after one year of treatment. In this study we describe age, gender, episodic or chronic migraine diagnosis, rates of MOH (Medication Overuse Headache) and MMD at the beginning of antiCGRP MAbs use. Persistence of treatment after one year is the major endpoint of the study. As erenumab (E), galcanezumab (G) (both from DEC-19) and fremanezumab (F) (from DEC-20) are available in Spain we will analyse them also separately. Reasons for discontinuation during first year of treatment are described. Dose modifying are also analysed. We will refer some measures after one year of treatment: MMD, MOH rates. In persitent treated patients we analyse the antiCGRP MAbs months of use nowadays.
Results: 5 different big hospitals with headache units in Spain referred data from a total of 706 patients in which antiCGRP MAbs were initiated. All of them were new patients for antiCGRP MAbs use. Mean age of patients was 49'10 years, being women 600 patients (84'99%) and 106 men (15'01%). There were 524 patients with Chronic Migraine (CM) diagnosis, a 74'22%, and the rest Episodic Migraine (EM) patients. 76'14% met MOH criteria at baseline. 280 patients were initiated on E, 228 on G and 198 on F.
Persistence of treatment after one year in 439 out of 702 patients. That means 62'54% maintaining first antiCGRP MAb ever used after one year of treatment. The persistence with E was 60'71%, for G 57'02% and 70'02% for F. Reasons for discontinuation during the first year of treatment: Mostly were due to lack of efficacy (223 patients, 31'59%), just 5 for high efficay, 22 due to adverse events (3'12%), 13 due to loss of follow-up and 11 for other reasons (few patients had more tan one reason).
Dose modifying: Patients who were initiated whith E 70 mg were increased to 140 mg in almost all cases to improve efficacy, in some cases even dosing each 21 days was used in patients with wearing off. E was dose modified around 20% of cases. In some cases (10%) G was used at 240 mg per month when efficacy decreased after some months of treatment. With F some patients were changed from 225 mg monthly to 675 mg quarterly or viceversa (10%) due to patient preferences, no adjustment of doses was needed.
Outcomes after one year: MMD decreased from 17'35 days at baseline to 7'38 after one year of treatment. With E 18'57 to 8'3 days; G 18'45 to 8'47 days; and F 14'35 to 5'81 days. MOH rate decreased from 76'14% at baseline to 16'61% after one year. In persistent patients the use of initial antiCGRP Mab lasts for an average of 26'24 months at the moment when data for present study was collected.
Conclusion: Persistence rate after one year of treatment with antiCGRP Mabs is very high: near 2/3 of patients. The major reason for discontinuation of treatment is lack of efficay (1/3 of patients); and just in 3% of patients due to adverse events. There are minor differences between all 3 antiCGRP Mabs outcomes. After one year of treatment MMD and MOH were markedly improved. Persistence of treatment is a very useful way to analyse real world evidence of preventive migraine treatments.
Disclosure of Interest: None Declared. All authors are usual speakers for all companies with marketed preventive migraine products in Spain.

IHC23-PO-281

Efficacy of CGRP monoclonal antibodies on chronic migraine and medication overuse: A systematic review and meta-analysis

Julyana M. Dantas[1], Mariana J. Oliveira[2], Sávio Batista[3], Amanda Godoi[4], Luciana A. O. Silva[5] and Daniel C. Schachter[6]

[1]*Federal University of Rio Grande do Norte, Natal, Brazil*
[2]*Faculdade de Ensino Superior da Amazônia Reunida, Redenção, Brazil*
[3]*Federal University of Rio de Janeiro, Rio de Janeiro, Brazil*
[4]*Cardiff University School of Medicine, Cardiff, Brazil*
[5]*Federal University of São Paulo, São Paulo, Brazil*
[6]*Unigranrio University, Rio de Janeiro, Brazil*

Objective: Medication overuse is a common occurrence in patients with primary headache syndromes, especially chronic migraine. Despite a high prevalence, there is still no consensus on the optimal approach to reduce acute medication use. We aimed to evaluate the efficacy of monoclonal antibodies (mAb) against calcitonin gene-related peptide (CGRP) in the population of patients with chronic migraine and overuse of analgesic medications.

Methods: PubMed, Embase, and Cochrane Library were searched for studies that compared mAb against CGRP versus placebo in patients with chronic migraine and medication overuse as defined by the International Classification of Headache Disorders, third edition. Unpublished data were sought on the subgroup of interest. A generic inverse-variance method was used to account for regression models in the original studies. Heterogeneity was examined with the Cochran Q test and I^2 statistics; p values inferior to 0.10 and I^2 >25% were considered significant for heterogeneity.

Results: We included 6 randomized clinical trials with 4732 patients, of whom 2434 (51.4%) had medication overuse. The mean follow-up was 12 weeks. Monthly number of days of acute medication use was significantly decreased in the mAb group compared to placebo (MD –2.55; 95% CI –3.15, –1.95; $p < 0.01$; $I^2 = 0$; figure 1A), as was the number of migraine days per month (MD –2.64; 95% CI –3.27, –2.00; $I^2 = 0$; $p < 0.01$). Reversion to no medication overuse was more common in patients treated with mAb (RR 0.78; 95% 0.71 to 0.85; $p < 0.01$; $I^2 = 55$; figure 1B). Similarly, patients in the mAb group experienced a significant decrease in disability, as measured by the Headache Impact Test (HIT-6) (MD –2.64; 95% CI –3.52, –1.76; $p < 0.01$; $I^2 = 0$; figure 1C).

Conclusion: These findings suggest monoclonal antibodies against CGRP are an effective treatment option for patients with chronic migraine and medication overuse.

Figure 1A. At 12 weeks, the average days of acute medication use was significantly lower in patients using anti-CGRP mAb compared to placebo.

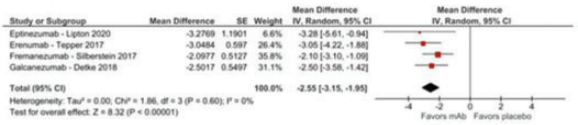

Figure 1B. Transition to no overuse of medications was more common with anti-CGRP mAb.

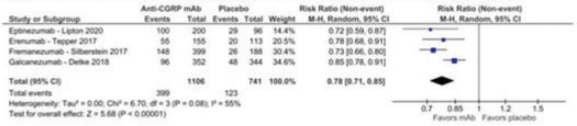

Figure 1C. Patients using anti-CGRP mAb had less headache related disability, as measured by the HIT-6.

Disclosure of Interest: None Declared

IHC23-PO-282

Sustained and Subsequent Response to Atogepant Among Individuals With Episodic Migraine With Prior Treatment Failure: Post Hoc Analysis of the ELEVATE Trial

Simona Sacco[1], Krisztian Nagy[2], Natty Chalermpalanupap[3], Fabrizio Vernieri[4], Jonathan H. Smith[5], Dagny Holle-Lee[6], Yingyi Liu[5], Karen Carr[5], Patricia Pozo-Rosich[7,8] and Richard B. Lipton[9]

[1]*University of L'Aquila, L'Aquila, Italy*
[2]*AbbVie, Budapest, Hungary*
[3]*AbbVie, Madison, NJ, USA*
[4]*Università Campus Bio-Medico di Roma, Roma, Italy*
[5]*AbbVie, North Chicago, IL, USA*
[6]*Department of Neurology, West German Headache and Vertigo Center Essen, University of Essen, Essen, Germany*
[7]*Vall d'Hebron University Hospital, Barcelona, Spain*
[8]*Universitat Autònoma de Barcelona, Barcelona, Spain*
[9]*Albert Einstein College of Medicine, Bronx, NY, USA*

Objective: Atogepant, an oral calcitonin gene–related peptide receptor antagonist, is approved in the United States for preventive treatment of migraine in adults, and in Puerto Rico, Canada, and Israel for the preventive treatment of episodic migraine in adults. This analysis was conducted to evaluate the proportions of (1) participants who sustained their initial response to atogepant over 12 weeks of treatment and (2) participants who did not experience an initial response but achieved a subsequent response with continued treatment.

Methods: This was a post hoc analysis of ELEVATE (NCT04740827), a phase 3, global, randomized,

double-blind, placebo-controlled trial of atogepant 60 mg once daily for the preventive treatment of episodic migraine among participants who had previously experienced an inadequate response with 2–4 classes of conventional oral preventive treatment. This analysis was conducted in the off-treatment hypothetical estimand (OTHE) population, which included all randomized participants who received ≥1 dose of study medication, had evaluable baseline data, and had ≥1 evaluable postbaseline 4-week period. Sustained response was assessed by calculating the proportion of participants with a reduction from baseline in monthly migraine days (MMDs) in month 1 who sustained at least that threshold of response in months 2 and 3. Response thresholds of ≥50%, ≥75%, and 100% were evaluated. Subsequent response was assessed by calculating the proportion of participants who did not experience a ≥30% or ≥50% reduction from baseline in MMDs in month 1 who experienced at least that response in subsequent months.

Results: Of 315 participants randomized to double-blind treatment, 309 were included in the OTHE population (placebo, n = 155; atogepant, n = 154; mean age 42.2 y; 89.6% female). The majority (61.3% [49/80]) of atogepant-treated participants who experienced an initial ≥50% MMD response in month 1 sustained this response throughout the trial (ie, a ≥50% response in both months 2 and 3). Additionally, 52.3% (23/44) and 47.6% (10/21) of participants who experienced a ≥75% or 100% initial response, respectively, sustained this response throughout the trial. Few participants remained nonresponders throughout the trial; only 12.7% (19/150) did not experience a ≥30% reduction from baseline in MMDs in any month, and only 22.3% (33/148) did not experience a ≥50% reduction in any month. Furthermore, a substantial proportion of participants who did not experience an initial response in month 1 experienced a response with continued treatment in month 2 or 3. Among participants who did not experience a ≥30% initial response, 32.5% (13/40) of these participants achieved a ≥30% response in month 2 and 48.6% (18/37) achieved this response in month 2 or 3. Among participants who did not experience a ≥50% initial response, 25.4% (17/67) achieved a ≥50% response in month 2 and 48.4% (31/64) achieved this response in month 2 or 3. Atogepant 60 mg once daily was well tolerated, and the safety results were consistent with the known safety profile of atogepant.

Conclusion: In the ELEVATE trial, atogepant was well tolerated and the majority of atogepant-treated participants who achieved an initial response in month 1 sustained their response throughout the 12-week treatment period. Among participants who did not experience a response to treatment in the first month, many went on to achieve a clinically meaningful reduction in MMDs with continued treatment.

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IHC23-PO-283

Adverse events leading to discontinuation of galcanezumab in Real Wold Evidence (RWE) in 1056 patients with migraine (Galca-Only Consortium).

Víctor Obach[1] and David Garcia-Azorin[2]

[1]*Hospital Clinic, Barcelona, Spain*
[2]*Hospital de Valladolid, Valladolid, Spain*

Objective: Anti-calcitonin gene-related peptide monoclonal antibodies are generally well tolerated, with few adverse effects and in most cases, mild in nature. We aim to describe the frequency of adverse events leading to discontinuation in a large series of patients treated with galcanezumab in a real world setting.

Methods: The "Galca-Only Consortium" is a multicenter ambisective cohort study. From November 15, 2019, to January 31, 2022, all consecutive patients with chronic migraine or high-frequency episodic migraine with prior failure to three or more migraine preventive drugs, treated with galcanezumab were included.

Patients were systematically assessed by headache experts and followed up quarterly for 12 months. A series of variables were gathered, related to patients' demographics, comorbidities, migraine diagnosis and situation and migraine burden. Response to treatment was according to the 50% responder rate, defined as the proportion of patients with who achieved a reduction of at least 50% in the number of headache days per month (HDM), compared to the baseline period.

During the entire study period, 12 months, the proportion of patients who discontinued galcanezumab due to adverse effects, in the opinion of the responsible physician, was assessed. Adverse events were classified according to the reported symptoms.

The study was approved by the Hospital Clinic of Barcelona Ethics Committee (HCB/2021/1327).

Results: During the study period, 70/1056 (6.6%) patients discontinued galcanezumab due to adverse events. A total of 90 adverse events were reported, summarized in the table.

Patients presenting adverse events leading to discontinuation did no differ in age, gender, years of migraine disease, HIT6 at baseline, compared to the rest of the patients.

There were differences in the proportion of patients with chronic migraines (92.9% vs 75.2%, p = 0.001), number of headache days per month at baseline (30 [25–39] vs 20 [14–30] p = 0.0.001) and frequency of comorbidities, such as mood disorders (58.3% vs 31.6%), fibromyalgia (21.7% vs 10.7%, p = 0–001), or other chronic pain (41.7% vs 18.4%, p = 0.001), respectively.

Conclusion: Galcanezumab discontinuation due to treatment emergent adverse effects in patients with migraine in a real world setting was infrequent. Half of them are due to dizziness or constipation.

Adverse Event (n = 90) in 70 patients	N (%)
Vertigo/Dizziness	31 (2.9)
Constipation	13 (1.2)
Local cutaneous pain o rash	9 (0.9)
Fatigue, drowsiness	9 (0.9)
Generalized cutaneous rash	7 (0.7)
Blood pressure instability	5 (0.3)
diarrhea, nausea, abdominal pain	4 (0.5)
Generalized pain	3 (0.3)
Others	9 (0.9)

Disclosure of Interest: None Declared

IHC23-PO-284

Randomized Controlled Trial of a Smartphone-Based Preventive Migraine Self-Management Program in the Emergency Department Setting: A Promising Teachable Moment

Mia T. Minen[1], Elizabeth Seng[2], Benjamin W. Friedman[3], Alexis George[1], Kristina Fanning[4], Ryan C. Bostic[4], Scott W. Powers[5] and Richard B. Lipton[3]

[1]*Department of Neurology, NYU Langone Health, New York, NY, USA*
[2]*Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA*
[3]*Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA*
[4]*MIST Research and Statistical Consulting, Wilmington, NC, USA*
[5]*Cincinnati Children's Hospital, Cincinnati, OH, USA*

Background: The emergency department (ED) is a critical point of contact with the health care system for many patients with migraine and an opportunity to initiate accessible non-pharmacologic migraine treatment. We examined whether a smartphone self-management progressive muscle relaxation (PMR) based therapy improved patient-centered outcomes for migraine compared to enhanced usual care (EUC).

Methods: We conducted a randomized controlled trial of the smartphone application RELAXaHEAD with and without PMR in patients who visited the ED for headache and met migraine criteria. We collected follow-up data on our main outcomes (migraine related disability (MIDAS), migraine related quality of life (MSQv2), and monthly headache days (MHDs) to determine whether there were improvements up to 3-months post-study initiation and report quantitative analyses.

Results: Of the 94 patients (Control (n = 48); PMR (n = 46)), 69/94 (73%) had baseline MIDAS and at least one follow-up MIDAS score. MIDAS mean change scores differed for the two groups (Control = 6.86 and PMR –25.09, p = 0.007. There was a statistically significant difference in the number of respondents improving by >5 MIDAS points for the PMR arm compared to the Control arm (PMR 28/34 (82.4%), Control 16/35 (45.7%), p = 0.002) and in the number of respondents improving by ≥10 MIDAS points, with (PMR 21/34 (61.8%), Control 13/35 (37.1%), p = 0.041). This effect persisted in Logistic Regression Models that included baseline MIDAS scores. For the MSQv2, Role function preventive and Emotional function change scores were higher among the PMR arm (n = 34) compared to Control (n = 35) with PMR 16.9 vs. Control 11.3 and PMR 26.5 vs. Control 19.8, respectively, while Role function restrictive change scores were similar

between groups (PMR 18.1 vs. Control 18.7) but independent sample t-tests found no statistically significant differences between PMR and Control groups for any MSQv2 subscale (RFR $p = 0.917$, RFP $p = 0.357$, EF $p = 0.409$). Of the 94 patients, 48 had three-month follow-up MHD data. PMR respondents ($n = 23$) had a -2.9 ± 8.0 mean MHD change, and those in the control group ($n = 25$) had a mean MHD change of -1.6 ± 6.5, $p = 0.533$).

Conclusion: In one of the few studies assessing how to help patients with migraine post-discharge from the ED, we found that a PMR-based self-management program yielded substantial clinically significant results in reducing migraine-related disability and a clinically though not statistically significant decrease in MHDs. Future work should examine how to implement this treatment into the ED workflow and how to make this treatment more accessible to patients.

IHC23-PO-285

Hull Prospective Analysis of OnabotulinumtoxinA (Botox)® in the treatment of chronic migraine; real-life data in 1306 patients; updated results on over 12 years experience

Rafiullah Khan[1], Modar Khalil[1], Alina BUTURE[1] and Fayyaz Ahmed[1,2]

[1]*Hull University Teaching Hospitals, Hull, United Kingdom*
[2]*Hull York Medical Shcool, Hull, United Kingdom*

Introduction: Chronic migraine (CM) is defined as headache on > 15 days/month for > 3 months of which > 8 days meet criteria for migraine with or without aura or respond to migraine-specific treatment, affects 2% of the general population and is the most disabling form of the disorder with substantial impact on quality of life.

Preventive treatment for episodic migraine may work in CM, however only topiramate has the established evidence. This and other oral agents have limitations due to poor tolerability, adverse effects and a considerable number of patients do not respond.

The efficacy and safety of OnabotulinumtoxinA in adults with CM was confirmed in the phase III Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) clinical programme leading to licensing authorities granting approval in CM. The real life prospective data from Hull in 254 patients was published in 2014.

OnabotulinumtoxinA was granted license in the UK by the Medicine and Healthcare product Regulatory Agency (MHRA) in July 2010, and in the USA by the Food and Drug Administration (FDA) in October 2010, and National Institute for Clinical Excellence (NICE) recommended its use in the National Health Service (NHS) in June 2012

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

Methods: Adult patients with CM attending the Hull migraine clinic were offered OnabotulinumtoxinA based on clinical needs. All patients had tried and failed at least one oral preventive migraine therapy and OnabotulinumtoxinA was delivered as per the PREEMPT study protocol. Patients were asked to maintain a headache diary for at least 30 days prior to and continuously after OnabotulinumtoxinA. Patients with medication overuse were included.

Data were extracted for headache days, migraine days, crystal clear (headache-free) days (primary outcome); also analgesic medication overuse, triptans use, and adverse events, before and after treatment (secondary outcome). Responder was defined according to Hull criteria defined as at least 50% reduction in either headache or migraine days or increment in headache free days twice that of the baseline or at least 6 headache free days in those less than 3 at baseline. Response rate was also measured as per NICE guidelines with 30% reduction on headache days post treatment.

1306 patients received 9485 cycles of OnabotulinumtoxinA, however we have included patients whom we have full data of their first cycle only (1132 patients), as including subsequent cycles will skew the results of our analysis.

Results: Of a series of 1306 patients, full data were available on 1132 patients (201 male, median age 45 years; range 14–79 years), 931 females (82% of the cohort) (median age 45 years, range 17–96 years). A total of 9485 treatment cycles were given. Patients had the diagnosis of CM for a median of 4 years (range 0.5–67 years). 1109/1132 (97.9%) had failed three preventive treatments. 588/1132 (51.9%) patients were overusing various analgesics. Mean headache and migraine days at baseline were 29 and 17 respectively.

The mean headache days reduced from 29 to 21 and migraine days reduced from 17 to 10 ($p < 0.001$) with HIT-6 score reduced from 68 to 62. 40% patients achieved at least 50% reduction in migraine days and 15% showed 75% reduction. 50% and 75% reduction in headache days were 23% and 8% respectively. A significant reduction in painkiller post treatment was observed. There was no difference in response in those with or without analgesic overuse.

·Adverse events reported were: Pain at the site of injection (10.3%), neck stiffness (10.3%), Ptosis (6.8%) and difficulty in swallowing (1%). Only 1% ($N = 11$) discontinued treatment due to side effects.

Conclusions: As far as we are aware this is the largest real-life data on patients receiving OnabotulinumtoxinA as a preventive treatment for CM. Our cohort represent

severely affected population than PREEMPT who had failed to respond to at least three first line treatment options. OnabotukinumtoxinA is an established, well tolerated, efficacious and safe preventive treatment option in CM.
Limitations: Our data is open-label and lacks a comparator hence a high placebo-response can not be eliminated.
Disclosure of Interest: FAYYAZ AHMED has received honorarium for being on the advisory board of Abbvie, Novartis, TEVA, Lundbeck, Eli Lilly, Pfizer, Electrocore, ENeura. He is a treasurer of the International Headache Society. Rafiullah Khan – None Modar Khalil – None Alina Buture – None

IHC23-PO-286

Two year outcome of fremanezumab in refractory chronic migraine patients: Real-world data from the Hull Migraine Clinic, UK

Rafiullah Khan[1], Somayeh Nasergivehchi[2], Modar Khalil[1], Helen Delroasario[1] and Fayyaz Ahmed[1,3]

[1]*Hull University Hospitals Nhs Trust, Hull, United Kingdom*
[2]*Hull University Teaching Hospitals, Hull, United Kingdom*
[3]*Hull York Medical School, Hull, United Kingdom*

Introduction: Fremanezumab is an anti-calcitonin gene-related peptide (CGRP) monoclonal antibody found to be efficacious for episodic (EM) and chronic migraine (CM) prevention in the HALO trials. It was approved in the UK by National Institute of Care and Clinical Excellence (NICE) for CM prophylaxis in patients unresponsive to $\geq$3 preventatives, with treatment cessation if $<$30% migraine frequency improvement after 12 weeks treatment (negative stopping rules). There are no restrictions on the duration of its use i.e., no positive stopping rules were recommended.
The efficacy and safety of fremanezumab for migraine prevention have been demonstrated in randomized, double-blind, placebo-controlled trials. Real-life data on safety and efficacy has been published recently by our group. There are reports on its safety and efficacy over 1–2 years although there is lack of literature on the long-term outcome on those that had responded to treatment. Many centres in the United Kingdom recommend treatment review after 12 months of treatment in responders. As per licensed indication most of the UK centres continue treatment if the monthly headache days exceed 4.
We report a two year follow up on a large cohort of refractory CM population who had failed a mean of 6 preventive treatment that responded at three month follow up.
Objectives: In this prospective audit, we evaluate the outcome on fremanezumab therapy at two year follow up from a tertiary headache clinic in the United Kingdom.
Methods: Patients with CM attending the Hull Headache Clinic at the Spire Hull and East Riding hospitals were recruited in the audit if they were prescribed fremanezumab for prophylaxis. Patients had already failed an average of 6 (range 5–11) previous preventive treatment inclusive of OnabotulinumtoxinA (91%). Patients were asked to maintain a headache diary for at least a month before commencing the treatment and continuously thereafter. To evaluate response all patients were reviewed at 3 months and those responding to treatment were asked to continue. At one year follow up, patients were asked to stop the treatment for three months if in the prior 3 months their monthly migraine days were $<$4 per month. In the subsequent three months the prescription was recommenced if the monthly headache days exceeded 4.
We measured monthly headache days (MHD), migraine days (MMD), headache-free days (HFD), acute analgesia medication days (AMD) and triptan days (TD), Headache Impact Test-6 (HIT-6) score monthly for three months to evaluate response months 9–12 at the 12 month follow up and 21–24 at 2 year follow up.
Results: 300 CM patient's refractory to an average of $>$6 preventatives who commenced monthly subcutaneous fremanezumab 225mg between Nov 2020 – Apr 2021 were recruited to the study. Patients were asked for verbal consent for an anonymised data collection and as this was a prospective audit, no ethical approval was required. Patients (N = 300) (221 F, 79 M), mean age 48.6 years (range 21–75). 243 patients (187 F, 56 M) at 3-month follow-up had baseline MHD, MMD and HFD of 28, 17 and 2 days, improving to 15, 6 and 15 days respectively were classed as responders and continued treatment for one year. The remaining 57 patients (34 F, 23 M) stopped treatment due to lack of response.
At one year 225 (92.5%) patients (213 F and 12 M) were still getting $>$5 days of headaches per month and continued treatment and only 18 (7.5%) patients (12 F, 6 M) were able to stop treatment. All but 3 had to restart therapy as the headache days exceeded $>$5 or more between 1–3 months following cessation of therapy. Hence 240/243 (98.7%) patients continued for the second year
At two year review (N = 240, 222F 18M) we were able to stop treatment on 33 patients with $<$4 days of headache in the previous three months. A further 17 patients were discontinued as they stopped responding to treatment with their monthly headache days reverting to baseline. 190 patients (178F, 12M) the prescription was renewed for the third year.
Conclusions: At two year follow up 22% of the initial cohort of responder were able to stop treatment. Only 15% stopped as their monthly headache days were $<$4. Remaining 7% stopped as they reverted to CM.
Disclosure of Interest: Fayyaz Ahmed is a treasurer of the International Headache Society. He has received honorarium for being on the advisory board of Abbvie,

Lundbeck, Novartis, Eli Lilly, Pfizer, Electrocore, ENeura. Rafiullah Khan – None Modar Khalil – None Somayeh Nasergivehchi – None Helen Delrosario – None

IHC23-PO-287

Do elderly patients with migraine have the same effectiveness and toleability to galacanezumab in Real Wold Evidence (RWE)? A series of 40 cases in Galca-Only Consortium.

Víctor Obach[1], Daniel Guisado[2], Antia Moreira[2], Elisa Cuadrado[2], Yesica Gonzalez Osorio[3], Alvaro Sierra[4] and David GArcia-Azorin[3]

[1]*Hospital Clinic, Barcelona, Spain*
[2]*Hospital del Mar, Barcelona, Spain*
[3]*Hospital de Valladolid, Valladolid, Spain*
[4]*Hsopital de Valladolid, Valladolid, Spain*

Objective: Patient over 70 years old with migraine are underrepresented in anti CGRP monoclonal antibody clinical trials. We analyze the tolerability and effectiveness of galcanezumab in this group of patients from a large multicentre registry.

Methods: The "Galca-Only Consortium" is a multicenter ambispective cohort study. All consecutive patients with chronic migraine or high-frequency episodic migraine with prior failure to three or more migraine preventive drugs, treated with galcanezumab were included. Patients were systematically assessed by headache experts and followed up quarterly for 12 months. A series of variables were gathered, related to patients' demographics, comorbidities, migraine diagnosis and situation and migraine burden. Response to treatment was according to the 50% responder rate (R50), defined as the proportion of patients with who achieved a reduction of at least 50% in the number of headache days per month, compared to the baseline period. Data of follow-up at 12 months are presented.

In the present sub-analysis, patients older than 70 years old were compared with the younger cohort.

Results: In our registry of 1055 patients, 46 patients (4.4%) were older than 70 years old. Demografics are shown in the table. The proporion of men is higher than in the younger group. They also presented higher number of MHDs and as expected, had longer period of migraine worsening before galcanezumad treatment was started.

At 12 month follow-up, the R50 was 47.8% similar to 41.0% in the yonger group. No differences were observed in Galcanezumab retention rate 65.2% and 71.6% and discontinuation due to adverse events 8.7% and 6.5%, respectively.

Conclusion: The effectiveness and safety of galcanezumab in migraine patients over 70 years old in RWE is similar to younger patients.

Variables	Patients over 70 years old n = 46	Patients 18 to 69 years old n = 1009	P value
Age, mean (SD)	74.8 (4.5)	48.6 (11.0)	0.001
Female, n (%)	31 (67.4)	844 (83.6)	0.006
Migraine worsening, years [IQR]	12 [7–21]	8 [4–13]	0.001
Chronic migraine, n (%)	40 (87.0)	766 (75.9)	0.08
Monthly Headache Days (MHDs), baseline [IQR]	30 [16–30]	20 [14–20]	0.008
Monthly Daily Headache (30 Days), n (%)	24 (52.2)	324 (32.1)	0.005
HIT6 baseline [IQR]	71 [67–74]	68 [65–72]	0.12
Mental disorders, n (%)	11 (30.6.9)	335 (39.7)	0.3
Chronic pain syndrome, n (%)	11 (30.6)	195 (23.1)	0.3

Disclosure of Interest: None Declared

Neuromodulation for headache

IHC23-PO-288

Biological effect and therapeutic potential of columbianadin on Blood-Brain Barrier permeability

Dinesh Kumar Patel

Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, India

Background: Plant derived natural products have important role in the medicine. Coumarins class phytochemicals are an important class of secondary metabolite found to be present in the varieties of plants. Chemically the coumarins have benzopyrone structures in their core which facilitate coumarins to attach with different receptors and enzymes through non-covalent bond.

Methods: Biological importance of columbianadin has been investigated in the medicine through scientific data analysis of different research work. Pharmacological potential of columbianadin for their effectiveness on human disorders have been investigated through scientific data analysis of different scientific research work. Biological effect of columbianadin on Blood-Brain Barrier permeability has been investigated through scientific data analysis of different scientific research work.

Results: Scientific data analysis of different scientific research revealed the biological potential of columbianadin in the medicine for their effectiveness against various forms of human disorders. Columbianadin is a coumarin class phytochemical found to be present in the Angelicae pubescentis. Biological effect of columbianadin on Blood-Brain Barrier permeability were investigated through scientific data analysis of various scientific research work and revealed moderate absorption.
Conclusion: Scientific data analysis revealed the biological effect of columbianadin on Blood-Brain Barrier permeability.
Disclosure of Interest: None Declared

IHC23-PO-289

Trigeminal autonomic cephalalgias and occipital neurostimulation: two case reports

Catarina Fernandes[1], Ricardo Pereira[2] and Isabel Luzeiro[1,3]

[1]*Neurology Department, Hospitalar and University of Coimbra, Coimbra, Portugal*
[2]*Neurosurgery Department, Hospitalar and University of Coimbra, Coimbra, Portugal*
[3]*Coimbra Health School/ESTeSC, Coimbra, Portugal*

Introduction: Trigeminal autonomic headache disorders include cluster headache (CH), paroxysmal hemicrania, hemicrania continua and short-lasting unilateral neuralgiform headache attacks (SUNCT). A wide range of pharmacologic treatments are available, but some patients do not respond to these treatments. Alternative options include injectable medications, surgical resection, and neurostimulation, such as occipital nerve stimulation (ONS). ONS is a nondestructive surgical option that is increasingly proving to be a safe and successful method.
Methods: Non-systematic literature review and characterization of the clinical and therapeutic response of two clinical cases of SUNCT and chronic CH.
Results: We present two clinical cases: a 54-year-old female patient diagnosed with SUNCT with severe impairment of quality of life. The patient reported that the frequency and intensity of attacks had not improved despite optimized medical treatment. Brain MRI showed no neurovascular contacts or structural lesions. She was proposed for a trial ONS. After 3 months, the patient showed a decrease in the intensity and duration of pain attacks, but no decrease in the frequency of attacks.The second patient, a 61-year-old woman with a history of refractory chronic CH, underwent a trial ONS after 5 years of diagnosis. She had a history of aneurysm of the internal carotid artery and reported only improvement in headache with lithium. Three months after implantation of ONS, the patient was attack-free and had optimal adaptation to the device.
Conclusion: These clinical cases showed significant improvement in the quality of life of patients with ONS. Neurostimulation techniques show promising results and should be considered as an early treatment option in the future.
Disclosure of Interest: None Declared

IHC23-PO-290

Randomized trial of non-invasive neuromodulation of the central μ-opioid system in migraine

Alexandre DaSilva[1,2], Dajung Kim[2,3], Manyoel Lim[2,2,4], Thiago Nascimento[2,3], Peter Scott[5], Yolanda Smith[6], Robert Koeppe[5], Jon-Kar Zubieta[7] and Niko Kaciroti[8]

[1]*Headache and Orofacial Pain Effort (H.O.P.E.) Laboratory, Department of Biologic and Materials Sciences & Prosthodontics, University of Michigan School of Dentistry, Ann Arbor, USA*
[2]*Michigan Neuroscience Institute, University of Michigan, Ann Arbor, USA*
[3]*Department of Biologic and Materials Sciences & Prosthodontics, University of Michigan School of Dentistry, Ann Arbor, USA*
[4]*Food Convergence Research Division, Korea Food Research Institute, Wanju, Korea, Republic of*
[5]*Department of Radiology, University of Michigan, Ann Arbor, USA*
[6]*Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, USA*
[7]*Department of Psychiatry, Mass General Brigham, Newton-Wellesley Hospital, Newton, USA*
[8]*Department of Biostatistics, University of Michigan, Ann Arbor, USA*

Objective: The migrainous brain remains underexplored as a target for neuromodulation to improve headache attacks and modulate our own opioid resources. This study aimed to determine whether high-definition transcranial direct current stimulation (HD-tDCS) over the primary motor cortex (M1) can improve clinical outcomes and endogenous μ-opioid receptor (μOR) availability for episodic migraineurs.
Methods: In a randomized, double-blind, and sham-controlled trial, 25 patients completed 10-daily 20-min M1 HD-tDCS, repeated Positron Emission Tomography (PET) scans with a selective agonist for μOR. Twelve age- and sex-matched healthy controls participated in the baseline PET/MRI scan without neuromodulation. The primary endpoints were moderate-to-severe (M/S)

headache days and responder rate ($\geq$ 50% reduction on M/S headache days from baseline), and secondary endpoints included headache intensity and the use of rescue medication over 1-month after treatment.
Results: Active M1 HD-tDCS, compared to sham, resulted in better clinical outcomes predominantly in higher-frequency individuals, as demonstrated by an interaction between treatment indicator and baseline migraine attack frequency on the M/S headache days and responder rate. These favorable outcomes were also observed for the secondary endpoints in higher-frequency patients (>3 attacks/month). The active treatment also increased the μOR concentration compared to the sham (and reversed it to healthy control levels) in the limbic and descending pain modulatory pathway, which, notably, mediated the clinical effectiveness of HD-tDCS in the higher-frequency patients.
Conclusion: The 10-daily M1 HD-tDCS has the potential to improve crucial clinical outcomes in episodic migraineurs, particularly those with a higher baseline frequency of migraine attacks (>3 attacks/month), which is possibly attributed to the increase in the endogenous μOR availability.
*Drs. DaSilva and Kim contributed equally to this work.

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IHC23-PO-291

A pilot randomized clinical trial study on M1 HD-tDCS effect on central μ-opioid receptor availability and pain sensitivity in temporomandibular disorder

Dajung Kim[1,2], Thiago Nascimento[1,2], Manyoel Lim[1,2,3], Theodora Danciu[4], Jon-Kar Zubieta[5], Peter Scott[6], Robert Koeppe[6], Niko Kaciroti[7] and Alexandre DaSilva[2,8]

[1]*Headache and Orofacial Pain Effort (H.O.P.E.) Laboratory, Department of Biologic and Materials Sciences & Prosthodontics, University of Michigan School of Dentistry, Ann Arbor, USA*
[2]*Michigan Neuroscience Institute, University of Michigan, Ann Arbor, USA*
[3]*Food Convergence Research Division, Korea Food Research Institute, Wanju, Korea, Republic of*
[4]*Department of Periodontics & Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, USA*
[5]*Department of Psychiatry, Mass General Brigham, Newton-Wellesley Hospital, Newton, USA*
[6]*Department of Radiology, University of Michigan, Ann Arbor, USA*
[7]*Department of Biostatistics, University of Michigan, Ann Arbor, USA*
[8]*Headache and Orofacial Pain Effort (H.O.P.E.) Laboratory, Department of Biologic and Materials Sciences & Prosthodontics, Ann Arbor, USA*

Objective: This study explored the association between experimentally induced pain sensitivity and μOR availability in patients with temporomandibular disorder (TMD) and further investigated any potential changes in pain and μOR availability after high-definition transcranial direct current stimulation (HD-tDCS) over the primary motor cortex (M1).
Methods: Nineteen patients with TMD participated in baseline Positron Emission Tomography (PET) with [11C] Carfentanil, a selective μOR agonist, consisting of early resting and late sustained masseteric pain challenge phase with an injection of 5% hypertonic saline to the most symptomatic side. Additionally, 7 patients with TMD received either active (n = 3) or sham M1 HD-tDCS (n = 4) for 10 sessions over 2 weeks, followed by a second PET scan.
Results: We observed that patients with more sensitive to pain, indicated by lower saline infusion rate, had less μOR availability in the right amygdala (MNI x = 28, y = −4, z = −14; at voxel-level $p < .005$ (uncorrected), with cluster-level family-wise error (FWE)-corrected $p < 0.05$) during the late phase of the PET scan. Active M1 HD-tDCS treatment, compared to sham, increased μOR availability in the thalamus (p for interaction = 0.11) during the resting state and amygdala, hippocampus, and, parahippocampal gyrus (p for interaction = 0.05, 0.06, and 0.11, respectively) during the late phase. Importantly, there was a correlation between enhanced μOR availability in limbic structures, including the amygdala and hippocampus, and a decrease in pain sensitivity.
Conclusion: The findings support the crucial role of the μOR system in regulating pain and highlight the potential utility of HD-tDCS as a therapeutic approach for TMD. However, larger-scale studies are needed to establish the clinical significance of our results.
Disclosure of Interest: This work was supported by grant grant numbers U01-DE025633 (Dr. DaSilva) and R56 DE022637-01 (Dr.DaSilva) from the National Institute of Dental and Craniofacial Research. No other disclosures were reported.

IHC23-PO-292

Occipital transcranial direct current stimulation in episodic migraine patients: effect on resting-state functional connectivity

Lars Michels[1], Nabin Koirala[2], Heiko Pohl[3], Peter Sandor[4], Marius Moisa[5], Christian Ruff[5], Roger Luechinger[6], Jean Schoenen[7], Franz Riederer[8], Andreas Gantenbein[9] and Muthuraman Muthuraman[10]

[1]*Department of Neuroradiology, Clinical Neuroscience Center, University Hospital Zurich, Zurich, Switzerland*
[2]*Child Study Center, School of Medicine, Yale University, New Haven, USA*
[3]*Department of Neurology, University Hospital Zurich, Zurich, Switzerland*
[4]*Department of Neurology and Neurorehabilitation, ZURZACH Care, Bad Zurzach, Switzerland*
[5]*Zurich Center for Neuroeconomics (ZNE), Department of Economics, University of Zurich, Zurich, Switzerland*
[6]*Institute for Biomedical Engineering, ETH Zurich and University of Zurich, Zurich, Switzerland*
[7]*Headache Research Unit, Department of Neurology-Citadelle Hospital, University of Liège, Liege, Belgium*
[8]*Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland*
[9]*Department of Neurology and Neurorehabilitation, ZURZACH Care, Bad Zurich, Switzerland*
[10]*Movement Disorders and Neurostimulation, Biomedical Statistics and Multimodal Signal Processing Unit, Department of Neurology, University Medical Center of Johannes Gutenberg University Mainz, Mainz, Germany*

Objective: Migraine patients also have functional brain abnormalities in the interictal period. This study examined between-network and within-network brain function interactions, comparing episodic migraineurs and healthy controls. In addition, it investigated the influence of anodal (excitatory) transcranial direct current stimulation (tDCS) on those interactions when applied over the medial occipital cortex. We hypothesized that only verum tDCS resulted in normalized directed connectivity.

Methods: We included healthy 20 adult controls (mean age: 31.6 ± 11.9 years, 17 females) and 22 female episodic migraineurs (mean age 37 ± 10.9 years, 15 with aura). After a 28-day baseline period (no stimulation) followed by a baseline visit, all migraine patients received daily active or sham anodal tDCS over the occipital lobe for the next 28 days. All participants underwent resting-state functional magnetic resonance imaging (fMRI) at baseline (B); migraine patients were also scanned shortly after the stimulation period and five months later. We conducted directed functional connectivity analysis at these time points to examine cortical (visual, somatomotor, fronto-parietal attention, dorsal attention, default mode, salience) and subcortical (limbic) network interactions.

Results: At baseline, migraine patients displayed lower between-network connectivity compared to controls in all seven cerebral networks as defined in (Yeo et al. 2011) especially eminent in the visual, somatomotor, default mode, and salience networks. This abnormality disappeared at the follow-up MRIs in in patients treated with tDCS ($n = 10$) but not in the sham ($n = 12$) tDCS group ($p < 0.001$; repeated-measures analysis of variance; main effect of time and group, and group $\times$ time interaction effect), and was replaced by an increased directed connectivity between those networks over time. In addition, tDCS reduced bidirectional (i.e. single-to-all and all-to-single) network interactions of the dorsal attention network to the other networks.

Network interactions originating from the limbic system and frontoparietal attention networks were not affected by tDCS. However, tDCS led to a progressive decrease in directed connectivity from the subcortical to cortical networks. Within-network connectivity normalized in the tDCS group. The number of migraine days correlated inversely with the within network-connectivity of the default mode network in the active group, most pronouncedly at the last MRI visit. Additionally, the active group showed a positive association between changes in migraine days (primary endpoint) and network interactions in the salience network.

Conclusions: Our results suggest that occipital anodal tDCS normalizes cortical network interactions. In addition, changes in migraine days may lead to within-network reorganization in patients with tDCS.

Disclosure of Interest: None Declared

IHC23-PO-293

Comparison of migraine with and without aura in a large cohort: Disease characteristics and response to Remote Electrical Neuromodulation (REN) treatment

Teshamae S. Monteith[1], Alit Stark-Inbar[2], Sharon Shmuely[2], Alon Ironi[2], Peter J. Goadsby[3,4], Richard B. Lipton[5] and Alan M. Rapoport[6]

[1]*Headache Division, Department of Neurology, University of Miami, Miller School of Medicine, Miami, USA*
[2]*Theranica Bio-Electronics, Netanya, Israel*
[3]*NIHR King's Clinical Research Facility & SLaM Biomedical Research Centre, and Wolfson CARD, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom*
[4]*Department of Neurology, University of California, Los Angeles, USA*

[5]Albert Einstein College of Medicine, Montefiore Headache Center, Bronx, USA
[6]The David Geffen School of Medicine at UCLA, Los Angeles, USA

Objective: Among people with ICHD-3 defined migraine about 30% have migraine with aura (MWA). Studies have shown that individuals with MWA may respond differently to acute and preventive treatments compared to those with migraine without aura (MWoA). Remote electrical neuromodulation (REN) is an FDA-cleared, safe, non-pharmacological, wearable device for the acute and/or preventive treatment of migraine with or without aura in patients 12 years of age or older. This study aims to characterize further the demographic and attack characteristic differences between patients with MWA versus MWoA, and to evaluate real-world efficacy and safety of acute treatment of migraine with REN for these patients.

Methods: Prospective real-world data were collected between October 2019 and February 2023 through the REN device (Nerivio®) smartphone application from all patients who chose to voluntarily report attack characteristics. Patients were classified as MWA if they reported the presence of aura during at least one attack, and MWoA if they reported no aura during any of their attacks. Data were analyzed on a patient level according to baseline reports at the beginning of treatment: pain intensity level (0–3 scale), presence/absence of aura and of each of the following associated symptoms (photophobia, phonophobia, nausea/vomiting, neck stiffness). We identified patients as suffering from each of the associated symptoms if they reported their presence in at least 50% of the attacks (corrected for multiple comparisons). We further identified patients as experiencing severe headache attacks if they reported pain intensity level = 3 in at least 50% of the attacks. We further analyzed consistent efficacy 2-hours post treatment in at least 50% of the REN treatments, as well as device safety.

Results: Real-world data were analyzed from 24,446 (87.0% female) patients who reported a total of 322,548 attacks. Of these, 9,468 patients reported having aura for at least one treated attack over a total of 171,451 attacks (MWA group); 14,978 patients never reported aura, over a total of 151,097 attacks (MWoA group). The MWA group was slightly younger (MWA, mean 37.9 ± SD 14.6, MWoA mean 39.9 ± SD 16.3; $P < 0.001$) and had a higher percentage of females (MWA 88.8% female, MWoA 86.0% female; $P < 0.001$). More patients in the MWA group reported severe pain intensity (34.1% vs. 28.1%; $P < 0.001$), as well as each of the associated symptoms: photophobia (78.9% vs 62.3%; $P < 0.001$), phonophobia (64.9% vs. 51.5%; $P < 0.001$), nausea and/or vomiting (44.1% vs. 31.4%; $P < 0.001$) and neck stiffness (41.1% vs. 34.8%; $P < 0.001$). REN was found to be highly effective in both subgroups, with approximately two out of three patients reporting pain relief (MWA 69.4%, MWoA 65.8%; $P < 0.05$) and one out of four patients reporting pain freedom (MWA 23.8%, MWoA 24.3%; $P = 0.657$). REN was found to be safe in both subgroups, with only 0.26% of patients reporting device-related adverse events, all non-serious.

Conclusion: These findings, from a large cohort, suggest that individuals with MWA have migraine with greater pain intensity and more frequent associated symptoms. Despite this, REN was found to be an effective and safe treatment option for those living with migraine, regardless of aura status.

Disclosure of Interest: Of direct relevance, AMR has consulted for Theranica; ASI, SS, and AI are employed by Theranica. TSM has received personal compensation for serving on advisory boards for Biohaven, Allergan/Abbvie, Lundbeck, Novartis, Amgen, Teva, Linpharma and Impel Neuropharmaceuticals. She has also served as a site principal investigator without direct compensation for Teva, Eli Lilly, Electrocore, Amgen, and Novartis; she has received grants from Amgen and Abbvie (to institution). She is on the editorial board for Brain and LIfe Magazine, Continuum Audio, and Neurology. She has received honoraria from Medscape, Springer (Neurodiem) and Massachusetts Medical Society, American Academy of Neurology and American Headache Society. She is an uncompensated co-author for studies sponsored by Abbvie and Pfizer. PJG reports, over the last 36 months, a grant from Celgene, and personal fees from Aeon Biopharma, Allergan/Abbvie, Amgen, CoolTech LLC, Dr Reddys, Eli-Lilly and Company, Epalex, GlaxoSmithKline, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, Shiratronics, Teva Pharmaceuticals and Tremeau, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer, and for medicolegal advice in headache, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee. RBL receives research support from the NIH: 2PO1 AG003949 (mPI), 1RF1 AG057531 (Site PI), RF1 AG054548 (Investigator), 1RO1 AG048642 (Investigator), R56 AG057548 (Investigator), RO1 AG060933 (Investigator), RO1 AG062622 (Investigator), 1UG3FD006795 (mPI), 1U24NS113847 (Investigator), U01 AT011005 (Investigator), 1R01 AG075758 (Pending—Investigator), 1R01 AG077639 (Pending—Investigator), K23 NS107643 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation, and research grants from TEVA, Satsuma, and Amgen. He serves on the editorial board of Neurology, is senior advisor to Headache, and is associate editor to Cephalalgia. He has reviewed for the NIA and NINDS, holds stock and

stock options in Biohaven Holdings as well as stock options in Manistee; serves as a consultant, advisory board member, or has received honoraria from: AbbVie (Allergan), American Academy of Neurology, American Headache Society, Amgen, Avanir, Axsome, Biohaven, BioVision, Boston Scientific, Dr. Reddy's (Promius), electroCore, Eli Lilly, eNeura Therapeutics, Equinox, GlaxoSmithKline, Grifols, Lundbeck (Alder), Merck, Pernix, Pfizer, Satsuma, Supernus, Teva, Trigemina, Vector, and Vedanta. He receives royalties from Wolff's Headache 7th and 8th editions, Oxford University Press, 2009, Wiley, and Informa. AMR serves as an advisor for AbbVie, Biohaven, Cala Health, Lundbeck, Pfizer, Satsuma, Teva Pharmaceutical Industries, Theranica and Xoc; he is on the Speakers Bureau of AbbVie, Biohaven, Impel, Pfizer and Teva Pharmaceutical Industries.

Other primary headache disorders

IHC23-PO-294

Other primary headache disorders: data from the head-MENA-A study in the Africa, Asia and, Middle East

Arife Çimen Atalar[1], Hamit Genç[2], Emel Ur Özçelik[1], Hayrunnisa Bolay[3], Derya Uludüz[4], Işın Unal-Cevik[5], Najib Kissani[6], Otgonbayar Luvsannorov[7], Mansoureh Togha[8], Aynur Özge[9], Betül Baykan[10,11] and Head-MENAA-A Study Group[12]

[1]*Kanuni Sultan Süleyman Education and Research Hospital, Department of Neurology, İstanbul, Turkey*
[2]*Van Training and Research Hospital, Van, Turkey*
[3]*Gazi University, Medical Faculty, Department of Neurology and Algology, Ankara, Turkey*
[4]*Istanbul University Cerrahpaşa, Medical Faculty, Department of Neurology, İstanbul, Turkey*
[5]*Hacettepe University, Medical Faculty, Department of Neurology, Ankara, Turkey*
[6]*Neuroscience Research Laboratory in Marrakesh Medical School, Cadi Ayyad University, Marrakech, Morocco*
[7]*Mongolian National University of Medical Sciences, Department of Neurology, Ulaanbaatar, Mongolia*
[8]*Tehran University of Medical Sciences, Department of Neurology, Tehran, Iran, Islamic Republic of*
[9]*Mersin University, Medical Faculty, Department of Neurology, Mersin, Turkey*
[10]*Istanbul University, Istanbul Faculty of Medicine, Department of Neurology, İstanbul, Turkey*
[11]*EMAR Medical Center, İstanbul, Turkey*
[12]*Head-MENA-A region Neurology Centers, İstanbul, Turkey*

Objective: Other primary headache disorders (OPHD) are under-investigated compared to the major primary headaches such as migraine, tension-type headache (TTH) and trigeminal autonomic cephalalgias (TACs). To recognize and differentiate OPHDs in practice, knowledge about the distribution and characteristics of subtypes is needed. We aimed to determine the prevalence and clinical characteristics of OPHDs, in patients from 13 countries worldwide, to guide the clinicians.

Methods: A large dataset derived from a cross-sectional study, titled Head-MENAA (Middle East, North Africa, Asia) conducted between April-May, 2022 was analyzed. Patients over 18 years, with headache as the primary reason for admission, were included from outpatient clinics, service, private clinics, and emergency/other inpatient services. A structured questionnaire, including the demographics, headache characteristics, accompanying symptoms, triggers were applied and headache subtypes were diagnosed by experts according to the ICHD-3 criteria as primary cough headache, primary exercise headache, primary headache associated with sexual activity, primary thunderclap headache, cold-stimulus headache, external-pressure headache, primary stabbing headache (PSH), nummular headache, hypnic headache and new daily persistent headache (NDPH).

Results: Of the cohort with a primary complaint of headache (n = 3722), 106 (2.85%) were diagnosed with OPHD. Fifty-two patients (1.39% of all patients with headache) had only OPHD, whereas 54 (1.45%) had both OPHD and a comorbid primary headache disorder (migraine, TTH or TAC). The most frequent subtypes were NPHD and PSH (0.2% among all patient cohort, each). All OPHDs were more frequent in females. Photophobia and phonophobia were the most frequent accompanying symptoms and physical activity (28.8%), stress (15.4%), and the Valsalva effect (15.4%) were the most common triggering factors in patients with OPHDs. The majority of the triggering factors were more explicit in patients with both migraine & OPHD diagnoses.

Conclusions: Other primary headache disorders are rare and heterogeneous; PSH and NDPH come forefront as the most frequent subtypes. The high comorbidity with major primary headaches, migraine in particular, suggests the presence of underlying predisposing factors such as common genetic background which supports the concept of "a headache continuum" for primary headaches. Besides, migraine comorbidity increases the vulnerability of the patient to triggers.

Disclosure of Interest: None Declared

IHC23-PO-295

A case of Primary Headache Associated with Sexual Activity (PHASA) presented with Persistent Genital Arousal Disorder (PGAD)

Woo-Seok Ha[1] and Hye-Kyung Baek[2]

[1]*Yonsei University College of Medicine, Seoul, Korea, Republic of*
[2]*Korean Institute for Sexual and Couple's Health, Seoul, Korea, Republic of*

We present a case of headache associated with sexual activity (PHASA) with persistent genital arousal disorder (PGAD). A 57-year-old woman with no history of headache, who had been sexually inactive with her partner for over 10 years, suffered from recurrent, unwanted episodes of genital arousal lasting 3∼5 days for 4 years. In March, 2021, she began to experience intense genital arousal that she had never experienced before. The arousal was accompanied by genital dysesthesia (tingling, buzzing), and was triggered by non-sexual stimuli, such as minute vibrations while driving. On the 4th day of symptom onset, while attempting coitus with her partner, she experienced an abrupt explosive headache, which was repeated during another coitus a week later. The patient underwent laboratory tests, brain MRI and MRA, all of which were normal. The patient was referred to a sexual medicine specialist and prescribed amitriptyline, escitalopram and propranolol with a diagnosis of PGAD. Her sexual arousal gradually diminished and when she stopped all medication three months later, all symptoms had disappeared. On further investigation, her spinal MRI revealed a Tarlov cyst, which is reported to be common in patients with PGAD. She has been in remission for two years. This case illustrates the co-occurrence of PHASA and PGAD and suggests a possible common pathophysiology between the two rare disorders.

Disclosure of Interest: None Declared

IHC23-PO-296

Identifying subtypes of primary new daily persistent headache using cluster analysis

Sanjay Cheema[1], Khadija Rantell[2] and Manjit Matharu[1]

[1]*Headache and Facial Pain Group, UCL Queen Square Institute of Neurology, London, United Kingdom*
[2]*Education Unit, UCL Queen Square Institute of Neurology, London, United Kingdom*

Objective: Primary new daily persistent headache (NDPH) is proposed to be a heterogenous group of disorders, but this is solely based on anecdotal evidence. We aimed to identify data-driven subtypes of primary NDPH using cluster analysis.

Methods: We used prospectively collected data on the demographics, headache phenotype, and comorbidities of 337 patients with primary NDPH according to ICHD-3 criteria. K-means cluster analysis with Gower distance was used to identify sub-clusters. Other linkage and distance clustering methods were also tested but none gave a better solution. We compared differences between the clusters using one-way ANOVA for continuous variables and Chi-squared for categorial variables, and we assessed whether treatment response differed between the clusters.

Results: We identified three clusters which differed by age, sex, headache intensity, migrainous features and headache number of headache triggers (see Table). Cluster 1 included older patients, a high proportion of males, and less severe headaches. Cluster 2 was predominantly female, had severe headaches, but few associated symptoms. Cluster 3 was young, predominantly female, with a high prevalence of migrainous symptoms and triggerability. Cluster 3 was most likely to respond to acute treatments (48%) compared to clusters 1 (30%) and 2 (24%), $X^2 = 12.4$, $p = 0.002$. There was no significant difference in response to preventive treatments.

Conclusion: We have identified three possible subphenotypes of primary NDPH. The features of Cluster 3 suggest a migraine-like biology. The mechanisms of cluster 1 and cluster 2 are unclear. Further testing is required to determine the biological basis of the groups and whether similar clusters are reproducible in other cohorts.

Table. Clinical variables which significantly differed between the three clusters

	Cluster 1 n = 148	Cluster 2 n = 103	Cluster 3 n = 86	P value
Age (years)	41.4	36.7	30.2	<0.001
Female sex (%)	48.7	70.9	72.1	<0.001
Background intensity (0–10 scale)	3.2	6.8	5.1	<0.001
Exacerbation intensity (0–10 VRS)	6.9	8.4	8.3	<0.001
Throbbing quality (%)	45.3	39.8	72.1	<0.001
Photophobia (%)	52.7	47.6	80.2	<0.001
Phonophobia (%)	54.1	51.5	75.6	0.001
Osmophobia (%)	15.5	9.7	32.6	<0.001
Number of triggers	2.2	1.8	6.5	<0.001

Disclosure of Interest: None Declared

IHC23-PO-297

New Daily Persistent Headache with Nutcracker Physiology and Spinal Epidural Venous Congestion: Case Series with Lumbar Vein Embolization as a Therapeutic Approach

Todd Rozen, Zlatko Devcic and Beau Toskich

Mayo Clinic Florida, Jacksonville, USA

Objective: To describe a case series of patients with treatment refractory new daily persistent headache (NDPH) and their response to lumbar vein coil embolization to alleviate spinal epidural venous congestion secondary to left renal vein compression.
Background: The authors have previously published on a unique subset of NDPH patients whose headaches worsened in the Trendelenburg position and who on time-resolved MR angiography demonstrated left renal vein (LRV) compression (nutcracker physiology NP) with retrograde left second lumbar vein flow (L2LV) and regional spinal epidural venous plexus congestion (EVP). The spinal cord EVP was hypothesized to cause NDPH via secondary cerebral vein congestion leading to an abnormal rest of CSF pressure to an elevated state. Previously renal autotransplant and other surgical techniques were the only treatments available to patients with symptoms related to NP. The authors recently published a case report utilizing minimally invasive endovascular lumbar vein embolization as a new therapeutic approach to NDPH in this specialized population. We now present a larger case series with long term follow-up.
Methods: Case series.

Procedure: In all cases catheter-based venography from the LRV demonstrated retrograde L2LV flow with regional spinal EVP congestion. Embolization of the L2LV was performed using microcoils. Repeat LRV venogram demonstrated no further flow into the L2LV with complete resolution of spinal EVP congestion.
Results: 4 patients have had coil embolization of which 3 are one year from their procedure while one patient is 9 months post treatment All met ICHD-3 criteria for NDPH. All patients were women ages: 19, 46, 59 and 59 years. Duration of NDPH prior to embolization was 8, 4, 5 and 5 years respectively. All failed at least 4 different headache preventive medications. Two patients had no triggering event for NDPH, while two were possibly triggered by airline travel. Post-embolization all four patients had improvement in their headaches. One patient is headache free and discontinued all headache medication. One patient was headache free for several weeks then had headache recurrence. A second embolization was performed to close an additional vein with retrograde EVP flow which developed after the first embolization. She is currently 90–95% improved with most days being completely headache free and requiring low dose prn usage of acetazolamide. A 3rd patient was headache free x 5 months off any medication but then had headache recurrence. She is now 90–95% improved headache wise with a substantial amount of daily pain free time on a small dose of acetazolamide which was ineffective prior to her initial embolization procedure. Finally, the youngest patient, who also had the longest duration of NDPH, has had only a 20% reduction in baseline pain intensity with no pain free time. However, she no longer experiences periods of severe pain exacerbation which used to occur multiple times per week, thus quality of life has improved. Of the 3 patients with the most improvement in headache, two awoke the day after the procedure with no pain while a 3rd was 75% better. These 3 patients all developed NDPH at age 40 years or older. There were no side effects from the procedure or procedure related complications. 3 patients had follow-up venography 6 months post embolization and this re-demonstrated the resolution of retrograde lumbar vein flow into the spinal EVP.
Conclusion: Our case series demonstrates that embolization of L2LV in treatment refractory NDPH in the setting of LRV compression, retrograde L2LV flow, and regional spinal EVP congestion may improve headaches. 3 of our 4 treated cases have had a significant headache response through one year follow-up. A possible positive predictive factor for doing well long-term is dramatic headache improvement 24–48 hours post procedure. Older age of onset of NDPH may also be a positive predictive factor. Coil embolization appears to cause permanently decreased retrograde spinal EVP flow on subsequent imaging but as some of our patients had headache recurrence other secondary pathways of retrograde venous flow and spinal EVP congestion may develop after the initial embolization. Lumbar vein embolization is a minimally invasive outpatient technique with no apparent side effects. It is less morbid than standard of care surgical techniques and provides a potential alternative treatment for NDPH with NP and spinal EVP congestion.
Disclosure of Interest: None Declared

IHC23-PO-298

Long-term Prognosis of New Daily Persistent Headache: A Clinic-Based Study

Yi-Hao Chen[1], Shuu-Jiun Wang[1,2], Yen-Feng Wang[1,2], Shih-Pin Chen[1,2], Wei-Ta Chen[1,2] and Jong-Ling Fuh[1,2]

[1]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*

Objective: To determine the prognosis of patients with new daily persistent headache in a tertiary hospital.
Background: New daily persistent headache (NDPH) is characterized by persistent daily headache of acute onset on a specific date. ICHD-3 criteria were revised in 2018 to include patients with either tension-type or migrainous features. Previous studies have shown that NDPH is refractory despite aggressive treatments.
Methods: We performed a single-center, retrospective chart review study of patients diagnosed with new daily persistent headache from 2008 through 2022. Patients were phone contacted for follow-up from 2020 to 2022 with a semi-structured questionnaire. For those not contacted, the last clinic records were used as the follow-up results. Primary outcome was monthly headache days at the last follow-up. Patients with >50% reduction of monthly headache days were considered to have a favorable outcome.
Results: Overall, 228 patients diagnosed with NDPH were recruited and of them, 199 patients (87%) and 29 patients (13%) have migrainous and tension-type features. In a mean duration of 30 months, 167 (73%) of them reported monthly headache days, including 96 by phone calls (57%) and 71 by chart review. A mean reduction of 48% in monthly headache days was observed at the last follow-up. In total, 38% of patients had a favorable outcome. On average, 25% NDPH patients reached >50% reduction at 1.5 years, 31% at 3 years, and 48% at 10 years. No differences in outcomes between patients with migrainous and tension-type features were observed. No other univariate factors were identified to predict the outcome in our study.
Conclusion: Through a mean follow-up duration of 2.5 years, around 40% patients with NDPH showed a favorable outcome at our headache center. Our results suggest NDPH might not be as grave as previously reported.
Disclosure of Interest: None Declared

IHC23-PO-299

Micro-structural white matter abnormalities in new daily persistent headache: a DTI study using TBSS analysis

Yanliang Mei[1], Wei Wang[1], Dong Qiu[1], Ziyu Yuan[1], Xiaoyan Bai[2], Hefei Tang[1], Peng Zhang[1], Xue Zhang[2], Yaqing Zhang[1], Xueying Yu[1], Binbin Sui[3] and Yonggang Wang[1]

[1]*Headache Center, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China*
[2]*Tiantan Neuroimaging Center of Excellence, China National Clinical Research Center for Neurological Diseases, Beijing, China*
[3]*Tiantan Neuroimaging Center of Excellence, China National Clinical Research Center for Neurological Diseases, Beijing, China*

Background: The pathogenesis of new daily persistent headache (NDPH) is still unclear, and there were few white matter imaging studies related to NDPH. The purpose of this study was to investigate the micro-structural abnormalities of white matter in NDPH and provided insight into the pathogenesis of this disease based on tract-based spatial statistics (TBSS).
Methods: Twenty-five healthy controls (HCs) and twenty-one patients with NDPH were included in this study. T1 structural and diffusion magnetic resonance imaging (MRI) was acquired from all participants. Differences in fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) between patients with NDPH and HCs were investigated using TBSS analysis.
Results: Significant decreased FA, increased MD and RD were found in patients with NDPH compared to HCs. White matter regions overlaid with decreased FA, increased MD and RD in 16 white matter tracks from the Johns Hopkins University ICBM-DTI-81 White-Matter Atlas and Johns Hopkins University White-Matter Tractography Atlas were found. After Bonferroni correction, there were no correlation between the FA values and clinical characteristics of patients with NDPH ($p > 0.05/96$).
Conclusion: The results of our research indicated that patients with NDPH might have a widespread abnormalities of the brain white matter.
Keywords: Tract-based spatial statistics; New daily persistent headache; Diffusion tensor imaging; Micro-structural abnormalities; Pain
Disclosure of Interest: None Declared

IHC23-PO-300

The Effects of Topical Clonazepam on Resting-State Functional Connectivity in Burning Mouth Syndrome Patients

Huann Tan[1,2], Jan Hoffmann[3], Tara Renton[1], Howard Matthew[4] and Elena Makovac[4]

[1]*Centre for Oral, Clinical & Translational Sciences, King's College London (KCL), London, United Kingdom*
[2]*Faculty of Dentistry, The National University of Malaysia, Kuala Lumpur, Malaysia*
[3]*Wolfson Centre for Age-Related Diseases, Institute of Psychiatry, Psychology & Neuroscience, KCL, London, United Kingdom*
[4]*Department of Neuroimaging, KCL, London, United Kingdom*

Objectives: Burning Mouth Syndrome (BMS) is a chronic intraoral burning sensation that remains challenging to treat due to its unclear aetiopathogenesis. Neuroimaging studies have shown BMS dysregulation in central nervous systems. To better understand BMS brain pathophysiology,

we investigated BMS patients' resting-state functional connectivity (FC) before and after administering an antinociceptive clonazepam mouthwash (CMW). We also examined differences between treatment responders and non-responders.

Methods: 26 BMS patients were tested in two sessions. In session 1, they received a clinical assessment and were familiarised with the imaging protocol. In session 2, pain scores (NRS, 0–10) and resting-state functional MRI scans were acquired before and after CMW. Seed-based FC analysis of the right anterior insula (RAI) cortex was performed, given reports that it mostly correlates with emotional and cognitive pain processing. Treatment responders reported a minimum of 50% of pain reduction from their baseline scores following clonazepam administration.

Results: Following clonazepam, BMS patients experienced reduced pain scores (mean –2.67, s.d $\pm$ 2.23), and 15 patients responded to treatment. A decrease in FC was identified between RAI and the left cerebellum (anterior lobe). Pre-CMW, treatment responders demonstrated lower FC than non-responders between RAI and right lateral occipital cortex and parietal lobe. Following treatment, responders had decreased FC network changes (Δ FC), compared to non-responders, between RAI and bilateral ventral prefrontal cortex but increased ΔFC between RAI and bilateral frontal medial cortex, paracingulate gyrus and right frontal orbital cortex.

Conclusion: We present evidence of alteration in the BMS patients' brain FC following CMW. The FC patterns seen in the responders could be potential predictive biomarkers in determining localised treatment response, and ΔFC between groups provide insight into the effect of topical clonazepam.

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IHC23-PO-301

Burning Mouth Syndrome Patients' Functional Connectivity and The Effect Of Inferior Alveolar Nerve Block in Relieving Pain Symptoms

Huann Tan[1,2], Jan Hoffmann[3], Tara Renton[1], Howard Matthew[4] and Elena Makovac[4]

[1]*Centre for Oral, Clinical & Translational Sciences, King's College London (KCL), London, United Kingdom*
[2]*Faculty of Dentistry, The National University of Malaysia, Kuala Lumpur, Malaysia*
[3]*Wolfson Centre for Age-Related Diseases, Institute of Psychiatry, Psychology & Neuroscience, KCL, London, United Kingdom*
[4]*Department of Neuroimaging, KCL, London, United Kingdom*

Objectives: Burning mouth syndrome (BMS) is a chronic idiopathic orofacial pain condition without known organic local or systemic causative pathology. The pathophysiology of BMS is poorly understood, making diagnosis and treatment challenging. Reports on altered resting-state functional connectivity (FC) in BMS patients' brain networks imply that BMS is neuropathic pain. To better understand BMS brain pathophysiology, blood oxygen level-dependent functional magnetic resonance imaging (fMRI) was employed to examine changes in brain and intra-oral pain area size (pain size) following bilateral dental local anaesthesia inferior alveolar nerve block (LA).

Methods: 15 patients were recruited and were tested in two sessions. They received clinical and neuropsychological assessments in session 1. In session 2, intra-oral pain size and resting-state fMRI scans were acquired before and after LA. Seed-based FC analysis of the ventromedial prefrontal cortex (vmPFC) was performed as the PFC region plays a central role in the pain modulation pathway.

Results: Before LA intervention, there was a positive correlation between patients' pain size in the oral cavity and the FC between vmPFC – left temporal lobe – frontal orbital cortex (FOC), insula, and amygdala. After LA administration, the pain size was significantly reduced by an average of –37.74 (s.d $\pm$ 16.89, $p < 0.001$). Following LA, stronger FC between vmFPC and bilateral FOC and temporal lobe and left insula were associated with greater pain size reduction (uncorrected PFWE = 0.005). However, we did not observe any significant correlation between FC network changes and pain size differences.

Conclusion: We demonstrated the relevance of afferent primary peripheral nerve branches of the trigeminal nerve in the pathomechanism of BMS. The association between baseline FC and changes in pain size provide preliminary insights that may serve as a potential marker to phenotype patients and to tailor patient-specific treatment.

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IHC23-PO-302

Secondary nummular headache: are they more common than we thought? Differences and similarities with primary nummular headache.

Antonio Sanchez Soblechero, Elisa Luque Buzo, Alberto Lozano Ros and Amparo Guillem Mesado

Hospital General Universitario Gregorio Marañon, Madrid, Spain

Objective: Nummular headache (NH) is considered as a primary headache. In previous series, few secondary

causes have been described (<15%). Our objective is to determinate secondary NH characteristics and to compare them with primary NH.
Methods: Retrospective study of a cohort of patients (2002–2022) with a NH diagnosis (CIC 3rdEd Criteria). Clinical data, results of complementary tests and evolution with treatment were collected. Statistical analysis was performed according to the variable (X^2 or t-student).
Results: 126 patients were included. Mean age was (51.8 ± 16.9) and 83(65.9%) were women. 43 patients (34.12%) previously had any time of headache and 33 (26.2%) suffered from hypertension.
Pain was more frequently located in parietal area (60;47.6%), with circular shape (94;75.8%), oppressive quality (42;39.6%), moderate (52;45.2%) or mild (51;44.3%) intensity and duration for hours (30;35.3%) or minutes (25;29.4%). 78 patients (63.9%) had sensory dysfunction on palpation. The preventive treatment more used was gabapentin (39;31%). 54 patients (54.1%) had chronic evolution and 37 (39.4%) a spontaneous remission. After at least 12 months of follow-up (2-360), only 14 patients (11.1%) recurred.
Cranial CT found a cause for NH in 11 out of 95 patients (11.57%); cranial MRI in 14 out of 76 (18.42%) and bone gammagraphy in 5 out of 23 (21.7%).
There were 38 patients (30.2%) with a diagnosis of secondary NH. Ten of them were due to bone alterations (four osteoid osteomas, four due to osteogenic activity in bone gammagraphy and two due to post-surgical bone deformities). Nine patients were considered as post-traumatic NH, five patients because of arachnoid cysts, five due to intracranial tumors (four meningiomas and one prolactinoma); three patients secondary to skin disorders (psoriasis plaque, piebaldism, skin nodule) and two patients because of hypertension.
Patients with secondary NH suffer more frequently from hypertension (15;39.4% vs 18;20.4; $p = 0.026$), previous headache (20;52.6% vs 23;26.1%; $p = 0.008$); and local sensory dysfunction (29;76.3% vs 49;55.6%; $p = 0.013$). There were no differences in the remaining clinical characteristics or evolution, except that the >50% response rate to the first preventive treatment was higher in patients with secondary NH (13;34.2% vs 12;13.6%; $p = 0.018$).
Conclusion: 30% of nummular headache in our cohort suffer from secondary nummular headache. Bone abnormalities, post-traumatic, arachnoid cysts and tumors were the most frequent causes. Previously diagnosis of any kind of headache, hypertension, and sensitive local dysfunction at presentation, are associated with a secondary nummular headache diagnosis. Treatment response is better in secondary cases, probably due to a specific etiological treatment in some cases.

IHC23-PO-303

Efficacy and safety of CGRP monoclonal antibody treatment for primary new daily persistent headache and comparison to chronic migraine

Sanjay Cheema, Susie Lagrata, Maha Ahmed, Rachel Pickering, Salwa Kamourieh and Manjit Matharu

UCL Queen Square Institute of Neurology and The National Hospital for Neurology and Neurosurgery, London, United Kingdom

Objective: To assess the efficacy and safety of CGRP monoclonal antibody treatment for primary new daily persistent headache (NDPH) and compare the efficacy in NDPH to chronic migraine (CM).
Methods: This prospective observational study included consecutive patients with NDPH and CM treated with Erenumab or Galcanezumab between January 2022 and January 2023. The primary endpoint was the proportion of patients who experienced a ≥30% improvement in monthly moderate-to-severe headache days (MSHD) from baseline to 12 weeks. Secondary outcome measures included monthly headache days, monthly migraine days, headache severity, the Headache Impact Test-6 (HIT-6) disability score and the visual analogue scale of the EQ-5D-5L quality of life measure. Outcomes were compared between NDPH and CM patients who did and did not have a daily headache.
Results: A total of 36 patients with NDPH and 168 patients with CM (97 of whom had a daily headache) were treated during the study period. Only seven patients with NDPH (19%) experienced a ≥30% improvement in MSHD, whereas 39 (40%) of those with daily CM and 59 (83%) of those with non-daily CM did. Only three patents with NDPH (8%) had an improvement in headache days (see Table). The most frequent side effects were constipation in 47 (23%) and fatigue in 25 (12%) and were similar in each group. There were no serious adverse events.
Conclusion: CGRP monoclonal antibody treatment, whilst well tolerated, is rarely effective in improving headache frequency or severity in NDPH. It appears to be less effective in NDPH than CM, especially those who do not have a daily headache. This suggests NDPH may have a different underlying biology and require a different treatment approach.
Disclosure of Interest: SC, MA, RP, SK: none SL: received fees for attending advisory meetings, presentations, and preparing presentation materials from Allergan, TEVA, Eli-Lilly and Novartis MM: chair of the medical advisory board of the CSF Leak Association, serves on the advisory board for Abbott, Allergan, Novartis, Eli Lilly, Medtronic, Autonomic Technologies Inc., and TEVA and has received payment for the development of educational

Abstract number: IHC23-PO-303
Table

	NDPH n = 36	Daily CM n = 97	Non-daily CM n = 71	X2	P value
Monthly moderate to severe days*	7 (19%)	39 (40%)	59 (83%)	48.1	<0.001
Monthly headache days*	3 (8%)	15 (15%)	52 (73%)	73.8	<0.001
Monthly migraine days*	16 (44%)	56 (58%)	54 (76%)	10.3	0.006
Mean headache severity*	8 (22%)	37 (38%)	33 (46%)	6.0	0.051
≥6 point improvement in HIT-6 score	9 (25%)	37 (38%)	35 (49%)	6.1	0.048
≥10 point improvement in EQ-5D-5L VAS	14 (39%)	37 (38%)	35 (49%)	2.3	0.319

*Proportion with ≥30% improvement

presentations from Allergan, electroCore, Eli Lilly, Novartis, and TEVA

IHC23-PO-304

Comparison of the efficacy of onabotulinumtoxinA in new daily persistent headache to chronic migraine

Sanjay Cheema, Susie Lagrata, Maha Ahmed, Salwa Kamourieh and Manjit Matharu

UCL Queen Square Institute of Neurology and The National Hospital for Neurology and Neurosurgery, London, UK, London, United Kingdom

Objective: To determine whether onabotulinumtoxinA (BoNT-A) is effective for the treatment of primary new daily persistent headache (NDPH) and to compare its effectiveness in NDPH to chronic migraine (CM).
Methods: We performed an observational study using prospectively collected data in consecutive patients with NDPH with migraine features, and CM, who were treated with BoNT-A between 2013 and 2022. Patients were treated with 2 cycles of BoNT-A as per the PREEMPT protocol and completed a headache diary and disability questionnaires at baseline and 12-week follow-up intervals. We compared treatment response in NDPH to patients with CM who had a daily headache at baseline (daily CM) and those who had between 15–27 headache days per month (non-daily CM). The primary outcome measure was the proportion of patients who experienced a ≥ 30% reduction in monthly moderate-to-severe headache days (MSHD) between baseline and 24 weeks.
Results: Inclusion criteria were met by 58 patients with NDPH, 153 with daily-CM, and 85 with non-daily CM. There was a ≥ 30% reduction in MSHD in 19 (33%) of patients with NDPH, 66 (43%) with daily-CM and 46 (55%) with non-daily CM (between groups X2 = 6.9, p = 0.031). There was an ≥ 30% improvement in monthly headache days in only five (8.6%) of patients with NDPH, 23 (15%) with daily-CM, and 37 (44%) of non-daily CM (between groups X2 = 33.4, p = <0.001). Despite this, there was a similar improvement in HIT-6 scores and patient estimate of improvement in all three groups. There were no serious adverse events, but mild side effects were experienced by 24% of patients, the most common of which were ptosis (4.7%) and worsening of headache (3.4%).
Conclusion: Although BoNT-A demonstrated a lower improvement of MSHD in NDPH compared to CM, it still led to significant improvements in quality of life across all groups. The discrepancy raises the possibility that patients with NDPH may have experienced improvements in non-headache symptoms, which could account for the similar enhancements in quality of life observed in CM patients, despite the lesser improvement in headache. Nonetheless, BoNT-A remains a safe and valuable treatment option for NDPH with migraine features.
Disclosure of Interest: SC, MA, SK: none SL: received fees for attending advisory meetings, presentations, and preparing presentation materials from Allergan, TEVA, Eli-Lilly and Novartis MM: chair of the medical advisory board of the CSF Leak Association, serves on the advisory board for Abbott, Allergan, Novartis, Eli Lilly, Medtronic, Autonomic Technologies Inc., and TEVA and has received payment for the development of educational presentations from Allergan, electroCore, Eli Lilly, Novartis, and TEVA

IHC23-PO-305

Successful relief of Glossopharyngeal neuralgia with syncope with OnabotulinumtoxinA: a case report.

Tamsin Hilliard[1,2], Elspeth Hutton[1,2], Jason Ray[1,2,3] and Richard Stark[1,2]

[1]*The Alfred Hospital, Melbourne, Australia*
[2]*Monash University, Melbourne, Australia*
[3]*The Austin Hospital, Melbourne, Australia*

Introduction: Glossopharyngeal neuralgia is a rare cause of facial pain that may be associated with bradycardia,

syncope, cardiac pauses and syncopal convulsions. We present a novel protocol for OnabotulinumtoxinA injections to treat this condition.

Case: We present a case of a 52-year-old woman with Glossopharyngeal Neuralgia with syncope. She described brief stabbing pains in the left ear, throat, and angle of the mandible triggered by yawning and swallowing, at times accompanied by hypotension and syncope. Magnetic Resonance Imaging revealed typical neurovascular compression. Carbamazepine was partially effective, but cognitive effects limited continued use, and gabapentin, baclofen and duloxetine were ineffective. Administration of OnabotulinumtoxinA to her left pre-auricular region achieved an excellent analgesic response and completely resolved the syncopal events.

Conclusion: Established surgical and pharmaceutical treatments for Glossopharyngeal neuralgia may be limited by tolerability or prone to procedural complications. Due to the rare association with cardiac pauses, there is a clear need for sustainable treatment options. We present the second published use of OnabotulinumtoxinA for this condition and demonstrate its efficacy in syncope using a novel and well-tolerated protocol.

Disclosure of Interest: Professor Stark has served on advisory boards and received payment for educational presentations from Allergan. Dr Hutton has served on advisory boards and received compensation for educational presentations from Allergan. Dr Ray has received compensation for educational presentations from Allergan and Dr Hilliard has no potential conflicts of interest to declare.

Other secondary headache disorders

IHC23-PO-306

Secondary headache due to aseptic meningitis – a case report of Mollaret's syndrome

Triin Helin Unt

West-Tallinn Central Hospital, Tallinn, Estonia. University of Tartu, Faculty of Medicine, Tartu, Estonia

Introduction: Secondary headache disorders are more common in the emergency department (ED), where headache is often the primary neurological complaint. The medical literature on the subject proposes 'red flags' to increase the likelihood of identifying secondary etiology of headache. Presentation of the triad of fever, nuchal rigitity, and decreased consciousness is variable and a lack of it does not rule out neuroinfection. Considering neuroinfection, including viral aseptic meningitis, as a headache cause is important because delay in diagnosis may have adverse results due to consequent delay in treatment. Recurrent episodes of aseptic meningitis that occur over a period of several years with complete resolution of symptoms in between is characteristic of Mollaret's meningitis. Herpes simplex virus type 2 (HSV-2) is describe as the most common causing agent, but there are also cases in which the causative agent remains unidentified.

Case report: 83-year-old man with a known history of 2 episodes of aseptic meningitis of unknown etiology followed by complete recovery, presented to the emergency department with recurrent severe headache, word finding difficulty and febrile temperatures. His medical history was significant for hypertension, aortic bioprosthesic valve and prostate carcinoma treated with radiation and hormone therapy. On examination he was slightly disoriented, had naming difficulties and meningeal signs of headache and nuchal rigidity. Computed tomography (CT) of the head showed vascular leukoencephalopathy without acute intracranial findings. Cerebrospinal fluid (CSF) analysis revealed lymphocytic pleocytosis of 90 cells $1^{6/L}$, protein 0,87 g/L, normal glucose and lactate levels, consistent with aseptic meningitis. Given the patient's history of noninfectious aseptic meningitis, complete recovery and symptom-free intervals in between, Mollaret's meningitis was suspected, and empiric treatment with acyclovir for HSV-encephalitis was initiated. All CSF studies, including HSV-1 and HSV-2 PCR, were negative and hence the antiviral treatment with acyclovir was discontinued after 3 days. Magnet resonance imaging (MRI) was performed as an additional radiological investigation showing multiple T2-intense foci in the white matter of the cerebral hemispheres, no diffusion restriction or contrast enhancement within the brain tissue, but meningeal contrast enhancement. Oligoclonal band, autoimmune encephalitis panels and onconeuronal antibodies in serum and CSF were negative. The patient's condition improved over 7 days and he was referred to general hospital's inpatient-clinic for further recovery where he remained for 4 days.

Conclusion: This case report presents a rare entity of recurrent aseptic meningitis – Mollaret's syndrome. Patients with headache and systemic features suspected of meningitis should undergo immediate lumbar puncture to facilitate proper diagnosis. The diagnosis of Mollaret's meningitis should be reserved for recurrent noninfectious meningitis cases. Early diagnosis may prevent prolonged hospital stay, unnecessary investigations, and exposure to unnecessary medications, with associated costs. In most Mollarets' syndrome cases a benign prognosis can be predicted.

Disclosure of Interest: None Declared

IHC23-PO-307

Resident's Awareness, Knowledge and Behavior towards medication overuse headache: A University hospital-based survey

Prakit Anukoolwittaya[1], Wanakorn Rattanawong[2] and Sekh Thanprasertsuk[1]

[1]*Chulalongkorn University, Bangkok, Thailand*
[2]*King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand*

Background and Objective: Medication overuse headache (MOH) poses a significant problem for headache patients in worldwide. Healthcare professionals play a critical role in preventing MOH among patients. However, physicians' knowledge, behavior, and awareness in this regard appear to be limited. This study aims to survey knowledge, behavior, and awareness about MOH among physicians in residency training programs.
Method: We conducted a survey among training residents, including those specializing in family medicine, internal medicine, neurology, and other subspecialties encountering headache patients at King Chulalongkorn Memorial Hospital (KCMH), Thailand. We designed a questionnaire to evaluate three aspects: awareness of MOH, knowledge of MOH, and behavior that may cause MOH in headache patients.
Results: A total of 70 residents were included in the study. Demographic data are presented below in table 1. In terms of awareness, 10% of residents were not aware that analgesic drugs can exacerbate headaches. Regarding knowledge, 25% of physicians did not know that MOH is a secondary headache. In addition, 31% of residents were unaware of the number of days that paracetamol or NSAIDs can be used without risking MOH, while 44% were unaware of the number of days that triptans, ergotamines, or opioids can be used without risking MOH. Furthermore, 14% of residents did not know how to manage MOH patients. In terms of behavior, 5% of physicians never ask patients about the frequency of their analgesic drug use. Additionally, 58% of physicians never advise headache patients to keep a headache diary, while 31% of physicians prescribed a number of analgesic drugs that may cause MOH. Finally, 22% of physicians prescribed opioid drugs to headache patients.

Table 1 Demographic data of the participant (N = 70)

Age, mean (SD)	30.2 (2.4)
Female, n(%)	35 (50.0)
Subspecialty, n(%)	
• Neurologist	24 (34.3)
• Internal medicine	25 (35.7)
• Family medicine and other involved subspecialties	21 (30.0)
Year as physician, mean(SD)	6.0 (2.2)

Conclusion: This study revealed substantial concerns regarding knowledge, behavior, and awareness of MOH among training residents in various specialties. Healthcare professionals play a vital role in preventing MOH among headache patients, but the findings of this study suggest that more education and training are necessary to improve their understanding and management of this condition. As MOH is a prevalent issue in worldwide, efforts should be made to incorporate education about MOH into medical training programs to prevent this condition's burden on patients and healthcare systems.
Disclosure of Interest: The findings of this study are particularly concerning, as they suggest a significant lack of knowledge, behavior, and awareness regarding MOH among training residents in various specialties. It is essential to address these gaps through education and training programs to improve physicians' understanding and management of MOH. As a prevalent issue worldwide, it is crucial to take steps to prevent the burden of this condition on patients and healthcare systems. I am particularly interested in exploring the implications of this study and how it may inform medical education and training programs. I believe that initiatives to incorporate education about MOH can lead to better outcomes for patients and improved healthcare delivery.

IHC23-PO-308

External validation of the Bern score for diagnosing spontaneous intracranial hypotension

So Youn Choi and Mi Ji Lee

Seoul National University Hospital, Seoul, Korea, Republic of

Background: A brain MRI-based composite score ("Bern score") to estimate the likelihood of spontaneous intracranial hypotension (SIH) was recently reported. We assessed patients with SIH to validate the diagnostic performance of the Bern scoring system.
Methods: We prospectively recruited patients with SIH from Seoul National University Hospital between April 2022 and February 2023. Age-sex-matched controls were selected from the headache clinic registry. All the

SIH patients underwent contrast-enhanced brain MRI and MR myelography, and selected patients underwent lumbar puncture if needed. The confirmative diagnosis of SIH was made based on at least one of the following: 1) typical brain or spinal imaging findings suggestive of SIH, 2) opening pressure <6 cmCSF relieved by the lumbar puncture, and 3) a typical clinical history and clear response to the epidural blood patch. Bern score was assessed and compared between the SIH group and controls using the receiver operating characteristic (ROC) curve.
Results: A total of 37 patients with SIH and 31 controls with primary headache disorders were included in the analysis. Based on the Bern score, the probability of CSF leakage in the SIH patients were classified as low (score ≤2) in 20 (54.1%), intermediate (score 3–4) in 10 (27%), and high (score ≥5) in 7 (18.9%). The AUC of the ROC curve was 0.704. The highest sum of sensitivity and specificity was observed at a Bern score of 3 or higher, with a sensitivity of 47.4% and specificity of 100%.
Of the patients in the low probability group, 65% were confirmed as having SIH based on either pachymeningeal enhancement or CSF leakage detected on spine MR myelography. The remaining 35% in the low probability group were image negative; however, they had an abrupt onset of moderate to severe orthostatic headache and showed a positive response to epidural blood patch (EBP) procedure.
Conclusion: In our study, about half of SIH patients had low Bern scores. Although our study findings validated the high specificity of Bern score for the diagnosis of SIH, the sensitivity was low. High Bern scores may be useful to diagnose SIH, while clinicians should consider the possibility of SIH in patients with the low Bern scores. Clinical suspicion should be prioritized than the brain MRI findings.

IHC23-PO-309

Analgesic effect of botulinum toxin on headache and muscle pain in temporomandibular disorder patients

Younjung Park, Min Jang, Sora Kim and Seong Taek Kim

Yonsei University College of Dentistry, Seoul, Korea, Republic of

(1) **Introduction:** Botulinum toxin (BoNT) is internalized into presynaptic cholinergic nerve terminals where it inhibits acetylcholine, thus inhibiting muscle contraction. Based on its muscle-relaxant properties, the aim of the present study was to evaluate analgesic effect of botulinum toxin on temporomandibular disorders (TMDs) patients suffering from headache and muscle pain.
(2) **Methods:** Twenty-one myogenous TMD and headache patients were randomly assigned into two groups. The control group received saline injections into each masseter, temporalis, splenius capitis, sternocleidomastoid, and trapezius muscle, and the treatment group received BoNT type A injections into each muscle presenting tenderness on palpation. The clinical effect, based on the pain intensity of orofacial pain and headache, and the number of tender areas, was evaluated at four time points: before and 4, 8, and 12weeks after the injection in both groups. A between-subjects factor, group, and a within-subjects factor, time, were analyzed using the Mann-Whitney test and the Friedman test, respectively.
(3) **Results:** Only BoNT group showed a decrease over time in the number of tender sites, and the intensity of headache and orofacial pain, with significant differences at each time point. The frequency of headache decreased in BoNT group 8 weeks after receiving an injection of BoNT. Pairwise comparisons show that the number of tender sites was significantly different between the control and BoNT group at 4 and 12 weeks.
(4) **Conclusions:** BoNT therapy was an effective treatment for TMD-related headache and muscle pain.
Disclosure of Interest: This research was funded by Hugel Inc. This trial was an investigator-initiated study fully supported by Hugel Inc., Chuncheon, Korea. They provided botulinum toxin (Botulax®, letibotulinumtoxinA) and supported a research grant.

IHC23-PO-310

Effect of Prednisolone for the Treatment of Medication-Overuse Headache: A 3-month result from a multicenter RELEASE study

Mi Ji Lee[1], Hong-Kyun Park[2], Sun-Young Oh[3], Jin-Ju Kang[3], Yooha Hong[4], Heui-Soo Moon[5], Tae-Jin Song[6], Min Kyung Chu[7] and Soo-Jin Cho[4]

[1]Seoul National University Hospital, Seoul, Korea, Republic of
[2]Department of Neurology, Inje University Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea, Republic of
[3]Department of Neurology, Chonbuk National University Hospital, Chonbuk National University School of Medicine, Jeonju, Korea, Republic of
[4]Department of Neurology, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of
[5]Department of Neurology, Kangbuk Samsung Hospital, Sungkyunkwan University College of Medicine, Seoul, Korea, Republic of
[6]Department of Neurology, Ewha Womans University Seoul Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of
[7]Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of

Background: The treatment of medication-overuse headache (MOH) is challenging, especially when withdrawal headache is manifested during cessation of overused medication. This study aimed to assess the efficacy of prednisolone in the treatment of MOH using a multicenter prospective registry (Registry for Load and Management of MEdicAtion OveruSE Headache [RELEASE]).
Methods: This was a sub-analysis of the RELEASE study. RELEASE is an ongoing project in which patients with MOH have been recruited from seven hospitals in Korea since April 2020. Clinical characteristics and disease profiles were assessed at baseline. The treatments for MOH were individualized by each investigator and were not controlled. Patients were followed-up at 1, 3, 6, and 12 months. In this study, using both univariate and multivariate models, we analyzed the effect of prednisolone on MOH reversal at 3 months.
Results: A total of 309 patients were enrolled in this study between April 2020 and October 2021. Steroids were prescribed to 59 (19.1%) patients. The prednisolone group had more monthly headache days (MHD) and higher headache-related disability at baseline than the non-prednisone group (median 30 [interquartile range 27–30] vs. 28 [20–30] days, $p < 0.001$; median headache impact test-6 scores 68 [65–72] vs. 65 [62–70], $p = 0.008$, respectively). A total of 228 patients (73.8%) completed the 3-month follow-up. The prednisolone group ($n = 41$) showed an MOH reversal rate of 75.6%, whereas MOH was reversed in only 57.8% of the 187 non-prednisolone patients ($p = 0.034$). The effect of steroids remained significant (adjusted OR 2.78, 95% CI 1.27–6.06, $p = 0.010$) showing an independent association with MOH reversal at 3 months after adjusting for the number of MHD at baseline, mode of discontinuation of overused medication, use of early preventive medications, and the number of preventive medications combined.
Conclusion: Our study supports the use of prednisolone for the treatment of MOH. The role of prednisolone can be better identified using outcome parameters of MOH reversal.
Disclosure of Interest: None Declared

IHC23-PO-311

A Mis(sed)diagnosis of headache

Gee Jin Ng

National Neuroscience Institute, Singapore, Singapore

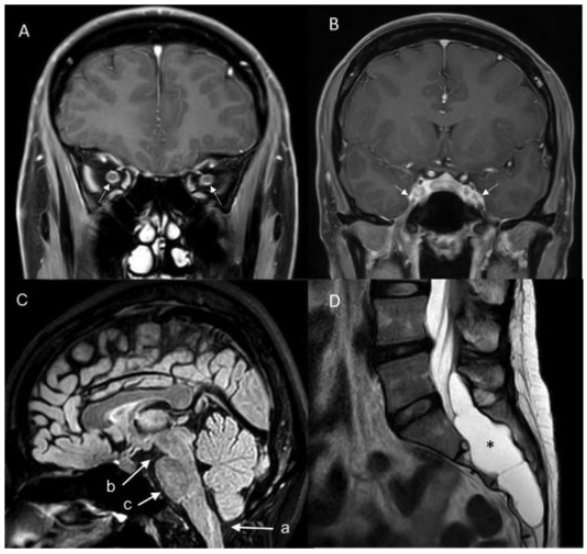
Objective: To describe a patient with spontaneous intracranial hypotension (SIH) from lumbosacral cyst fistula with subtle Magnetic resonance imaging (MRI) changes.
Case: A 27-year-old lady (body mass index 20) presented with throbbing headache associated with nausea and intermittent binocular diplopia, without orthostatic exacerbation in pain. There was no fever, ptosis, swallowing impairment, limb weakness, numbness or slurring of speech. Clinical examination revealed a left 6th nerve palsy, fundoscopy show normal optic disc. Systemic reviews were unremarkable.
Contrasted MRI brain showed bilateral optic nerve sheath and tentorial enhancement, mild bulkiness of cavernous sinuses and pituitary gland, without cerebellar descent, low lying tonsil, reduce of ponto-medullary distance, flattening of ventral pons and subdural fluid collection (Fig. 1A–1C).
Cerebrospinal fluid (CSF) opening pressure was 80 mm H2O. Diagnostic workup for meningeal inflammatory/infiltrative conditions such as infective meningitis, autoimmune disease, Immunoglobulin G4 disease, neurosarcoidosis and lymphoma were negative. Headache responded to oral naproxen and transient diplopia resolved.
Episodic headaches occurred over the next year, followed by a subsequent presentation with severe headache, which worsened on standing. Repeat MRI Brain showed persistent abnormalities (Fig. 1A–1C). CSF opening pressure was 45 mm H2O. Diagnosis of SIH was made. MRI spine showed a lumbosacral, extradural cyst (Fig. 1D), no definite site of CSF leak was demonstrated radiologically.
Conservation management such as caffeine, bedrest and epidural blood patch (EPB) was unsuccessful. Decompressive surgery was subsequently done and multiple fistulae were noted intra-operatively (histology: arachnoid cyst). Headache resolved within 2 months post-surgery.
Discussion: SIH has an estimated incidence of 5 per 100,000 cases and is often due to dural leakage.[1] Diagnosis is often missed or delayed,[1] especially when patient does not present with orthostatic headache, reported 3% of patients.[2] Other symptoms may include posterior neck pain, tinnitus, nausea, vomiting and photophobia, leading to a misdiagnosis of a migraine or tension headache.[1,2] Cranial nerve palsies, most commonly abducens (83% of opthalmoplegia cases)[3] may occur. Imaging findings of SIH include diffuse smooth pachymeningeal enhancement (73%), brain sag (43%), subdural collection (35%), pituitary enlargement (38%), venous engorgement (57%), and distortion of the midbrain.[2]
Diagnostic criteria for SIH requires CSF pressure <60 mm H2O, or evidence of CSF leakage on imaging, and exclusion of other possible causes of orthostatic headache.[3] CSF opening pressure may be normal in 32% patients.[2] The difficulty in diagnosis of SIH was illustrated in our patient's first presentation, without orthostatic headache, MRI brain show subtle changes and CSF opening pressure was normal.
Spinal arachnoid cysts are rare and often asymptomatic; complications usually arise from compression of the spinal cord (myelopathy).[4] Arachnoid cyst rupture causing SIH has been rarely reported in literature.[5]

Management of SIH includes conservative measures – bed rest, hydration, caffeine, theophylline,[1] however only 28% responded.[2] A comprehensive workup for identification of possible site(s) of CSF leak is indicated in all patients. Surgical treatment is indicated for a definite structural abnormality causing CSF leak.1 For patients with suboptimal response to oral medications or severe symptoms, EBP is utilised, and may require to be repeated, responsive rate of first EBP is 64%.[2]

In conclusion, diagnosis of SIH is easily missed. A high index of suspicion is critical for an early diagnosis.

Figure (Fig.)

Fig. 1 Coronal post-gadolinium MRI brain: (A) bilateral optic nerve sheath enhancement (arrows), and (B) bulkiness of the cavernous sinuses (arrows) and pituitary gland. (C) Sagittal MRI brain: (a) no brain sag (b) normal pontomedullary distance, and (c) no flattening of ventral pons. (D) MRI of the lumbosacral spine: a CSF signal extradural arachnoid cyst (*)



Disclosure of Interest: CONFLICT OF INTEREST: There is no conflict of interest. CONSENT: Informed written consent had been obtained from the patient for the presentation.

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IHC23-PO-312

Utility of lasmiditan in treating thunderclap headache associated with reversible cerebral vasoconstriction syndrome

Yasutaka Sadamoto[1] and Hironobu Harada[2]

[1]*Takanoko Hopital, Matsuyama, Japan*
[2]*Harada Neurosurgery, Matsuyama, Japan*

Background and Objectives: Reversible cerebral vasoconstriction syndrome (RCVS) is a neurological disorder characterized by the sudden onset of thunderclap headaches (TCH), and segmental cerebral artery stenosis. RCVS is commonly seen in middle-aged women who have a history of migraine. Treatment typically involves rest and medications such as nifedipine, verapamil, and magnesium sulfate to manage vasospasm. However, commonly used symptomatic treatments for headaches, such as Non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol, are sometimes inadequate, so more effective treatments are required.

Headaches in RCVS can resemble migraine, but triptans, which are often used to treat acute migraine, are not recommended for RCVS due to the risk of vasoconstriction caused by their effects on the 5-hydroxytryptamine (5-HT) 1B receptor. Lasmiditan is a drug used to treat the acute stage of migraine that works by targeting the 5-HT1F receptor. Unlike other medications, it does not affect the 5-HT1B receptor.

We encountered two cases of migraine-like TCH in patients with RCVS who had a history of migraine. Lasmiditan proved to be highly effective in managing their symptoms.

Cases: Case 1: A 53-year-old woman experienced TCH during lunch, and presented to our department on the first day of her illness. We performed head magnetic resonance imaging (MRI), and diagnosed RCVS. She was admitted to the hospital on the same day.

Case 2: A 41-year-old woman experienced TCH onset during bathing, with recurrence during both bathing and defecation. She was diagnosed with RCVS on the 13th day of illness at the clinic and was referred to our department on the same day.

Both patients had a history of migraine and were initially prescribed verapamil, NSAIDs, and paracetamol, but these treatments were ineffective for TCH. The first patient was

prescribed lasmiditan on the 7th day of illness, and the second patient was prescribed lasmiditan on the 14th day of illness. Following this, both patients showed a significant improvement in symptoms. No new foci of cerebrovascular disease were observed in either case.

Discussion: The pathophysiology of RCVS is still unclear. Along with endothelial damage and disruption of the blood-brain barrier (BBB), abnormal sympathetic responses of the cerebral blood vessels have been proposed to be important in the etiology of RCVS. The parenchymal arteries of the brain are innervated by the superior cervical ganglion, and the release of norepinephrine and neuropeptides from sympathetic nerve endings is thought to cause vasoconstriction. Since TCH usually recurs frequently within 2–3 weeks of onset, and vasoconstriction of the major cerebral arteries becomes prominent around three weeks post-onset, it is unlikely that vasoconstriction of the major and middle cerebral arteries is the cause of headache. Instead, the involvement of the distal arteries is likely the primary trigger that activates the trigeminal vasoceptive pathways.

Receptors for calcitonin gene-related peptide (CGRP), a potent vasodilator, are expressed in vascular smooth muscle. Although CGRP does not regulate steady-state vascular tonus, it is released from trigeminal nerve endings during vasoconstrictive stimulation to restore vascular tone. This suggests that CGRP may be involved in a reflex mechanism to counter cerebral vasoconstriction.

Migraine headaches are initiated by the stimulation of nociceptors innervating the dura mater and the subsequent release of CGRP. In fact, direct injection of CGRP has been shown to trigger headaches and migraine attacks. In RCVS patients with a history of migraine, the increase in CGRP concentration associated with cerebral vasoconstriction may be responsible for inducing headaches. However, in these two cases, it is also possible that RCVS exacerbated the preexisting migraine and caused severe headache attacks.

5-HT1F receptors are present in both peripheral trigeminal nerve endings and the central nervous system, and regulate pain signaling associated with migraine. Lasmiditan is a drug that exhibits high selectivity for human 5-HT1F receptors. Lasmiditan activates 5-HT1F receptors in the peripheral nervous system, inhibits the presynaptic release of CGRP from trigeminal nerve endings, crosses the BBB, and activates 5-HT1F receptors in the central nervous system, thus modulating central sensitization.

Conclusion: In cases of RCVS where patients have a history of migraine with no new foci of cerebrovascular disease, lasmiditan may be a promising treatment option when NSAIDs and paracetamol are ineffective against TCH.

IHC23-PO-313

Headache & Complete Ophthalmoplegia following Herpes Zoster Ophthalmicus – a Case Report from Sri Lanka.

Shanindra De Alwis and Bimsara Senanayake

Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka

Introduction: Herpes zoster, also known as shingles, results from reactivation of latent Varicella Zoster virus that gained access to sensory ganglia during the primary infection with the virus. Herpes zoster is characterized by a painful, unilateral vesicular eruption, which usually occurs in a single or two contiguous dermatomes.

Herpes zoster ophthalmicus (HZO) is defined as herpes zoster involvement of the ophthalmic division of the fifth cranial nerve. This entity is considered a potentially sight-threatening condition due to the complication of acute keratitis leading to progressive corneal scarring. It is also reported to be associated with other complications such as episcleritis, glaucoma and cataracts.

Here we report a patient who presented with headache and ophthalmoplegia following HZO infection.

Case Report: 60-year-old patient with a history of diabetes mellitus for 10 years complained of a painful rash in her left forehead. This was treated as Herpes Zoster with oral acyclovir. 2 weeks later, she developed a left sided headache with diplopia. Examination revealed a left sided ptosis, proptosis and a healed vesicular rash over the V1 region (Figure 01).

Left sided complete ophthalmoplegia was observed with a dilated poorly reactive pupil. Visual acuity was preserved. Inflammatory markers were normal. CSF analysis revealed lymphocytes with a marginally high protein. MRI of the left orbit showed high signal intensity and swelling in the lateral & medial extra-ocular muscles with a fullness in the left superior orbital fissure.

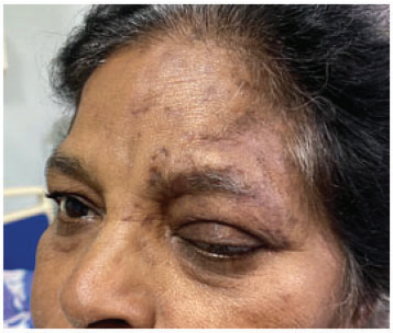
She was treated with high dose IV Methylprednisolone for 3 days along with a slow taper of oral prednisolone. She was discharged 1 week later as her symptoms were improving.

Discussion: Ophthalmoplegia as part of the sequelae of HZO, is typically described as a late complication, often up to 2 months after the initial herpetic rash.

Following reactivation of VZV in the Trigeminal ganglion, the virus migrates along the ophthalmic division (V1) of the Trigeminal nerve and spreads to the corresponding dermatome. As the virus spreads along V1, direct tissue infection along with an immune response may take place within the orbit. This may involve the orbital apex, extra-ocular muscles (myositis), blood vessels (vasculitis) and/or nerve sheaths (perineuritis).

The involvement of orbital tissue ipsilateral to the cutaneous lesions support the view that the pathogenesis is likely

to be due to direct viral infection of orbital cells and consequent immune cell attack.
In our patient, the increased signal change and swelling of extra ocular muscles in the MRI supports myositis as the possible etiology behind the presentation.
Diagnosis of this condition is essentially a clinical one. Limited data suggests that systemic corticosteroids and a course of oral acyclovir can be used as treatment. The prognosis for full recovery after complete ophthalmoplegia following HZO is good.
Figure 01



Disclosure of Interest: None Declared

IHC23-PO-314

Clinical characteristics of reversible cerebral vasoconstriction syndrome: A large Korean multicenter study

Soohyun Cho[1], Byung-Kun Kim[2] and Mi Ji Lee[3]

[1]*Uijeongbu Eulji Medical Center, Uijeongbu, Korea, Republic of*
[2]*Nowon Eulji Medical Center, Seoul, Korea, Republic of*
[3]*Seoul National University Hospital, Seoul, Korea, Republic of*

Background: Reversible cerebral vasoconstriction syndrome (RCVS) is an important cause of thunderclap headaches that can lead to neurological complications. We previously demonstrated the characteristics of RCVS in a single center in Korea. The present multicenter study investigated the clinical characteristics of RCVS in more large sample size of Korean patients
Methods: In this multicenter study, patients with only angiogram-proven RCVS were enrolled. Angiogram-proven RCVS was defined when the multifocal vasoconstrictions were normalized within 3–6 months. We finally recruited 230 patients with angiogram-proven RCVS. Clinical features, etiologies, trigger factors, neurological manifestations and complications, and treatments were evaluated in included patients.
Results: Patients with RCVS were median 49 years (interquartile range, 38.0–60.0 years), with a female predominance (81.3%). In etiology, idiopathic RCVS (73.9%) was reported most frequently, followed by emotional stress (15.2%). Trigger factors of thunderclap headaches were reported in 187 (81.3%) patients in which, Valsalva maneuver (46.5%) was most common. During the follow-up period, neurological complication was reported in only 22 (9.5%) patients and modified Rankin score was 0 (98.7%) after three-month follow-up. For the treatment of RCVS, nimodipine was used in almost all patients (96.1%).
Conclusion: Korean patients with RCVS appear to have idiopathic and benign RCVS. Compared to Western patients, lower prevalence of secondary etiology and neurological complications were observed. This may imply that clinical outcomes can be affected according to genetic, social and environmental factors in RCVS.
Disclosure of Interest: None Declared

IHC23-PO-315

Reversible cerebral Vasoconstriction syndrome intERnational CollaborativE (REVERCE) network: Rationale and design of a multicentre research collaboration

Kristin Sophie Lange[1,2], So Youn Choi[3], Yu-Hsiang Ling[4,5], Shih-Pin Chen[4,2,8], Jérôme Mawet[9], Claire Duflos[10], Mi Ji Lee[3], Anne Ducros[2,11], Shuu-Jiun Wang[4,5,6] and Alessandro Pezzini[12]

[1]*Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany*
[2]*Department of Neurology, CHU Montpellier, Gui de Chauliac Hospital, Montpellier, France*
[3]*Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*
[4]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[5]*School of Medicine, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[6]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[7]*Division of Translational Research, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan*
[8]*Institute of Clinical Medicine, College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[9]*Emergency Headache Center, Department of Neurology, Lariboisière Hospital, Assistance Publique des Hôpitaux de Paris, Paris, France*
[10]*Clinical Research and Epidemiology Unit, Department of Public Health, CHU Montpellier, Montpellier University, Montpellier, France*
[11]*Charles Coulomb Laboratory, CNRS UMR5221, Montpellier University, Montpellier, France*

[12]Department of Clinical and Experimental Sciences, Neurology Clinic, University of Brescia, Brescia, Italy

Objective: Reversible cerebral vasoconstriction syndrome (RCVS) is a rare, but increasingly recognised cerebrovascular condition. Evidence on risk factors, optimal treatment and prognosis is scarce and based mainly on national cohorts. The REversible cerebral Vasoconstriction syndrome intERnational CollaborativE (REVERCE) project aims to elucidate the epidemiological and clinical characteristics of RCVS by investigating risk factors and triggering conditions, pathophysiology, treatment, functional outcome, long-term risk of recurrent events and death, with special emphasis on ethnic and regional variation.
Methods: REVERCE is an international network of neurological centres with specific expertise on RCVS, aimed at recruiting adult patients with definite first-ever RCVS in the setting of a multi-centre observational study. Data on risk factors and triggering conditions, imaging, neurological complications, functional outcome, recurrent vascular events, death and the use of specific treatments will be collected. Subgroup analyses will be made based on age, gender, etiology, ethnicity and geographical region of residence. Currently, individual patient data of approximately 800 patients from four countries (France, Italy, Taiwan and South Korea) are available. Ethical approval for the REVERCE study has been obtained at the University Hospital Montpellier (IRB-MTP_2021_02_202100734), and will be obtained from national or local institutional review boards in the participating centres.
Summary: The aim of REVERCE is to provide a better description and understanding of clinical and epidemiological characteristics of RCVS patients, and to contribute to the improvement of clinical management and therapeutic options. First results are anticipated in 2023.
Disclosure of Interest: Comments: *These authors contributed equally. Conflicting interests: The authors do not have any conflicts of interest related to the submitted work. KSL reports personal fees (Teva, Acticor Biotech). JM reports personal fees (Abbvie, GEP Sante, Lundbeck, Homeperf, Teva, Lilly, Lundbeck, Pfizer). MJL reports personal fees (Eli Lilly, Lundbeck, Pfizer, NuEyne Co., Teva, Abbvie, SK chemical, CKD Pharm, YuYu Pharma), research grants (Eli Lilly, Otsuka, Novartis, Allergan, BioHaven, Lundbeck, Eli Lilly/Ildong), and funding (National Research Foundation of Korea grant funded by the Korea government (MSIP), Seoul National University New Faculty Startup Fund, Yuhan company). AD reports personal fees (Allergan Abbvie, Lilly, Teva, Lundbeck, Pfizer, SOS). SJW reports personal fees (AbbVie, Pfizer, Eli Lilly, Biogen), research grants (Eli Lilly, Novartis) and has been principal investigator in sponsored trials (Novartis, Lundbeck and Orient Europharma). The other authors have nothing to disclose.

IHC23-PO-316

Is the Proof in the Pain? Association of Headache and Vessel Pathology on Follow-Up in Cervical Artery Dissection

Miranda Stattmann[1], Susanne Wegener[1,2] and Jil Baumann[3]

[1]University Hospital Zurich, Zurich, Switzerland
[2]Clinical Neuroscience Center, Zurich, Switzerland
[3]University of Zurich, Zurich, Switzerland

Objective: Unilateral head and neck pain is a hallmark of cervical artery dissection (CAD). While pain is conceived as an alarming sign for patients and often leads to discovery of the dissection, it is not known if persistence of pain is associated with course of CAD. One reason to suspect pain would be irritation of perivascular pain-sensitive nerves caused by mechanical compression or direct stimulation of pain receptors in the vessel wall. Potentially, pain could indicate persisting vessel pathology, and thus guide treatment decisions aimed at reducing risk of ischemic stroke in CAD.
Methods: We performed a retrospective analysis of data from patients with CAD treated at the University Hospital Zurich (USZ). Only patients with information about the presence of pain, independence after CAD according to the modified Rankin Scale (mRS), and imaging-based information on vessel status were included. Patients were grouped according to presence/absence of head and/or neck pain on admission and 3-months follow up. We used descriptive statistics and logistic regression to reveal a potential association between pain on admission and pain on follow up with status of the dissected vessel on follow up (open, stenosed, occluded). We screened 139 patients with CAD between 2014 and 2019, and included 68.
Results: In our cohort of patients with CAD, headache was a common initial clinical presentation, which rarely persisted until 3 months. Pain persisted until follow-up at 3 months in only 22% of patients with pain on admission. Fifty-nine patients (86.8%) had pain on admission, which was resolved in 46 (68%) at follow-up. In patients with headache, vessel pathology and pain were mostly ipsilateral. There was no statistically significant difference between the groups regarding the location of the dissected vessel (anterior vs posterior circulation, $p = 0.131$) and the extent of the vessel pathology (occlusion vs. stenosis, $p = 0.196$). There were no differences between the three patient groups in descriptive analysis of comorbidities and demographic factors. Logistic regression analysis for vessel status on follow up did not show an association with pain on admission or follow up.
Conclusion: In conclusion, we found that vessel pathology after CAD on follow-up was independent of headache status. Thus, our findings provide a point of reassurance for patients who might be concerned about the

persistence of pain after CAD. Judging from our data, pain does not suggest persisting vessel pathology. However, more studies with a larger cohort of patients are needed to understand the specific type of pain in CAD and the time course of its evolution. This is especially important, as some patients with CAD only report headache and have no other focal neurologic signs.
Disclosure of Interest: None Declared

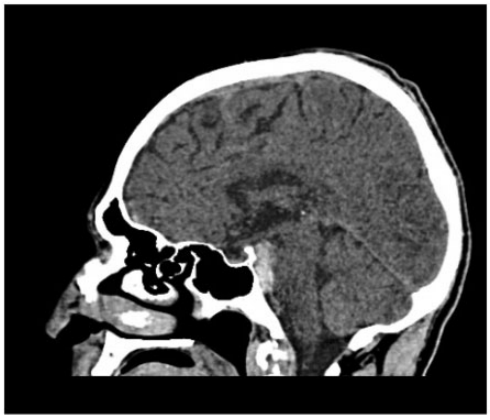
IHC23-PO-317

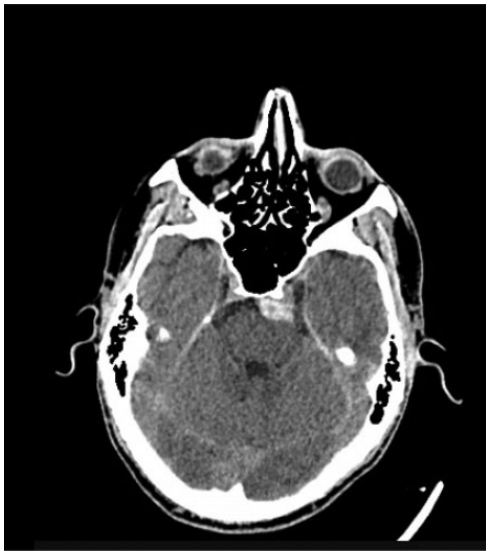
A case of secondary headache associated with sexual activity induced by vertebral artery dissection mimicking fusiform aneurysm in an adult patient.

Anna Serga, Igor Nelin, Daria Artemieva and Maria Mikhailyukova

Clinical Hospital №2, Krasnodar, Russian Federation

Objective: We present a case of a secondary headache associated with sexual activity in a man with vertebral artery dissection mimicking fusiform aneurysm.
Methods: Case report
Results: A 41-year-old male had a pain in the head and neck brought on by and occurring only during sexual activity during last 14 days. His pain was increasing in intensity with increasing sexual excitement and accompanied by abrupt explosive intensity just before or with orgasm. His medical history there is no history of trauma, or excessive physical activity or usage of any medication. Although his medical history includes hepatitis B. He was away on business and went to see a general practitioner upon return. No clinical signs were found and patient went to the emergency room.
A non-contrast-enhanced computed tomography showed changes in left vertebral artery (PICTURE 1 and 2)





and a computed tomography angiography revealed fusiform aneurysm, blood vessel ultrasound showed constriction of the left extra cranial part of the vertebral artery. Spinal tab showed blood in spinal fluid. So, a diagnosis was formulated as non-traumatic subarachnoid haemorrhage from fusiform aneurysm of the left vertebral artery. The patient was admitted to ICU.
The patient was consulted by a neurosurgeon by telemedicine. As a result, cerebral angiography was ordered. Cerebral angiography did not confirm an aneurysmal disease but constriction of the left intra cranial part of vertebral artery was confirmed. So, a diagnosis was changed to a dissection of the left intra cranial part of vertebral artery with non-traumatic subarachnoid haemorrhage. Dissection and haemorrhage into vessel regressed in dynamic and headache regressed too.
Conclusion: A clinical symptoms of secondary headache associated from subarachnoid haemorrhage or from dissection artery vary from migraineurs to thunderclap. The present case showed a diagnostic journey of the patient with a headache associated with sexual activity.
Disclosure of Interest: None Declared

IHC23-PO-318

Headache as the primary symptom of central nervous system vasculitis: a case report

Kadri-Hebo Kukumägi

Tartu University Hospital, Tartu, Estonia

A 33 year old male fell ill with severe headaches, which in the first months were episodic. Then the pain escalated – he had daily headaches that lasted even through the night. At first, the pain located all over the head, but after

a couple of months, he felt it more on the temporal region on the left. Headaches were not accompanied by other complaints. Previously performed blood tests showed mild leukocytosis and eosinophilia.

After having headaches approximately for half a year, he had a computed tomography (CT) scan of the head done in the emergency department (ED). It was found that he had an old lacunar stroke lesion in the caudate nucleus region, but the angiography of cerebral blood vessels did not show any pathology.

A month after the ED visit, he was hospitalized in the neurology department due to repeated transient ischemic attacks of the left carotid system. On the second CT angiography, the left medial cerebral artery (MCA) was about 50% narrower than in the previous study. On the magnetic resonance imaging (MRI) performed on the third day of hospitalization, narrowing of the MCA M1 arteries were developed bilaterally, also acute lacunar ischemic lesions were formed on the left side of MCA and posterior cerebral artery (PCA) supply area. Cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis (31 E6/L), mildly elevated protein level (0.49 g/L), positive intrathecal oligoclonal synthesis and chemokine CXCL13. The panels of viruses and bacteria from the CSF (including analyses for mycobacterium, Borrelia burgdorferi, T. pallidum) all remained negative.

For differential diagnosis it was considered both infectious and autoimmune vasculitis. A long duration of symptoms (more than 6 months) and the presence of pleocytosis in the CSF were not suitable for reversible vasoconstriction syndrome.

Because the Toxocara canis serology was positive, and according to the literature it can cause eosinophilic meningitis and central nervous system vasculitis, he was treated as a possible patient with neurotoxocariasis. The patient was prescribed treatment with albendazole in addition to pulse therapy with methylprednisolone, oral prednisolone and aspirin. The patient's condition improved during hospitalization, headaches disappeared, a slight right-sided hemiparesis remained.

Soon he was hospitalized for the second time due to right hemiparesis and added mild left hemiparesis. On the CT angiography, aggravation of multiple cerebral artery stenoses were observed, causing recurrent transient ischemic attacks and lacunar cerebral infarctions. To clarify the diagnosis, a brain biopsy was taken, but no changes in small blood vessels or other pathology suitable for vasculitis was found. Autoantibodies indicating systemic vasculitis were also negative. In the hospital, the patient's condition had negative dynamics with methylprednisolone pulse therapy. It was decided to escalate the treatment to intravenous cyclophosphamide.

During the next three month time period he was hospitalized two more times because of multiple transitory ischemic attacks and new multilocular strokes. CT angiography showed negative dynamics, in the arteries there were new stenoses and preocclusions formed. Multiple angioplasty procedures of the cerebral arteries were performed. Because of the previously failed cyclophosphamide treatment, it was decided to treat the patient with Rituximab, which was successful. Now two years after the treatment, there have been no new exacerbations and the patient has only mild right-sided hemiparesis. Taking all of the above into consideration, a diagnosis of primary central nervous vasculitis was established.

IHC23-PO-319

Supraventricular Tachycardia Presenting As Cardiac Cephalalgia

Usman Ashraf

St Vincent's Hospital, Sydney, Australia

Introduction and Objective: Cardiac cephalalgia is a secondary headache where the symptom of headache can preclude serious and potentially fatal cardiac events. Presentation of headache with an associated cardiac symptom warrants further consideration of this diagnosis. We present a case of headache associated with an underlying supraventricular tachycardia.
Case Description and Methods: A 79 year old man presented to hospital after six stereotyped episodes in 1 week of headache. The headache is described as a mild (3/10 severity) sharp pain from behind his right eye that immediately radiated to the top of his right scalp and was mild in severity. Each time this headache lasted for 2–5 seconds and then was followed by 2–3 seconds of unsteadiness and then syncope. He had no other associated symptoms with these episodes. All of these episodes occurred whilst he was walking in his garden. He never had a previous history of headaches or syncope but had a relevant past medical history of suspected supraventricular tachycardia for which he was on Flecainide 50mg BD.
Results: Postural blood pressure measurements, blood tests including troponin and CT Brain imaging with angiogram from aortic arch to Circle of Willis did not yield any abnormalities. He was attached to continuous telemetry monitoring when admitted to hospital, which twice captured episodes of supraventricular tachycardia of 150 beats per minute for duration of 15 seconds, each episode was preceded by his stereotyped headache and followed by syncope. Transthoracic echocardiogram showed severe apical hypokinesis and aneurysmal deformity. A permanent pacemaker was inserted by an interventional cardiologist and the patient did not have further episodes of headache.
Conclusion: The case presented above highlights the importance of considering cardiac cephalalgia as a

secondary headache diagnosis in patients with cardiac symptoms such as syncope associated with headache, particularly as this can herald a potentially serious or fatal event that can otherwise be treated or prevented. The pathophysiology for cardiac cephalalgia remains incompletely understood, but is potentially explained by involvement of vagal cardiac afferent fibres and their interaction with trigeminal nerves in the spinal trigeminal nucleus.
Disclosure of Interest: None Declared

IHC23-PO-320

Aseptic meningitis after BNT-162b2 COVID-19 vaccination: case report and literature review

Yuji Kato[1], Takashi Osada[1], Nobuo Araki[2], Shinichi Takahashi[1] and Satoshi Suda[1]

[1]*Department of Neurology and Cerebrovascular Medicine, Saitama Medical University International Medical Cente, Hidaka, Japan*
[2]*Yomiuri Land Keiyu Hospital, Tokyo, Japan*

Objective: Aseptic meningitis is a rare, but possible severe side effect after COVID-19 vaccine. Headache is a common complication after vaccination and these symptoms are usually ignored or managed with conservative therapy. The purpose of this study is to clarify the clinical picture of aseptic meningitis after COVID-19 vaccine.
Methods: Case report and literature review.
Results: We describe a-27-year-old female patient who had prior history of migraine and developed refractory severe headache and photophobia after the first dose of COVID-19 vaccine. Intravenous methylprednisolone significantly improved her symptoms. On reviewing the literature, we could find only nine similar cases, over half among women aged 20 to 40 years. Clinical meningitis symptoms in three patients were already present on the first day after vaccine administration, as opposed to a period of 1 to 2 weeks in other patients. Six out of ten previous cases were treated with steroids, which led to a rapid improvement.
Conclusion: Aseptic meningitis should be kept in mind the differential diagnosis of patients with persistent or delayed onset of headache and fever following COVID-19 vaccinations. Clinical suspicion and careful investigation infer rare adverse events such as aseptic meningitis and led to prompt and appropriate treatment.
Disclosure of Interest: None Declared

IHC23-PO-321

The Transition of Medication Overuse Status By Acute Medication Categories in Episodic or Chronic Migraine Patients to Non-overuse Status After Receiving Anti-CGRP Monoclonal Antibodies: A Systematic Review and Meta-Analysis

Akkanat Panto[1], Chananchida Sirilertmekasakul[1], Pattanan Lekhalawan[1], Pariyada Panyarachun[1], Porpim Jindasakchai[1] and Wanakorn Rattanawong[1,2]

[1]*Faculty of Medicine, King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand*
[2]*The Thai Headache Society, Bangkok, Thailand*

Objective: The objective of this systematic review and meta-analysis was to determine whether patients with episodic (EM) or chronic migraine (CM), who were treated with anti-CGRP antibodies, showed a reversal from medication overuse (MO) or medication overuse headache (MOH) status at their baseline to non-overuse status. Furthermore, this study aimed to establish which acute headache medication (AHM) categories responded more effectively to anti-CGRP antibodies.
Methods: A systematic search was conducted in the PubMed database for relevant studies from January 2013 to April 2023. We included phase three randomized controlled trials to examine the role of anti-CGRP antibodies in patients with EM or CM, and their MO status. A meta-analysis was conducted to find the association between anti-CGRP antibodies and the number of EM and CM patients with MO or MOH at baseline that reverted to non-MO status or below MOH threshold.
Results: The initial search yielded a total of 344 studies. After removing duplicates and screening with inclusion criteria, four studies fulfilled our conditions. 1695 cases participated in total. Each study reviewed the response of change in MO status of patients after receiving anti-CGRP antibodies, including epinizumab, fremanezumab, galcanizumab, and erenumab, compared to placebo. Our study analyzed three AHM categories: triptans, simple analgesics, and multiple drugs.
The overall relative risk (RR) was 1.46 (95% CI, 1.28 to 1.66; p-value <0.001). The RRs for triptans, simple analgesics, and multi-drug groups were 1.74 (95% CI, 1.55 to 1.96; p-value <0.001), 1.28 (95% CI, 0.997 to 1.64; p-value 0.053), and 1.24 (95% CI, 1.05 to 1.45; p-value 0.009) respectively.
Conclusion: The meta-analysis has shown that anti-CGRP antibodies were statistically significant in reducing the number of acute medication days, and hence, transitioning from MO or MOH status to non-MO status or below the MOH threshold (RR = 1.46) for all included

studies as well as all AHM categories except for simple analgesics. Patients from the triptan group had the highest RR of 1.74 with p-value <0.001, while the simple analgesics group had RR of 1.28, however, with p-value >0.05. Interestingly, this analysis can be interpreted as that anti-CGRP antibodies might not be effective in reducing simple analgesics use in EM or CM patients. Further studies are needed to investigate these matters.

Disclosure of Interest: None Declared

IHC23-PO-322

Post COVID headache, in 510 cases presented in emergency department on Regional Hospital Durres, Albania in period November 2020 –November 2022

Edlira Shemsi (Harizi)[1,2], Ferid Domi[3], Kledisa Shemsi[4], Nensi Qerimi (Sulstarova)[5] and Gjergji Qerimi[3]

[1]*Durres, Durres, Albania*
[2]*Regional Hospital Durres, Neurology Department, Durres, Albania*
[3]*Regional Hospital Durres, Emergency Department, Durres, Albania*
[4]*Bezirkskliniken Schwaben, BKH Psycjiatrie und Psychotherapie, Ulm, Germany*
[5]*Regional Hospital Durres, Infection Disease, Durres, Albania*

Background: SARSCoV2 the virus responsible for the COVID19 pandemic had not only respiratory symptoms, butalso neurological symptoms, and headache is a frequent complaint.Pathophysiologyof headache in the context of COVID 19 has some mechanisms that can be involved in persistence of headache after acute stage of the disease. These mechanisms include systemic inflammation that can stimulate cytokine storm, canactivate trigeminovascular-system at the meninges, andin some patients this inflammatory response may be sustained after infection and can play role at post Covid headache.

Methods: We have seen 510 patients that have been presented at emergency department and neurology consult at SRD with headache after covid19(2–10months after infections).15%of patients had severe covidinfections with respiratory insuficienceand have been recovered in hospital(76 patients)and85%(434 patients) have been treated ambulatory.themost of patients had bilateral frontal headache(52%)and holocranicheadache(22%), and hemicranic-migraine type(26%).

Results:

Conclusions: Themechanisms of persistent headache for months after covid19 infections means to be stimulate by inflammatory mechanisms with stimulation of the trigeminovascularsystem, and CGRP(calcitonigene-related peptide) released by pulmonary endings nerve during viral infections may stimulate migraine.

Conclusions: Most of patients had oppressive pain,72% (367 patients)had moderate headache and 28% (143patients) had severe continousheadache. Middle age of patients was52years old and65%were female(331)and 35%male(179) and mean time of headache was 3.6month from all patients 30%(153 patients) have been known with primary headache, and76%had migraine (116 patients,78 female,38 male),22%tensive type headache (34 patients, 20 female and 14 male) and2% had cluster headache (3patients were mens) .From all 510 of patients 45% (230) had also other post covidsymptoms like dizziness, memoryproblems, insomnia, brainfog, depressionand anxiousestate etc.

IHC23-PO-323

Role of brain MRI with contrast and whole spine MRI in the first-line investigation of SIH.

Dwij Mehta, Sanjay Cheema, Salwa Kamourieh, Parag Sayal, Ayman Qureshi, Indran Davagnanam and Manjit Matharu

University College London (UCL) Queen Square Institute of Neurology and The National Hospital for Neurology and Neurosurgery, London, United Kingdom

Objectives: To investigate the role of MRI brain with contrast and whole spine MRI in the first-line radiological work-up of spontaneous intracranial hypotension (SIH). The secondary objective was to compare the prevalence of typical MRI signs associated with SIH in relation to symptom-duration at time of imaging.

Methods: A retrospective study of patients with imaging-positive SIH. The first brain MRI with contrast and whole spine MRI which had been performed for each patient were reviewed for evidence of classical signs associated with SIH. The frequency of radiological signs in relation to duration of symptoms was compared.

Results: The cohort consisted of 80 patients. The most frequently observed sign on brain MRI with contrast was the venous distension sign, present in 81% of patients. Pachymeningeal enhancement as a solitary sign of SIH on intracranial MRI was observed in 3.8% of patients and extradural spinal collection in absence of intracranial features of SIH was noted in 5.1% of patients. Brain sagging had a greater prevalence in patients imaged in the chronic phase of SIH ($p = 0.004$), whilst the converse was true for spinal collection ($p = 0.001$).

Conclusions: Patients with suspected SIH should have screening imaging that includes both brain MRI with contrast and whole spine MRI to avoid missing the diagnosis in

an estimated 9% of patients. Longer symptom-duration is associated with a greater prevalence of brain sagging, whereas the opposite is true for extradural spinal collection.
Disclosure of Interest: None Declared

IHC23-PO-324

Characteristics of headache, with various encephalopathies developed against the background of chronic kidney disease

Sevara Khudayarova and Gulnora Rakhmatullaeva

Tashkent Medical Academy, Tashkent, Uzbekistan

Relevance: Headache in patients with chronic kidney disease is one of the most frequent clinical manifestations.
The purpose of the study: To study the frequency and characteristics of headache of various types of encephalopathy in patients with CKD
Materials and Methods: 75 patients with CKD were studied. Patients were diagnosed with the following: hypertensive encephalopathy (n = 33), uremic encephalopathy (n = 31), acute hypertensive encephalopathy (PRES) syndrome (n = 10).
Results of the study: In patients with hypertensive encephalopathy (n = 33), 31 (93.3%) patients complained of headaches. The GB score on the VAS scale was 7 ± 1.2 ($P < 0.05$). Of these, 25 (75.7%) patients associated headaches with hypertension, and noted a decrease in headaches with a decrease in blood pressure. The pains were paroxysmal, compressive, pulsating, localized mainly in the occipital 15 (60%) and parietal-occipital regions (10 (40%). With uremic encephalopathy (n = 31), all 100% complained of headache. The intensity of GB on the VAS scale was 5 ± 2.3 (($P < 0.05$). However, here the headaches were of the nature of aching, persistent pain of a chronic nature, patients noted a decrease in the intensity of pain after the hemodialysis procedure. The pain was diffuse and localized mainly in the frontotemporal 14 (45.1%) and parietotemporal areas. In patients with acute hypertensive encephalopathy (n = 10), headache was also one of the first clinical manifestations. However, the pain here was acute, burning in nature, patients describe the pain as an electric shock, lightning. The score on the VAS scale was 9.6 ± 3.2. Headaches were accompanied by visual impairment in the form of decreased visual acuity 4 (40%), a feeling of shroud 6 (60%) and flickering flies in front of the eyes 6 (60%), nausea 10 (100%) and vomiting 4 (40%).
Conclusions: Headache in patients with CKD is one of the most frequent clinical manifestations, which have different characteristics and localization, as well as intensity depending on the type of encephalopathy.

IHC23-PO-325

Isolated Non-traumatic Convexity Subarachnoid Haemorrhage; Report of a Challenging Diagnosis

Devasmitha Wijesundara and Bimsara Senanayake

Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka

Introduction: Subarachnoid haemorrhage (SAH) most commonly occurs due to aneurysmal rupture, where blood is found around the circle of Willis or Sylvian fissure. Rarely, bleeding may be limited to the convexities of the brain. We report a case of convexity SAH presenting as recurrent thunderclap headaches with normal angiography.
Case report: A 53-year-old female presented with three episodes of thunderclap headache over a five-day period. This was accompanied by vomiting and vertigo. She denied ever having an episodic headache disorder. Her history was significant for ischemic heart disease for which she had undergone coronary stenting and was on aspirin. No vasoconstrictive triggers were identified. Her blood pressure was 130/80 mmHg, with a normal general examination. There was no neck stiffness, papilledema, nor any focal neurological deficits. Basic blood investigations, inflammatory markers and coagulopathy screen were normal. Non-contrast computerized tomography (CT) brain revealed hyper-density within the sulci of the left temporo-occipital lobe suggestive of SAH (figure 1A). This was confirmed by magnetic resonance imaging (MRI) (figure 1B-D). There were no other abnormalities. She was started on oral nimodipine and kept under observation. Vascular imaging in the forms of CT angiography, MR angiography, and digital subtraction angiography (DSA) as well as MR venography were all normal (figure 2). Aspirin was restarted on day 5 and she was discharged on day 12, following an uneventful hospital stay. DSA performed after 2 weeks was also unremarkable. The patient remains under close follow up.
Discussion: Convexity SAH is an uncommon entity which occurs secondary to venous thrombosis, amyloid angiopathy, vasculitis, arteriovenous malformations/fistulae, or internal carotid artery stenosis. Reversible cerebral vasoconstriction syndrome (RCVS) and posterior reversible encephalopathy syndrome (PRES) also give rise to this condition. Although, her history was suggestive of RCVS, with a RCVS2 score of 7, this could not be radiologically confirmed. We conclude this to be a rare case of "angio-negative" convexity SAH.
Conclusion: Subarachnoid haemorrhage may rarely manifest as isolated bleeding into sulci. Although it has a good prognosis, etiology should always be sought.

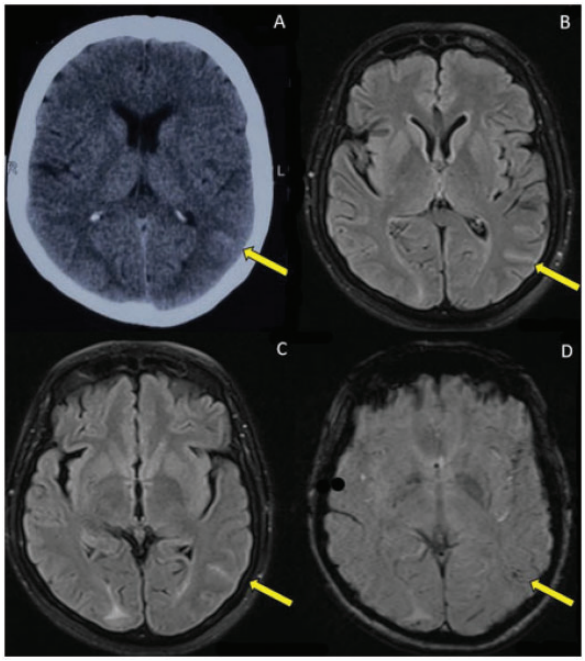


Figure 1- Brain imaging. A- Non-contrast CT, B, C- MRI-FLAIR sequence, D – MRI-SWI sequence

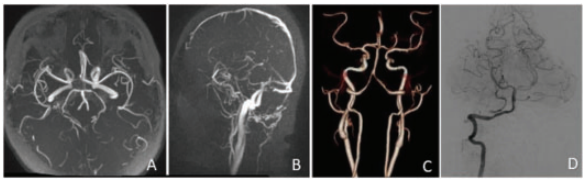


Figure 2- Vessel imaing. A-MR-angiogram, B-MR-venogram, C-CT-angiogram, D-Digital subtraction angiogram

Disclosure of Interest: None Declared

IHC23-PO-326

A Case of Craniopharyngioma Presenting with Isolated Persistent Stabbing Headache

Sun-Ku Han[1], Jae Yong Lee[1] and Byung-Su Kim[2]

[1]Bundang Jesaeng General Hospital, Daejin Medical Center, Seongnam, Korea, Republic of
[2]Ewha Womans University Mokdong Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of

Background: Although most stabbing headaches are primary, isolated stabbing headache can uncommonly arise from a serious intracranial pathology. Herein, we report an interesting case with persistent stabbing headache as the presenting manifestation of craniopharyngioma

Case: A 49-year old woman visited our outpatient headache clinic due to persistent stabbing headache. Approximately 10 years ago, she had recurrent stabbing headache episodes usually relapsing-remitting within several days. However, the current stabbing headache was lasting for 1 month. Her headache was moderate-intensity pain and fixed in the right posterior head without cutaneous allodynia. She has no headache history of migraine or tension-type headache. Except persistent stabbing headache, she was apparently healthy and had no past medical history. Neurological examination revealed no neurological deficit.

She undertook brain magnetic resonance imaging (MRI) to identify a possible intracranial pathology related to her isolated persistent stabbing headache. MRI of her brain demonstrated a 4 cm sized lobulating solid and cystic mass in the suprasellar cistern with upward extension of the cystic portion to the 3rd ventricle leading to presumed elevation of the 3rd ventricle floor and obstructive hydrocephalus. She was referred to other hospital for surgical treatment.

Conclusions: Given that the majority of patients with craniopharyngioma have been reported to present with neurological deficits and hormonal disturbance, her isolated stabbing headache is a rare manifestation of this disease. Since she had a history of typical primary stabbing headache and no focal neurological deficit, persistence of fixed site stabbing headache was the only clue for early suspecting secondary serious intracranial pathology. Therefore, we need to focus such distinguishing headache characteristics to anticipatively identify secondary etiology in headache clinical practice.

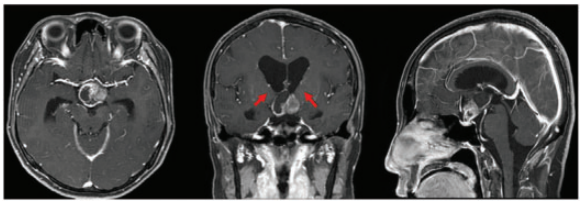


Figure. Neuroimaging findings. Brain MRI (T1 contrast-enhanced images) reveals a 4 cm sized lobulating solid and cystic mass with rim enhancement and calcification in the suprasellar cistern. The mass has a core of T1 high signal intensity and thin wall enhancement. There is no attachment or compression of midbrain. The superior dominance was related to upward extension of the cystic portion to the 3rd ventricle with presumed elevation of the 3rd ventricle floor, resulting in obstructive hydrocephalus (red arrows). These MR findings indicate that the mass pathology is probably craniopharyngioma.

Disclosure of Interest: None Declared

IHC23-PO-327

Three-month prognoses of medication overuse headache depending on the acute symptomatic medications and the treatment strategies

Jin-Ju Kang[1], Sun-Young Oh[1], Soo-Jin Cho[2], Hong-Kyun Park[3], Mi-Kyoung Kang[2], Yooha Hong[2], Heui-Soo Moon[4], Tae-Jin Song[5], Mi Ji Lee[6] and Min Kyung Chu[7]

[1]*Department of Neurology, Jeonbuk National University Hospital & School of Medicine, Jeonju, Korea, Republic of*
[2]*Department of Neurology, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, Republic of*
[3]*Department of Neurology, Inje University Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea, Republic of*
[4]*Department of Neurology, Kangbuk Samsung Hospital, Sungkyunkwan University College of Medicine, Seoul, Korea, Republic of*
[5]*Department of Neurology, Ewha Womans University Seoul Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of*
[6]*Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*
[7]*Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of*

Background: Medication-overuse headache (MOH) is a common global health problem, severely disabling the majority of the patients affected. Despite MOH being a widespread headache disorder, there is no consensus on the most effective approach to its treatment. The prognosis for MOH seems to depend on several factors.
Objective: To characterize the clinical prognostic features of patients with MOH according to the class of acute medications being overused and treatment strategies.
Methods: As part of the RELEASE study, a longitudinal, prospective, observational study of MOH patients involving seven neurology clinics in the Republic of Korea from April 2020, a follow-up further analysis was conducted.
Results: A total of 375 patients with MOH were enrolled in the RELEASE study between April 2020 and March 2022, but 169 patients completed 3-month follow-up. Except for the number of missed days per month in E-MOH and the GAD-7 scores in N-MOH, significant improvement was presented in almost all parameters after 3 months of initiating MOH treatment, regardless of the type of drug overused. Except the number of pharmacy visit days per month, there was a significant main effect of visit on clinical parameters, indicating that the frequency and severity of MOH, as well as related disability, were lower post-treatment compared to pre-treatment. There was no significant interaction between overused medication type and visit, suggesting that the effect of overused medication on MOH patients was not differed depending on the type of acute symptomatic medications. The analysis revealed a significant between-subject effect for overused drug type ($F(4, 161) = 3.414$, $p = 0.010$, $\eta p2 = 0.079$), indicating that changes in monthly acute medication days varied depending on the causative drug. Additionally, repeated measures analysis of variance on the number of headache days per month revealed a significant between-subject effect for discontinuation strategy ($F(2, 163) = 4.072$, $p = 0.026$, $\eta p2 = 0.047$), indicating that changes in the number of headache days per month varied depending on the discontinuation strategy. Repeated measures analysis of variance for the number of severe headache days per month ($F(3, 156) = 3.552$, $p = 0.016$, $\eta p2 = 0.064$) and the number of acute medication intake days per month ($F(3, 156) = 4.298$, $p = 0.006$, $\eta p2 = 0.076$) revealed the visit effect as well as the type of preventive treatment effect.
Conclusion: Regardless of the type of causative drug, starting MOH treatment immediately after diagnosis contributes to rapid improvement, and reducing or discontinuing the overused medications is recommended for MOH treatment.

IHC23-PO-328

Description of the clinical characteristics of headache in patients with loss of cervical lordosis and other spinal deformities: Study of a series of 14 cases

Maria Novoa

National Institute of Neurological Sciences, Lima, Peru

Objective: The aim of this study was to describe the clinical characteristics of headaches associated with loss of cervical lordosis and other spinal deformities.
Methods: We evaluated 132 patients seen for the first time in the headache clinic of the National Institute of Neurological Sciences, from January to March 2023. The 132 patients, who after being evaluated by the headache specialist for their main complaint, headache, complete spine radiographs were requested as part of the examination protocol for patients with headaches and suspected cervicogenic headaches.
We excluded 118 cases, 112 with degenerative disc disease and osteoarthritis and only 06 with normal radiographs. We included 14 patients, between 18–33 years old, with headaches and deformities in the entire spine, without age-associated degenerative changes seen in total

spine radiographs. We observed loss of cervical lordosis in 14 cases, more dorsal scoliosis in 13 cases, and lumbar scoliosis in 12 of the 14 cases (see tables 2 and 3).
Results: Of the 14 cases, 13 were women and 01 was male. All young people between 18 to 33 years of age. With a history of head and spinal trauma in 12 cases. Whereas, the 14 cases revealed bad postures in general. The 14 cases reported that the onset of their headache occurred at a very early age, between 5 and 25 years of age, mainly after the traumas. The location of the pain was referred to only on one side in 09 cases. While 12 cases accused that the high intensity of the pain incapacitated them. And with greatly increased frequencies (>15d/>3 months). In 11 of the cases the duration of pain was greater than 01 day. Associated with instability with vertigo in 11 cases and with tinnitus in only 06 cases. While, in 11 cases nausea was also added and of these same cases, only in 04 cases the vomiting was occasional. The 14 cases had different types of autonomic disorders such as; allodyneas of different location, facial ruddiness, red eyes, paleness, etc. (see table 1). When applying the ICHD-3 criteria, 10 of the 14 cases met the criteria for chronic migraine (CM) and 04 for episodic migraine (ME). Being, 09 of the 14 cases, migraines sideLocked wit autonomic features.
Discussion: We describe 14 headaches that met ICHD-3 criteria for MC and ME, all of them with autonomic disorders; 05 with bilateral symptoms and 09 blocked to one side, with abnormalities of the anatomical curvature of the neck and the rest of the spine. None of the 14 cases met the ICHD-3 criteria of being cervicogenic headaches, and although there was a history of direct or indirect cervical and spinal trauma in most of the patients in the series and with precipitation of pain from digital pressure, mainly in the roots of the greater cervical and lesser cervical.
And although there is still no clear relationship in this regard, it is undeniable that the spine is an extension of the central nervous system, therefore, existing anomalies in its anatomical structure could be related to both bilateral headaches and side blocked headaches, before anomalies from both central and peripheral structures. However, a prospective study in this regard could shed more light on the clinical picture of these headaches associated with deformities of the spine, mainly with the loss of cervical lordosis.
Disclosure of Interest: None Declared

IHC23-PO-329

Early nimodipine treatment prevents worsening of reversible cerebral vasoconstriction syndrome: a serial Transcranial Doppler study

Soohyun Cho[1] and Mi Ji Lee[2]

[1]*Department of Neurology, Uijeongbu Eulji Medical Center, Eulji University School of Medicine, Uijeongbu, Korea, Republic of*
[2]*Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea, Republic of*

Background: Nimodipine is commonly used for the treatment of reversible cerebral vasoconstriction syndrome (RCVS). However, no prospective study has been conducted to test its disease-modifying effect. This study aimed to prospectively track changes in cerebral blood flow using Transcranial Doppler (TCD) in patients with RCVS and investigate the effect of nimodipine on preventing worsening of vasoconstriction.
Methods: We prospectively recruited patients with recent-onset (<3 weeks within the first thunderclap headache) RCVS. All participants underwent TCDs for the evaluation of mean flow velocities (MFVs) of bilateral middle cerebral arteries (MCAs) at baseline and serially followed up after 10, 20, 30, and 90 days. Oral nimodipine was started after the baseline TCD. To estimate worsening of vasoconstriction, we calculated the area of time with MFVs above baseline ("MFV area"). We tested the correlation between the days after onset to the start of nimodipine and MFV areas and linear regression analysis to examine the independent association of earlier nimodipine treatment with MFV areas.
Results: A total of 33 patients with RCVS (mean age 51.7 [SD 10.2] years; 91% female) completed this study. Baseline TCD was performed at a mean 7.1 (SD 4.1) days after the onset of thunderclap headache. A statistically significant correlation between days after onset to the start of nimodipine treatment and MFV areas ($r = 0.45$, $p = 0.015$). This association remained significant after adjusting age and sex (regression coefficient 65.32 [95% CI = 6.15 to 124.49], adjusted $p = 0.039$) in the multivariable linear regression.
Conclusions: Our analysis revealed an independent association of the timing of nimodipine administration with worsening of vasoconstriction in patients with RCVS, suggesting earlier nimodipine treatment is associated with less worsening of vasoconstriction. Nimodipine may have disease-modifying effect in the treatment of RCVS.
Disclosure of Interest: S. Cho: None Declared, M. J. Lee Conflict with: This study was supported by Samjin Pharmaceutical Co. and the National Research

Foundation of Korea (NRF) grants funded by the Korean government (MSIP) (No. 2020R1A2B5B01001826). The funders had no role in study design, data analysis, and interpretation of results.

IHC23-PO-330

Spontaneous orthostatic headache improved after occipital nerve block: A case report.

Sue Hyun Lee

Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Korea, Republic of

Spontaneous orthostatic headache is prominent feature of intracranial hypotension. Occasionally, postural orthostatic tachycardia syndrome (POTS) shows orthostatic headache. The presence of tachycardia with upright posture differentiates POTS from intracranial hypotension. Massive hydration and epidural blood patch at the leaking site are first-line treatment for spontaneous intracranial hypotension.

Occipital nerve block is an injection of steroids or anesthetics into regions of the greater occipital nerve and the lesser occipital nerve. This procedure is commonly used for treating occipital neuralgia, chronic migraine, cervicogenic headache, and cluster headache. However, occipital nerve block is not a recommendation for headache management of spontaneous intracranial hypotension or POTS. This report describes a case of spontaneous orthostatic headache improved after occipital nerve block.

A 69-year-old female visited outpatient clinic of Neurology department due to sudden incidence of headache. She recently diagnosed hypothyroidism and controlled properly by taking mediation. Hypothyroidism was her only medical history and she did not have history of spinal puncture or trauma. In the past, she had headache when she stayed under the sun for a long time. In addition, she had headache for one week after each COVID-19 vaccine and for one month after COVID-19 infection. Those headaches were mild intensity and did not have associated symptoms. However, one month before her visit to Neurology department, headache started suddenly. She continuously felt heavy, tight, and needle poking pain through her posterior head which had moderate intensity. Indigestion was associated with headache. She also reported phonophobia, but this was always present and did not aggravate by headache. Her headache was always aggravated by upright positioning and disappeared by supine position. Her questionnaires were as follows: Headache Impact Test-6 (HIT-6) 68, Migraine Disability Assessment (MIDAS) 0. She brought brain magnetic resonance image (MRI) which showed slight enlargement in pituitary. She reported that this MRI was taken right after headache began. Her heart rate and blood pressure showed little difference during position change.

She was admitted for massive hydration and epidural blood patch. While starting her preventive medication for migraine, her headache remained same after 3 days of massive hydration. Therefore, we consulted Anesthesiology department for epidural blood patch. However, Anesthesiology department wanted to try occipital nerve block first due to posterior location of headache and migrainous features such as indigestion and moderate intensity. After some discussion, we decided to occipital nerve block prior to epidural patch. Anesthesiologist injected 5cc of 1% mepivacaine in greater occipital nerve and lesser occipital nerve. The patient was discharged same day of occipital nerve block because the patient insisted. She visited outpatient clinic after 2 weeks of discharge. She reported that 1 week after the nerve block, her headache was greatly improved but some heaviness of brain was present. She stopped taking acute pain medication due to mildness of headache. Preventive medication is maintained, and she had another occipital nerve block.

This case had both features of intracranial hypotension and migraine. By the International Classification of Headache Disorder-3 (ICHD-3), this case can be diagnosed to intracranial hypotension than migraine. However, epidural patch was difficult because target site was not clear. Therefore, when target site is not clear enough for epidural patch, prior treatment of migraine needs to be considered for mixed features like our case.

Disclosure of Interest: None Declared

IHC23-PO-331

Summary of calcific tendinitis of longus coli muscle in Japan.

Shinji Morita[1], Tatsuya Monzen[1] and Fumihiko Sakai[2]

[1]*Ota Memorial Hospital, Ota City, Gunma Prefecture, Japan*
[2]*Saitama International Headache Center, Saitama, Japan*

Objective: Calcific tendinitis of the longus coli muscle is a cause of headache and is classified as cervicogenic headache in the International Classification of Headache, 3rd edition. Although case reports and papers have been published on this disease in the past, it is a rare disease. In Japan, there are almost no opportunities to learn about it in medical education. We examined patients diagnosed with calcific tendinitis of the longus coli muscle at our hospital between 2014 and 2023. We also searched and reviewed the literature using the Japanese medical

literature search engine, Ichushi Web, and summarised literatures in Japan.

Methods: Patients diagnosed with calcific tendinitis of the longus coli muscle who visited our hospital between April 2014 and March 2023 were investigated. We also searched the literature using Ichushi Web to clarify the current condition of calcific tendinitis of the longus coli muscle in Japan. A total of 48 references, 86cases, were examined, excluding duplicate publications and those which the text could not be verified.

Results: Only one case of calcific tendinitis of the longus coli muscle was diagnosed at our hospital. The patient was brought to the emergency department with a complaint of sudden headache. Subarachnoid hemorrhage and vertebral artery dissection was suspected. Contrast-enhanced head CT and neck CT were performed. However, instead of vascular abnormalities, calcification in front of cervical spine was found. The pain became better by using painkiller.

A search of Ichushi revealed a total of 86 cases (male: 50, female: 36). The mean age of the patients was 45.4 ± 12.7. All patients were improved with analgesics including NSAIDs. The time to symptom improvement is 9.0 ± 8.2 days. The main symptoms were back neck pain and swallowing pain. The most important differential diagnosis was pharyngeal abscess and antibiotics were used in many cases. Headache was present in just 5 cases and was a rare symptom of calcific tendinitis of the longus coli muscle, a rare condition.

Conclusion: In case of sudden headache, a history of pain on swallowing and neck pain should be obtained. CT should include the cervical region when patients complained of headache with swallowing or neck pain.

Medical education at universities may be useful as part of an awareness campaign on Calcific tendinitis of the longus coli muscle.

IHC23-PO-332

Effect of continuous epidural injection of hydroxyethyl starch on spontaneous intracranial hypotension

Yuwen Zhang[1], Jing Ding[2], Changhong Miao[3], Shichao Li[3], Jiang Lin[4] and Wei xingzi Xu[4]

[1]Department of Neurology, Zhongshan Hospital, Fudan Univetsity, Shanghai, China
[2]Department of Neurology, Zhongshan Hospital, Fudan Univetsity, Shanghai, China
[3]Department of anesthesiology, Zhongshan Hospital, Fudan Univetsity, Shanghai, China
[4]Department of radiology, Zhongshan Hospital, Fudan Univetsity, Shanghai, China

Objective: To investigate the effect and safety of continuous epidural pumping of hydroxyethyl starch in the treatment of spontaneous intracranial hypotension (SIH).

Methods: We enrolled 22 patients with SIH hospitalized in Zhongshan Hospital Fudan University from June 2020 to May 2022.The clinical features, MRI features, MR myelography (MRM), computed tomography myelogram (CTM) features and lumbar puncture results were analyzed. Initial treatment consisted of bed rest, hydration with IV fluids and simple analgesics. However, after 1 week of conservative treatment, only 2 patients had symptoms resolved. The remaining 20 patients had no improvement, so they were given continuous epidural pumping of hydroxyethyl starch. The patients taked a lateral position and the anesthesiologist located the intervertebral space according to the results of CTM. After the puncture needle reached the ligamentum flavum, the needle core was removed, and the epidural catheter is inserted through the puncture needle. First, 30–40 ml hydroxyethyl starch was injected slowly, then it was pumped 6–10 ml per hour, finally, the tube was removed after 48h.The disappearance of symptoms such as orthostatic headache was considered effective. One month later, we followed up the patient's brain MRI and MRM again.

Results: Among the 22 patients, 11 were males and 11 were females. The average age of patients was 40.18 ± 9.39 years old. 50% of patients had low cerebrospinal fluid (CSF) pressure ($<60 mmH_2O$), 50% had normal pressure ($60–180 mmH_2O$). Abnormal brain MRI signs were found in 20 patients (90.91%). Diffuse pachymeningeal enhancement was the most common sign (90.91%), followed by pituitary enlargement (63.64%) and venous sinus dilatation (36.36%). CTM was performed in all 22 patients and CSF leakage was found in 21 cases (95.45%). The most common leak location was the cervicothoracic spine(45.45%), followed by the thoracic spine (40.91%) and the cervicothoracic lumbar spine (9.09%). MRM was performed in 21 patients and abnormal CSF accumulation was found in all patients (100%). Only 2 patients had improvement in symptoms after 1 week of conservative treatment. The remaining 20 patients were treated with epidural puncture and continuous pumping of hydroxyethyl starch. After 2 days, the patients were asked to get up and observe whether there was headache in sitting position to evaluate the treatment effect. The patients' symptoms improved significantly and the orthostatic headache disappeared completely, which was considered effective. Of the 20 patients, 18 patients had first successful treatment (effective rate 90.0%), including 2 patients who had previously received epidural blood patch therapy. The success rate of continuous epidural injection of hydroxyethyl starch on SIH was higher than that of epidural blood patch therapy reported in the literature (64%, according to JAMA neurology). Two patients had no significant improvement after the first treatment,

and they received a second epidural continuous hydroxyethyl starch therapy a week later. Eventually their symptoms improved significantly. No serious adverse events were found after therpy. The minor transient adverse events included back pain and head swelling. We followed up the patient's brain MRI and MR myelogram one month later. It can be seen that the dural enhancement was reduced or disappeared and the MRM showed obvious cerebrospinal fluid absorb.

Conclusion: Continuous epidural infusion of hydroxyethyl starch can effectively treat spontaneous intracranial hypotension with high success rate, simple and easy operation, no obvious complications, and can be used as a new treatment method.

Keywords: Spontaneous intracranial hypotension; hydroxyethyl starch; Epidural

Disclosure of Interest: None Declared

IHC23-PO-333

55 year old male presenting with migraine-like headache and hyponatremia post-recombinant adenovirus vaccination to COVID-19: a case report

James Im[1] and William Kingston[1,2]

[1]*University of Toronto, Toronto, Canada*
[2]*Sunnybrook Health Sciences Centre, Toronto, Canada*

Objective: This case report describes first onset headache imitating a primary migraine disorder with subsequently discovered hyponatremia.

Methods: A 55 year old healthy male presented to the emergency room with a 2–3 week history of a recurrent new onset pulsatile headache with associated photophobia and phonophobia 3–4 weeks after exposure to his first dose of the (AstraZeneca Oxford) ChAdOx1 SARS COV 2 vaccination. The patient was informed with regards to the details and the nature of this case report and agreed to release his anonymized medical details for academic study.

Results: Clinical examination revealed no abnormalities with vital signs and cardiopulmonary examination noting that the patient appeared euvolemic. CT/CTA of the brain revealed no abnormalities. MRI/MRV brain with contrast revealed no abnormalities other than an incidental stable appearing right posterior parasagittal focus of signal favoured to be a lipoma or a potential Rathke's cyst without mass effect. Additionally, COVID 19 was not detected by viral PCR. The patient is a non-smoker, however a CT chest abdomen and pelvis was performed. This revealed no malignant focus.

The patient's serum on initial investigations were normal but subsequently was found to have serum sodium of 117, serum osmolality of 249 mmol/kg, urine sodium of 88 mmol/L and urine osmolality at the lowest found at 255 mmol/kg. He was diagnosed with syndrome of inappropriate antidiuretic hormone (SIADH) and improved with fluid restriction and simple analgesia and was subsequently discharged 4 days later. He has not had a recurrence of his headache up to one year in follow-up at the time of report submission.

Conclusion: Given the lack of another ostensible trigger, emergence of migraine-like headache in an otherwise healthy individual with no history of headache, rapid improvement and a possible, albeit delayed, temporal relationship, this case report purports the vaccine as the underlying cause of his headache and hyponatremia. Given the importance of side effect recognition in widely distributed vaccinations, this symptom presentation should be studied further in this vaccine formulation and in other similar case studies.

Disclosure of Interest: None Declared

IHC23-PO-334

Obstructive sleep apnea syndrome and headache

Isil Yazici Gencdal[1] and R. Gokcen Gozubatik-Celik[2]

[1]*Department of Neurology, Bakirkoy Research and Training Hospital for Neurologic and Psychiatric Diseases, University of Health Science, Istanbul, Turkey*
[2]*Department of Neurology, Bakirkoy Research and Training Hospital for Neurologic and Psychiatric Diseases, University of Health Science, ıstanbul, Turkey*

Introduction: Morning headaches may be important to obstructive sleep apnea syndrome (OSAS). Hypercapnia, hypoxemia, increased blood pressure, interrupted sleep, and impaired cerebral blood flow may cause headaches.

Objective: Our study aimed to evaluate the relationship between the severity of the headache and polysomnography findings and the clinical response to continuous positive airway pressure (CPAP) treatment.

Methods: Demographic information of 312 patients who were followed up with the diagnosis of OSAS in the sleep outpatient clinic of our hospital and received CPAP treatment for six months, presence of sleep apnea headache before and after treatment according to the International Classification of Headache (ICHD-3); The severity of headache using the Visual Analogue Scale (VAS); Polysomnography findings such as minimum oxygen saturation, total sleep time, sleep efficiency, desaturation index, mean heart rate, and mean oxygen saturation were evaluated retrospectively.

Results: Between March 2020 and June 2022, 50 patients (21 female, 29 male) out of 312 patients who applied to

our sleep laboratory with the diagnosis of OSAS and started CPAP treatment had complaints consistent with sleep apnea syndrome headache. The mean age was 52.1 ± 7.8 years and the mean body mass index was 34.4 ± 7.3. All patients reported improvement in their headaches due to CPAP treatment. The initial median value of VAS pain scores was 7 (4–9), and this value decreased to 1.2 (0–5) after treatment. In our study, a significant correlation was observed between the severity of the disease and the severity of headaches in our patients with OSAS. A statistically significant decrease was observed in the severity of headache after PAP treatment in patients with polysomnography findings with low min O2 hours, low mean O2 hours, high desaturation index, and high AHI.

Conclusion: Headache is common in patients with sleep disorders, and the sleep pattern and quality of patients who apply to the neurology outpatient clinic should be questioned. In our study, a statistically significant relationship was observed between the severity of the disease and polysomnography findings and the severity of headaches in our patients with OSAS. Clinical improvement was observed in patients with CPAP therapy.

Disclosure of Interest: None Declared

IHC23-PO-335

Evaluation of the headache features in acute and chronic stages after cerebral venous thrombosis from 2017–2023 in patients admitted to Valiasr Hospital in Zanjan, iran

Nooshin Yamani

Zanjan University of Medical Sciences, Zanjan, Iran, Islamic Republic of

Background: Cerebral venous thrombosis (CVT) could be a neurovascular disease caused by a thrombotic occlusion of either a dural sinus or cerebral vein. Headache has been reliably detailed as the foremost common symptom of cerebral venous thrombosis and as the foremost frequent presenting feature. There's restricted data around the frequency and phenotype of headache, weeks to months after cerebral venous thrombosis (postcerebral venous thrombosis headache, PCH). Purpose of this survey is to characterize CVT, depict the headache pattern, and, at last, to evaluate the recurrence, characteristics and indicators of PCH.

Methods: In this cross-sectional study, patients with a definite diagnosis of CVT referred to Valiasr hospital (zanjan University of Medical Sciences) from 2017 to 2022 were included. We recruited conscious CVT patients who were able to give reliable history after consent. Institutional ethics approval was obtained. The diagnosis of CVT was based on the clinical and imaging parameters. The frequency and characteristics of PCH were surveyed in cerebral venous thrombosis survivors. Patients were met at least three months after the cerebral venous thrombosis diagnosis and discharge. Clinical and imaging characteristics at the time of cerebral venous thrombosis determination, as well as history of headache earlier to cerebral venous thrombosis were compared in subjects with (GroupPCH) and without PCH (Group control).

Results: Subjects (n = 50) were assessed. PCH was present in 31(62%) of the patients, phenotypes of tension-type-like headache were present in 16 (51.6%) and of migraine-like headache in 14(45.2%). The mean age was significantly more common (P = 0.007) in Group PCH (42.65 ± 14.3) than in Group control (31.7 ± 11). History of primary headache prior to cerebral venous thrombosis was significantly more common (OR: 4.6; 95% CI: 1.04–27.5) in GroupPCH (38.7%) than in Groupcontrol (10.5%).

Conclusion: Headache is the most common patient presentation. The quality of this headache is highly variable with no specific location or pattern. PCH was present in more than half of the patients. History of prior headache may be a risk factor for PCH. In group PCH patients with history of headache had a higher intensity of headache compared to patients without a history of headache.

Key Words: Cerebral venous thrombosis, postcerebral venous thrombosis headache, headache disorders, migraine disorders, tension-type headache.

Disclosure of Interest: None Declared

IHC23-PO-336

Spontaneous intracranial hypotension complicated by cerebral venous thrombosis: a case report

Gabriel Keller, Diogo Guilherme Leão Edelmuth, Ida Fortini and Marcio Nattan Portes Souza

Universidade de Sao Paulo, Sao Paulo, Brazil

Objective: Cerebral Venous Thrombosis (CVT) has been rarely reported as a complication of Spontaneous Intracranial Hypotension (SIH). Venous sinus dilation causing blood flow slowing combined with dural sinus anatomical distortion due to brain sagging were two proposed mechanisms by which SIH could precipitate CVT. However, a few case studies have reported a clear temporal association between the two conditions, with SIH preceding the occurrence of CVT. We report a patient with SIH who presented with postural headache, with an initially normal venous CT angiography, and had an MRI

performed one week later confirming SIH and revealing the development of CVT.

Methods:

Case report:

Results: A 47 years-old female patient with medical history of episodic migraine and use of oral contraceptive experienced a sudden onset of a severe bilateral headache associated with neck pain, tinnitus, dizziness, and ear fullness. The pain progressed over the following hours and became daily persistent, being relieved by lying supine and restarting a few minutes after standing. One week after symptoms had started, she had a head CT with venous angiography performed, which returned normal. Her headache persisted over the following week and she evolved with a focal motor seizure. An MRI angiography was then performed and revealed pachymeningeal diffuse enhancement, subdural effusions, decreased mamillopontine distance, and enlarged venous sinuses with thrombosis of the superior sagittal sinus and cortical veins. Extensive investigation for genetic and acquired thrombophilia was performed with normal findings. She received enoxaparin for the CVT treatment, and a dynamic CT myelography revealed a dural contrast leak at the T12-L1 spinal level. A guided epidural blood patch was performed, and the patient evolved with complete headache remission after a few days.

Conclusion: CVT has recently been reported as a rare complication of SIH. Despite the presence of putative mechanisms relating the two conditions, there is still controversy over their causal relationship. By showing a temporal progression from SIH to CVT in this case, we reinforce the concept that SIH could lead to CVT.

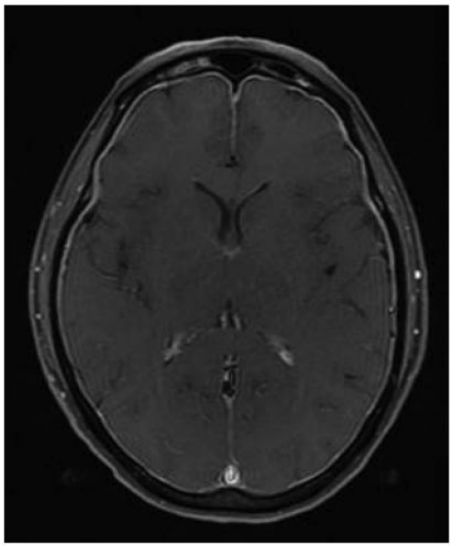


Fig. 1 – Pachymeningeal diffuse enhancement

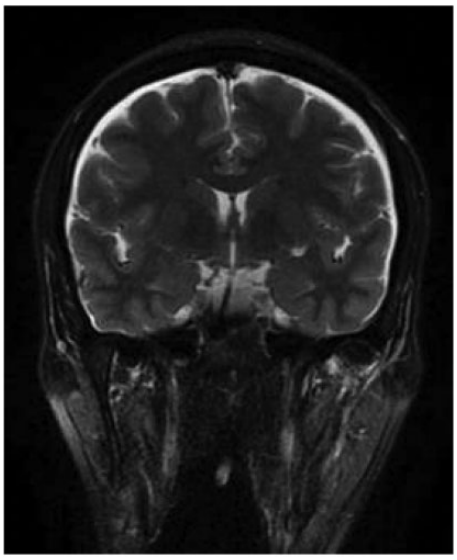


Fig. 2 – Subdural effusions

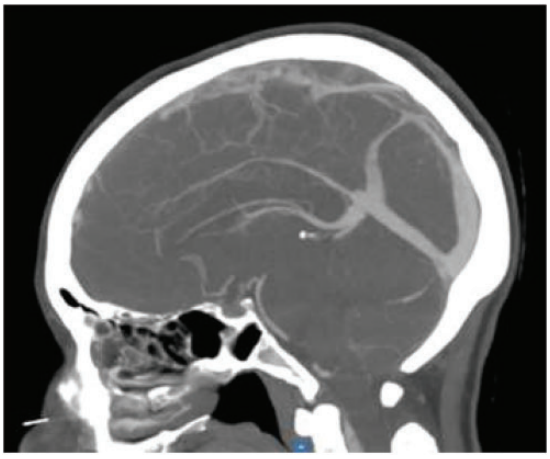


Fig. 3 – Superior sagittal sinus thrombosis

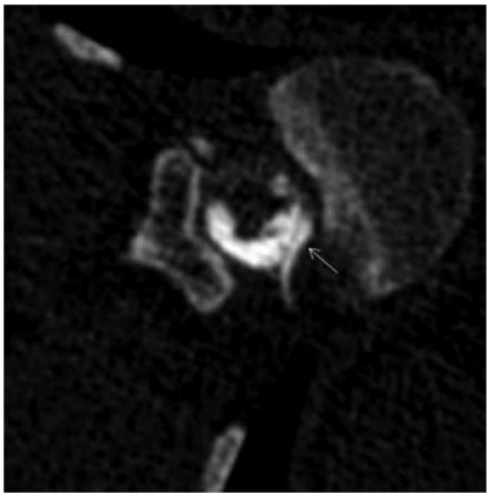


Fig. 4. Dynamic CT mielography at T12-L1 level showing contrast leak

Disclosure of Interest: None Declared

IHC23-PO-337

Sex Differences in the Clinical Manifestations and Treatment Outcomes in a Large Cohort of Spontaneous Intracranial Hypotension

Yen-Feng Wang[1,2], Po-Tso Lin[1,2], Shu-Shya Hseu[1,2], Jong-Ling Fuh[1,2], Jiing-Feng Lirng[1,2], Shih-Pin Chen[1,2], Wei-Ta Chen[1,2,3] and Shuu-Jiun Wang[1,2]

[1]*Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*National Yang Ming Chiao Tung University, Taipei, Taiwan*
[3]*Ministry of Health and Welfare Keelung Hospital, Keelung, Taiwan*

Objective: To determine sex differences in clinical profiles and treatment outcomes in spontaneous intracranial hypotension (SIH).
Methods: Medical records of consecutive patients with SIH in a tertiary medical center between December 1997 and August 2021 were systematically reviewed. Clinical profiles, imaging findings, and treatment responses were compared between the sexes. Outcome measures included response to the first epidural blood patching (EBP) and complications.
Results: In total, 442 patients with SIH (277F/165M, mean age 40.3 ± 10.0 years) were included in the analysis. Men had longer delays between disease onset and initial hospital presentation (20.8 ± 21.5 vs. 38.2 ± 67.4 days, $p = 0.002$), and were less likely to have nausea, vomiting, photophobia, and tinnitus compared with women (all $P < 0.05$) despite comparable radiologic findings. Among the 374 patients treated with EBPs, men were more likely to fail the first EBP (58.0% vs. 39.0%, odds ratio [OR] = 2.2 [95% confidence interval = 1.4–3.3], $P < 0.001$). However, the cumulative responder rates after up to two EBPs were comparable between men and women (86.2% vs. 87.7%, $P = 0.680$). Men were at a higher risk of having SDH (29.7% vs. 10.8%, OR = 3.5 [95% CI = 2.1–5.8], $P < 0.001$). Among patients with SDH, men had greater thickness (12.8 ± 4.3 vs. 8.1 ± 5.9 mm, $P < .001$) and were more likely to receive surgical drainage (55.1% vs. 10.0%, OR = 11.0 [95% CI = 3.0–41.3], $P < 0.001$) than women. Two of the three patients with mortality or significant disability were men, and the only death in women was attributed to underlying malignancy.
Conclusions: SIH in men is characterized by a delayed presentation, poorer response to the first EBP, and a higher risk of SDH. Cautions should be exercised in the management of men with SIH, and more aggressive measures, such as early and multiple EBPs, may be helpful.

Disclosure of Interest: YF Wang has received honoraria as a speaker from Taiwan branches of Allergan/AbbVie, Chugai, Eli Lilly, Novartis, Pfizer, Sanofi, UCB, and Viatris, and Hava Bio-Pharma, and Orient EuroPharma. He has received research grants from the Taiwan Ministry of Science and Technology, and Taipei Veterans General Hospital. SJ Wang has served on the advisory boards of Daiichi-Sankyo, Eli Lilly and Novartis; has received honoraria as a moderator from Allergan/AbbVie, Pfizer, Eli Lilly, Biogen and Eisai and has been the PI in trials sponsored by Eli Lilly, Novartis, and Allergan/AbbVie. He has received research grants from the Taiwan Minister of Technology and Science (MOST), Brain Research Center, National Yang Ming Chiao Tung University from The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan, Taipei Veterans General Hospital, Taiwan Headache Society and Taiwan branches of Eli Lilly, Novartis, and Pfizer. PT Lin, SS Hseu, JL Fuh, JF Lirng, SP Chen, and WT Chen reported no disclosures relevant to the manuscript.

IHC23-PO-338

A case of neuronal intranuclear inclusion disease initiated by headache and hemianopia

Ahro Kim, Seulgi Hong, Seong Jin Jeon, MinJee Kim, Seungjin Choi and Ji-Yun Park

Ulsan University Hospital, Ulsan, Korea, Republic of

Background: Neuronal intranuclear inclusion disease (NIID) is a rare slowly progressive neurodegenerative disease characterized by intranuclear inclusions in the central, peripheral, and autonomic nervous systems and visceral organ cells. The clinical manifestations of NIID are highly variable, including movement disorders, dementia, neuropathy, and autonomic dysfunction, which makes its early diagnosis difficult. Detecting intranuclear inclusions (both morphologically and immunohistochemically) in skin or central nervous system tissues is valuable for diagnosing both familial and sporadic NIID cases. We investigated a patient who suffer from headache and hemianopsia episodes and had been misdiagnosed as migraine.
Case: A 55-year-old man visited the emergency room with headache, nausea, and vomiting that had started two weeks ago with no prior medical history. His symptoms began with blurred vision and the right side visual field was disturbed, followed by a headache and that lasted for 3 hours. He vomited for two days with no relief. He described his headache as a squeezing pain that was somewhat alleviated by lying down. The patient also reported

experiencing dizziness, generalized weakness, and slurred speech, and was confused for a period during which he failed to recognize his family. Computed tomography(CT) and Magnetic Resonance (MR) imaging (Figure 1a) and angiography were conducted, but the findings were non-specific. A cerebrospinal fluid(CSF) exam was performed to rule out encephalitis, and no definitive abnormalities were found. The patient returned to the outpatient clinic one week later, reporting recurrent headaches since his previous ER visit. An Electroencephalogram was performed, revealing no definitive abnormalities. On the basis of history and exam, he was diagnosed with migraine with aura.

One year later he revisited emergency room, presenting with severe headache, confusion, and dysarthria that had developed a few days ago. On neurological examination, the patient presented with a drowsy mental status and confusion, as well as right gaze preference, left central-type facial palsy, and left side weakness. The patient's MRI revealed a diffuse lesion with restricted diffusion in the cortex of the right frontal, parietal, occipital, and temporal lobes. Additionally, there was enhancement observed in the same lesion. A CSF exam was performed again, and no definitive abnormalities were found. At the time of admission, it was discovered that some of his siblings had experienced similar symptoms and were diagnosed with NIID. A skin biopsy was performed, revealing eosinophilic intranuclear inclusions in the sweat glands and adipose tissue, which were consistent with NIID. The patient's history of recurrent headaches and encephalitis-like episodes, positive family history, and the findings from skin biopsy and brain MRI led to the final diagnosis of adult onset NIID. The patient's condition deteriorated, and he became bedridden, eventually requiring transfer to a nursing home. One month later, he died of aspiration pneumonia and sepsis.

Conclusion: Initially, the patient was suspected to have migraine with aura, as all the diagnostic tests conducted were normal. However, when the patient presented with recurrent headaches, accompanied by atypical symptoms such as dysarthria and confusion, further diagnostic workup was necessary. Therefore, it is important to consider the possibility of NIID in such cases, even if the patient's symptoms are consistent with migraines.

IHC23-PO-339

A rare cause of thunderclap headache- a cervical spinal cord haemangioendothelioma with sub arachnoid haemorrhage localised to spinal cord

Udari Tankana Samarasiri and Bimsara Senanayake

Institute of Neurology National hospital of Sri Lanka, Colombo, Sri Lanka

A 24 year old female presented with hyperacute occipital head and neck pain while bending forward to lift a weight, followed by a two hour period of drowsiness. On regaining consciousness noted continuing low grade neck pain, vertigo, vomiting, bilateral drooping of eyelids with accompaning double vision.

On examination her GCS was 15/15. Nuchal rigidity was present. Bilateral complete occulomotor nerve palsy with fixed dilated pupils of 6mm was observed. She had spastic quadripareisis with extensor planter response with power of MRC grade +4/5.

Non contrast CT brain CT cerebral angiogram was normal. However there was persistent blood stained CSF on a lumbar puncture done on day two. CT angiography and digital subtraction angiography of neck vessels revealed a vascular lesion at C4 spinal level with two feeding arteries arising from right vertebral at C7 level and right anterior spinal artery. There was a delay in contrast clearance of the lesion. MRI spine revealed an avidly contrast enhancing T2/Flair hyperintense intramedullary lesion with perilesional oedema extending upto lower medulla oblongata and syrinx formation of spinal cord caudal to the lesion. Bilateral occulomotor nerves also was shown to be contrast enhancing. Midbrain imaging was normal.

Dorsal midline myelotomy with excision of lesion following embolization of the main feeding artery was performed successfully. Preliminary histological assessment was suggestive of spinal cord haemangioendothelioma. Further immunohisthochemical assessment is pending.

This is a case of cervical cord haemangioendothelioma presenting as a thunderclap headache due to sub arachnoid haemorrhage localised to spinal cord. This is an extremely rare cause of a thunder clap headache. The acute onset occulomotor nerve palsy with pupillary involvement was radiologicaly explained by avidly enhancing verves possibly due to neuritis. However a cause the acute onset neuritis is yet to be confirmed currently even persisting beyond 2weeks of the event. Irritation by sub arachnid blood was thought as a plausible explanation however pointers against this was that the initial CT brain was negative for cerebral sub arachnoid blood and secondly the symptoms persisted even two weeks after the event.

This signifies the importance of recongising vascular spinal cord tumors leading to sub arachnoid haemorrhage localised to spinal cord in cases of thunderclap headache with negative brain imaging.

Disclosure of Interest: None Declared

IHC23-PO-340

Distinguishing Between Migraine and Cervicogenic Headache: Key Factors for Differential Diagnosis

Esra Aciman Demirel[1], Nesrin Ergin[2], Nevra Oksuz[3], Dilan Bayar Narin[3], Burcu Karpuz Seren[4], Fatma Gulhan Sahbaz[5], Senem Ertugrul Mut[6], Buse Cagla Ari[7], Pinar Gelener[8], Tulin Gesoglu Demir[9], Nermin Tepe[10], Huseyin Tugrul Atasoy[1], Derya Uludüz[11] and Aynur Ozge[3]

[1]Department of Neurology, Faculty of Medicine, Bulent Ecevit University, Zonguldak, Turkey, zonguldak, Turkey
[2]Department of Neurology, Pamukkale University, Medical Faculty, Denizli, Turkey, denizli, Turkey
[3]Mersin University Faculty of Medicine, Department of Neurology, Mersin, Türkiye, mersin, Turkey
[4]Department of Neurology, Zonguldak Ataturk State Hospital, Zonguldak, Turkey, zonguldak, Turkey
[5]Department of Neurology, Afyonkarahisar State Hospital, afyonkarahisar, Turkey
[6]1University of Kyrenia, Faculty of Medicine, Department of Neurology, Kyrenia, Kyrenia, Cyprus
[7]Bahcesehir University Medical Faculty, Neurology Department, Istanbul, Turkey, istanbul, Turkey
[8]1University of Kyrenia, Faculty of Medicine, Department of Neurology, Kyrenia, TRNC, kyrenia, Cyprus
[9]Department of Neurology, Faculty of Medicine, Harran University, Urfa, Turkey, urfa, Turkey
[10]Department of Neurology, Balıkesir University, Balıkesir, Turkey, balıkesir, Turkey
[11]Istanbul University, Cerrahpasa Faculty of Medicine, Department of Neurology, Istanbul, Türkiye, istanbul, Turkey

Background: Migraine and cervicogenic headache (CEH) are common primary and secondary headaches. However, their overlapping symptoms pose challenges in accurately diagnosing them, resulting in incorrect diagnoses in approximately half of cases and subsequent inappropriate treatment choices. CEH is characterized by reduced range of motion in the neck, attacks triggered by neck movements or external pressure on the greater occipital nerve of the C2 root, ipsilateral shoulder/arm pain, and consistent unilaterality. Conversely, these features are typically absent in common migraine. Typical migraine symptoms such as nausea, vomiting, photophobia, and phonophobia can also occur in CEH but with lower frequency and intensity. However, there are several overlapping cases for both types of headache disorders that require clearer insight.

Objective: This study aims to identify key factors that can aid in the differential diagnosis between migraine and cervicogenic headache, enhancing the accuracy of diagnosis and facilitating appropriate treatment choices.

Materials and Methods: A prospective study was conducted, involving 314 consecutive patients diagnosed with cervicogenic headache from 15 different headache outpatient departments as a preliminary report of an ongoing national project. These patients were receiving follow-up care at neurology services in hospitals.

Results: The study included 314 patients, of which 68.5% were female. The highest incidence was observed in the 30–40 age range. Among the patients, 94.3% reported pain originating from the neck and spreading to the head. The duration of headache episodes most commonly ranged from 1 to 5 years. The attack duration varied, with 41.4% lasting between 1 and 4 hours and 40.1% lasting between 5 and 72 hours. About 50.2% of patients experienced 3–4 attacks per month, and the mean attack severity was rated as 6–7 on a scale. The occipital and cranio-cervical junctions were the most intense regions of headache sensation for 21.7% of patients, followed by the cranio-cervical junction alone for 11.8%. The most common pain qualification reported was constrictor (23.2%), followed by pressure-pressure (20.1%). Throbbing headache was less prevalent, described by only 15.6% of patients. In terms of headache location, 44.3% experienced pain solely on one side of the neck, while 43.6% experienced pain on one side of the neck that occasionally spread to the opposite side. Shoulder pain, limited neck movement, and dizziness were the most common accompanying symptoms of headache. Neck pain severity varied among patients, with 14% reporting severe pain, 28.7% mild pain, 47.8% moderate pain, and 9.6% no neck pain. Routine physical activity triggered pain in 66.6% of patients, while 73.6% experienced trigger from posture. The flexion-rotation test yielded positive results in 60.2% of patients. Pressure applied to the upper cervical spine (C1-3) triggered headache in 63.1% of patients, while pressure on the occipital region triggered headache in 55.4%. Cervical imaging commonly revealed cervical radiculopathy and cervical flattening. Simple analgesics and nonsteroidal anti-inflammatory drugs were the most frequently used treatments for headache attacks, with over 50% of patients responding favorably to NSAIDs. Tricyclic antidepressants, SNRIs, and SSRIs were commonly prescribed for prophylactic treatment. Gon blockade and trigger point injections were the most frequently employed interventional methods, with over 75% of patients benefiting from these procedures. Only 31.8% of patients underwent physical therapy, with exercise being the most

common method (12.9%), followed by TENS (9.0%) and massage (7.1%).
Regarding treatment, our study found that simple analgesics and nonsteroidal anti-inflammatory drugs were the most commonly used medications for managing headache attacks in cervicogenic headache patients, with favorable response rates exceeding 50%. Prophylactic treatment often involved the use of tricyclic antidepressants, SNRIs, and SSRIs. Interventional methods such as GON blockade and trigger point injections were found to be beneficial for a significant majority of patients. However, it is worth noting that the utilization of physical therapy methods was relatively low, with exercise being the most common approach.
Conclusion: Our study revealed several distinguishing factors between migraine and cervicogenic headache. While both types of headaches share some similarities, such as unilateral pain and a higher prevalence among females, they exhibit significant differences. Our findings contribute to a better understanding of the characteristics, triggers, and treatment patterns of cervicogenic headache, highlighting the need for a comprehensive approach to differentiate it from migraine and provide optimal tailored management strategies for patients.

IHC23-PO-341

Clinical Correlates of Bern Score in Patients with Spontaneous Intracranial Hypotension: a critical reappraisal

So Youn Choi[1], Hoe Jong Jeong[2], Eunji Lee[3] and Mi Ji Lee[1]

[1]Seoul National University Hospital, Seoul, Korea, Republic of
[2]Veterans Healthcare Service Medical Center, Seoul, Korea, Republic of
[3]Soonchunhyang University Seoul Hospital, Seoul, Korea, Republic of

Background: Spontaneous intracranial hypotension (SIH) is a dynamic disorder in which clinical manifestation and radiological findings change in time. Recently, the "Bern Score" has been suggested to estimate the likelihood of SIH based on brain MRI findings. In this study, we aimed to investigate the clinical correlates of the Bern Score in patients with SIH.
Methods: Between April 2022 and February 2023, we prospectively recruited patients with SIH admitted to Seoul National University Hospital. All patients underwent contrast-enhanced brain MRI and MR myelography. Clinical and radiological characteristics and treatment outcomes were collected. The Bern Score was assigned to each patient based on brain MRI findings. Number of spinal segments with extradural cerebrospinal fluids (CSF) was counted to represent the extent of extradural CSF demonstrated in MR myelography. We performed the Pearson's correlation analysis to assess the correlation between clinical variables and the Bern score.
Results: Clinical and radiological features of 37 patients with SIH were analyzed. A moderate negative correlation was found between the Bern Score and disease duration ($r = -0.388$, $p = 0.018$). The Bern score showed a moderate positive correlation with good response to epidural blood patch (EBP) ($r = 0.469$, $p = 0.003$). The number of spinal segments with visible extradural CSF positively correlated with the Bern Score ($r = 0.452$, $p = 0.005$).
Conclusion: We found that the Bern Score normalizes as disease duration increases and higher Bern Scores are associated with better treatment outcomes. Higher Bern Scores also correlate with more visible CSF leakage. Taken together, a special caution should be paid when interpreting the Bern Score to diagnose SIH in patients with longer disease duration and those without extradural CSF. A low Bern Score does not rule out the possibility of SIH in such patients, and treatment outcome can be even worse in patients with lower Bern Scores.

IHC23-PO-342

Cervical Vertebral Artery Dissection Manifesting the First-Onset Migraine With Aura-Like Attack

Hynji Kim, Sumin Kim and Byung-Su Kim

Ewha Womans University Mokdong Hospital, Ewha Womans University College of Medicine, Seoul, Korea, Republic of

Background: Cervical vertebral artery dissection (VAD) can present with a variety of cervical pain, headache, and neurological deficits. Since VAD has a potential risk of distal embolization and subsequent cerebral ischemia in the acute phase, migraine aura-like symptoms may theoretically occur at stroke or transient ischemic stroke-onset in VAD. Nonetheless, migraine with aura-like presentation attributed to VAD has rarely been reported in previous literature. Hence, we report a case of traumatic cervical VAD, chiefly manifesting migraine with aura-mimicking attack.
Case: A 27-year-old woman visited the headache clinic with a chief complaint of the first-onset visual symptom and following headache attack one day earlier. She described her visual symptom as scintillating scotoma in the left visual field lasting approximately for 10 minutes. She reported a following headache started 20 minutes after the visual symptoms ended. The headache characteristics were as follows: severe headache intensity (10–visual analogue scale: 9), bilateral, pulsatile, aggravation by routine activity, nausea, and attack duration: 12 hours. She

also had been experiencing dull pain in her right cervical region since receiving a massage one week earlier.
In fact, she had a history of headache that had been persisting for ≥10 years. Her prior headache was compatible with migraine without aura. Her migraine disease course was stationary, and recent average attack frequency was about 4 times per month. She reported the new headache was stronger than her usual migraine attack, and her usual over-the-counter drug was differently ineffective in relieving the headache pain.
She promptly underwent MRI to determine whether her new headache attack was due to secondary etiology. No intracranial abnormalities, including acute cerebral infarction, were observed on diffusion-weighted imaging (DWI) and brain MRI. On supra-aortic contrast-enhanced magnetic resonance angiography, bead-like irregularity and stenosis of the right V2 segment were found. Antithrombotic therapy of aspirin with 300 mg loading doses was initiated. Three months later, she was followed up with brain CT angiograpy, the stenosis in the right V2 was no longer observed. She had no more attack of visual symptom and following headache during the follow-up.
Conclusions: In this case, the new headache attack in the acute phase of VAD considerably resembles typical attack of migraine with aura. Given that the new headache attack occurred during the persistence of neck pain following the massage, the patient was finally diagnosed with cervical VAD. A possible explanation for this novel presentation is that her active cycle of migraine without aura can further enhance a potential of microemboli from the segment of cervical artery dissection to induce cortical spreading depression as a direct pathophysiology for the migraine with aura-like attack. In clinical aspect, physicians had better keep in mind that the first attack resembling migraine with aura may be due to secondary etiology.

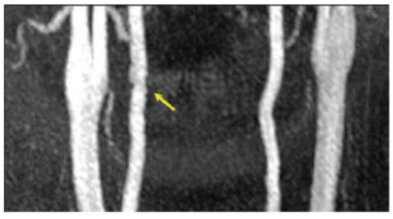


Figure. Note bead-like irregularity and stenosis of the right V2 segment (yellow arrow).

Disclosure of Interest: None Declared

IHC23-PO-343

Clinical Characteristics of Headache in Patients with Alopecia Areata: A Case Series

Yung-Hua Chu[1,2,3], Yen-Feng Wang[1,2,3], Li-Ling Hope Pan[1,3], Chih-Chiang Chen[1,2,4] and Shuu-Jiun Wang[1,2,3]

[1]*Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan*
[2]*College of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[3]*Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[4]*Department of Dermatology, Taipei Veterans General Hospital, Taipei, Taiwan*

Objective: Alopecia areata (AA) is an autoimmune disease characterized by hair loss due to inflammatory responses that target hair follicles. AA accompanied by headache was rarely reported in previous studies. The objective of the present study was to characterize headache profiles in AA.
Patients and Methods: We report a case series of patients presenting with concomitant AA and headache. The patients were all diagnosed with AA by a dermatologist and received topical or oral steroid treatment. Patients were interviewed by headache specialists for their headache phenotypes. Allodynia was defined as pain triggered by a stimulus that would not normally provoke pain, such as light touch, winds, or combing hair. Quantitative sensory testing (QST) was carried out to obtain thresholds for cold pain, heat pain, and mechanical punctate pain. Headache-related disability was assessed by using Migraine Disability Assessment (MIDAS). Psychological disturbances and sleep quality were evaluated by Hospital Anxiety and Depression Scale (HADS), including anxiety (HADS-A) and depression (HADS-D) subscales, and Pittsburgh Sleep Quality Index (PSQI).
Results: In total, sixteen patients (12F/4M, mean age 40.9 ± 13.0 years) were included. The headache was migrainous in five patients (31.3%), and was stabbing, pressing, or throbbing pain in others. Hair loss was temporally correlated with headache onset in 13 patients (81.3%), although headache persisted after hair regrowth in 11 patients (68.8%). Five of these patients (4F/1M, mean age 44.6 ± 3.6 years) (31.3%) reported allodynia. Only one patient (20%) in this group had migrainous features. When compared with those without, patients with allodynia had lower heat pain thresholds at the hair loss region (46.9 ± 4.0 °C vs. 49.0 ± 1.2 °C, $p = 0.013$) and less severe symptoms of anxiety (HADS-A = 6.5 ± 2.1 vs. 8.1 ± 5.1, $p = 0.037$). However, the average pain severity (4.4 ± 2.1 vs. 6.2 ± 2.5 on the numerical rating scale, $p = 0.599$), the

presence of nausea (20% vs. 44.4%, p = 0.360), vomiting (0% vs. 22.2%, p = 0.255), photophobia (20% vs. 44.4%, p = 0.360) or phonophobia (40% vs. 77.8%, p = 0.158), functional disability (MIDAS = 21.0 ± 33.8 vs. 24.8 ± 43.3, p = 0.820), symptoms of depression (HADS-D = 4.5 ± 3.7 vs. 6.4 ± 5.7, p = 0.440), and sleep quality (PSQI = 19.7 ± 16.3 vs. 29.1 ± 14.0, p = 0.848), as well as the thresholds for cold pain (6.5 ± 9.8 vs. 6.2 ± 7.4, p = 0.534) and mechanical punctate pain (78.3 ± 60.7 vs. 124.7 ± 80.0, p = 0.821) were comparable.

Conclusion: Headache in patients with AA is only occasionally migrainous and was temporally correlated with hair loss in most cases. Approximately a third reported allodynia, and these patients had reduced heat pain thresholds and fewer symptoms of anxiety. However, more cases are needed to further characterize the association between hair loss and headache.

Disclosure of Interest: None Declared

IHC23-PO-344

Fasting headache during the month of Ramadan

khadija saghir[1], Ouassim Mansoury[2], Fatma Gülhan Şahbaz[3], Emel Ur Özçelik[4], Semih Taşdelen[5], Aynur Özge[6], Arife Çimen Atalar[7], Hamit Genç[8], Samia Ben Sassi[9], Rabha Ali El sahly[10], Yaqoub Alabwah[11], Yahya Dehal[12], Shaimaa abdalaleem abdalgeleel[13], Mona AF Nada[14], Nevin Shalaby[15], Sarkhan Amirguliyev[16], Fatimata Hassane Djibo[17], Yared Z Zewde[18], Mory M. Camara[19], Mohamed Amine[2] and Najib Kissani[1]

[1]*Neurology Department, Centre Hospitalier Universitaire Mohammed VI de Marrakech, Cadi Ayyad University, Marrakesh, Morocco*
[2]*Department of Public Health, Epidemiology and Community Medicine, Laboratory of Biosciences and Health, Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakesh, Morocco*
[3]*Department of Neurology, Afyonkarahisar State Hospital, Afyonkarahisar, Turkey*
[4]*Departments of Neurology and Clinical Neurophysiology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey*
[5]*Department of Neurology, Istanbul University Faculty of Medicine, Istanbul, Turkey*
[6]*Department of Neurology and Algology, Mersin University Faculty of Medicine, Mersin, Turkey*
[7]*Health Sciences University Kanuni Sultan Süleyman Education and Research Hospital, istanbul, Turkey*
[8]*Gaziantep Dr. Ersin Arslan Training and research Hospital, Department of Neurology, Gaziantep, Turkey*
[9]*Mongi Ben Hmida National Institute of Neurology, Tunis, Tunisia*
[10]*medical college Benghazi university, tripoli, Libya*
[11]*Kuwait University, Health Science Center, Kuwait, Kuwait*
[12]*Centre Hospitalier des spécialités, Naoukchott, Mauritania*
[13]*Cancer Epidemiology and Biostatics, National Cancer Institute Cairo University, Cairo, Egypt*
[14]*Department of Neurology, Cairo University, cairo, Egypt*
[15]*Department of Neurology, Cairo University, Cairo, Egypt*
[16]*Republic Diagnostic Center, Baku, Azerbaijan*
[17]*National Hospital of Amirou Boubacar DIALLO, Niamey, Niger*
[18]*Addis Ababa University, College of health Sciences, Department of neurology, Addis Ababa, Ethiopia*
[19]*Hopital Anaim de Kamsar. Département de médecine polyvalente, Conakry, Guinea*

Objective: During the month of Ramadan, Muslims all over the globe practice fasting. They refrain from drinking, eating, and smoking from dawn until sunset. Our study aims to estimate the prevalence, intensity, and characteristics of headaches during Ramadan and identify the commonly used analgesics.

Methods: We conducted a descriptive multicenter cross-sectional study, using an online-self-administered questionnaire during the whole month of Ramadan; between March 22, 2023, and April 22, 2023. We included the general population from fourteen countries, and volunteer sampling was used. The data was collected in Google Forms and analyzed using SPSS version 23.

Results: 2397 participants responded to our survey. The male: female sex ratio was 2,05. Overall, 32,1% of responders belonged to the 26 to 35-year age group. 41,5% did not have a medical history of chronic headaches. The prevalence of fasting headache during this year's Ramadan was 73.8% with a 95% CI of [72.08%, 75.60%], compared to 69,2% in last year's Ramadan. Fasting headache was more common in females 68,6% than in males 31, 4%, and also among individuals who used to start their day with a cup of coffee or tea 64, 2%, however only 18,7% of smokers had fasting headache. Half of the participants 54,7% with fasting headache were relieved after breaking the fast. The characteristic of headache was tension or heaviness 55,8% and pulsation 53,2%, the headache was bilateral in one-third of the cases and localized mainly in the forehead in 43,4% of cases. Its main intensity was 6, 5 ± 1, 9 on a Likert scale from 1 to 10. Using medications to relieve the headache was common as 80. 6% of responders used medications. Among them, the most consumed drugs were paracetamol (62,7%), Naproxen (28.3%), and ibuprofen (19.5%).

Conclusion: fasting headache is frequent during Ramadan, it can occur in subjects who had or had not a history of chronic headache. Our study explored its main characteristics. however, more studies are needed to understand the complex physiopathology of fasting headache.

Disclosure of Interest: None Declared

IHC23-PO-345

Recurrent Thunderclap Headache as the Initial Presentation of Carotid Body Tumors: A Case Report and Implications for Imaging.

Yichen Lee

Department of Neurology, National Taiwan University Hospital Hsin-Chu Branch, Hsin-Chu, Taiwan

Carotid body tumors are rare neuroendocrine tumors with a reported incidence of 1–2 per 100,000. According to a multinational registry of 1432 patients with carotid body tumors, headache was reported in only 2% of cases.

Thunderclap headache is an important red flag for secondary headaches. A lesion outside of the brain is not a common cause of thunderclap headache. We report a case of a 13-year-old boy with a carotid body tumor who had recurrent thunderclap headaches as the initial presentation.

The patient had never experienced headaches before, but about 1.5 months prior to the clinic visit, he had a sudden onset of left-sided headache after coughing. He described the headache as severe pounding pain around the left temporal area, which lasted for about an hour and was not relieved by painkillers.

About 1 month later, while resting in the afternoon, he had a sudden onset of severe holocephalic headache. He described the pain as an explosion in his head, which peaked within seconds. The pain was so intense that he could only howl and roll on the floor. The excruciating pain subsided about 4–5 hours later, and he was able to fall asleep. The explosive headache recurred in the afternoon of the next day and almost every afternoon around seven to eight o'clock, subsiding around 4 hours later.

Brain MRI (magnetic resonance imaging) and MR angiography revealed a 3.8cm hypervascular tumor in the left carotid space with slight separation and lateral displacement of the left external and internal carotid artery. The patient received embolization followed by tumor removal. Pathology confirmed a paraganglioma. The patient's headaches gradually improved after the surgery.

Thunderclap headache is an important red flag for secondary headache, and brain imaging, including CT (computed tomography), CT angiography, MRI, or MR angiography, is recommended to exclude structural or vascular lesions. The experience of treating this patient suggests that the scope of CT angiography or MR angiography should be extended to include the neck.

IHC23-PO-346

A rare cause of thunderclap headache secondary to a dissecting basilar artery fusiform aneurysm

Indrachapa Ranasinghe[1], A D P Athukorala[2] and Bimsara Senanayake[1]

[1]*Institute of Neurology, National Hospital of Sri Lanka, Colombo, Sri Lanka*
[2]*Department of Interventional Radiology, National Hospital of Sri Lanka, Colombo, Sri Lanka*

Background: Basilar artery aneurysms (BAA) account for only 2.1% of all intra cranial aneurysms (1) (2). BAA can present as subarachnoid hemorrhage (SAH), stroke or found incidentally. Thunderclap headache due to dissecting basilar artery aneurysm without SAH is exceptionally seldom reported. (3). However Basilar artery thrombosis (BAT) gives rise to thunderclap headache more often in about 20–53% (4).

Case presentation: A 59-year-old male with hypertension and dyslipidemia presented with thunderclap headache. A typical thunderclap headache starting in the occipital region awakened him from sleep. He developed dysarthria with right sided weakness after about 10 minutes of onset of the headache. Left sided bulbar and facial palsy with right hemiparesis was noted on examination.

Non contrast computer tomography (NCCT) brain revealed an abnormally dilated basilar artery (Figure 1). Magnetic resonance imaging (MRI) brain revealed left brainstem and right cerebellar infarctions. Multiple lumens within the basilar trunk were noted in magnetic resonance angiogram (MRA) causing fusiform aneurysm formation (Figure 2). Digital subtraction angiogram (DSA) confirmed fusiform aneurysm with luminal irregularity (Figure 3). These radiological findings suggested basilar trunk dissection with underlying thrombosis. Neurosurgical or endovascular interventions were not possible due to acute thrombosis and dissection. Flow diverters were not available.

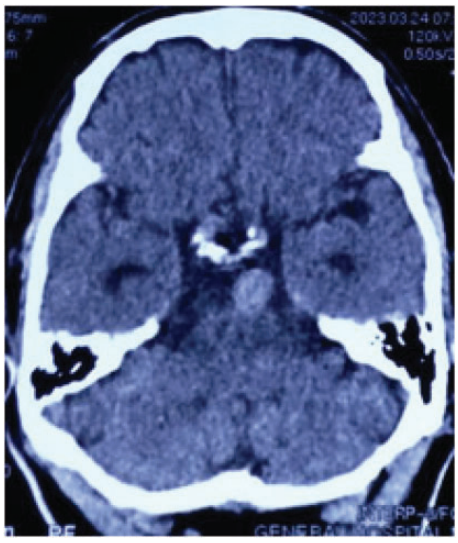


Figure 1: NCCT brain showing dilated basilar artery.

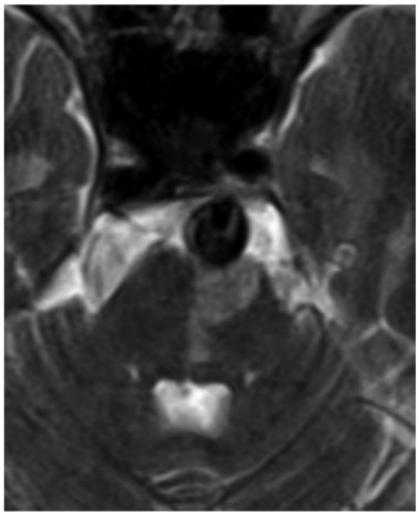


Figure 2: MRI T2 image showing multiple lumens in Basilar trunk. Left median pontine infarction is also shown.

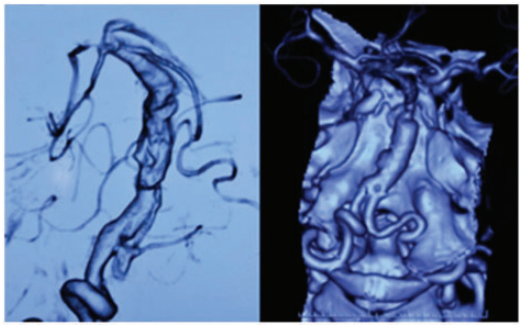


Figure 3: DSA showing basilar trunk fusiform aneurysm

Patient was started on Apixaban in addition to optimization of anti-hypertensives and statins. After 2 weeks course of in-patient rehabilitation, he was discharged with modified Rankin scale 4 disability with the plan of follow up MRI brain with MRA in 3 months' time.

Discussion: Four types of BAA are recognized: chronic mural bleeding ectasia, saccular aneurysm, segmental fusiform ectasia and acute dissecting aneurysm in order of incidence (1). Dissecting aneurysms present with neurological deficit or SAH with high morbidity and mortality (5). Acute thrombosis with true and false lumens suggested that our patient had acute dissecting BAA. Thunderclap headache is usually not known to occur with basilar artery dissection though it is well documented in basilar thrombosis. Only one case report could be found in literature reporting thunderclap headache associated with basilar artery dissection (3). In our patient thunderclap headache preceded neurological deficit which would suggest thunderclap headache was associated with acute dissecting BAA rather than secondary thrombosis and brain stem infarctions. We believe that our case provides evidence that basilar artery dissection as a rare cause of thunderclap headache.

Disclosure of Interest: None Declared

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Post-traumatic headache

IHC23-PO-347

Hypersensitivity to PACAP-38 in Post-Traumatic Headache: A Randomized Clinical Trial

Haidar Al-Khazali[1], Rune Christensen[1], David Dodick[2], Basit Ali Chaudhry[1], Faisal Mohammad Amin[1], Rami Burstein[3] and Hakan Ashina[1,3]

[1]*Danish Headache Center, Copenhagen, Denmark*
[2]*Mayo Clinic, Scottsdale, USA*
[3]*Harvard Medical School, Boston, USA*

Objective: To ascertain whether intravenous infusion of pituitary adenylate cyclase-activating polypeptide-38 (PACAP-38) induces migraine-like headache in people with persistent post-traumatic headache (PTH).
Methods: A randomized, double-blind, placebo-controlled, 2-way crossover trial conducted at a single center. Eligible participants were adults diagnosed persistent PTH attributed to mild traumatic brain injury who had no history of migraine. Participants were randomly assigned to receive a 20-minute continuous intravenous infusion of PACAP-38 (10 pmol/kg/min) or placebo (isotonic saline) on two separate experimental days with a 1-week wash-out period in between. The primary outcome was the difference in incidence of migraine-like headache between PACAP-38 and placebo during the 12-hour observational period after infusion. A site investigator recorded outcome data every 10 minutes until 60 minutes following infusion start, after which participants were discharged and instructed to fill out a headache diary every 60 minutes until 12 hours after infusion start.
Results: A total of 49 individuals were assessed for eligibility, with 21 being enrolled and completing the trial. The participants had a mean age of 35.2 years, and 16 (76%) were women. Most of them (19 [90%] of 21) had a migraine-like phenotype. During the 12-hour observational period, 20 (95%) of 21 participants developed migraine-like headache after intravenous infusion of PACAP-38, compared with 2 (10%) participants after placebo ($P = 0.001$). Furthermore, the baseline-corrected area under the curve for median headache intensity scores during the 12-hour observational period was higher after PACAP-38 than placebo ($P = 0.001$).
Conclusion: In people with PTH, PACAP-38 was shown to be a potent inducer of migraine-like headache. Targeting PACAP-38 signaling might hold promise for the treatment of PTH.

Disclosure of Interest: D.W.D. reports the following competing interests. Consulting: Amgen, Atria, CapiThera Ltd., Cerecin, Ceruvia Lifesciences LLC, CoolTech, Ctrl M, Allergan, AbbVie, Biohaven, GlaxoSmithKline, Lundbeck, Eli Lilly, Novartis, Impel, Satsuma, Theranica, WL Gore, Genentech, Nocira, Perfood, Praxis, AYYA Biosciences, Revance, Pfizer. Honoraria: American Academy of Neurology, Headache Cooperative of the Pacific, Canadian Headache Society, MF Med Ed Research, Biopharm Communications, CEA Group Holding Company (Clinical Education Alliance LLC), Teva (speaking), Amgen (speaking), Eli Lilly (speaking), Lundbeck (speaking), Pfizer (speaking), Vector Psychometric Group, Clinical Care Solutions, CME Outfitters, Curry Rockefeller Group, DeepBench, Global Access Meetings, KLJ Associates, Academy for Continued Healthcare Learning, Majallin LLC, Medlogix Communications, Medica Communications LLC, MJH Lifesciences, Miller Medical Communications, WebMD Health/Medscape, Wolters Kluwer, Oxford University Press, Cambridge University Press. Non-profit board membership: American Brain Foundation, American Migraine Foundation, ONE Neurology, Precon Health Foundation, International Headache Society Global Patient Advocacy Coalition, Atria Health Collaborative, Arizona Brain Injury Alliance, Domestic Violence HOPE Foundation/Panfila. Research support: Department of Defense, National Institutes of Health, Henry Jackson Foundation, Sperling Foundation, American Migraine Foundation, Henry Jackson Foundation, Patient Centered Outcomes Research Institute (PCORI). Stock options/shareholder/patents/board of directors: Aural analytics (options), Axon Therapeutics (shares/board), ExSano (options), Palion (options), Man and Science, Healint (options), Theranica (options), Second Opinion/Mobile Health (options), Epien (options), Nocira (options), Matterhorn (shares), Ontologics (shares), King-Devick Technologies (options/board), EigenLyfe (shares), AYYA Biosciences (options), Cephalgia Group (shares/board), Atria Health (options/employee). Patent 17189376.1–1466:vTitle: Onabotulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (Non-royalty bearing). Patent application submitted: Synaquell® (Precon Health). F.M.A. reports personal fees from Eli Lilly, Lundbeck, Pfizer, and Teva, outside of the submitted work. R.B. reports research support received from Allergan, Dr. Reddy's Laboratories, Eli Lilly, and Teva, outside of the submitted work. In addition, R.B. has received honoraria, acted as a consultant or advisory board member for Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, CGRP Diagnostics, Dr. Reddy's Laboratories, ElectroCore, Eli Lilly, GlaxoSmithKline, Merck, Pernix, Teva, and Trigemina. R.B. also reports receiving CME fees from Healthlogix, Medlogix, and WebMD/Medscape, and holds patents for several products, including (9061025, 11732265.1, 10806890, US2021-0015908, WO21007165, US2021-0128724, WO21005497). R.B. is a reviewer for the National Institute of Neurological Disorders and Stroke (NINDS) and holds stock options in Allay Lamp and Percept, outside of the submitted work. H.A. reports

personal fees from Teva, outside of the submitted work. The remaining authors declare no competing interests.

Psychological and behavioural factors and management

IHC23-PO-348

Quality of Life, Mental Health and Sleep-Quality in Patients Diagnosed with Tolosa-Hunt Syndrome; Evaluation of long-term outcomes

H Shafeeq Ahmed and Hamsa Lokanath

Bangalore Medical College and Research Institute, Bangalore, India

Objective: Tolosa Hunt syndrome (THS) is a rare headache disorder of unknown aetiology. Steroids are the mainstay of treatment. The current study aims to evaluate the Health-related Quality of Life (HRQOL) in THS patients.
Methods: Telephone based interviews was conducted in patients having a diagnosis of THS, of at least 6 months go and within 6 years were included for the present study. The study included several questionnaires including the World Health Organisation Quality of Life Questionnaire (WHOQOL-BREF), Patient Health Questionnaire-9 (PHQ-9) for depression, Generalised Anxiety Disorder-7 (GAD-7) for anxiety and the Pittsburgh Sleep Quality Index (PSQI). Higher scores in PSQI indicate worse sleep quality.
Results: A total of 51 patients were included, and all the four questionnaires showed normal distribution and high internal consistence validity. There was a high correlation between Psychological and Environmental parameters at 0.471 ($p = 0.01$) in the WHOQOL-BREF with a Cronbach's Alpha was 0.768 and hence the internal consistency of the scale was found to be valid. 34 (66.6%) of the patients had sever depression whereas 27 (52.9%) had severe anxiety wherein higher levels of anxiety correlated with lower levels of quality of life ($p = 0.07$). the mean PSQI score with standard deviation was 15.34 (4.77) where higher scores were correlated with worse anxiety and depression ($p = 0.02$). The internal consistency of the PSQI was found to be valid with a Cronbach's Alpha was 0.712.
Conclusion: The HRQOL of THS patients on long-term observation showed a direct relationship with progression in time wherein mental health and sleep quality deteriorated over time. WHOQOL-BREF indicated that environmental factors directly impacted psychological well-being.
Disclosure of Interest: None Declared

IHC23-PO-349

Comprehensive questionnaire study on migraine triggers in Japan

Tsubasa Takizawa[1], Narumi Watanabe[1,2], Tamir Enkhtaivan[1], Naoki Miyazaki[3], Ryota Ishii[3], Mamoru Shibata[4], Ryo Takemura[3] and Jin Nakahara[1]

[1]*Department of Neurology, Keio University School of Medicine, Tokyo, Japan*
[2]*Department of Laboratory Medicine, Keio University School of Medicine, Tokyo, Japan*
[3]*Biostatistics Unit, Clinical and Translational Research Center, Keio University Hospital, Tokyo, Japan*
[4]*Department of Neurology, Tokyo Dental College Ichikawa General Hospital, Ichikawa, Japan*

Background: It is well-known that migraineurs have triggers such as stress and sleep. Although there are studies focusing on migraine triggers worldwide, only few previous studies have assessed limited types of migraine triggers in Japan. This study aimed to identify such factors in a more comprehensive manner.
Methods: Migraine patients ($n = 220$; mean age 47.3 ± 13.2 years, female patient ratio: 87%) at the outpatient clinic of Keio University Hospital completed a survey assessing 48 potential triggering factors of migraine including stress, sleep, diet and weather. As a measure of causality, respondents reported the frequency of migraine attacks associated with each triggering factor (i.e., rarely, approximately 50%, often, and always).
Results: All patients reported at least one triggering factor. The most frequently reported trigger was fatigue (87.5%), followed by stress (86.8%), low barometric pressure (82.6%), menstrual cycles (81.3%), and lack of sleep (78.6%). Well-recognized dietary factors, such as consumption of cheese and chocolate (16.4%–24.2%), were less common. Regarding weather factors, more patients reported items related to barometric pressure (73.9%–82.6%) than to temperature (48.1%–52.3%). Factors associated with the highest causality (i.e., "always") were menstrual cycle (35.5%), red wine (16.2%), typhoon (14.7%), low barometric pressure (14.2%), and stress (11.4%).
Conclusion: This study clarified migraine triggers frequently reported by Japanese patients with migraine. Factors such as stress and sleep turned out to be frequently-reported triggers as in previous studies conducted outside Japan. Factors related to weather and menstrual cycle seemed to be more common among Japanese migraineurs.
Disclosure of Interest: TT is a consultant/advisor and/or served as advisory board for Eli Lilly, Otsuka, Amgen, Pfizer, and Teijin. TT received speaker honoraria from Eli Lilly, Daiichi Sankyo, Otsuka, Amgen, Kowa, Kyowa Kirin,

Eisai, UCB Japan, Takeda, and Santen Pharmaceutical, and research funding from Eli Lilly and Tsumura outside the submitted work. JN received honoraria and research scholarships from Amgen and Daiichi Sankyo.

IHC23-PO-350

Association between temporomandibular joint pain and psychological factors in patients with central sensitization (CS). multiple linear regression analysis

Sebastián Martín Pérez[1,2], Isidro Martín Pérez[2], José Andrés Díaz Córdova[3], Leidy Milena Posada Cortés[3] and José Luis Alonso Pérez[3,4]

[1]Universidad Europea de Canarias, Europea de Canarias, Faculty of Health Sciences, Musculoskeletal Pain and Motor Control Research Group, Santa Cruz de Tenerife, Spain
[2]Departamento de Farmacología y Medicina Física, Área de Radiología y Medicina Física, Secciones de Enfermería y Fisioterapia, Facultad de Ciencias de la Salud, San Cristóbal de la Laguna, Santa Cruz de Tenerife, Spain
[3]Universidad Europea de Canarias, Europea de Canarias, Faculty of Health Sciences, Musculoskeletal Pain and MotorControl Research Group, Santa Cruz de Tenerife, Spain
[4]Universidad Europea de Madrid, Faculty of Sport Sciences, Musculoskeletal Pain and Motor Control Research Group, Villaviciosa de Odón, Madrid, Spain

Introduction: Psychological variables and their relationship with pain intensity in patients with temporomandibular joint disorders (TJD) with or without central sensitization (CS).
Method: A cross-sectional study with non-probability convenience sampling was conducted. It was carried out between January 2022 and June 2023 at the European University of the Canary Islands (Spain). Participants over 18 years of age with informed consent, who are within the inclusion criteria, were selected. Pain intensity (NPRS), anxiety (STAI), catastrophism (PCS), perceived stress (PSS), and sleep quality (PSQI) were assessed. In addition, statistical analysis was performed using the software SPSS v.20 (IBM®, USA), performing the descriptive analysis, normality test ($p < 0.05$), and multiple linear correlation analysis.
Results: From a total of 52 subjects (34 women and 18 men), 26 participants with and 26 without CS were obtained using the CSI aged between 28 and 67 years were selected. On the one hand, in subjects with TJD with CS, it was detected that higher anxiety levels were significantly associated with greater pain intensity ($\beta = 0.4467$, $t = 2.477$, $p = 0.021$). Regarding sleep quality was inversely associated with pain intensity in a non-statistical significant relation ($\beta = -0.1616$, $t = -0.933$, $p = 0.361$). On the other hand, in TJD without CS it was detected that higher anxiety levels were significantly associated with greater pain intensity ($\beta = 0.5087$, $t = 2.672$, $p = 0.014$) and in relation to sleep quality was positively associated with pain intensity, but not significantly ($\beta = 0.0511$, $t = 0.253$, $p = 0.803$).
Conclusions: In the group with central sensitization (CS) higher levels of anxiety were significantly associated with higher pain intensity, while higher levels of pain catastrophization and perceived stress were not significantly associated with higher pain intensity.

IHC23-PO-351

A Case-Control Study Investigating the Association between Sleep Disturbances and Migraine Frequency and Severity

Mohammed Omer

Gadarif University, Gadarif, Sudan

Background: Migraine is a common and debilitating neurological disorder characterized by recurrent episodes of moderate-to-severe headaches and associated symptoms. Previous research has suggested a potential link between sleep disturbances and migraine, but the relationship between specific sleep-related factors and migraine frequency and severity remains unclear. This study aimed to investigate the association between sleep disturbances and migraine frequency and severity in a case-control setting.
Methods: We conducted a case-control study involving 500 migraineurs (cases) and 500 age- and sex-matched controls without migraine. Data on sleep disturbances, including sleep duration, sleep quality, insomnia, and sleep apnea, were collected using the Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI). Migraine frequency and severity were assessed using the Migraine Disability Assessment (MIDAS) questionnaire and a visual analog scale (VAS) for pain. Multivariable logistic regression models were employed to examine the associations between sleep disturbances and migraine frequency and severity, adjusting for potential confounders.
Results: Cases had significantly higher PSQI and ISI scores compared to controls, indicating a higher prevalence of sleep disturbances among migraineurs. Poor sleep quality (PSQI score > 5) was significantly associated with a higher migraine frequency (OR = 2.45, 95% CI: 1.63–3.67) and severity (OR = 1.85, 95% CI: 1.26–2.72). Insomnia (ISI score > 14) was also found to be significantly associated with increased migraine frequency (OR = 1.97, 95% CI: 1.30–2.99) and severity (OR = 1.58, 95% CI: 1.06–2.35).

Sleep duration and sleep apnea showed no significant associations with migraine frequency or severity.
Conclusion: This case-control study provides evidence for a significant association between sleep disturbances, particularly poor sleep quality and insomnia, and increased migraine frequency and severity. These findings highlight the importance of addressing sleep disturbances in the management of migraine and suggest that improving sleep quality may be a potential strategy to reduce migraine burden. Further research is needed to explore the underlying mechanisms and evaluate the effectiveness of sleep-focused interventions in migraine management.
Disclosure of Interest: None Declared

IHC23-PO-352

Psychological profiles of super responders and non responders to cgrp-monoclonal antibodies: data from a 6-month follow-up

Sara Bottiroli[1,2], Gloria Vaghi[2,3], Roberto De Icco[2,3], Daniele Martinelli[2], Grazia Sances[2] and Cristina Tassorelli[2,3]

[1]*Giustino Fortunato University, Benevento, Italy*
[2]*IRCCS Mondino Foundation, Pavia, Italy*
[3]*University of Pavia, Pavia, Italy*

Objectives: To evaluate the psychological predictors of a super response to anti-CGRP monoclonal antibodies (mAbs) in a 6-month follow-up in subjects with chronic migraine (CM) or episodic migraine (EM).
Methods: One hundred and sixteen patients (age: 48.2 ± 10.5, F: 77%) with CM or EM (ICHD-III criteria) who had already failed at least three preventive therapies underwent treatment with CGRP-targeting mAbs. At baseline (T0), patients received also a full psychological evaluation according to DSM 5 criteria comprising mood, anxiety, and personality disorders as well as childhood traumas, current stressors and alexithymia traits by using self-report qestionnaires (Childhood Trauma Questionnaire, the Stressful life-events Questionnaire, and the Toronto Alexithymia Scale). Patients were then followed up at 6 months for their clinical condition.
Results: At the 6-month follow-up, 41% of patients (n: 47, age: 49.7 ± 8.8, F: 81%) reported a reduction of at least 75% in monthly migraine days (MMD) (Super Responder, SR); whereas 16% (n: 19, age: 49.6 ± 11.9, F: 74%) a ≤25% MMD reduction with respect to T0 (Non Responders, NR). When compared to SR, NR patients were characterized by a higher prevalence of anxiety (90% vs 57%, $p = .012$) and personality disorders (94% vs 34%, $p = .003$), in particular those belonging to Cluster C (avoidant, dependent, and obsessive-compulsive personality disorders) (74% vs 30%, $p = .001$). They also showed a higher number of very serious current stressors (2.0 ± 3.1 vs 0.2 ± 0.7, $p < .001$) as well as more alexithymic traits (53.6 ± 13.4 vs 43.5 ± 12.9, $p = .005$). The SR and NR groups were instead similar as regards mood disorders and childhood traumas.
Conclusions: We confirm the marked effectiveness of CGRP-targeting mAbs also in patients with difficult-to-treat forms of migraine and a high burden of psychological comorbidities. Our results, although preliminary because of the small sample size, show that patients who achieve two extreme responses (super response vs. absolute non-response) to mAbs also significantly differ in their psychological profiles. In particular, our data highlight the impact of an "anxious-fearful" personality, anxiety, current stressors and alexithymic traits in those patients particularly refractory to many preventive treatments, including mAbs.
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Disclosure of Interest: The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: CT received honoraria for the participation in advisory boards or for lecturing from: Allergan, Dompé, Eli-Lilly, Novartis, and Teva. CT has no ownership interest and does not own stocks of any pharmaceutical company. RDI received honoraria for lecturing from: Eli-Lilly, and Teva. GS received honoraria for the participation in advisory boards or for lecturing from: Eli-Lilly, Novartis, and Teva. The remaining authors have no conflicts of interest.

Tension-type headache

IHC23-PO-353

Prevalence of cranial autonomic symptoms in episodic tension-type headache

Marcin Straburzyński[1], Marta Waliszewska-Prosół[2], Magdalena Nowaczewska[3], Ewa K. Czapińska-Ciepiela[4], Anna Gryglas-Dworak[5] and Sławomir Budrewicz[2]

[1]*Department of Family Medicine and Infectious Diseases, University of Warmia and Mazury, Olsztyn, Poland*
[2]*Department of Neurology, Wroclaw Medical University, Wrocław, Poland*
[3]*Department of Otolaryngology, Head and Neck Surgery and Laryngological Oncology, Ludwik, Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Bydgoszcz, Poland*
[4]*Epilepsy and Migraine Treatment Centre, Kraków, Poland*
[5]*Headache Center, Wrocław, Poland*

Objective: To assess the prevalence of lacrimation, conjunctival injection, ptosis, nasal congestion, rhinorrhoea and facial sweating among subjects fulfilling diagnostic criteria for episodic tension-type headache (TTH).
Methods: The Migraine in Poland study was a nationwide cross-sectional online survey conducted from August 2021 to June 2022. Survey protocol included questions assessing diagnostic criteria for, among others, migraine without aura (MwoA) and tension-type headache according to International Classification of Headache Disorders, 3rd edition. Moreover, the questionnaire examined the presence of cranial autonomic symptoms (CAS) and their relation to headache attacks.
Results: 3225 respondents took part in the survey (age 13–80 – mean 38.9; 87.1% women). Among 1141 subjects meeting criteria for TTH, 210 respondents fulfilled diagnostic criteria for isolated episodic TTH (without cooccurring migraine attacks or other primary headache disorders). In the latter cohort, 116 (55.2%) respondents reported at least one CAS during their headache attacks: lacrimation n = 72 (34.3%), ptosis n = 40 (19.1%), nasal congestion n = 38 (18.1%), rhinorrhoea n = 37 (17.6%), conjunctival injection n = 37 (17.6%), facial sweating n = 35 (16.7%) and myosis n = 23 (11.0%). CAS in episodic TTH were less prevalent than in the MwoA cohort (55.2% vs 63.0%).
Conclusions: The prevalence of retrospectively reported CAS is high among episodic TTH patients. Similarly as in the case of migraine, this may potentially contribute to misdiagnosing TTH as a disorder with highly prevalent CAS (e.g. trigeminal autonomic cephalalgias, rhinosinusitis).
Disclosure of Interest: None Declared

Trigeminal neuralgia and other cranial neuropathies

IHC23-PO-353

Trigeminal Neuralgia and Its Comorbidities: A Nationwide Disease Trajectory Study

Jacob Worm[1], Isabella Friis Jørgensen[2], Ólafur Birgir Davídsson[1,3], Henrik Winther Schytz[1], Lars Bendtsen[1], Søren Brunak[2], Thomas Folkmann Hansen[1,2] and Stine Maarbjerg[1]

[1]*Department of Neurology, Danish Headache Center, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark*
[2]*Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, Copenhagen, Denmark*
[3]*Department of Epidemiology Research, Statens Serum Institut, Glostrup, Denmark*

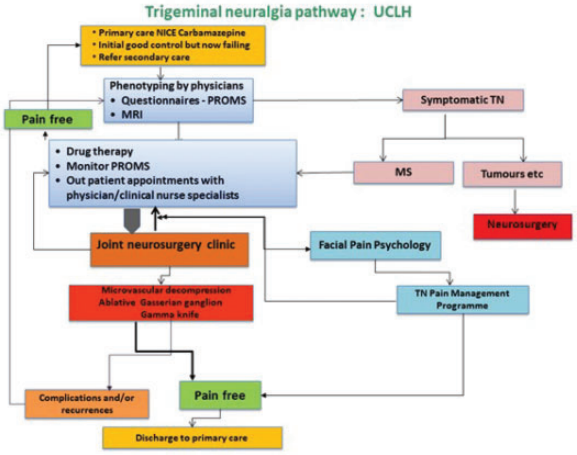
Objective: To investigate specific temporal associations in trigeminal neuralgia comorbidities using a novel population-based method: disease trajectories.
Methods: We included 7.2 million unique individuals from the Danish National Patient Register (DNPR) from 1994 to 2018 to cover all individuals diagnosed with trigeminal neuralgia. To identify comorbidities more prevalent in trigeminal neuralgia, we used 10,000 randomly selected controls matched on age, sex, and discharge week, for comparison. We determined if these comorbidities were diagnosed before or after trigeminal neuralgia and used a disease trajectory network to track the progression of diseases over time and identify significant patterns that individuals with trigeminal neuralgia follow. Finally, we conducted a post hoc Cox-regression analysis using the Danish National Prescription Register and DNPR data to investigate whether risk of stroke was associated with carbamazepine or oxcarbazepine treatment.
Results: Of 7,141 participants with trigeminal neuralgia included in the study, 64% were women and the mean age at diagnosis was 59 years. Among these participants, 27 specific comorbidities were found to be significantly linked to trigeminal neuralgia with an increased risk of 18 preceding diseases. Following a diagnosis of trigeminal neuralgia, participants had an increased risk of developing nine diseases, including ischemic stroke. Furthermore, participants treated with carbamazepine or oxcarbazepine had a higher risk of stroke compared to those treated with other anti-seizure medications.
Conclusions: We discovered specific and significantly temporal associated comorbidities in a Danish trigeminal neuralgia population. Participants with trigeminal neuralgia have higher risk of stroke than the general Danish population, which may be related to first-line treatment and the results are indicating a need for vascular screening in individuals with trigeminal neuralgia.
Disclosure of Interest: None Declared

IHC23-PO-355

Developing and evaluating a multidisciplinary care-pathway for patients with trigeminal neuralgia

Joanna Zakrzewska and Staff Facial Pain

UCLH NHS Trust, London, United Kingdom



Objective: Develop a multidisciplinary care-pathway for patients with trigeminal neuralgia (TN) to ensure that all patients are provided with a personalised evidence base approach to management.

Method: Over a period of eleven years a care-pathway was developed in a large London teaching hospital based in a postgraduate dental hospital. Patients are referred from medical and dental primary care as well as other specialist services from all parts of the UK. As the service was built up each of the components of the service were evaluated by independent observers and the results published. Staff included oral physicians, oral surgeons, headache neurologists, pain medicine specialists, neurosurgeons, clinical nurse specialists, physiotherapists, psychologists, statisticians. Over 50 people were involved in its development and evaluation. Phenotyping of patients was carried out using the ICHD criteria and patient related outcome measures (PROMS) collected at each encounter. Imaging protocols supervised by a senior neuroradiologist were put in place. Ethical approval was in place.

Results: A review of 225 patients with TN showed that TN resulted in a significant impact on quality of life and mood Doi. 10.1097/j.pain.0000000000000853. A qualitative study of the impact on 15 patients showed that services needed to offer more psychological support Doi: 10.1007/s00701-015-2515-4. The medical therapies used were informed by international guidelines and by assessing their side effects DOI: 10.1111/ane.12901, DOI: org/10.1186/s10194-020-01156-9, DOI: 10.1186/s10194-015-0563-z. The protocol for acute therapies were based on a systematic review DOI:10.1016/j.bja.2019.05.026. A clinical nurse was trained to become an independent prescriber and her telephone consultations were evaluated by a couple of medical students DOI.org/10.1177/2049463719892027. The 55 patients interviewed reported high satisfaction with the service and it reduced outpatient appointments. Patients consulted not just about their medication but overall management. The clinical psychologists and physiotherapist developed a TN management program to help patients cope with fear and uncertainty and was open for anyone who wished to utilise it. The first program for 15 patient was independently evaluated and showed that it was considered a positive experience and that a cognitive behaviour therapy program is useful Doi 009:13:486–491. All patients once phenotyped and with appropriate MRIs were seen in a clinic with a specialist neurosurgeon and a pain specialist. A satisfaction survey of this clinic showed that the 55 patients who attended during one year appreciated this approach and the opportunity to participate in decision making DOI 10.1177/20494637211045877. A review of 11 years of this clinic attended by 334 patients showed that 55% underwent some form of surgery and of these 55% were pain free and off drugs. Overall 28% were totally pain free and off medication DOI 10.1186/s10194-022-01489-7

A separate review of 20 patients with TN and MS showed that these patients were more likely to be on polytherapy and needed repeated ablative procedures to control their pain DOI:10.2217/pmt-2021-0001C

Conclusion: An independent review of this pathway showed that in 129 patients with a mean follow up of 6 years, 79% expressed significant improvement since beginning treatment in this service. DOI:10.1186/s10194-020-01198-z. This pathway has been incorporated into the UK national guidelines https://www.rcseng.ac.uk/dental-faculties/fds/publications-guidelines/clinical-guidelines/

Disclosure of Interest: Biogen who did one of the reviews.

IHC23-PO-356

Development of a Core Outcome Set for Trigeminal Neuralgia for use in clinical trials

Carolina Venda Nova[1], Sarah Baker[2], Richeal Riordain[3,4] and Joanna Zakrzewska[1]

[1]*UCL Eastman Dental Institute, London, United Kingdom*
[2]*School of Clinical Dentistry University of Sheffield, Sheffield, United Kingdom*
[3]*Cork University Dental School, Cork, Ireland*
[4]*UCL Eastman Dental Hospital, London, United Kingdom*

Objectives: Trigeminal neuralgia (TN) is a unilateral episodic severe facial pain. It can be managed with medicines and with surgery but the best treatment option, has not yet been identified. Important outcomes of treatment i.e ones that are meaningful to patients have not been determined.
The aim of this project was to develop a Core Outcome Set for TN – a group of outcomes that can be used in all future studies and which are meaningful to clinicians, researchers but more importantly, to patients. If all studies used the same outcomes patients would be able to decide what the best treatment for this condition may be for them.
Methods: Two systematic reviews (SR) were completed. One on the current use of outcomes, mapped to the IMMPACT six core domains, and the second on the psychometric properties of outcome measures, according to the COSMIN guidelines. Three online focus groups were held with UK patients to determine their views on what they considered to be core outcomes. Thematic analysis was then conducted on the focus group transcripts. Following this stage, an online Delphi study was carried out to determine the views of patients, clinicians, and researchers as to the core outcome domains. Three rounds were conducted. The final stage was a consensus online meeting to determine which of the outcomes for which consensus was not reached should be used for future research and clinical practice.
Results: The systematic review identified outcomes used in 467 studies. Most of these studies collected data on pain and TN side effects with only 46 studies collecting information on the physical impact of treatment, and 17 studies assessing emotional functioning. Of the included studies, 35 collected data on patient satisfaction. Up to 10 different questionnaires were used for assessment of pain relief and nine were used for assessment of pain intensity,
The SR on psychometric properties used in TN yielded few results. Six studies were included in the analysis and only five questionnaires were appraised. There was moderate quality evidence for sufficient content validity of the Penn Facial Pain Scale-Revised.
Three online focus groups were attended by 14 patients with TN. The analysis identified four themes: 1 uncertainty about TN aetiology and prognosis; 2 descriptions of the mental, social, and physical impact of TN which contrasts with coping mechanisms developed over time; 3 participants' views of what a successful treatment means, what specific outcomes they expect and patient's willingness to self-manage their conditions; 4, the importance of appropriate and timely access to healthcare and the importance of peer support. There were 14 subthemes. Many of these highlighted the importance of moving beyond just pain relief and the need to assess quality of life from the patient's perspective.
The Delphi study involved 70 participants of whom 38 were patients, 26clinicians, and 6 researchers. The participants were presented with a list of 40 outcomes derived from the earlier phases of the study. From this, 17 outcomes were considered crucial by 70% or greater of all participants. A follow-up consensus meeting was attended by 13 participants of whom six were patients, to discuss 23 outcomes for which no consensus was reached and ratify the final core outcome domains. The final 11 mandatory core outcome domains from this process were: pain relief, duration of pain relief, pain intensity, pain interference, pain free on medication, ability to participate in social roles/activities, health related quality of life, overall response to treatment, satisfaction with treatment, side effects of medication and surgery. Other domains considered of importance were quality of pain, fear of pain, coping, self-care, eating, talking.
Conclusion: Working with patients, clinicians and researchers made it possible to develop a TN core outcome set (COS). This COS is an important step for combining and contrasting study results and to meaningfully draw conclusions from research studies. Using outcomes relevant to those most affected by TN has the potential to translate into improved and more efficient access to care. The next step is to identify suitable measures that map on to the TN COS domains.
Disclosure of Interest: Rosetrees Trust funded the PhD student

Other

IHC23-PO-357

Correlation of Migraine Headache with Electroencephalogram Findings of Epileptiform Discharges

Miriam Catherine Bernal Dantes and
Marc Laurence Fernandez

The Medical City, Ortigas, Philippines

Objective: Even before the existence of electroencephalography (EEG), the relationship between headache, especially migraine, and epilepsy have long been postulated because of their similar features. With clinical and epidemiological studies showing that migraine and seizures are highly co-morbid disorders, a relationship between the 2 has been recognized, despite having an unclear association between them. The topic of recent reports and studies include the common factors, clinical features, genetics, pathophysiology and treatment of the 2 disorders. In this study, we reviewed the relationship between migraine headaches and findings of epileptiform discharges in the EEG.

Methods: The EEG findings and demographic profile of adult patients with a diagnosis of migraine headaches, either migraine with aura, or migraine without aura, were reviewed. The patients, who underwent EEG in the Neurophysiology Laboratory, were recruited within a period of 3 months.
Results: A total of 38 patients were included in the final study sample. The participants were mostly females, with mean age of 35 years. For the types of migraine, 65.8% of the participants had migraine without aura, and 34.2% had migraine with aura.
For the EEG findings, all participants had a background activity of "generalized, well-modulated medium voltage alpha rhythm" with a range of 8 to 11 hertz.
During photic stimulation, "bilateral occipital driving response" was observed among 23.7% (n = 9) of respondents.
In hyperventilation, 13.2% (n = 5) of the participants had presence of generalized short bursts of delta activity, and 2.6% (n = 1) presented with "intermittent theta activity" in the right region of the brain.
7.9% (n = 3) of the included participants had presence of epileptiform discharges in the EEG. One patient had migraine with visual aura, and the other 2 had migraine without aura. For these 3 patients, there were no headache and seizure episodes during the EEG study.
For the test on relationship between the presence of epileptiform discharges in EEG and migraine type, the results of Fisher's Exact Test show that presence of epileptiform discharges and the type of migraine were not significantly related with each other with a p-value of 0.973. The odds ratio of 0.958, was also not significant. Statistical analysis between findings in photic stimulation and hyperventilation, and presence of epileptiform discharges were not significantly related with having presence of epileptiform discharges, with a p-value of 0.682 and 0.412, respectively.
Conclusion: In the study, no significant correlation were seen in migraine headaches, and EEG findings of epileptiform discharges.
However, in the 3 patients with presence of epileptiform discharges in the EEG, it conveys that the diagnosis between the 2 may still pose the possibility of diagnostic confusion.
The EEG may specifically confirm the diagnosis of seizures, or direct towards another diagnosis if the symptoms are clinically similar and uncertain.
Disclosure of Interest: None Declared

IHC23-PO-358

Coffee consumption and migraine: a population-study

Soomi Cho, Kyung Min Kim and Min Kyung Chu

Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of

Background: Caffeine has been linked with migraine and coffee is the most consumed caffeinated beverage. Caffeine is a trigger of migraine. However, it promotes headache relief in migraine attack. Although several studies on the association between coffee and the prevalence of headache/migraine have been reported, information on the effect of coffee consumption on clinical characteristics of migraine is limited. This study aimed to investigate the effect of coffee consumption on the prevalence and clinical characteristics of migraine using data of a nation-wide study.
Methods: We used data of CHASE study in Korea. Daily coffee consumption was classified as no-to-low consumption (<1 cup/day), medium consumption (1–2 cups/day) and high consumption (>2 cups/day).
Results: Of the 3,030 participants,170 (5.6%) and 1768 (58.3%) were classified as having migraine and non-migraine headache. 1137 (37.5%), 1410 (46.5%) and 483 (15.9%) were identified as no-to-low coffee consumption, moderate consumption and high consumption, respectively. The prevalence of high consumption was not significantly different among participants with non-headache, non-migraine headache and migraine (19.4% vs. 15.8% vs. 15.6%, p = 0.437). Of 170 participants with migraine and 1768 participants with non-migraine headache, headache days per 30 days, severe headache days per 30 days and days with acute medications were not significantly different among participants with no-to-low coffee consumption, moderate consumption and high consumption groups. Acute treatment responses were significantly different among participant with no-to-low coffee consumption, moderate consumption and high consumption groups (The migraine Treatment Optimization Questionnaire-6 score, 19.00 [16.75–22.00] vs. 23.00 [17.75–26.25] vs. 22.00 [17.00–24.00], p = 0.026). In contrast, acute treatment responses were not significantly different among participants with non-migraine headache (23.50 [19.00–27.00] vs. 24.00 [20.00–28.00] vs. 22.00 [17.00–24.00], p = 0.542).
Conclusions: Prevalence and clinical characteristics of migraine were not significantly different according to daily coffee consumption in migraine. However, acute treatment response of migraine differs according to coffee consumption.
Disclosure of Interest: None Declared

IHC23-PO-359

Average-steps per day as marker of treatment response in adults with chronic migraine: a cross-sectional study

Frederik Thal Jantzen, Basit Ali Chaudhry, Ina Nørgaard, Christopher Kjaer Cullum, Thien Phu Do and Faisal Mohammad Amin

Danish Headache Center, Copenhagen, Denmark

Objective: Physical activity can worsen migraine, leading to reduced activity levels in adults with chronic migraine. This study has investigated change in average steps per day, as a surrogate marker of physical activity, in adults with chronic migraine treated with monoclonal antibody against calcitonin gene-related peptide or its receptor.
Methods: Adults with chronic migraine, who were classified as responders to preventive treatment with monoclonal antibodies, were enrolled. The primary endpoint was the difference in mean number of steps per day between the 3-months prior to treatment initiation and the first 3-months after treatment. The secondary endpoint was the correlation between the change in steps per day and the change in monthly migraine days.
Results: Twenty-two (20 females) participants were enrolled with a median age of 48.5 years. The median number of steps per day increased from 4,421 at baseline to 5,241 after treatment. We found a positive correlation between the increase in steps per day and the treatment response.
Conclusions: Increase in physical activity was significantly correlated with treatment response with monoclonal antibodies. Automatically registered data on step count might be used to monitor physical activity as a response to preventive treatment in adults with chronic migraine.
Disclosure of Interest: F.T.J., B.A.C, C.K.C have no conflicts of interests to report. T.P.D. reports personal fees from Teva, outside of the submitted work. F.M.A. has received Honoria or personal fees from Pfizer, Teva, Novartis, Lundbeck and Eli Lilly for lecturing or participating in advisory boards; is principal investigator for phase IV trials sponsored by Novartis and by Teva; serves as president of Danish Headache Society and board member of the European Headache Federation; serves as associate editor for Acta Neurol Scand, Front Neurol, Front Res Pain, and Headache Medicine; serves as junior associate editor for Cephalalgia and Cephalalgia Reports; member of the editorial board of J Headache Pain

IHC23-PO-360

Migraine: An Abnormal Crosstalk Between Increased Neural Activities and Lowered Firing Thresholds

Mohammad Dawood Rahimi

Herat University, Herat, Afghanistan

Although noise or variance is needed to support adaptability in a complex system like the brain, the amount of noise a brain with a migraine can hold intact is inverse to its ability. If neural activities and firing thresholds are not sequential at a single moment, then the variance between neural activities and firing thresholds can be highly harmful. In such a condition, the excitatory postsynaptic potentials produce excessive current flow at synapses. This is large because of abnormal distribution of variance or stochastic resonance abnormalities. The current is excessive but not strong enough to reach the axonal terminals. Therefore, the process of signaling could not be completed. Based on associative learning, a third factor often influences the excessive but weak synaptic input. The third factor is often vital feedback or behavioral input which becomes associated with weak synaptic input. In a brain with a migraine, the third factor is usually a stressor, and the output is a stress-response activity. This phenomenon has a detrimental effect on the somatic membrane potentials and firing probability. Dendritic spikes-related depolarizations are subthreshold. Prolonged and cumulative weak neural firings working on membrane polarization, plastic induction, cell motility, and immune responses via inactivation of sodium channels during repetitive stress-response activities or allostatic load. This type of modification of synaptic strength is known as synaptic scaling. The results of such scaling are quasi-fractal connectivity and coherence-incoherence patterns. Though, time-delayed feedback by inappropriate coupling strengths inversely disturbs correlation, coordination, and habituation between pre- and postsynaptic firings in the brains with migraine. This perspective or review may supply promising targets for novel functional and structural directed research, which can move forward to find balanced approaches to modulate both desirable and undesirable sources of variances in a brain with migraine.
Disclosure of Interest: None Declared

IHC23-PO-361

The ability of a collection of gait indexes generated from trunk acceleration to describe imbalanced gait in patients with migraine without aura between attacks.

Chiara Abagnale, Gabriele Sebastianelli, Francesco Casillo, Stefano Filippo Castiglia, Dante Trabassi, Nicola Seget, Greta Seveso, Cherubino Di Lorenzo, Mariano Serrao and Gianluca Coppola

Sapienza University of Rome Polo Pontino-ICOT, Department of Medico-Surgical Sciences and Biotechnologies, Latina, Italy

Objectives: Of the various possible ramifications of migraine within the nervous system, sensorimotor involvement is one of the most insidious and under-investigated. It is not uncommon for subjects suffering from migraine to experience static and dynamic balance impairment, as well as a reduction in the limits of stability, which leads to a reduction in anticipatory postural adjustments and an increased risk of falling [1–3]. The aims of this study were: (i) to assess the ability of 16 gait stability indexes to identify gait instability in subjects with episodic migraine without aura (MO) regardless of age and gait speed and (ii) to investigate their correlations with clinical and kinematic variables.
Materials: This study included 23 walking trials from subjects with MO and 23 age, gender, and gait speed matched healthy subjects (HS) acquired using a single lumbar-mounted inertial measurement unit.
Methods: The harmonic ratios, percent recurrence, percent determinism (RQAdet), coefficient of variation, normalized jerk scores, and maximal Lyapunov's exponents for short time series (LLE) were calculated based on trunk acceleration patterns in the anteroposterior (AP), medio-lateral (ML), and vertical (V) directions. To assess the ability of the gait indexes to characterize the gait of MO, independent sample t-tests, Cohen's d, and the area under the receiver operating characteristic curves were calculated. To assess the correlations between clinical scales and gait parameters, partial Pearson's correlation coefficients were calculated, excluding the effects of gait speed.
Results: LLEML values $\geq$1.04, LLEV values $\geq$1.06, and RQAdetAP values $\geq$96.32 characterized MO with 78%, 70%, and 75% probabilities, respectively, regardless of gait speed. LLEML correlated with the duration of the migraine attacks ($r = 0.48$, $p = 0.01$), VAS ($r = 0.42$, $p = 0.02$), MIgraine Disability Assessment Score ($r = 0.38$, $p = 0.03$), Dizziness Handicap Inventory scores ($r = 0.44$, $p = 0.04$). LLEV correlated with Allodynia Symptoms Checklist scores ($r = 0.46$, $p = 0.01$) and pain intensity ($r = 0.42$, $p = 0.02$). RQAdetAP correlated with the Activities Balance Confidence scale scores ($r = -0.40$, $p = 0.03$).
Discussion: LLE can capture the subtle gait imbalance experienced by MO, reflecting a loss of local dynamic stability in ML and V directions, and a reduced ability to respond adequately to small perturbations during gait. As a result of their perceived imbalance, MO increase their gait regularity, particularly in the AP direction, as evidenced by higher RQAdet when compared to HS. LLEML, LLEV, and RQAdet are accurate biomarkers of gait instability that reflect the severity and disability of migraine presentation.

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IHC23-PO-362

The Nocebo Response in Pharmacologic Treatments of Primary Headache: A Systematic Review and Meta-Analysis

Zheman Xiao, Yu Zhang, Yingying Xu and Shuping Liu

Renmin Hospital of Wuhan University, Wuhan, China

The nature and magnitude of nocebo responses in primary headache disorders are still unknown. To assess the distribution and possible predictors of nocebo responses in primary headache treatments, databases, including PubMed, EMBASE, and Cochrane Library were searched from 1988 to December 31, 2020, for parallel-group, double-blind, randomized placebo-controlled trials of pharmacologic treatments of primary headaches. The nocebo responses were calculated using a random effects meta-analysis model. Subgroup and metaregression analyses were performed to determine the associations of study design and demographic characteristics with nocebo responses. A total of 178 randomized controlled

trials that satisfied the inclusion criteria were included. Prophylactic treatments elicited stronger nocebo responses than acute treatments. The majority of nocebo adverse events were mild to moderate in severity, with the nervous and digestive systems being the most commonly affected. There was a strong correlation between the active medication and control groups in terms of adverse events, both quantitatively and qualitatively. Long treatment duration, a high proportion of subjects receiving active medications, multicenter design, North America, high body mass index, women, previous treatment experiences, and a high proportion of patients with migraine headache with aura were all found to be significant positive predictors of nocebo responses, whereas the year of publication was found to be inversely related to them. Nocebo effects should be noticed for their contribution to discontinuation of or lack of adherence to active treatments. Clarifying these nocebo-related risk factors can aid in their clinical prevention and management.

Disclosure of Interest: None Declared

IHC23-PO-363

Co-occurrence Measures Indicate Visual Snow and Tinnitus Involve Separate Mechanisms

Amy Claire Thompson, Jarrod Morris, Dolores Mifsud, Patrick Goodbourn and Jason Forte

Melbourne School of Psychological Sciences, the University of Melbourne, Parkville, Vic, Australia

Objective: Visual snow (VS) is a positive perceptual anomaly characterised by persistent flickering dots across the visual field. It is the primary phenomenon associated with Visual Snow Syndrome (VSS). Some researchers have hypothesised that VS is a visual analogue of tinnitus and that they involve a shared mechanism. This study explored the association between onset timing of VS and tinnitus, and perceived severity of the two conditions, to investigate this theory.

Methods: 324 undergraduate students were screened for VS, perceptual phenomena associated with VSS, and tinnitus using a novel screening tool based on the European School Interdisciplinary Tinnitus Research Screening Questionnaire (ESIT-Q). Participants were aged 17 years or older, were fluent in English, and had no prior knowledge of VS or VSS.

Results: Of 290 participants included for analysis, 205 were female, 81 were male, 3 were non-binary and 1 preferred not to say. Participants' mean age was 19.53 years ($SD = 3.32$, range 17–54). In total, 149 participants experienced VS some of the time, of whom 33 met the criteria for VSS (notwithstanding some more complex explanation for their symptoms), and 62 also experienced tinnitus. 66 either had migraine diagnoses or probably experienced migraine.

Among participants who experienced both VS and tinnitus, there was no association between the time of onset of the two conditions, $\chi^2(20) = 27.7$, $p = .12$. However, there was a significant association between the perceived severity of the two conditions, $r(59) = .44$, $p < .001$, 95% CI [.21, .62].

Conclusion: Our results indicate that people with both VS and tinnitus did not experience the initial onset of the two symptoms together. If the two symptoms began concurrently, this would support theories which suggest they share a common mechanism: our results indicate this may not be the case. However, the significant association between the perceived severity of both conditions suggests that, like tinnitus, the perceived severity of VS may be impacted by psychological factors; and may be independent of the objective severity of the condition.

IHC23-PO-364

Effect of COVID vaccination on monthly migraine days: A longitudinal cohort study

Britt W.H. van der Arend, Mirthe M. Bloemhof, Alle G. van der Schoor, Erik W. van Zwet and Gisela M. Terwindt

Leiden University Medical Center, Leiden, Netherlands

Background: This longitudinal cohort study aimed to investigate changes in migraine-related outcomes following COVID-19 infection and vaccination.

Methods: We identified 547 clinically diagnosed migraine patients from the Leiden Headache Center who kept a headache E-diary during the COVID-19 pandemic (February 2020 – August 2022). We sent a questionnaire to register their COVID-19 infection and/or vaccination dates. After applying inclusion criteria, $n = 59$ participants could be included in the infection analysis and $n = 147$ in the vaccination analysis. Primary outcome was the change in Monthly Migraine Days (MMD) between 1 month prior and 1 month post COVID-19 infection or vaccination. Secondary outcome variables were change in Monthly Headache Days (MHD) and Monthly Acute Medication Days (MAMD).

Results: Vaccination against COVID-19 was associated with an increase in MMD (1.06, 95% CI: 0.57–1.55, $p < 0.001$), MHD (1.52, 95% CI: 0.91–2.14, $p < 0.001$) and MAMD (0.72, 95% CI: 0.33–1.12, $p < 0.001$) in the first month post-vaccination. COVID-19 infection solely increased the number of MAMD (1.11, 95% CI: 0.10–1.62, $p = 0.027$), but no statistically significant differences in MMD or MHD were observed.

Conclusion: Our findings imply that vaccination against COVID-19 is associated with an increase in migraine, indicating a possible role of inflammatory mediators in migraine pathophysiology.
Disclosure of Interest: B.W.H. van der Arend and G.M. Terwindt report independent support from the Dutch Research Council (849200007) and the Dutch Brain Foundation (HA2017.01.05). G.M. Terwindt reports consultancy or industry support from Abbvie/Allergan, Lilly, Lundbeck, Novartis, and Teva, and independent support from the European Community, Dutch Heart and Brain Foundations, Dutch Research Council, and Dioraphte. E. W. van Zwet, M.M. Bloemhof and A.G. van der Schoor report no disclosures.

IHC23-PO-365

A Case Report of Persistent Aura without Infarction in a Patient with Migraine

Mohammed Omer

Gadarif University, Gadarif, Sudan

Introduction: Migraine is a common neurological disorder characterized by recurrent episodes of moderate-to-severe headaches and associated symptoms. Persistent aura without infarction (PAWOI) is a rare phenomenon in migraine, in which the aura symptoms persist beyond the typical duration without evidence of cerebral infarction. This case report describes the clinical presentation, diagnostic workup, and management of a patient with PAWOI.
Case Presentation: A 42-year-old female with a history of migraine with aura presented with persistent visual disturbances, including scintillating scotoma, lasting for more than two weeks following a typical migraine attack. The patient denied any history of head trauma, recent infection, or substance use. Neurological examination revealed no focal deficits or signs of increased intracranial pressure. Brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were unremarkable, ruling out cerebral infarction, arteriovenous malformations, or other structural abnormalities. Electroencephalogram (EEG) demonstrated no epileptiform activity.
Management and Outcome: The patient was treated with a combination of intravenous sodium valproate and oral topiramate, which led to a gradual resolution of the persistent aura symptoms within four weeks. At the three-month follow-up, the patient reported no recurrence of persistent aura and a reduction in the frequency of her migraine attacks.
Conclusion: This case report highlights the rare occurrence of PAWOI in a patient with migraine and emphasizes the importance of a thorough diagnostic workup to rule out other potential causes of persistent aura symptoms. Early recognition and appropriate treatment of PAWOI may prevent potential complications, reduce patient distress, and improve overall outcomes. Further research is needed to understand the pathophysiology of PAWOI and identify optimal management strategies for this rare phenomenon.
Disclosure of Interest: None Declared

IHC23-PO-366

The individual burden of migraine in patient with non specific treatment

Bolortsetseg Davaasuren[1] and Otgonbayar Luvsannorov[2]

[1]*General Hospital for State Special Servant, Ulaanbaatar, Mongolia*
[2]*Health Science University of Mongolia, Ulaanbaatar, Mongolia*

Keywords: migraine, burden of migraine, migraine non-specific drugs, nocebo
Introduction: Migraine is one of the most common neurological diseases and most disabling neurological conditions in the world, often causing individual burden and a substantial impairment of daily activities. Patients with difficult-to-treat migraine often cycle through different therapies. Migraine treatment is aimed at stopping symptoms and preventing future attacks that is most important part of migraine management. The treatment of migraine includes acute and preventive treatments, which can classify as migraine-non-specific or migraine-specific and pharmacological or non-pharmacological treatments. In our country, Mongolia, we can not use enough migraine-specific drugs (triptans, ditans, and onabotulinumtoxin etc) and migraine-specific treatments consist of Calcitonin genere-related peptide (CGRP) monoclonal antibodies, and gepants in migraine treatment. We aimed to characterize and assess the individual burden of migraine in patients with nonspecific treatment attending in our outpatient clinic General Hospital for State Special Servant and District hospital of Bayangol, Mongolia.
Aim: To assess individual burden of migraine and corresponding non-specific treatment
Methods: Using standardized methodology with cluster random sampling, we selected Mongolian adults (aged 18–65 years) from outpatients in outpatient clinic General Hospital for State Special Servant and District hospital of Bayangol. They were interviewed by neurologists, using Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) structured questionnaire following pilot-testing. ICHD-3 beta diagnostic criteria were applied. Hospital based cross

sectional study of patients with migraine using standardized HARDSHIP questionnaire.
Results: The total of 34 outpatients aged between 18–65 were participated in the study of whose 97.0% are women and 3.0% are men and the mean age of the participants is 37.5. Of those 34 outpatients, 76.4% employed, 14.7 unemployed, 5.8% retired and 2.9% student in our study. Mean frequency of the migraine was 15 day/month. Most of the patient with moderate to severe headache (16.7%,83.3%). Ictal state of migraine continued up to 12.5% of the duration of the migraine while disability level for individual was 5.5%. Participant without migraine had significantly higher (i.e better) subjective wellbeing-4 scores than those with migraine ($p < 0.005$). There were 22 kind of drug (combination analgesics 47.8%, NSAID 30.9%, vitamin 11.2%, other 9.8%) in our study. Subjective wellbeing-4 score correlated inversely with drug usage. Thus, patient with citramon, poldaming, citromax had lower (i.e. worse) scores than those with NSAID and other nonspecific drug such as piracetam, carbamazepine, cinnarizin etc. (24.1 ± 4.7 vs 28.4 ± 5.1; $p < 0.05$)
Conclusion: This study depicts, for the first time, migraine attributed individual burden and impact on subjective wellbeing psychology. Migraine disorder also highly individual burden. Mean frequency of the migraine was 15 day/month and most of the patient with moderate to severe headache. Ictal state of migraine continued up to 12.5% of the duration of the migraine while disability level for individual was 5.5% in our study, that is also high in developed country. We always use non-specific drugs and pharmacological non-specific migraine preventatives in our treatment. There is a substantial requirement in migraine specific treatment in our country. Structured healthcare services for migraine need to be urgently put in place.

IHC23-PO-367

Headache in emergency room, an Albanian experience

Redon Uruçi[1,2] and Jera Kruja[1,2]

[1]*University of Medicine, Tirana, Albania*
[2]*UHC Mother Teresa, Tirana, Albania*

Introduction: The neurologist undertakes the role of differentiating a small number of patients with life-threatening headaches from the large number of cases presented with primary benign headaches in the Emergency Department. A delay in diagnosis can result in major consequences for the patient, from the installation of neurological deficits to even life-threatening outcomes. This study seeks to highlight that headache is not properly assessed in EDs, thus increasing the cost of health care, especially in terms of imaging investigation.
Method: Admissions chart data of visits to the neurological emergency department of UHC Mother Teresa were collected, during the January-March 2022 time frame. The statistical program SPSS 20.0 was used for data analysis. Continuous variables are summarized as mean standard deviation (SD). The percentage of patients in each category was calculated for the categorical variables. The X2 test was used to compare the percentage between categorical variables. Student's t test was used to compare the means of the parameters of the continuous variables. The value of $p \leq 0.05$ was considered statistically significant. All statistical tests are two-sided.
Results: In total there were 6338 patients admitted to the USB QSUT Emergency, of which 175 or 2.7% of them were diagnosed with headache. There was a predominance of women in the ratio 1.92: 1 ($p < 0.01$). The average age of patients is 48.6 years. 88.7% of patients had primary headache, while only 11.3% of them had secondary pain. Only 5 (2.9%) patients did not perform CT of the head ($p < 0.01$). 25 patients (14.3%) were hospitalized. A significant trend of increasing hospitalization rate was found with increasing age group ($p < 0.01$)
Conclusion: The high number of chronic headaches in the ED demonstrates the need of spreading a genuine "culture of headache" in the medical community, beyond that of neurology. The high percentage of patients undergoing emergency neuroimaging evaluation speaks to the necessity of implementing a headache management algorithm, based on standardized international protocols. Unnecessary radiation levels carry unwanted effects that go beyond the overload of medical staff, directly affecting the development of neoplastic processes in the patients in question. The necessary changes also extend to the symptomatic treatment of emergency headache, as mannitol continues to lead the first-line emergency headache therapy, an outdated and unfounded approach to recent guidelines.
Disclosure of Interest: None Declared

IHC23-PO-368

The Regional Outreach Programme of the International Headache Society in sub-Saharian Africa in partnership with the DREAM program: First on-site course in Malawi

Daniele Martinelli[1], Cristina Tassorelli[1,2], Freda Dodd-Glover[3], Manjit Matharu[4], Derya Uluduz[5], Victor Tamba Tolno[6] and Massimo Leone[7,8]

[1]*IRCCS Mondino Foundation, Pavia, Italy*

[2]Department of Brain and Behavioral Sciences, University of Pavia, pavia, Italy
[3]Korle Bu Teaching Hospital, accra, Ghana
[4]Headache and Facial Pain Group, UCL Queen Square Institute of Neurology and National Hospital for Neurology and Neurosurgery, London, United Kingdom
[5]Istanbul University, Cerrahpasa School of Medicine, Neurology Department, istambul, Turkey
[6]DREAM project, Blantyre, Malawi
[7]Neuroalgology Unit, IRCCS C. Besta Neurologic Institute, Milan, Italy
[8]DREAM Program, Rome, Italy

Objectives: Due to doctors' shortage in sub-Saharan Africa (SSA), primary care non-physician clinicians (called clinical officers, CO) provide most of the care to the population.
In November 2022, the Regional Outreach Programme of the IHS organised the first on-site course dedicated to "Headache, head pain syndromes, migraine and related disorders". It was developed in partnership with the Disease Relief through Excellent and Advanced Means (DREAM) program to improve CO headache education.
The aim of this initiative is to improve the management of headache in an area of SSA.
Methods: Building on the DREAM healthcare facilities operating in Malawi, the 2-day course was organised in Blantyre and was attended by COs working in several primary care facilities in Malawi.
The teaching modules foresaw a high degree of interaction with the audience; the treatment approach was focused on the use of the WHO list of essential drugs. The final session foresaw the group discussion of multiple clinical cases.
Here we report the results of a survey conducted before and after the training to evaluate the participants' training, needs, and knowledge about headache.
Results: Thirty-four COs participated: 10 women, median age 33 years, with 9 years of work experience.
The survey highlighted the lack of proper training in neurology and headache. The after-course survey showed a great improvement in their knowledge of neurology, pain, and primary and secondary headache.
The trainees were highly satisfied, much appreciated the lectures and the provided practical tips as well. They strongly recommended the course and wished to change their approach to headache patients.
Conclusions: Poor education hampers proper care for headache patients in SSA. Fruitful partnerships between International Societies and established local providers can provide headache education at the primary care level where most patients are seen. Long-term follow-up, tailored task-shifting and task-sharing are necessary. The IHS-DREAM program in SSA adheres and contributes to the objectives of the WHO Intersectoral Global Action Plan.
Disclosure of Interest: None Declared

IHC23-PO-369

Verification of a clinical decision support system for the diagnosis of headache disorders based on patient–computer interactions: A multi-center study

Han Xun[1], Wan Dongjun[2], Zhang Shuhua[1], Yin Ziming[3], Huang Siyang[4], Xie Fengbo[4], Guo Junhong[5], Qu Hongli[6], Yao Yuanrong[7], Xu Huifang[8], Li Dongfang[9], Chen Sufen[10], Wang Faming[11], Wang Hebo[12], Chen Chunfu[13], He Qiu[14], Dong Ming[15], Wan Qi[16], Xu Yanmei[17], Chen Min[18], Yan Fanhong[19], Wang Xiaolin[1], Wang Rongfei[1], Zhang Mingjie[1], Ran Ye[1], Jia Zhihua[1], Liu Yinglu[1], Chen Xiaoyan[1], Hou Lei[1], Zhao Dengfa[1], Dong Zhao[1] and Yu Shengyuan[1]

[1]Department of Neurology, The First Medical Center, Chinese PLA General Hospital, Beijing, China
[2]Department of Neurology, The 940th Hospital of Joint Logistic Support Force of Chinese People's Liberation Army, Lanzhou, China
[3]School of Health Science and Engineering, University of Shanghai for Science and Technology, Shanghai, China
[4]AffaMed Therapeutics, Beijing, China
[5]Department of Neurology, First Hospital of Shanxi Medical University, Taiyuan, China
[6]Department of Neurology, The First Affiliated Hospital of Xiamen University, Xiamen, China
[7]Department of Neurology, Guizhou Province People's Hospital, Guiyang, China
[8]Department of Neurology, Wuhan NO.1 Hospital, Wuhan, China
[9]Department of Neurology, Second Hospital of Shanxi Medical University, Taiyuan, China
[10]Department of Neurology, Changsha Central Hospital Affiliated to University of South China, Changsha, China
[11]Department of Neurology, Tiantai People's Hospital of Zhejiang Province, Taizhou, China
[12]Department of Neurology, Hebei General Hospital, Shijiazhuang, China
[13]Department of Neurology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, China
[14]Department of Neurology, The People's Hospital of Liaoning Province, Shenyang, China
[15]Department of Neurology and Neuroscience Center, The First Hospital of Jilin University, Jilin, China
[16]Department of Neurology, Jiangsu Province Hospital, Nanjing', China
[17]Department of Neurology, Dingyuan General Hospital, Chuzhou, China
[18]Department of Neurology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China
[19]Department of Neurology, Linyi Jinluo Hospital, Linyi, China

Background: Although headache disorders are common, the current diagnostic approach is unsatisfactory. Previously, we designed a guideline-based clinical decision support system (CDSS 1.0) for diagnosing headache disorders. However, the system requires doctors to enter electronic information, which may limit widespread use.
Methods: In this study, we developed the updated CDSS 2.0, which handles clinical information acquisition via human–computer conversations conducted on personal mobile devices in an outpatient setting. We tested CDSS 2.0 at headache clinics in 16 hospitals in 14 provinces of China.
Results: Of the 653 patients recruited, 18.68% (122/652) were suspected by specialists to have secondary headaches. According to "red-flag" responses, all these participants were warned of potential secondary risks by CDSS 2.0. For the remaining 531 patients, we compared the diagnostic accuracy of assessments made using only electronic data first. In Comparison A, the system correctly recognized 115/129 (89.15%) cases of migraine without aura (MO), 32/32 (100%) cases of migraine with aura (MA), 10/10 (100%) cases of chronic migraine (CM), 77/95 (81.05%) cases of probable migraine (PM), 11/11 (100%) cases of infrequent episodic tension-type headache (iETTH), 36/45 (80.00%) cases of frequent episodic tension-type headache (fETTH), 23/25 (92.00%) cases of chronic tension-type headache (CTTH), 53/60 (88.33%) cases of probable tension-type headache (PTTH), 8/9 (88.89%) cases of cluster headache (CH), 5/5 (100%) cases of new daily persistent headache (NDPH), and 28/29 (96.55%) cases of medication overuse headache (MOH). In Comparison B, after combining outpatient medical records, the correct recognition rates of MO (76.03%), MA (96.15%), CM (90%), PM (75.29%), iETTH (88.89%), fETTH (72.73%), CTTH (95.65%), PTTH (79.66%), CH (77.78%), NDPH (80%), and MOH (84.85%) were still satisfactory. A patient satisfaction survey indicated that the conversational questionnaire was very well accepted, with high levels of satisfaction reported by 852 patients.
Conclusions: The CDSS 2.0 achieved high diagnostic accuracy for most primary and some secondary headaches. Human–computer conversation data were well integrated into the diagnostic process, and the system was well accepted by patients. The follow-up process and doctor–client interactions will be future areas of research for the development of CDSS for headaches.

IHC23-PO-370

Impact of headache on the clinical and psychological characteristics of temporomandibular disorders

Seonghae Kim[1], Jung Hwan Jo[2,3] and Ji Woon Park[2,3]

[1]*Dental Research Institute, Seoul National University, Seoul, Korea, Republic of*
[2]*Seoul National University School of Dentistry, Seoul, Korea, Republic of*
[3]*Seoul National University Dental Hospital, Seoul, Korea, Republic of*

Objective: Headache is a well-known comorbidity of temporomandibular disorders (TMD) and their co-occurrence has been reported through numerous previous studies. In most cases, various factors are known to be shared in their pathogenesis with central sensitization playing a major role. TMD patients with headache have been reported to show a higher level of pain and disability compared with those with only TMD, underlining the need to diagnose and manage headache in this disease population in a timely manner. Therefore, the purpose of this study was to analyze the differences in clinical characteristics and psychological status according to the presence of headache in a well-defined group of TMD patients to identify specific clinical factors to understand and approach.
Methods: Patients seeking care due to TMD symptoms between 1 Dec, 2019 to 31 Apr, 2022 were analyzed. The presence of headache was verified based on subjective report and TMD was diagnosed based on the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). The Graded Chronic Pain Scale (GCPS) version 2 of DC/TMD Axis II was used to measure pain intensity and disability level. Symptom Checklist-90-Revision (SCL-90-R) was applied to evaluate psychological status.
Results: Of the 793 TMD patients, 290 reported headache (37%). Those in their 30s to 50s showed the highest headache prevalence. Females showed a significantly higher headache prevalence ($p = 0.025$). TMD patients with headache reported a significantly higher level of pain intensity on a 0–10 numeric rating scale (NRS) with more patients showing higher than moderate level of pain ($p = 0.005$). Patients with headache more frequently reported pain on palpation of the masticatory muscle ($p = 0.031$) and temporomandibular joint ($p = 0.007$) area. Patients with headache more frequently reported clenching ($p = 0.016$) along with sleep disturbance ($p < 0.001$) and insomnia symptoms ($p < 0.001$). Also, those with headache more frequently reported pain of other body parts including low back, arm and leg, neck and shoulder. More patients with headache showed moderately limiting levels of disability due to symptoms

($p = 0.002$). TMD patients with headaches showed significantly higher levels of somatization ($p < 0.001$), depression ($p = 0.045$), anxiety ($p = 0.005$), and paranoid ideation ($p = 0.022$).
Multiple regression analysis showed age, sleep disturbance, and somatization were significantly associated with Characteristic Pain Intensity (CPI) levels. Logistic regression analysis showed that presence of sleep disturbance (odds ratio [OR] = 1.405), neck and shoulder pain (OR = 2.255), and gastrointestinal problems (OR = 1.755) were associated with headache while for psychological factors, somatization (OR = 1.114), and paranoid ideation (OR = 1.049) increased and psychoticism decreased the likelihood of headaches (OR = 2.181).
Conclusion: TMD patients with concomitant headache showed higher pain intensity and disability levels compared to those free of headache. Also, the psychological condition of those positive for headache were worse. Sleep disturbance and pain of other body parts were factors related to the presence of headache in TMD patients indicating the need to identify such conditions in the diagnostic process and furthermore to provide appropriate management of headache for improved prognosis in TMD patients.
Disclosure of Interest: None Declared

IHC23-PO-371

Is There a Relationship Between Body Mass Index and Allodynia in Migraine Patients?

Buse Rahime Hasirci Bayir[1], Arife Çimen Atalar[2] and Betül Baykan[3]

[1]*Haydarpaşa Numune Education and Research Hospital, Neurology Department, İstanbul, Turkey*
[2]*Kanuni Sultan Süleyman Education and Research Hospital, Neurology Department, İstanbul, Turkey*
[3]*İstanbul Faculty of Medicine, Neurology Department, İstanbul, Turkey*

Aim: There are studies showing that the presence of allodynia, which is the clinical manifestation of central sensitization, is associated with an increase in body mass index (BMI). The aim of this study is to examine the relationship between BMI, which is a marker of mild inflammation, and allodynia in patients with migraine.
Material and Method: Patients who were followed up with a diagnosis of migraine in the Headache Outpatient Clinic between January 2019 and June 2022 and had ≥ 4 attacks per month were included in the study. The patients were divided into two groups according to their BMI. The first group included low and normal weight patients with BMI < 25kg/m2, and the second group included overweight and obese patients with BMI≥ 25 kg/m2. Demographic data such as gender, age, educational status and headache characteristics of the patients were recorded. Headache severity was evaluated by visual analog scale (VAS), migraine-related limitation was measured with MIDAS, and presence of allodynia was evaluated with the Allodynia Symptom Checklist-12.
Results: A total of 94 patients (85 females) with BMI < 25kg/m2 and 50 patients (46 females) with BMI≥ 25kg/m2 were included in the study. The mean age of the group with higher BMI was higher (p:0.007) and the education level was lower ($p < 0.001$). Migraine duration was also higher in this group (p: 0.018). Presence of aura, duration of attack, number of days with headache, use of analgesic and prophylactic treatment were similar in both groups. There was no statistical significance between the VAS, MIDAS and allodynia scores of the patients.
Conclusion: The increase in BMI may lead to the chronicity of migraine by contributing to the development of central sensitization in migraine patients or inflammatory mechanisms. We observed that patients with long-lasting migraine had a higher BMI. However, no correlation was found between BMI and allodynia in these patients, suggesting different underlying mechanisms.
Disclosure of Interest: None Declared

IHC23-PO-372

The Effect of Cannabidiol on the Excitability of Nociceptive Mice Trigeminal Neurons – A Pilot Study

Shanya Watthanaphothithorn[1], Aree Wanasuntronwong[2], Ukkrit Jansri[1] and Anan Srikiatkachorn[1]

[1]*Faculty of Medicine, King Mongkut's Institute of Technology Ladkrabang, à,°Bangkok, Thailand*
[2]*Department of Oral Biology, Faculty of Dentistry, Mahidol University, à,°Bangkok, Thailand*

Objective: Cannabidiol (CBD), a non-psychotropic cannabinoid extracted from the Cannabis Sativa plant, has been shown to interact with various receptors in the nociceptive pathway. CBD's interaction with these target molecules makes it a potential alternative analgesic medication to current treatments such as non-steroidal anti-inflammatory drugs (NSAIDs) and opioids. Although there have been multiple preclinical studies on the analgesic effects of CBD via reduction of inflammation, there are still limited studies assessing CBD's effect on peripheral nociceptive neurons by electrophysiological parameters. This study aims to evaluate the effect of CBD on the electrophysiologic characteristics of nociceptive trigeminal ganglion neurons.

Methods: A whole cell patch clamp method was used to assess neuronal excitability of small-to-medium sized trigeminal ganglion neurons harvested from adult male Jcl: ICR mice, comparing between trigeminal ganglion neurons treated with 0.5uM CBD for 1–2 hours to a control group. A 1ms current was injected in 5pA increments to measure the excitability of individual neurons. The primary outcome is the excitability measured by the resting membrane potential (RMP), threshold potential, and rheobase. Secondary outcomes include action potential (AP) parameters of height, overshoot, rising and falling time, duration, and depth. All data is reported as means and standard error of means, and statistical analysis is performed using the Mann-Whitney U test.

Results: A sample of $n = 8$ was obtained from each group with the average neuronal diameter in the control and CBD group being 24.79 ± 1.92um and 30.68 ± 1.32um ($p = 0.074$) respectively. The CBD treated group showed no significant difference in terms of RMP (control, -51.11 ± 4.06 mV vs CBD, -55.02 ± 1.72 mV, $p = 0.141$), and rheobase (control, 17.78 ± 2.24pA vs CBD, 23.13 ± 3.13pA, $p = 0.248$), however there is a significant difference in threshold potential (control, -9.20 ± 5.08mV vs CBD, -16.46 ± 2.83mV, $p < 0.005$). For the secondary outcomes there is a significant difference in the parameters of AP rising time (control, 2.68 ± 0.34ms vs CBD, 0.9 ± 0.14ms, $p < 0.01$), AP falling time (control, 12.64 ± 1.75ms vs CBD, 2.58 ± 0.55ms, $p < 0.05$), and AP duration (control, 20.33 ± 1.99ms vs CBD, 3.48 ± 0.61ms, $p < 0.005$).

Conclusion: Overall there is an increase in excitability of small-to-medium sized trigeminal neurons treated with 0.5uM CBD seen by the significantly lower threshold potential, shorter AP rising time, shorter AP falling time, and a shorter AP duration. This result contradicts the initial hypothesis that CBD will decrease the excitability of nociceptive neurons as shown in previous research studying the activity of CBD on individual receptors, however this could be due to confounding glial responses and the nature of the sample being a normal trigeminal neuron culture instead of an inflammatory culture. Nevertheless, this warrants a full further investigation on the electrophysiological profile of nociceptive neurons as well as glial cells treated with CBD.

Disclosure of Interest: None Declared

IHC23-PO-373

Visual Snow Syndrome: The impact of real-time functional magnetic resonance imaging neurofeedback on resting-state functional connectivity

Lars Michels[1], Reza Mazloum[1], Raphaela Schöpfer[1], Philipp Stämpfli[2], Konrad Weber[3,4], Leah Disse[3], Christopher Schankin[5] and Fabienne Fierz[4]

[1]*Department of Neuroradiology, University Hospital Zurich, Zurich, Switzerland*
[2]*Department of Psychiatry, Psychotherapy and Psychosomatics, Zurich, Switzerland*
[3]*Department of Ophthalmology, University Hospital Zurich, Zurich, Switzerland*
[4]*Department of Neurology, University Hospital Zurich, Zurich, Switzerland*
[5]*Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland*

Objective: Visual snow syndrome (VSS) is a distressing condition with unrelenting and persistent disturbing visual phenomena that is characterized by continuous perception of innumerable flickering dots. The disease is often accompanied by comorbidities such as migraine, tinnitus, depression, and anxiety. Neuronally, VSS patients show cerebral hypermetabolism in parts of the visual cortex, resulting in altered neuronal excitability, as well as increased grey matter volume and functional hyperconnectivity. We hypothesized that real-time functional magnetic resonance imaging (rtfMRI) neurofeedback (NFB) will allow patients to learn to regulate their lingual gyrus activity (outcome). Moreover, the investigators predicted that stronger regulation of activity from the lingual gyrus would correlate with a prospective decrease (3-month after the NFB intervention) in VS symptoms (primary endpoint).

Methods: In this double blind, randomized and sham-controlled experiment, the investigators used rtfMRI-NFB allowing patients to downregulate activity in or outside of the visual cortex. We included 18 healthy controls (mean age 24.1 years $\pm$ 6 years, 11 females) without signs of a neurological disorder (e.g. migraine), who only had a baseline MRI scan, and 18 patients with VSS (mean duration: 7.02 ± 8.6 years, mean age: 32.4 years $\pm$ 6 years, 6 females) of which 14 had tinnitus and eight migraine (6 . with aura, HARDSHIP questionnaire). Patients had a clinical interview (before and 3 months after NFB) assessing VSS symptoms, and filled out the VSS questionnaire (Puledda et al. 2020), before and after the NFB sessions, as well as a migraine and anxiety and depression questionnaire. In addition, patients had anatomical MRI, MR-spectroscopy, and resting-state fMRI using a 3 Tesla Philips Achieva scanner before the NFB sessions.

As intervention, only patients had two consecutive rtfMRI-NFB sessions (each 1-hour, baseline, 4 NFB runs and transfer run per session, maximally a week apart). During the NFB sessions, patients had to either regulate parts of the right lingual gyrus (verum region; Aldusary et al., 2021) or rectus gyrus (sham region; matched in size to the lingual gyrus) using intermittent and implicit (i.e. patients self-selected a strategy) NFB.

Outcome was the regulation success that was by comparing the first (baseline) to the last (10th) run without feedback (transfer run). After the NFB sessions, resting-state fMRI was recorded. Functional connectivity (FC) seed-to-voxel (seeds: lingual and rectus gyrus) and atlas-based region-to-region (ROI-to-ROI) analyses were performed with the CONN toolbox, following pre-processing (e.g. motion correction) and subsequent group analysis. Using a general linear model, we compared the groups by two-sample, two-tailed t-tests ($p < 0.05$ cluster-corrected). Covariates were VS severity, VSS duration, migraine and tinnitus.

Results: Before NFB, the ROI-to-ROI revealed hyperconnectivity in patients with VSS compared to controls, predominately between the thalamus and visual brain regions. Post-NFB ROI-to-ROI analysis demonstrated normalized FC in the verum group compared to persistent hyperconnectivity in the sham group, including connectivities from the lingual gyrus to the posterior cingulate cortex, when controlled for age, sex, VSS severity, duration, migraine, and tinnitus. Within-group seed-to-voxel analysis revealed that the verum group showed increased FC after NFB in parts of the visual cortex (not lingual gyrus), prefrontal cortex, and angular gyrus. In contrast, the sham group stronger FC compared to pre-NFB in brain areas outside the visual cortex. The clinical outcome will be presented elsewhere.

Conclusions: Our results indicate that rtfMRI-NFB of the visual cortex reduced hyperconnectivity in the verum NFB group. These functional changes might represent the first modification of a potential VSS-biomarker that could be associated with a reduction of VSS symptoms. In the future, this method might represent a non-invasive approach to successfully and specifically improve severity of the hitherto difficult to treat VSS.

Disclosure of Interest: None Declared

IHC23-PO-374

Microphysiological on-chip systems for modelling brain disease using human induced pluripotent stem cells

Jean-Philippe Frimat and Arn van den Maagdenberg

Leiden University Medical Center, Leiden, Netherlands

Models of brain disorders typically involve the use of rodents, which is time consuming and resource intensive, and has ethical considerations. More relevant even, rodent models may not accurately predict (all) features of human disease. Also, in many cases, findings from animal models have been shown to be poor predictors of human responses. Hence there is a rational to develop microphysiological on-chip systems (MPS), which are cellular models that replicate aspects of organ and tissue function in vitro. They are distinct from conventional cell cultures in that microfluidic components may include features such as gas- and fluid flow; for this reason, some are referred to as microfluidic Organs-on-Chip (OoCs). These advanced models can provide specific cues to cells as in real tissues, typically use human induced pluripotent stem cells (iPSC), creating systems with the potential to impact understanding of human physiology and disease, but also toxic effects of the environment or drugs and even the identification of novel therapeutics. Here, we use MPS of the brain to illustrate advancement of in vitro on-chip models for various brain disorders that include migraine and epilepsy. For migraine, we propose a human iPSC-based model comprising a compartmentalized microfluidic device, fabricated using polydimethylsiloxane (PDMS) replica molding, that is combined with a multi-electrode array (MEA, multichannel systems, 120 electrodes) to monitor the status of the neuronal culture. Each chamber is 250 μm wide, 50 μm high and 1 cm long and with designed outgrowth isolation and directionality (arrow heads). In addition, we propose human iPSC-derived endothelial and/or vascular smooth muscle cell-based vessels-on-chip that can later link neuronal and vascular components. In addition, we will underline the importance of standardized analysis pipelines with, for example, the development of semi-automated software for electrophysiological interpretation of MEA recordings and sensors (e.g. pH) to in detail assess conditions of the cellular models.

Disclosure of Interest: None Declared

IHC23-PO-375

Status of diagnosis and preventative treatment of primary headache disorders in China: a multicenter cross-sectional study

Huanxian Liu[1,2], Wei Gui[3], Kaiming Liu[4], Zhihua Jia[1], Ming Dong[5], Yingying Cheng[5], Yudan Lv[5], Kang Qu[5], Hongru Zhao[6], Jianjun Chen[7], Dan Zhang[8], Zhiliang Fan[9], Xiaosu Yang[10], Dongmei Hu[11], Hongyan Xie[11], Mingxin Li[12], Bing Wen[12], Sufen Chen[13], Peng Xu[14], Qingqing Rong[14], Qiu He[15], Zhanxiu Ren[15], Fanhong Yan[16], Heling Zhao[16], Min Chen[17], Tingmin Yu[18], Hongli Qu[19], Xingkai An[19], Huailian Guo[20], Xinhua Zhang[20], Xiaoping Pan[21], Xiaojuan Wang[21], Shi Qiu[22], Lvming Zhang[22], Hongling Zhao[23], Xin Pan[23], Qi Wan[24], Lanyun Yan[24], Jing Liu[1,2], Zhe Yu[1,2], Mingjie Zhang[1,2], Ye Ran[1,2], Xun Han[1,2], Shengyuan Yu[1,2] and Zhao Dong[1,25]

[1]*Department of Neurology, the First Medical Center of Chinese PLA General Hospital, Beijing, China*
[2]*International Headache Center, Chinese PLA General Hospital, Beijing, China*
[3]*Department of Neurology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China*
[4]*Department of Neurology, Second Affiliated Hospital, School of Medicine, Zhejiang University, Zhejiang, China*
[5]*Department of Neurology and Neuroscience Center, The First Hospital of Jilin University, Jilin, China*
[6]*Department of Neurology, The First Affiliated Hospital of Soochow University, Jiangsu, China*
[7]*Department of Neurology, Lishui Municipal Central Hospital, Zhejiang, China*
[8]*Department of Neurology, Sir Run Run Shaw Hospital, Zhejiang, China*
[9]*Department of Neurology, Xing Tai People's Hospital, Hebei, China*
[10]*Department of Neurology, Xiangya Hospital, Central South University, Hunan, China*
[11]*Department of Neurology, The Second Affiliated Hospital of Shandong First Medical University, Shandong, China*
[12]*Department of Neurology, Qilu Hospital, Shandong, China*
[13]*Department of Neurology, Changsha Central Hospital Affiliated to the University of South China, Hunan, China*
[14]*Department of Neurology, Affiliated Hospital of Jining Medical University, Shandong, China*
[15]*Department of Neurology, The People's Hospital of Liaoning Province, Liaoning, China*
[16]*Department of Neurology, Linyi Jinluo Hospital, Shandong, China*
[17]*Department of Neurology, Zhengzhou University first affiliated Hospital, Henan, China*
[18]*Department of Neurology, The Second Hospital of Jilin University, Jilin, China*
[19]*Department of Neurology, The First Affiliated Hospital of Xiamen University, Jilin, China*
[20]*Department of Neurology, People's Hospital, Peking University, Beijing, China*
[21]*Department of Neurology, Guangzhou First People's Hospital, Guangdong, China*
[22]*Department of Neurology, Aerospace Center Hospital, Beijing, China*
[23]*Department of Neurology, Da Lian Municipal Central Hospital, Liaoning, China*
[24]*Department of Neurology, Jiangsu Province Hospital, Jiangsu, China*
[25]*International Headache Center, Chinese PLA General Hospital, Beijing, China*

Background: Headache disorders are common worldwide and place a considerable economic burden on people and society. Misdiagnosis and under-treatment continue to be major problems worldwide. In the past decade, there is still a lack of assessment of the status of diagnosis and preventative treatment of primary headache disorders in China.

Methods: We analyzed the questions established in the Survey of Fibromyalgia Comorbidity with Headache (SEARCH) study regarding previous diagnoses and preventative treatment of primary headache disorders. This cross-sectional study included adults with primary headache disorders treated at 23 Chinese hospitals from September 2020 to May 2021.

Results: 2,868 participants were included in the analyses. Migraine and tension-type headaches (TTH) account for 74.1% (2,124/2,868) and 23.3% (668/2,868), respectively. 8.1% (231/2,868) of patients with primary headache disorders had a combination of medication overuse headache (MOH). A total of 56.6% (1,624/2,868) of individuals with primary headaches were undiagnosed. The previously reported correct diagnosis for migraine, TTH, TACs, and MOH was 27.3% (580/2,124), 8.1% (54/668), 23.2% (13/56), and 3.5% (8/231), respectively. "Nervous headache" was the most common misdiagnosis among individuals with migraine (9.9%, 211/2,124), TTH (10.0%, 67/668), trigeminal autonomic cephalalgias (TACs; 17.9%, 10/56), and other primary headache disorders (10.0%, 2/20). Only 16.5% (77/468) of individuals with migraine and 4.7% (2/43) with TTH have been previously prescribed preventative medication.

Conclusions: Although the rate of correct diagnosis of primary headache disorders has increased compared to 10 years ago, misdiagnosis and inadequate treatment of primary headaches continue to be major problems in China. More efforts are needed in the future to improve the diagnosis and preventive treatment of primary headache disorders.

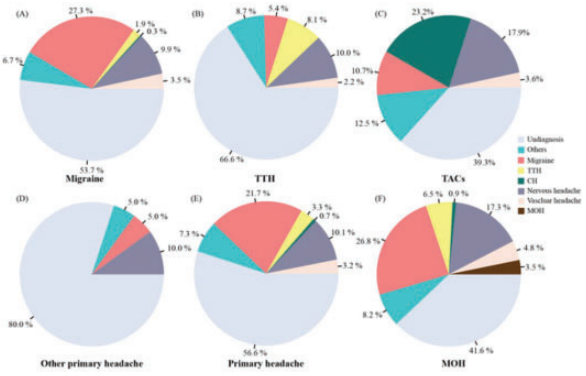

Figure 1. Percentage of previous diagnoses of primary headache disorders and MOH. The cumulative percentage was over 100% due to a patient having multiple previous diagnoses. TTH, tension-type headache; TACs: trigeminal autonomic cephalalgias; CH, cluster headache; MOH: medication overuse headache.

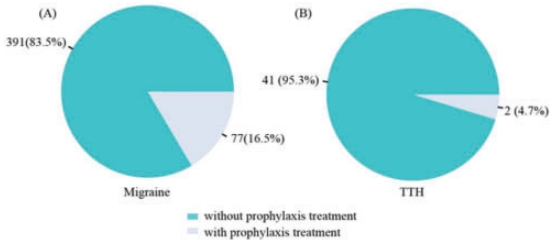

Figure 2. Percentage of previous prophylaxis treatment of migraine (A) and TTH (B). TTH, tension-type headache.

Disclosure of Interest: None Declared

IHC23-PO-376

Headache Code: a protocol to optimize the care of headache patients in the emergency department

Javier A Membrilla[1], Laura Gómez-Dabo[2], Raúl García-Yu[3], Eduardo Mariño[3], Javier Díaz- de-Terán[3], Alicia Alpuente[2] and Patricia Pozo-Rosich[2]

[1]*Hospital Francesc de Borja, Gandía, Spain*
[2]*Hospital Universitario Vall d'Hebron, Barcelona, Spain*
[3]*Hospital Universitario La Paz, Madrid, Spain*

Objective: To design a protocol to optimize the care of patients with headache in the emergency department, facilitating diagnosis and shortening treatment times.
Methods: A narrative literature review was conducted through a MEDLINE search in October 2021 using the terms "headache," "emergency department," "red flags," "treatment," and/or "length of stay."
Results: A flow chart has been designed that includes 3 assessments in the form of scores for the prioritization of care and the establishment of treatment according to the level of emergency. The first two scores are performed in triage. Score 1 aims to identify secondary headaches with high morbidity and mortality, requiring emergency medical attention, using as items vital signs and guiding symptoms of subarachnoid hemorrhage and meningitis (score $\geq$2). If the patient does not score on score 1, score 2 is used, which includes the leading symptoms of migraine status, VAS, and vitals. Scores $\geq$2 are managed as cases suggestive of status migrainosus or other headache with functional limitation and will receive medical attention in a box with decreased environmental stimuli, with symptomatic treatment $<$30 min. Finally, emergency department doctors will use a third score that reviews the remaining "red flags" of secondary headaches to guide the ordering of complementary tests and make a diagnosis.
Conclusions: This protocol can optimize resources and improve the care of patients consulting for headache in the emergency department. The protocol should be validated by comparing it with usual clinical practice.
Disclosure of Interest: None Declared

IHC23-PO-377

Migraine and aura frequency in patients with polycythemia vera and essential thrombocythemia.

Tegan Ake[1], Carson Sautter[1], Jyotika Singh[2], Melissa Cortez[1], Seniha Ozudogru[3], Josef Prchal[1], Brynn Parsegov[1], Cecilia Martindale[1], KC Brennan[1] and Kathleen Digre[1]

[1]*University of Utah, Salt Lake City, USA*
[2]*Cleveland Clinic, Cleveland, USA*
[3]*University of Pennsylvania, Philadelphia, USA*

Background: Polycythemia vera (PV) and essential thrombocythemia (ET) are two myeloproliferative disorders that have been associated with migraine and neurologic manifestations. The mechanism of this susceptibility may be due to microvascular thrombosis and hypoxia, which are both triggers for cortical spreading depression, the mechanism of migraine aura. The objective of the current study was to evaluate the disease burden of migraine and aura in patients with ET and PV.
Study Methods: Study participants were identified from a clinical database containing all patients evaluated in Hematology at the University of Utah over a 5-year period. Inclusion criteria: ICD-10 diagnoses of PV (D45)

and ET (D47.3); ages >18 years old. Exclusion criteria: ICD-10 diagnoses of hypercoagulable conditions such as Factor V Leiden, antithrombin III deficiency, protein C and S deficiency, antiphospholipid syndrome, hyperhomocysteinemia, prothrombin gene mutation, and secondary thrombocythemia, and/or brain tumor.

Qualifying participants were then contacted by phone and offered the opportunity to participate in a telephone survey related to headache history and related symptoms, including a Structured Migraine Interview, Visual Aura Rating Scale (VARS), Headache Impact Test (HIT-6) and Migraine Quality of Life questionnaires. A retrospective chart review was also performed to collect clinical background data (labs, treatments, demographics, and neurologic evaluation).

Results: The database yielded 212 patients who met the criteria for this study. 109 (57%) patients were female, and the average age was 60.2 (range 19–88).

Of the 212 patients, 69 declined to participate or were found to be deceased. Sixty-five patients were unreachable. Seventy-eight participants agreed to participate in the study. Of the 78 patients who agreed to participate in the study, survey data have been completed on 72.

Thirty-eight (52.8%) of these patients reported recurrent headaches and 17 (21.8%) met criteria for migraine (with or without aura); 12 (16.7%) had migraine with aura determined by a VARS score of greater than 5. Mean HIT-6 score was 56.8 (range 36–76), equating with a substantial impact on quality of life. Mean migraine specific QOL scores were 13.9 (range 4–38).

Conclusions: Among survey respondents, consisting of 78 patients with PV or ET, over half reported recurrent headaches. Of these, 23.6% met ICHD-3 based criteria for migraine-type headaches and of those 70.6% had migraine with aura. Notably, these proportions are greater than expected in the general population, where about 12% report migraine, of which about 25% are expected to have aura. These findings imply that patients with PV and ET are at a higher risk of migraine and migraine aura. HIT-6 and migraine specific QOL scores revealed a significant disease burden. These results support proposed theories related to platelet dysfunction in migraine. It is possible that migraine and aura in these patients are overlooked disease markers that could help to guide treatment. Future studies might investigate change in HIT-6 and mQOL scores in response to treatment of patients' underlying hematologic disorder.

Disclosure of Interest: None Declared

IHC23-PO-378

Reliability and Validity of Turkish Version of Mıgraine Interictal Burden Scale-4 (MIBS-4) in Patients with Migraine

Rahşan Karacı[1], Esra Aydın Sünbül[1], Pınar Yalınay Dikmen[2], Elif Ilgaz Aydınlar[2], Fehmi Bilgiç[3], Nevra Öksüz[4], Emel Ur Özçelik[5], Arife Çimen Atalar[5], Semih Taşdelen[6], Esme Ekizoğlu[6], Ezgi Uludüz[7], Derya Uludüz[8], Aynur Özge[9] and Saime Füsun Domaç[10]

[1]*University of Health Sciences Erenköy Psychiatry and Neurological Diseases Training and Research Hospital, istanbul, Turkey*

[2]*Neurology Department, School of Medicine, Acibadem University, istanbul, Turkey*

[3]*Mersin University School of Medicine, neurology Department, Mersin, Turkey*

[4]*Mersin University School of Medicine, Neurology Department, Mersin, Turkey*

[5]*Department of Neurology, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, istanbul, Turkey*

[6]*Department of Neurology, Istanbul Faculty of Medicine, Istanbul University, Çapa, istanbul, Turkey*

[7]*Koç University, School of Medicine, Medical Student, istanbul, Turkey*

[8]*İstanbul University, Cerrahpaşa Faculty of medicine, Neurology department, istanbul, Turkey*

[9]*Department of Neurology, Mersin University Faculty of Medicine, Mersin, Turkey*

[10]*Department of Neurology, University of Health Sciences, Erenkoy Mental Health and Neurological Disorders Training and Research Hospital, İstanbul, Turkey*

Background and Aim: Migraine is described as one of the major causes of disability worldwide. Number of studies on migraine have shown impairment in academic, occupational. social, leisure, and family life leading to a poor quality of life during and between attacks. The aim of this study is to assess reliability and validity of Turkish version of MIBS-4 questionnaire in patients with migraine.

The Migraine Interictal Burden Scale (MIBS-4) measures migraine-related interictal burden in 4 domains related to difficulty in planning at work or school, family and social life, and emotional/affective and cognitive stress. MIBS-4 is a 4-item self-administered questionnaire for clinical use or screening.

Methods: A total of 179 patients with migraine were enrolled in this multicenter, prospective study in two consecutive interviews with 4-week intervals. The comprehensibility, patient-physician reliability, internal consistency, test-test repetition reliability and validity of Turkish translation of MIBS-4 were analyzed.

Results: In terms of clarity of all MIBS-4 questions, a statistically significant agreement was obtained between the patient and the physician (ICC = 0.713; $p < 0.001$, ICC = 0.851; $p < 0.001$, ICC = 0.637; $p < 0.001$, ICC = 0.760; $p < 0.001$).
No statistically significant difference was found between the intelligibility distributions of the 1st, 2nd, 3rd and 4th questions of MIBS-4 according to the patient- administered and the physician-administered interviews (p values were 0.167, 0.068, 0.121, 0.225, respectively).
A significantly very good consistence was obtained between the 1st and 2nd interview values (ICC = 0.891; $p < 0.001$). Cronbach's alpha coefficient was obtained between 0.818 and 0.845, and the scale was obtained with high reliability.
A statistically significant positive correlation was obtained between the 1st and 2nd interview MIBS values and HIT-6, and the correlation coefficients were obtained as 0.158 and 0.330, respectively ($p = 0.036$, $p < 0.001$)
Conclusion: These results demonstrated that the Turkish translation is equivalent to English version of MIBS-4 in terms of internal consistency and it has high test-retest reliability and validity as correlated with HIT-6 scores.

IHC23-PO-379

The extended phenotype of migraine in children and adolescents: a prospective study from a large specialist paediatric headache clinic

Nazia Karsan

King's College London, London, United Kingdom. Great Ormond Street Hospital for Children, London, United Kingdom

Objectives: Non-headache migraine symptoms are considerably less explored in children and young people compared to adults. The migraine phenotype may have differences in this patient group which are not formally recognised in the current International Classification of Headache Disorders (ICHD3). This, and a lack of recognition of the extended migraine phenotype, may lead to diagnostic challenges and delayed management, whereas furthering understanding in this area could promote prompt and effective diagnosis and acute attack management, as well as appreciation of the entirety of migraine-related disability.
We set out to perform prospective systematic phenotyping of patients with migraine presenting to a large tertiary specialist Children's Headache Clinic, to characterise the extended phenotype of paediatric migraine and highlight possible phenotypic differences to adults.

Methods: Consecutive new patients with migraine presenting to the Children's Headache Clinic at Great Ormond Street Hospital for Children between 8th January 2022- 8th February 2023 seen by the authors were included ($n = 105$).
Data was collected prospectively from the first clinical encounter, during which a detailed systematic headache history is taken by a trained headache physician from the child and their parent(s) and/or guardian. Demographic and phenotypic information including age, gender, headache diagnosis, disease duration, gestational age at birth, infantile migraine markers, triggers for attacks and for headache onset including history of head injury, migraine phenotype (including headache laterality, premonitory symptoms (PS), vertigo, allodynia and cranial autonomic symptoms (CAS)), attack duration and preventive use was acquired. Some patient histories at the time of the data capture contained information on migraine postdrome symptoms, and we have been more systematic about capturing such information since.
Data were tabulated and analysed (IBM SPSS v 28). Descriptive statistics, Cohen's kappa (k) measure of agreement and Pearson correlation (r) analyses were used to examine the data. Significance was assessed at $P < 0.01$, as Bonferroni multiple comparison correction was applied for the number of statistical tests performed (5).
Results: Patients were 65% female and aged 5–17 years (median 14, IQR 11–15), with a mean disease duration of 4.7 years (SD 2.8). Baseline monthly headache frequency was 1–30 days (median 30, IQR 12–30). Chronic migraine was the most common diagnosis (55%), and 42% were on migraine preventive therapy. Attack duration varied between 2–168 hours (median 12, IQR 5–72). The majority (81%) had bilateral headache and 34% could identify a potential trigger associated with migraine onset. Aura was present in 41% (49% visual, 30% mixed, 7% sensory, 7% hemiplegic and 7% brainstem). At least one infantile migraine marker was present in 65%, with travel sickness (58%) and colic (52%) being the most common. At least one PS was reported by 93% (range 0–7; of which mood change, tiredness and concentration difficulty were the most common), at least one CAS by 58% (range 0–6; of which pallor, lacrimation and flushing were the most common) and premonitory CAS by 23%. Vertigo (53%; 39% external, 23% internal, 4% mixed and 34% unclassified) and craniofacial allodynia (16%; one patient reported this as a PS) were also reported. The most common perceived migraine triggers were stress, bright lights and loud sounds. The laterality of headache and CAS showed moderate agreement ($k = 0.5$, $P < 0.001$). Vertigo and allodynia showed slight agreement ($k = 0.2$, $P = 0.009$). Information on postdrome symptoms was present in 62% (malaise, concentration difficulty, anorexia, thirst and cravings were the most commonly reported). There was a positive correlation ($r = 0.36$, $P < 0.001$) between disease duration

and number of PS. There was slight agreement between the perception of loud sounds as a migraine trigger and attack-related phonophobia ($k = 0.2$, $P = 0.002$).

Conclusion: The extended paediatric migraine phenotype includes several non-canonical migraine symptoms including PS, CAS, vertigo and allodynia. Paediatric PS may be more limbic in phenotype compared to sensory in adults. The paediatric postdrome needs to be further evaluated for prevalence and phenotype. CAS tend to lateralise with headache and despite generally shorter headache durations in this group, should not deter from a migraine diagnosis. There is a suggestion of a more enriched PS phenotype with disease chronicity, and non-headache migraine manifestations may co-exist in the same individual. The perception of loud sounds as a trigger may be the misattribution of attack-related phonophobia. Further systematic evaluation of similar potential trigger-symptom associations in larger samples is required.

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Author Index

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2023, Vol. 43(1S) 334–361

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(continued)

Continued

Author name	Program Codes
	IHC23-PO-199
	IHC23-PO-344
	IHC23-PO-347
	IHC23-PO-359
Amirguliyev, Sarkhan	IHC23-OR-014
	IHC23-PO-197
	IHC23-PO-344
Amores, Fred	IHC23-PO-265
An, Xingkai	IHC23-PO-375
Ancochea, Julio	IHC23-PO-078
Andreou, Anna	IHC23-PO-156
	IHC23-PO-171
	IHC23-PO-173
	IHC23-PO-221
Andrini, Giorgia	IHC23-PO-249
Aninditha, Tiara	IHC23-PO-122
	IHC23-PO-253
Anizon, Fabrice	IHC23-PO-154
Ann, So-Ei	IHC23-PO-245
Antoniou, Anastasia S	IHC23-PO-103
Anukoolwittaya, Prakit	IHC23-PO-024
	IHC23-PO-027
	IHC23-PO-109
	IHC23-PO-307
Apostolakopoulou, Loukia	IHC23-OR-007
Arakawa, Ichiro	IHC23-PO-028
Araki, Nobuo	IHC23-PO-320
Aranceta, Sonsoles	IHC23-DP-015
	IHC23-PO-278
Aranyi, Csaba Sándor	IHC23-PO-187
Aranzeta, Sonsoles	IHC23-PO-279
Argyriou, Andreas A	IHC23-PO-103
	IHC23-PO-268
Artemieva, Daria	IHC23-PO-317
Artola, Alain	IHC23-PO-154
Arı, Buse Cagla	IHC23-PO-141
Asawavichienjinda, Thanin	IHC23-PO-050
Ashina, Håkan	IHC23-PO-120
	IHC23-PO-198
	IHC23-PO-199
	IHC23-PO-347
Ashina, Messoud	IHC23-DP-018
	IHC23-DP-038
	IHC23-DP-040
	IHC23-OR-002
	IHC23-OR-014
	IHC23-PO-120
	IHC23-PO-130
	IHC23-PO-131
	IHC23-PO-136
	IHC23-PO-137
	IHC23-PO-197
	IHC23-PO-198
	IHC23-PO-199
	IHC23-PO-229

(continued)

Continued

Author name	Program Codes
Ashina, Sait	IHC23-IND-002
	IHC23-IND-013
	IHC23-PO-132
	IHC23-PO-270
Ashraf, Usman	IHC23-PO-108
	IHC23-PO-319
Asskour, Laila	IHC23-PO-080
Atalar, Arife Çimen	IHC23-OR-007
	IHC23-PO-141
	IHC23-PO-294
	IHC23-PO-371
	IHC23-PO-378
Atasoy, Huseyin Tugrul	IHC23-PO-340
Athukorala, A D P	IHC23-PO-346
Aurilia, Cinzia	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261
	IHC23-PO-273
Aurora, Sheena	IHC23-PO-217
Avino, Gianluca	IHC23-PO-182
Aydın Sünbül, Esra	IHC23-OR-010
	IHC23-PO-378
Ayton, Sarah	IHC23-IND-006
Azimova, Julia	IHC23-PO-276
Azuma, Yasuhiro	IHC23-PO-116
Babe, Emma Anastasie	IHC23-PO-052
Bacila, Ana	IHC23-PO-194
	IHC23-PO-196
Bae, Dae-Woong	IHC23-OR-008
	IHC23-PO-020
	IHC23-PO-035
Baek, Hye-Kyung	IHC23-PO-295
Baek, Jang-Hyun	IHC23-PO-245
Bagdy, Gyorgy	IHC23-PO-013
	IHC23-PO-187
Bai, Xiaoyan	IHC23-PO-179
	IHC23-PO-180
	IHC23-PO-181
	IHC23-PO-299
Baker, Josephine	IHC23-PO-104
	IHC23-PO-224
	IHC23-PO-225
Baker, Sarah	IHC23-PO-356
Baksa, Daniel	IHC23-PO-013
	IHC23-PO-185
Banasik, Karina	IHC23-PO-069
Barash, Steve	IHC23-IND-009
Barbanti, Piero	IHC23-IND-014
	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261

(continued)

Continued

Author name	Program Codes
	IHC23-PO-273
Barloese, Mads	IHC23-PO-045
Barral, Eliseo	IHC23-DP-013
Bartezaghi, Marta	IHC23-PO-271
Bartolini, Marco	IHC23-PO-016
	IHC23-PO-273
Bartolome, Carla Vianca	IHC23-PO-208
Batista, Sávio	IHC23-PO-281
Battucci, Simona	IHC23-PO-264
Baumann, Jil	IHC23-PO-316
Bayar Narin, Dilan	IHC23-PO-340
Baydina, Ekaterina	IHC23-PO-220
Baykan, Betül	IHC23-DP-009
	IHC23-OR-007
	IHC23-PO-053
	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-256
	IHC23-PO-294
	IHC23-PO-371
Bayramoglu, Banu	IHC23-PO-100
Beaulieu, Claudie	IHC23-PO-155
Bebek, Nerses	IHC23-PO-053
Becker Ifantides, Kim	IHC23-PO-264
Begasse de Dhaem, Olivia	IHC23-OR-009
	IHC23-PO-138
Beier, Dagmar	IHC23-OR-006
Beiersdorf, Johannes	IHC23-PO-190
Belopasova, Anastasia	IHC23-PO-220
Belvis, Robert	IHC23-PO-280
Ben Sassi, Samia	IHC23-PO-344
Bendtsen, Lars	IHC23-PO-353
Bertuzzo, Davide	IHC23-PO-016
	IHC23-PO-260
Bezerra, Daniel	IHC23-PO-212
Bharadwaj, Vimala	IHC23-DP-033
Bighiani, Federico	IHC23-DP-023
	IHC23-JT-003
	IHC23-JT-005
	IHC23-PO-230
Bilgiç, Fehmi	IHC23-PO-061
	IHC23-PO-378
Bilias, Konstantinos	IHC23-PO-103
Blatchley, Chris	IHC23-PO-277
Bloemhof, Mirthe M	IHC23-PO-364
Blumenfeld, Andrew	IHC23-IND-004
	IHC23-IND-015
	IHC23-PO-264
Bolay, Hayrunnisa	IHC23-OR-007
	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-141
	IHC23-PO-157
	IHC23-PO-294
Bolchini, Marco	IHC23-PO-266

(continued)

Continued

Author name	Program Codes
	IHC23-PO-267
Bonamico, Lucas	IHC23-PO-269
Bonassi, Stefano	IHC23-PO-014
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261
	IHC23-PO-273
Bondone, Claudia	IHC23-PO-090
Bono, Francesco	IHC23-PO-260
	IHC23-PO-273
Bonuccelli, Alice	IHC23-PO-090
Boon, Mariëtte R	IHC23-PO-023
Borrello, Laura	IHC23-PO-251
	IHC23-PO-273
Bose, Pyari	IHC23-PO-178
Bose, Ray	IHC23-OR-004
Bose, Rohini	IHC23-PO-252
Boserup, Line Pickering	IHC23-DP-040
	IHC23-PO-229
Bostic, Ryan C	IHC23-PO-284
Bottiroli, Sara	IHC23-OR-013
	IHC23-PO-352
Boucherie, Deirdre M	IHC23-DP-004
Boyacıoğlu, Hayal	IHC23-PO-124
	IHC23-PO-125
Brancaccio, Carla	IHC23-PO-230
Brandt, Roemer	IHC23-PO-021
Bravo, Alba	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Bravo, Yasmin	IHC23-PO-269
Brekke, Ole-Lars	IHC23-PO-068
Brennan, KC	IHC23-PO-377
Breukel, Cor	IHC23-PO-169
Brin, Mitchell	IHC23-DP-041
Briode, Ron	IHC23-DP-041
Broadhurst, Sarah	IHC23-PO-258
Broessner, Gregor	IHC23-PO-255
	IHC23-PO-275
Brunak, Søren	IHC23-PO-069
	IHC23-PO-353
Bruun, Mie Topholm	IHC23-PO-069
Buchholz, David	IHC23-DP-002
Budrewicz, Sławomir	IHC23-PO-353
Burgdorf, Kristoffer S	IHC23-PO-069
Burish, Mark	IHC23-DP-044
Burstein, Rami	IHC23-DP-041
	IHC23-PO-347
Buse, Dawn C	IHC23-DP-011
	IHC23-DP-043
	IHC23-IND-001
	IHC23-IND-002
	IHC23-IND-003
	IHC23-PO-132
	IHC23-PO-142

(continued)

Continued

Author name	Program Codes
	IHC23-PO-270
Buture, Alina	IHC23-PO-236
	IHC23-PO-285
Buysman, Erin	IHC23-IND-010
	IHC23-IND-011
Bömers, Jesper Peter	IHC23-PO-162
Cadiou, Francois	IHC23-PO-009
Cafer, Vugar	IHC23-PO-139
Cagla Ari, Buse	IHC23-PO-340
Cagol, Alessandro	IHC23-PO-198
Cakir, Seda	IHC23-PO-063
Calabresi, Paolo	IHC23-PO-075
	IHC23-PO-123
Calderaro, Marcelo	IHC23-PO-212
Calistri, Lucia	IHC23-PO-090
Callesen, Ida	IHC23-PO-069
Calvo, Daniela	IHC23-PO-269
Calzada, María José	IHC23-PO-078
Camara, Mory M	IHC23-PO-344
Camarda, Cecilia	IHC23-PO-016
	IHC23-PO-251
Camiña Muñiz, Javier	IHC23-PO-262
Cammarota, Francescantonio	IHC23-DP-023
	IHC23-JT-005
	IHC23-PO-230
Campoy, Sergio	IHC23-PO-280
Can, Ayşe İrem	IHC23-PO-139
	IHC23-PO-141
Canbaloglu, Kubra	IHC23-PO-201
Canella, Mattia	IHC23-PO-231
Cantello, Roberto	IHC23-PO-182
Cao, Feng	IHC23-IND-010
	IHC23-IND-011
Cao, Xiangqi	IHC23-PO-193
Capriglia, Elena	IHC23-DP-023
Caratozzolo, Salvatore	IHC23-PO-266
Carmine Belin, Andrea	IHC23-PO-022
	IHC23-PO-044
Carneiro Junior, José Luiz	IHC23-PO-212
Carnevale, Antonio	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-260
	IHC23-PO-261
Caronna, Edoardo	IHC23-PO-080
Carr, Karen	IHC23-PO-282
Carvalho, João José	IHC23-PO-212
Casillo, Francesco	IHC23-DP-024
	IHC23-JT-004
	IHC23-PO-361
Castellazzi, Gloria	IHC23-PO-194
	IHC23-PO-196
Castiglia, Stefano Filippo	IHC23-PO-361
Castonguay, William	IHC23-PO-170
Cattaneo, Federica	IHC23-PO-182
Cavanzo, Paula	IHC23-PO-235

(continued)

Continued

Author name	Program Codes
Ceccardi, Giulia	IHC23-PO-266
	IHC23-PO-267
Celebisoy, Nese	IHC23-PO-256
Cerrahoglu Şirin, Tuba	IHC23-PO-053
Cerri, Silvia	IHC23-DP-023
Cetingok, Halil	IHC23-PO-110
Cetta, Ilaria	IHC23-PO-242
	IHC23-PO-271
Cevoli, Sabina	IHC23-PO-030
	IHC23-PO-242
	IHC23-PO-249
	IHC23-PO-260
	IHC23-PO-261
Cha, Yong Sung	IHC23-PO-005
Chai-Adisaksopha, Chatree	IHC23-PO-114
Chaimano, Siwahdol	IHC23-PO-114
Chalermpalanupap, Natty	IHC23-PO-282
Chalmer, Mona Ameri	IHC23-DP-031
	IHC23-PO-069
Chandra, Avinash	IHC23-PO-119
Chandra, Ayush	IHC23-PO-119
Charles, Andrew	IHC23-PO-134
Charleston IV, Larry	IHC23-IND-004
Charoensri, Koth	IHC23-PO-113
Chaudhry, Basit Ali	IHC23-PO-347
	IHC23-PO-359
Cheema, Sanjay	IHC23-DP-025
	IHC23-PO-296
	IHC23-PO-303
	IHC23-PO-304
	IHC23-PO-323
Chen, Chih-Chiang	IHC23-PO-343
Chen, Chunfu	IHC23-PO-046
Chen, Hung-Chieh	IHC23-DP-014
Chen, Jian-Bang	IHC23-JT-002
Chen, Jianjun	IHC23-PO-375
Chen, Keren	IHC23-PO-134
Chen, Min	IHC23-PO-375
Chen, Shih-Pin	IHC23-DP-008
	IHC23-JT-002
	IHC23-PO-033
	IHC23-PO-056
	IHC23-PO-088
	IHC23-PO-127
	IHC23-PO-149
	IHC23-PO-177
	IHC23-PO-188
	IHC23-PO-189
	IHC23-PO-298
	IHC23-PO-315
	IHC23-PO-337
Chen, Shu-Ting	IHC23-OR-012
	IHC23-PO-033
Chen, Sufen	IHC23-PO-034
	IHC23-PO-375

(continued)

Continued

Author name	Program Codes
Chen, Wei-Hung	IHC23-DP-012
	IHC23-PO-087
Chen, Wei-Ta	IHC23-PO-033
	IHC23-PO-088
	IHC23-PO-149
	IHC23-PO-298
	IHC23-PO-337
Chen, Xiaoyan	IHC23-PO-034
Chen, Yi-Hao	IHC23-PO-298
Chen, Yun-Ning	IHC23-JT-002
Chen, Zheng	IHC23-DP-044
Cheng, Roger	IHC23-PO-001
	IHC23-PO-083
	IHC23-PO-086
Cheng, Shuli	IHC23-PO-234
	IHC23-PO-235
Cheng, Yingying	IHC23-PO-375
Cheng, Yu	IHC23-PO-009
Cheng, Yu-Chen	IHC23-PO-133
Cherchi, Rossella	IHC23-PO-016
Chessell, Iain	IHC23-PO-247
Chessell, Tharani	IHC23-PO-247
Cheung, Sing Ngai	IHC23-PO-032
Chi, Nai-Fang	IHC23-PO-189
Chiang, Chia-Chun	IHC23-OR-012
	IHC23-PO-009
Chiang, Jeremy Chung Bo	IHC23-PO-079
Chiou, Lih-Chu	IHC23-DP-034
Cho, Joong-Yang	IHC23-PO-140
Cho, Soo-Jin	IHC23-DP-003
	IHC23-OR-008
	IHC23-PO-018
	IHC23-PO-019
	IHC23-PO-020
	IHC23-PO-035
	IHC23-PO-060
	IHC23-PO-115
	IHC23-PO-243
	IHC23-PO-310
	IHC23-PO-327
Cho, Soohyun	IHC23-PO-020
	IHC23-PO-035
	IHC23-PO-174
	IHC23-PO-246
	IHC23-PO-314
	IHC23-PO-329
Cho, Soomi	IHC23-PO-084
	IHC23-PO-205
	IHC23-PO-358
Choi*, So Youn	IHC23-PO-315
Choi, Seungjin	IHC23-PO-338
Choi, So Youn	IHC23-PO-308
	IHC23-PO-341

(continued)

Continued

Author name	Program Codes
Choi, Yun-Ju	IHC23-OR-008
	IHC23-PO-035
Chou, Shao-Kai	IHC23-DP-034
Chowdhury, Debashish	IHC23-DP-028
	IHC23-JT-006
Chowdhury, Samiran	IHC23-PO-146
Christensen, Casper Emil	IHC23-OR-002
Christensen, Rune H	IHC23-PO-120
	IHC23-PO-198
	IHC23-PO-199
	IHC23-PO-347
Christensen, Sarah Louise	IHC23-DP-006
	IHC23-PO-045
Christiansen, Isabella Mai	IHC23-PO-160
Christoforou, Konstantinos	IHC23-PO-257
	IHC23-PO-265
Christophilos, Savvas	IHC23-PO-221
Chu, Min Kyung	IHC23-DP-003
	IHC23-OR-008
	IHC23-PO-018
	IHC23-PO-020
	IHC23-PO-035
	IHC23-PO-047
	IHC23-PO-084
	IHC23-PO-205
	IHC23-PO-243
	IHC23-PO-310
	IHC23-PO-327
	IHC23-PO-358
Chu, Yung-Hua	IHC23-PO-343
Chunfu, Chen	IHC23-PO-369
Chung, Chin-Sang	IHC23-PO-035
Chung, Jae Myun	IHC23-OR-008
	IHC23-PO-035
Chung, Pil-Wook	IHC23-OR-008
	IHC23-PO-035
	IHC23-PO-038
	IHC23-PO-245
Coelho, Mariana	IHC23-PO-055
Colombo, Bruno	IHC23-PO-242
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-271
Cook, James	IHC23-DP-034
Coppola, Alfonso	IHC23-PO-016
Coppola, Gianluca	IHC23-DP-024
	IHC23-JT-004
	IHC23-PO-361
Cordelli, Duccio Maria	IHC23-PO-090
Corrado, Michele	IHC23-DP-023
	IHC23-JT-005
	IHC23-PO-230
Cortez, Melissa	IHC23-PO-377

(continued)

Continued

Author name	Program Codes
Crema, Santiago	IHC23-PO-269
Cremascoli, Riccardo	IHC23-DP-023
Cuadrado, Elisa	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
	IHC23-PO-287
Cuadrado, María-Luz	IHC23-PO-039
	IHC23-PO-041
Cullum, Christopher Kjaer	IHC23-PO-359
Czapińska-Ciepiela, Ewa K	IHC23-PO-353
D'Alonzo, Renato	IHC23-PO-090
D'Amico, Domenico	IHC23-PO-263
D'Onofrio, Florindo	IHC23-PO-016
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261
	IHC23-PO-273
d'Onofrio, Luigi	IHC23-PO-251
da Silva Borges, Gisela	IHC23-PO-154
	IHC23-PO-155
Dabruzzo, Brett	IHC23-DP-041
	IHC23-DP-043
	IHC23-IND-002
	IHC23-PO-132
	IHC23-PO-142
Dahlgren, Anna	IHC23-PO-044
Dai, Wei	IHC23-OR-011
Daković, Marko	IHC23-PO-176
Dalldorf, Lara K	IHC23-DP-032
Dallel, Radhouane	IHC23-PO-154
	IHC23-PO-155
Dammers, Ruben	IHC23-DP-004
Danciu, Theodora	IHC23-PO-291
Danno, Daisuke	IHC23-PO-066
	IHC23-PO-206
	IHC23-PO-244
Danser, A H Jan	IHC23-DP-004
	IHC23-DP-026
	IHC23-OR-003
Dantas, Julyana M	IHC23-PO-281
Dantes, Miriam Catherine Bernal	IHC23-PO-357
Dardiotis, Efthymios	IHC23-PO-081
DaSilva, Alexandre	IHC23-PO-191
	IHC23-PO-290
	IHC23-PO-291
Davaasuren, Bolortsetseg	IHC23-PO-366
Davagnanam, Indran	IHC23-DP-025
	IHC23-PO-323
David, Lisa	IHC23-PO-143
Davidsson, Olafur	IHC23-PO-069
Davletov, Bazbek	IHC23-PO-156
Davídsson, Ólafur Birgir	IHC23-PO-353
Dawson, Angelina M	IHC23-DP-032
De Abreu Ferreira, Rosa	IHC23-DP-042
De Alwis, Shanindra	IHC23-PO-313

(continued)

Continued

Author name	Program Codes
de Boer, Irene	IHC23-PO-076
	IHC23-PO-138
	IHC23-PO-200
De Icco, Roberto	IHC23-DP-023
	IHC23-JT-005
	IHC23-OR-013
	IHC23-PO-194
	IHC23-PO-196
	IHC23-PO-230
	IHC23-PO-352
De la Fuente, Hortensia	IHC23-PO-077
	IHC23-PO-078
De los Santos, Ignacio	IHC23-PO-078
de Luis-García, Rodrigo	IHC23-PO-186
	IHC23-PO-202
de Ruijter, Joëlle E.T	IHC23-PO-239
De Simone, Roberto	IHC23-PO-016
de Vries, Tessa	IHC23-DP-026
Dehal, Yahya	IHC23-PO-344
Del Campo Guerola, Luciana	IHC23-PO-078
Del Corso, Benedetta	IHC23-PO-263
Delahaye, Laurent	IHC23-PO-131
Deligianni, Christina	IHC23-OR-002
	IHC23-OR-014
	IHC23-PO-221
	IHC23-DP-035
Delima-Tchombe, Paule-Rose	IHC23-PO-091
	IHC23-PO-092
Delroasario, Helen	IHC23-PO-286
Dengfa, Zhao	IHC23-PO-369
Denysenko, Lex	IHC23-IND-014
Deorari, Vaibhav	IHC23-DP-028
Dermitzakis, Emmanouil	IHC23-PO-081
	IHC23-PO-103
	IHC23-PO-268
Descheemaeker, Amélie	IHC23-PO-154
Devcic, Zlatko	IHC23-PO-297
Dewhurst, Stephen	IHC23-DP-002
Dhurjati, Rupasvi	IHC23-PO-008
Di Clemente, Laura	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-260
Di Fiore, Paola	IHC23-PO-260
	IHC23-PO-273
Di Lorenzo, Cherubino	IHC23-DP-024
	IHC23-JT-004
	IHC23-PO-361
Di Nardo, Giovanni	IHC23-PO-090
Di Pasquale, Michele	IHC23-PO-266
	IHC23-PO-267
Di Puccio-Sicuteri, Leonardo	IHC23-PO-144
Diamante, Pearl Angeli	IHC23-PO-204
Dickerson, Ian	IHC23-OR-001
Didriksen, Maria	IHC23-PO-069
Digre, Kathleen	IHC23-PO-377

(continued)

Continued

Author name	Program Codes
Ding, Jing	IHC23-PO-332
Dinh, Khoa Manh	IHC23-PO-069
Dipasquale, Ottavia	IHC23-OR-004
DiPuccio-Sicuteri, Leonardo	IHC23-DP-005
Disse, Leah	IHC23-PO-373
Do, Thien Phu	IHC23-DP-018
	IHC23-OR-014
	IHC23-PO-007
	IHC23-PO-130
	IHC23-PO-359
Dobos, Dora	IHC23-PO-185
Dobrynina, Larisa	IHC23-PO-220
Dodd-Glover, Freda	IHC23-PO-368
Dodick, David W	IHC23-OR-009
	IHC23-PO-009
	IHC23-PO-347
	IHC23-IND-007
	IHC23-IND-012
Domaç, Saime Füsun	IHC23-PO-378
Domi, Ferid	IHC23-PO-322
Domingues, Renand	IHC23-PO-212
Dong, Ming	IHC23-PO-375
Dong, Zhao	IHC23-OR-011
	IHC23-PO-017
	IHC23-PO-046
	IHC23-PO-165
	IHC23-PO-166
	IHC23-PO-375
Dongfang, Li	IHC23-PO-369
Dongjun, Wan	IHC23-PO-369
Donmez-Demir, Buket	IHC23-PO-163
Doretti, Alberto	IHC23-PO-273
Dorricott, Nicholas	IHC23-PO-170
Doumbe, Jacques	IHC23-PO-091
	IHC23-PO-092
Doyle Strauss, Lauren	IHC23-PO-143
Drago, Flavia	IHC23-PO-090
Drakoulis, Nikolaos	IHC23-PO-081
Dreier, Jens P	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
	IHC23-PO-190
Duan, Molly	IHC23-IND-006
	IHC23-PO-274
Ducros, Anne	IHC23-PO-315
Duet, Mary	IHC23-PO-143
Duflos, Claire	IHC23-PO-315
Duggal, Ashish	IHC23-DP-028
Duggal, Ashishkumar	IHC23-JT-006
Duong, Thomas	IHC23-PO-170
Dupont-Benjamin, Laure	IHC23-PO-274
Dussol, Manon	IHC23-PO-155
Dylander, August	IHC23-DP-018
Díaz Córdova, José Andrés	IHC23-PO-350
Díaz Insa, Samuel	IHC23-PO-280

(continued)

Continued

Author name	Program Codes
Díaz-de-Terán, Javier	IHC23-PO-039
	IHC23-PO-041
	IHC23-PO-376
Dømgaard, Mikala	IHC23-DP-018
	IHC23-PO-130
Echavarria Iñiguez, Ana	IHC23-PO-279
Echeberria, Amaya	IHC23-PO-279
Echeverria, Amaya	IHC23-DP-015
	IHC23-PO-278
Edress, Mohamed	IHC23-PO-071
Edvinsson, Lars	IHC23-PO-160
	IHC23-PO-162
Egeo, Gabriella	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261
	IHC23-PO-273
Eiros Bouza, José María	IHC23-PO-128
Ekizoğlu, Esme	IHC23-DP-009
	IHC23-OR-007
	IHC23-PO-053
	IHC23-PO-378
El sahly, Rabha Ali	IHC23-PO-344
Eliaçık, Sinan	IHC23-PO-141
Emri, Miklós	IHC23-PO-187
Enkhtaivan, Tamir	IHC23-PO-349
Erdogan Soyukibar, Tuba	IHC23-PO-201
	IHC23-PO-254
	IHC23-PO-256
Ergen, Mehmet	IHC23-PO-201
Ergin Toktas, Hayal	IHC23-PO-256
Ergin, Nesrin	IHC23-PO-141
	IHC23-PO-340
Erikstrup, Christian	IHC23-PO-069
Ernstsen, Charlotte	IHC23-DP-006
Ertas, Elif	IHC23-PO-139
Ertaş, Mustafa	IHC23-OR-007
	IHC23-PO-063
	IHC23-PO-256
Ertugrul Mut, Senem	IHC23-PO-340
Erwin Wells, Rebecca	IHC23-PO-143
Esparcia, Laura	IHC23-PO-078
Essomba, Emmanuel	IHC23-PO-092
Estebas, Carlos	IHC23-PO-039
Ettrup, Anders	IHC23-DP-038
	IHC23-DP-040
Evlice, Ahmet	IHC23-PO-129
Eyupoglu, Sevim	IHC23-PO-139
Fabregat, Neus S	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Falsaperla, Raffaele	IHC23-PO-090
Faming, Wang	IHC23-PO-369
Fan, Zhiliang	IHC23-PO-375

(continued)

Continued

Author name	Program Codes
Fang, Xuemin	IHC23-PO-009
Fanhong, Yan	IHC23-PO-369
Fanning, Kristina	IHC23-DP-043
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	IHC23-IND-002
	IHC23-IND-003
	IHC23-PO-132
	IHC23-PO-142
	IHC23-PO-284
Faro, Scott	IHC23-PO-203
Favoni, Valentina	IHC23-PO-016
	IHC23-PO-030
	IHC23-PO-235
	IHC23-PO-242
	IHC23-PO-249
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Fengbo, Xie	IHC23-PO-369
Ferilli, Michela Ada Noris	IHC23-PO-097
	IHC23-PO-098
	IHC23-PO-101
Fernandes, Catarina	IHC23-PO-055
	IHC23-PO-289
Fernandes, Linford	IHC23-PO-265
Fernandez Fernandez, Santiago	IHC23-PO-279
Fernandez, Marc Laurence	IHC23-PO-357
Fernandez-Fernandez, Santiago	IHC23-DP-015
	IHC23-PO-278
Fernández-Lázaro, Iris	IHC23-PO-078
Ferrarese, Carlo	IHC23-PO-117
	IHC23-PO-231
Ferrari, Michel	IHC23-PO-021
Ferro, Valentina	IHC23-PO-090
Fierz, Fabienne	IHC23-PO-373
Figueroa, Alexandra	IHC23-PO-279
Filali, Yassine	IHC23-DP-037
Filippi, Massimo	IHC23-PO-242
	IHC23-PO-260
	IHC23-PO-271
	IHC23-PO-273
Finkelstein, Ian	IHC23-PO-235
Finnegan, Michelle	IHC23-DP-019
	IHC23-DP-042
	IHC23-IND-007
Finocchi, Cinzia	IHC23-PO-251
	IHC23-PO-260
Fiorentini, Giulia	IHC23-PO-014
	IHC23-PO-016
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Fitzek, Mira Pauline	IHC23-PO-048
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	IHC23-PO-051
Flinn, Harold	IHC23-PO-170
Fogang-Fogoum, Yannick	IHC23-PO-092
Foiadelli, Thomas	IHC23-PO-090
Forde, Grace	IHC23-PO-264
Forrester, Lewis M	IHC23-DP-032
Forte, Jason	IHC23-PO-363
Fortini, Ida	IHC23-PO-336
Foster, Emma	IHC23-PO-108
Fox, Janosch	IHC23-PO-031
Franklin, Brooke	IHC23-PO-059
Frattale, Ilaria	IHC23-PO-095
	IHC23-PO-101
Frediani, Fabio	IHC23-PO-016
	IHC23-PO-260
Frejvall, Ulf	IHC23-PO-233
Friedman, Benjamin W	IHC23-PO-284
Frimat, Jean-Philippe	IHC23-PO-374
Fronczek, Rolf	IHC23-PO-021
	IHC23-PO-023
Fuh, Jong-Ling	IHC23-DP-008
	IHC23-PO-033
	IHC23-PO-088
	IHC23-PO-177
	IHC23-PO-189
	IHC23-PO-298
	IHC23-PO-337
Fujii, Akihiro	IHC23-DP-001
Fujita, Hiroaki	IHC23-PO-237
Fujita, Shugo	IHC23-PO-219
Fukazawa, Ryosuke	IHC23-DP-001
Gabilondo, Hugo	IHC23-IND-017
Gabrie, Ligia	IHC23-PO-078
Gago-Veiga, Ana Beatriz	IHC23-PO-039
	IHC23-PO-041
	IHC23-PO-077
	IHC23-PO-262
Gai, Annalisa	IHC23-PO-014
	IHC23-PO-273
Galambos, Attila	IHC23-PO-185
Galic, Maja	IHC23-IND-014
Gallardo, Víctor J	IHC23-PO-080
Gams Massi, Daniel	IHC23-PO-052
Gandhi, Pranav	IHC23-DP-019
	IHC23-IND-006
	IHC23-IND-012
	IHC23-PO-274
Gantenbein, Andreas	IHC23-PO-292
García-Azorín, David	IHC23-PO-077
	IHC23-DP-017
	IHC23-PO-128
	IHC23-PO-186
	IHC23-PO-202
	IHC23-PO-262
	IHC23-PO-287
	IHC23-DP-015
	IHC23-OR-007

(continued)

(continued)

Continued

Author name	Program Codes
	IHC23-PO-138
	IHC23-PO-150
	IHC23-PO-278
	IHC23-PO-279
	IHC23-PO-283
Garcia-Monco, Juna Carlos	IHC23-PO-278
	IHC23-PO-279
	IHC23-DP-015
García López, David	IHC23-PO-183
García Ull, Jessica	IHC23-PO-183
García-Yu, Raúl	IHC23-PO-376
Garelja, Michael	IHC23-PO-153
	IHC23-PO-185
Garelja, Michael L	IHC23-DP-020
	IHC23-DP-032
Gascón Giménez, Francisco	IHC23-PO-183
Gasperi, Marianna	IHC23-PO-059
Gaul, Charly	IHC23-DP-016
	IHC23-PO-031
	IHC23-PO-238
	IHC23-PO-255
	IHC23-PO-275
Ge, Zhaoli	IHC23-PO-034
Gecse, Kinga	IHC23-PO-012
	IHC23-PO-013
	IHC23-PO-185
	IHC23-PO-187
Gelener, Pınar	IHC23-PO-340
Genç, Hamit	IHC23-OR-007
	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-141
	IHC23-PO-294
	IHC23-PO-344
Gendolla, Astrid	IHC23-DP-038
Gendron, Louis	IHC23-PO-155
Genovese, Federica	IHC23-PO-242
Gens, Helena	IHC23-PO-055
George, BA, Alexis	IHC23-PO-284
Gerontology Students, Istanbul	IHC23-PO-124
Gesoğlu Demir, Tülin	IHC23-PO-141
	IHC23-PO-340
Ghadri-Sani, Mona	IHC23-PO-258
Ghezzi, Cristina	IHC23-DP-023
Ghiotto, Natascia	IHC23-OR-013
	IHC23-PO-230
Ghouri, Reza	IHC23-PO-057
	IHC23-PO-061
Giannini, Giulia	IHC23-PO-030
Gil Gimeno, Rosario	IHC23-PO-183
Gil Luque, Sendo	IHC23-PO-279
Giossi, Riccardo	IHC23-PO-231
Gioè, Daniela	IHC23-PO-090
GIPMER, Headache Group	IHC23-JT-006
Giusti, Lorenzo	IHC23-PO-030

(continued)

Continued

Author name	Program Codes
Glover, Sophie	IHC23-DP-025
Goadsby, Peter J	IHC23-IND-007
	IHC23-PO-025
	IHC23-PO-026
	IHC23-PO-131
	IHC23-PO-032
	IHC23-PO-151
	IHC23-PO-178
	IHC23-PO-257
	IHC23-PO-265
	IHC23-PO-293
	IHC23-OR-004
	IHC23-DP-013
Godoi, Amanda	IHC23-PO-281
Goebel, Hartmut	IHC23-PO-238
Goicochea, Maria Teresa	IHC23-PO-138
	IHC23-PO-269
Gong, Zihua	IHC23-JT-001
	IHC23-PO-152
	IHC23-PO-166
Gonzalez-Martinez, Alicia	IHC23-PO-077
	IHC23-PO-078
González, Andrea	IHC23-PO-073
González-García, Nuria	IHC23-PO-039
	IHC23-PO-041
González-Martínez, Alicia	IHC23-PO-039
	IHC23-PO-041
González-Osorio, Yésica	IHC23-DP-017
	IHC23-PO-077
	IHC23-PO-128
	IHC23-PO-186
	IHC23-PO-262
	IHC23-PO-279
	IHC23-PO-287
González-Quintanilla, Vicente	IHC23-PO-073
	IHC23-PO-074
	IHC23-PO-262
González-Álvaro, Isidoro	IHC23-PO-078
Gooch, Reid	IHC23-PO-203
Goodbourn, Patrick	IHC23-PO-363
Gooddy, Benjamin	IHC23-OR-004
Gorbacheva, Nina	IHC23-PO-089
Gori, Bendetta	IHC23-PO-182
Gosalia, Helin	IHC23-PO-025
	IHC23-PO-026
Gossrau, Gudrun	IHC23-PO-235
Goto, Tetsuya	IHC23-PO-002
Gozubatik-Celik, R. Gokcen	IHC23-PO-100
	IHC23-PO-334
Granhall, Charlotte	IHC23-OR-002
Granziera, Cristina	IHC23-PO-198
	IHC23-PO-199

(continued)

Continued

Author name	Program Codes
Grazzi, Licia	IHC23-PO-016
	IHC23-PO-117
	IHC23-PO-231
	IHC23-PO-260
	IHC23-PO-263
	IHC23-PO-271
	IHC23-PO-273
Grech, Olivia	IHC23-DP-036
Greco, Filippo	IHC23-PO-090
Greenway, Agatha	IHC23-PO-170
Greenwood, Fiona	IHC23-PO-257
	IHC23-PO-265
Grillo, Valentina	IHC23-DP-023
	IHC23-JT-005
REINMUN-COVID and EDEPIMIC	IHC23-PO-078
Grugno, Rosario	IHC23-PO-016
Gryglas-Dworak, Anna	IHC23-DP-040
	IHC23-PO-353
Gu, Qun	IHC23-PO-034
Guaschino, Elena	IHC23-OR-013
	IHC23-PO-230
Guastafierro, Erika	IHC23-PO-263
Gubanova, Maria	IHC23-PO-220
Guerrero Peral, Ángel Luis	IHC23-DP-015
	IHC23-DP-017
	IHC23-PO-077
	IHC23-PO-128
	IHC23-PO-186
	IHC23-PO-202
	IHC23-PO-262
Guerrieri, Simone	IHC23-PO-242
Guglielmino, Valeria	IHC23-PO-075
Gui, Wei	IHC23-DP-022
	IHC23-PO-375
Guigue, Alexis	IHC23-PO-250
Guilherme Leão Edelmuth, Diogo	IHC23-PO-336
Guillem Mesado, Amparo	IHC23-PO-302
Guisado, Daniel	IHC23-PO-287
Gulzhan, Zhulamanova	IHC23-DP-029
Guo, Aihong	IHC23-PO-207
Guo, Hua	IHC23-DP-042
Guo, Huailian	IHC23-PO-375
Guo, Song	IHC23-OR-014
Guo, Yi	IHC23-PO-210
Gurlek, Onur Cagin	IHC23-PO-167
Gutierrez, Teresa	IHC23-PO-269
Gárate, Gabriel	IHC23-PO-073
	IHC23-PO-074
Gómez García, Andrea	IHC23-PO-280
Gómez-Dabo, Laura	IHC23-PO-376
Gökçen Gözübatık, Rabia	IHC23-OR-007
Göçmez Yılmaz, Gülcan	IHC23-PO-057
	IHC23-PO-061
Güleç, Hüseyin	IHC23-OR-010
Gülhan Şahbaz, Fatma	IHC23-PO-344

(continued)

Continued

Author name	Program Codes
Ha, Huy	IHC23-PO-131
Ha, Woo Seo	IHC23-PO-205
Ha, Woo-Seok	IHC23-PO-295
Haanes, Kristian Agmund	IHC23-PO-160
	IHC23-PO-161
	IHC23-PO-162
Hadjikhani, Nouchine	IHC23-PO-191
	IHC23-PO-198
	IHC23-PO-199
Haghdoost, Faraidoon	IHC23-PO-008
Halker Singh, Rashmi	IHC23-IND-015
Hamann, Xenia	IHC23-PO-255
	IHC23-PO-275
Hammer, Angéla	IHC23-PO-187
Han, Chorong	IHC23-DP-044
Han, Junhee	IHC23-PO-020
Han, Kyungdo	IHC23-PO-004
	IHC23-PO-147
Han, Sun-Ku	IHC23-PO-326
Han, Xun	IHC23-PO-034
	IHC23-PO-375
Hansen, Jakob Møller	IHC23-PO-136
	IHC23-PO-137
Hansen, Nadja Skadkær	IHC23-OR-006
Hansen, Thomas Folkmann	IHC23-PO-069
	IHC23-PO-136
	IHC23-PO-137
	IHC23-PO-353
Harada, Hironobu	IHC23-PO-312
Harriott, Andrea	IHC23-IND-012
	IHC23-IND-015
Harris, Dagan	IHC23-IND-015
Haruyama, Yasuo	IHC23-PO-237
Hasirci Bayir, Buse Rahime	IHC23-PO-371
Hassane Djibo, Fatimata	IHC23-PO-344
Hauberg, Daniel Sloth	IHC23-PO-136
	IHC23-PO-137
Hay, Debbie L	IHC23-DP-020
	IHC23-DP-032
	IHC23-PO-153
	IHC23-PO-185
He, Jiahui	IHC23-PO-072
He, Qiu	IHC23-PO-375
Hebo, Wang	IHC23-PO-369
Helle, Megan	IHC23-PO-241
Hemstock, Matthew	IHC23-PO-274
Heo, Kyoung	IHC23-PO-047
Herr, Keira	IHC23-PO-252
Higashimoto, Yuki	IHC23-DP-001
Hilliard, Tamsin	IHC23-PO-305
Hipp, Joachim	IHC23-PO-275
Hirano, Makito	IHC23-PO-066
Hirata, Koichi	IHC23-PO-003
	IHC23-PO-006
	IHC23-PO-237

(continued)

Continued

Author name	Program Codes
Hjalgrim, Henrik	IHC23-PO-069
Hoekman, John	IHC23-PO-217
Hoffmann, Jan	IHC23-DP-016
	IHC23-PO-300
	IHC23-PO-301
Holland, Philip R	IHC23-DP-027
	IHC23-DP-036
	IHC23-PO-159
Holle-Lee, Dagny	IHC23-PO-282
Holm, Anja	IHC23-DP-006
Holmen Poulsen, Amanda	IHC23-PO-198
Holton, Kathleen	IHC23-PO-240
Hong, Seulgi	IHC23-PO-338
Hong, Yoo-ha	IHC23-PO-115
Hong, Yooha	IHC23-DP-003
	IHC23-PO-018
	IHC23-PO-019
	IHC23-PO-243
	IHC23-PO-310
	IHC23-PO-327
Hongli, Qu	IHC23-PO-369
Hori, Satoko	IHC23-PO-228
Horvath, Zsolt	IHC23-PO-009
Hou, Tsung-Wei	IHC23-DP-014
	IHC23-PO-088
Hovelsø, Nanna	IHC23-PO-136
	IHC23-PO-137
Hoyt, Margaret	IHC23-IND-010
	IHC23-IND-011
Hseu, Shu-Shya	IHC23-PO-337
Hsiao, Yi-Ting	IHC23-DP-039
Hsu, David	IHC23-DP-033
Hsu, Hsiang-Ting	IHC23-PO-088
Hsu, Tun-Wei	IHC23-DP-008
Hu, Dongmei	IHC23-PO-034
	IHC23-PO-375
Huang, Iris	IHC23-IND-005
	IHC23-IND-008
Huang, Ming	IHC23-IND-005
	IHC23-IND-008
Huang, Peijian	IHC23-PO-209
Huang, Tzu-Chou	IHC23-PO-056
Huebner, Michael	IHC23-PO-148
	IHC23-PO-170
Huerta, Mariano	IHC23-PO-280
Huifang, Xu	IHC23-PO-369
Hultman, Rainbo	IHC23-DP-037
Hung, Kuo-Sheng	IHC23-PO-070
Hutton, Elspeth	IHC23-PO-224
	IHC23-PO-225
	IHC23-PO-234
	IHC23-PO-305
Hwang, Heewon	IHC23-PO-005
Jensen, Rigmor H	IHC23-OR-006
	IHC23-PO-045
Hüttebräucker, Tomás	IHC23-PO-202

(continued)

Continued

Author name	Program Codes
Idrovo, Luis	IHC23-PO-265
Igarashi, Hisaka	IHC23-PO-116
Iglesias, Fernando	IHC23-PO-279
Ihara, Keiko	IHC23-PO-228
Ikegawa, Atsuko	IHC23-PO-066
Ilgaz Aydinlar, Elif	IHC23-PO-063
	IHC23-PO-201
	IHC23-PO-254
	IHC23-PO-256
	IHC23-PO-378
Im, Hee-Jin	IHC23-PO-018
	IHC23-PO-060
Im, James	IHC23-PO-333
Imai, Noboru	IHC23-PO-112
Imbiakha, Brian	IHC23-DP-002
Inuyama, Lyo	IHC23-PO-006
Ironi, Alon	IHC23-IND-015
	IHC23-PO-293
Ishida, Miki	IHC23-PO-259
Ishii, Ryota	IHC23-PO-349
Ishii, Ryotaro	IHC23-DP-001
ISHIZAKI, Kumiko	IHC23-PO-206
Ishizuchi, Kei	IHC23-PO-228
Ito, Yasuo	IHC23-PO-219
Jackson, Nicholas	IHC23-PO-134
Jager, Mason	IHC23-DP-002
Jaimes, Alex	IHC23-PO-039
	IHC23-PO-041
	IHC23-PO-280
Jain, Neelu	IHC23-PO-203
Jain, Samayak	IHC23-PO-211
Jang, Hyemin	IHC23-PO-222
Jang, Ki Moon	IHC23-PO-205
Jang, Min	IHC23-PO-309
Jansem, Priabprat	IHC23-PO-027
Jansen, Nico	IHC23-PO-168
	IHC23-PO-169
Jansen-Olesen, Inger	IHC23-DP-006
Jansri, Ukkrit	IHC23-PO-372
Jantzen, Frederik Thal	IHC23-PO-359
Jao, Chi-Wen	IHC23-DP-012
	IHC23-PO-087
Jenkins, Bronwyn	IHC23-PO-234
Jennysdotter Olofsgård, Felicia	IHC23-PO-022
	IHC23-PO-044
Jensen, Mette Nyholm	IHC23-PO-162
Jensen, Sidsel	IHC23-PO-229
Jeon, Seong Jin	IHC23-PO-338
Jeong, Hoe Jong	IHC23-PO-341
Jia, Zhihua	IHC23-PO-034
	IHC23-PO-375
Jindasakchai, Porpim	IHC23-PO-321
Jing, Ji	IHC23-IND-005
	IHC23-IND-008
Jion, Yasmin Binte Idu	IHC23-PO-252

(continued)

Continued

Author name	Program Codes
Jo, Jung Hwan	IHC23-PO-370
Johnson, Kirk	IHC23-DP-027
Jones, Martyn	IHC23-PO-171
	IHC23-PO-173
Joshi, Shivang	IHC23-IND-013
Josiassen, Mette Krog	IHC23-DP-038
	IHC23-DP-040
	IHC23-PO-229
Juhasz, Gabriella	IHC23-PO-012
	IHC23-PO-013
	IHC23-PO-185
	IHC23-PO-187
Juhl Korsbæk, Johanne	IHC23-OR-006
Junhong, Guo	IHC23-PO-369
Jusupova, Asel	IHC23-PO-107
Jørgensen, Isabella Friis	IHC23-PO-353
Jørgensen, Niklas Rye	IHC23-PO-045
Jürgens, Tim P	IHC23-DP-016
K. Moawad, Mona	IHC23-PO-036
Kaciroti, Niko	IHC23-PO-191
	IHC23-PO-290
	IHC23-PO-291
Kale, Alp Kagan	IHC23-PO-139
Kallela, Mikko	IHC23-DP-016
Kamaci, İbrahim	IHC23-PO-110
Kamble, Nitish	IHC23-PO-062
Kamel, Mohamed Abdelmonem	IHC23-PO-218
Kamourieh, Salwa	IHC23-DP-025
	IHC23-PO-303
	IHC23-PO-304
	IHC23-PO-323
Kang, Jin-Ju	IHC23-DP-003
	IHC23-PO-243
	IHC23-PO-310
	IHC23-PO-327
Kang, Jinkyu	IHC23-PO-106
Kang, Mi-Kyoung	IHC23-PO-018
	IHC23-PO-115
	IHC23-PO-243
	IHC23-PO-327
Kang, Wenyan	IHC23-PO-209
Karacı, Rahşan	IHC23-OR-010
	IHC23-PO-010
	IHC23-PO-256
	IHC23-PO-378
Karadaş, Ömer	IHC23-OR-007
Karakuş, Esin	IHC23-PO-124
	IHC23-PO-125
Karatas, Hulya	IHC23-PO-163
	IHC23-PO-164
	IHC23-PO-167
Karlen, Walter	IHC23-PO-023
Karlsson, William Kristian	IHC23-OR-002
Karlı, Necdet	IHC23-PO-256
Karpuz Seren, Burcu	IHC23-PO-340

(continued)

Continued

Author name	Program Codes
Karsan, Nazia	IHC23-OR-004
	IHC23-PO-178
	IHC23-PO-379
Kashiwaya, Yoshihiro	IHC23-PO-244
Kato, Hirohisa	IHC23-PO-116
Kato, Yuji	IHC23-PO-320
Katsarava, Zaza	IHC23-IND-001
	IHC23-IND-003
	IHC23-PO-131
Katsarou, Martha-Spyridoula	IHC23-PO-081
Katsuki, Masahito	IHC23-PO-002
Kaube, Holger	IHC23-DP-016
Kawasaki, Hitoshi	IHC23-PO-219
Keller, Gabriel	IHC23-PO-336
Kennedy, Gina	IHC23-IND-017
Keski-Säntti, Petra	IHC23-DP-016
Khalil, Modar	IHC23-PO-236
	IHC23-PO-285
	IHC23-PO-286
Khan, Rafiullah	IHC23-PO-236
	IHC23-PO-285
	IHC23-PO-286
Khudayarova, Sevara	IHC23-PO-145
	IHC23-PO-324
Kies, Dennis A	IHC23-PO-076
Kikui, Shoji	IHC23-PO-206
	IHC23-PO-244
Kim, Ahro	IHC23-PO-338
Kim, Byung-Kun	IHC23-OR-008
	IHC23-PO-019
	IHC23-PO-020
	IHC23-PO-035
	IHC23-PO-246
	IHC23-PO-259
	IHC23-PO-314
Kim, Byung-Su	IHC23-OR-008
	IHC23-PO-035
	IHC23-PO-326
	IHC23-PO-342
Kim, Daeyoung	IHC23-OR-008
	IHC23-PO-035
Kim, Dajung	IHC23-PO-191
	IHC23-PO-290
	IHC23-PO-291
Kim, Eunju	IHC23-DP-044
Kim, Gilwan	IHC23-IND-010
	IHC23-IND-011
	IHC23-PO-270
Kim, Hynji	IHC23-PO-342
Kim, Jae-Moon	IHC23-PO-035
Kim, Jiyoung	IHC23-PO-115
Kim, Kyung Min	IHC23-PO-005
	IHC23-PO-047
	IHC23-PO-084
	IHC23-PO-205

(continued)

Continued

Author name	Program Codes
	IHC23-PO-358
Kim, Manho	IHC23-PO-232
Kim, MinJee	IHC23-PO-338
KIM, Namoh	IHC23-PO-004
Kim, Seong-Taek	IHC23-PO-106
	IHC23-PO-309
Kim, Seonghae	IHC23-PO-370
Kim, Seonghoon	IHC23-PO-011
Kim, Seung Ae	IHC23-PO-147
	IHC23-PO-222
Kim, Seung Jae	IHC23-PO-084
Kim, Soo-Kyoung	IHC23-OR-008
	IHC23-PO-035
	IHC23-PO-115
Kim, Sora	IHC23-PO-309
Kim, Sumin	IHC23-PO-245
	IHC23-PO-342
Kim, Sun Young	IHC23-DP-044
Kim, Yong Beom	IHC23-PO-245
Kim, Yoo Hwan	IHC23-PO-115
Kingston, William	IHC23-PO-333
Kissani, Najib	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-294
	IHC23-PO-344
Kivelevitch, Gabriela	IHC23-PO-259
Klarenbach, Scott	IHC23-PO-250
Klein, Antonia	IHC23-PO-190
Klukinov, Michael	IHC23-DP-033
Kocasoy Orhan, Elif	IHC23-PO-110
Koch, Mirja	IHC23-PO-238
Kocsel, Natalia	IHC23-PO-185
Koeppe, Robert	IHC23-PO-191
	IHC23-PO-290
	IHC23-PO-291
Koga, Nobuyuki	IHC23-PO-003
	IHC23-PO-259
Kogelman, Lisette J. A	IHC23-PO-069
Koh, Akihito	IHC23-PO-002
Koirala, Nabin	IHC23-PO-292
Kokonyei, Gyongyi	IHC23-PO-185
Kokoti, Lili	IHC23-PO-197
Kondo, Hiroyuki	IHC23-PO-003
Kondziella, Daniel	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Kordcal, Sanjay Rao	IHC23-JT-006
Korobkova, Daria	IHC23-PO-276
Kortazar, Izaro	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Kota, Vidyasagar	IHC23-PO-008
Kouroudi, Aikaterini	IHC23-PO-103
Kovalchuk, Nadezhda	IHC23-PO-058
Krasenbaum, Lynda J	IHC23-IND-009

(continued)

Continued

Author name	Program Codes
	IHC23-IND-014
	IHC23-PO-259
Kraya, Torsten	IHC23-PO-255
	IHC23-PO-275
Krishnan, Arun	IHC23-PO-079
Kristensen, David M	IHC23-DP-006
Kristjansson, Ragnar P	IHC23-PO-069
Kruit, M.C	IHC23-PO-200
Kruja, Jera	IHC23-PO-367
Kuate-Tegueu, Callixte	IHC23-PO-052
	IHC23-PO-091
	IHC23-PO-092
Kukumägi, Kadri-Hebo	IHC23-PO-318
Kulkarni, Girish B	IHC23-PO-062
Kull, Pia	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Kumar, Sahel	IHC23-PO-013
Kumar, Sandhya	IHC23-PO-143
Kuo, Yu	IHC23-PO-177
Kuster, Gustavo	IHC23-PO-212
Kwon, Ki-Han	IHC23-PO-115
Károlyi, Norbert	IHC23-PO-187
kısabay ak, Ayşın	IHC23-PO-141
Labastida-Ramirez, Alejandro	IHC23-DP-036
	IHC23-PO-159
Labib, Dalia	IHC23-PO-071
Lagrata, Susie	IHC23-PO-303
	IHC23-PO-304
Lai, Kuan-Lin	IHC23-DP-008
	IHC23-DP-039
	IHC23-PO-033
	IHC23-PO-149
	IHC23-PO-188
Laikhter, Elizabeth	IHC23-PO-143
Lammers, Gert J	IHC23-PO-023
Landete, Pedro	IHC23-PO-078
Lang, Clemens	IHC23-PO-190
Lange, Kristin Sophie	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
	IHC23-PO-315
Lanteri-Minet, Michel	IHC23-DP-019
	IHC23-DP-042
	IHC23-IND-001
	IHC23-IND-003
	IHC23-PO-131
Larissa, Kuanova	IHC23-DP-029
Larripa, Natalia	IHC23-PO-269
Lau, Chi Ieong	IHC23-DP-012
	IHC23-PO-087
Lauritzen, Sabrina Prehn	IHC23-DP-006

(continued)

Continued

Author name	Program Codes
Lavania, Sagar	IHC23-PO-211
Layos, Almudena	IHC23-PO-279
Leach, Justin	IHC23-DP-002
Lee, Eunji	IHC23-PO-341
Lee, Euyhyun	IHC23-DP-011
Lee, Hye Jeong	IHC23-PO-084
	IHC23-PO-205
Lee, Hyoung Cheol	IHC23-PO-246
Lee, Jae Yong	IHC23-PO-326
Lee, Jenny	IHC23-PO-134
Lee, Jiyun	IHC23-PO-047
Lee, Kyung Won	IHC23-PO-011
Lee, Mi Ji	IHC23-DP-007
	IHC23-OR-008
	IHC23-PO-004
	IHC23-PO-020
	IHC23-PO-035
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	IHC23-PO-315
	IHC23-PO-327
	IHC23-PO-329
	IHC23-PO-341
	IHC23-DP-003
Lee, Pei-Hsin	IHC23-PO-087
Lee, Sang-Hwa	IHC23-PO-020
Lee, Solam	IHC23-PO-005
Lee, Sorae	IHC23-PO-245
Lee, Sue Hyun	IHC23-PO-084
	IHC23-PO-330
Lee, Wonwoo	IHC23-PO-047
Lee, Yi-Chung	IHC23-PO-088
Lee, Yichen	IHC23-PO-345
Lee, Young-gun	IHC23-PO-140
Leen, Annie J	IHC23-DP-032
Lei, Hou	IHC23-PO-369
Lei, Xiangyu	IHC23-PO-175
Lekhalawan, Pattanan	IHC23-PO-321
Leone, Massimo	IHC23-PO-368
Leroux, Elizabeth	IHC23-IND-001
	IHC23-IND-003
	IHC23-PO-131
Levine, Joshua E	IHC23-PO-210
Lewis, David	IHC23-DP-016
Li, Heng	IHC23-PO-017
Li, Joshua	IHC23-PO-134
Li, Ke	IHC23-PO-034
Li, Mingxin	IHC23-PO-375
Li, Ruibing	IHC23-OR-005

(continued)

Continued

Author name	Program Codes
Li, Shichao	IHC23-PO-332
Li, Yajie	IHC23-PO-034
Li, Zhiye	IHC23-PO-180
	IHC23-PO-181
Lian, Yajun	IHC23-PO-034
Lian, Yu	IHC23-PO-034
Liaw, Yi Chia	IHC23-PO-033
Lightman, Stafford L	IHC23-PO-023
Lim, Ji Ye	IHC23-DP-044
Lim, Manyoel	IHC23-PO-191
	IHC23-PO-290
	IHC23-PO-291
Limberg, Nicole	IHC23-PO-234
Lin, Gang	IHC23-IND-005
	IHC23-IND-008
Lin, Jiang	IHC23-PO-332
Lin, Po-Tso	IHC23-PO-337
Lin, Yu-Ching	IHC23-OR-012
Lin, Yu-Kai	IHC23-PO-070
Ling, Yu-Hsiang	IHC23-PO-149
	IHC23-PO-177
	IHC23-PO-188
	IHC23-PO-189
	IHC23-PO-315
Linley, John	IHC23-PO-247
Linnenbank, Chelsey	IHC23-PO-169
Linstra, K.M	IHC23-PO-200
Lipton, Richard B	IHC23-IND-014
	IHC23-DP-043
	IHC23-IND-001
	IHC23-IND-002
	IHC23-IND-003
	IHC23-IND-006
	IHC23-IND-007
	IHC23-IND-012
	IHC23-PO-132
	IHC23-PO-142
	IHC23-PO-270
	IHC23-PO-282
	IHC23-PO-284
	IHC23-PO-293
Lirng, Jiing-Feng	IHC23-DP-008
	IHC23-PO-177
	IHC23-PO-189
	IHC23-PO-337
Liu, Chengcheng	IHC23-IND-007
Liu, Chenyu	IHC23-PO-175
Liu, Huanxian	IHC23-PO-034
	IHC23-PO-375
Liu, Hung-Yu	IHC23-PO-188
liu, Jiale	IHC23-PO-034
Liu, Jianguang	IHC23-PO-207
Liu, Jing	IHC23-PO-034
	IHC23-PO-375
Liu, Kaiming	IHC23-IND-005

(continued)

Continued

Author name	Program Codes
	IHC23-IND-008
	IHC23-PO-072
	IHC23-PO-184
	IHC23-PO-375
Liu, Lin	IHC23-DP-011
Liu, Qin	IHC23-PO-175
Liu, Shuping	IHC23-PO-362
Liu, Tzu-Ting	IHC23-JT-002
Liu, Xiaoning	IHC23-IND-005
	IHC23-IND-008
Liu, Yi	IHC23-PO-070
Liu, Yingyi	IHC23-PO-282
Liu, Yu	IHC23-PO-207
	IHC23-PO-215
Llorente-Ayuso, Lucía	IHC23-PO-039
	IHC23-PO-041
Lloyd, Joseph	IHC23-PO-156
	IHC23-PO-171
	IHC23-PO-173
Lo-Ciganic, Wei-Hsuan	IHC23-PO-210
Lokanath, Hamsa	IHC23-PO-348
Lopes de Souza, Sandra	IHC23-PO-172
Lopez, Alberto Andres	IHC23-PO-279
Lopez, Cristina Lopez	IHC23-OR-014
Louise Christensen, Sarah	IHC23-DP-010
Lozano Alonso, Jose Eugenio	IHC23-DP-017
	IHC23-PO-128
Lozano Ros, Alberto	IHC23-PO-302
Lozano-Ros, Alberto	IHC23-PO-039
Lozano-Ros, Antonio	IHC23-PO-041
Lozanp, Alberto	IHC23-PO-279
Lu, Kaifeng	IHC23-IND-007
Lu, Zhihong	IHC23-PO-207
	IHC23-PO-215
Luccarini, Philippe	IHC23-PO-155
Luebke, Anne	IHC23-DP-002
	IHC23-OR-001
Luechinger, Roger	IHC23-PO-292
Lund, Nunu	IHC23-PO-045
Luo, Guogang	IHC23-PO-175
	IHC23-PO-193
Luo, Lei	IHC23-DP-019
Luo, Yi	IHC23-IND-005
	IHC23-IND-008
Luque Buzo, Elisa	IHC23-PO-302
Luu, Huong	IHC23-PO-250
Luvsannorov, Otgonbayar	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-294
	IHC23-PO-366
Luzeiro, Isabel	IHC23-PO-055
	IHC23-PO-289
Lv, Yudan	IHC23-PO-375
Láinez Andrés, José Miguel	IHC23-PO-183
López-Sanz, Celia	IHC23-PO-078

(continued)

Continued

Author name	Program Codes
Lønberg, Ulla Sofie	IHC23-PO-136
	IHC23-PO-137
Ma, Julia	IHC23-IND-012
Ma, Liheng	IHC23-PO-216
Maarbjerg, Stine	IHC23-PO-353
Maassen van den Brink, Antoinette	IHC23-DP-004
	IHC23-DP-026
	IHC23-OR-003
	IHC23-PO-200
	IHC23-PO-239
Machado Kopruszinski, Caroline	IHC23-PO-247
Mackenzie, Elyse	IHC23-PO-001
Macías Saint-Gerons, Diego	IHC23-PO-128
Madera, Jorge	IHC23-PO-073
Madjid, Irma Savitri	IHC23-PO-253
Magnerou, Annick Mélanie	IHC23-PO-052
	IHC23-PO-091
	IHC23-PO-092
Makovac, Elena	IHC23-PO-300
	IHC23-PO-301
Malaventura, Cristina	IHC23-PO-090
Mamitsuka, Hiroshi	IHC23-PO-012
Maniataki, Stefania	IHC23-PO-257
	IHC23-PO-265
Manni, Raffaele	IHC23-DP-023
Mansoury, Ouassim	IHC23-PO-344
Mao, Jingrui	IHC23-PO-034
Mapoure, Njankouo Yacouba	IHC23-PO-052
Marchante-Reillo, Ginebra	IHC23-PO-186
Marco, Teresa	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Marcos-Jiménez, Ana	IHC23-PO-078
Marcotte, Thomas	IHC23-DP-011
Margani, Erika	IHC23-PO-090
Mariela, Grandinetti	IHC23-PO-269
Marino, Silvia	IHC23-PO-090
Mariño, Eduardo	IHC23-PO-376
Markoulli, Maria	IHC23-PO-079
Marmura, Michael	IHC23-IND-014
Marshall, Joseph	IHC23-DP-013
Martami, Fahimeh	IHC23-PO-240
Marteletti, Paolo	IHC23-OR-007
Martimianaki, Georgia	IHC23-IND-017
Martin Bujante, Maria	IHC23-PO-279
Martin, Ines	IHC23-DP-015
Martin-Bujanda, Maria	IHC23-DP-015
Martindale, Cecilia	IHC23-PO-377
Martinelli, Daniele	IHC23-JT-005
	IHC23-PO-194
	IHC23-PO-196
	IHC23-PO-271
	IHC23-PO-352
	IHC23-PO-368
Martins, Karen	IHC23-PO-250

(continued)

Continued

Author name	Program Codes
Martín Pérez, Isidro	IHC23-PO-350
Martín Pérez, Sebastián	IHC23-PO-350
Martín-Gallo, Enrique	IHC23-PO-078
Martín-Martín, Carmen	IHC23-PO-186
Martínez-Badillo, Cristina	IHC23-PO-262
Martínez-Fleta, Pedro	IHC23-PO-078
Mascarella, Davide	IHC23-PO-030
	IHC23-PO-249
Masi, Stefano	IHC23-PO-090
Massi-Gams, Daniel	IHC23-PO-092
Mateu-Albero, Tamara	IHC23-PO-078
Matharu, Manjit	IHC23-DP-025
	IHC23-IND-001
	IHC23-IND-002
	IHC23-IND-003
	IHC23-IND-013
	IHC23-PO-131
	IHC23-PO-132
	IHC23-PO-224
	IHC23-PO-225
	IHC23-PO-296
	IHC23-PO-303
	IHC23-PO-304
	IHC23-PO-323
	IHC23-PO-368
Mathew, Paul G	IHC23-PO-217
Mathur, Sahil	IHC23-PO-062
Matsumori, Yasuhiko	IHC23-PO-002
	IHC23-PO-112
Matthew, Howard	IHC23-PO-300
	IHC23-PO-301
Mavridis, Theodoros	IHC23-PO-221
Mawet, Jérôme	IHC23-PO-315
May, Arne	IHC23-DP-016
	IHC23-PO-138
Mayda Domaç, Füsun	IHC23-OR-010
	IHC23-PO-010
	IHC23-PO-065
	IHC23-PO-256
Mayorita, Cita	IHC23-PO-122
Mazloum, Reza	IHC23-PO-373
Mazzocchetti, Chiara	IHC23-PO-090
Mbonda, Paul	IHC23-PO-092
McAllister, Peter	IHC23-IND-014
Md Isa, Nur Amalina	IHC23-PO-079
Mecklenburg, Jasper	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Medrano, Christopher	IHC23-PO-241
Mehta, Dwij	IHC23-DP-025
	IHC23-PO-323
Mehta, Mitul	IHC23-OR-004
Mei, Ruyi	IHC23-IND-005
	IHC23-IND-008
Mei, Yanliang	IHC23-DP-030

(continued)

Continued

Author name	Program Codes
	IHC23-PO-179
	IHC23-PO-299
Meijer, Onno C	IHC23-PO-023
Melo-Carrillo, Agustine	IHC23-DP-041
Membrilla, Javier A	IHC23-PO-039
	IHC23-PO-041
	IHC23-PO-376
Mendizabal, Adys	IHC23-PO-134
Meno-Tetang, Guy	IHC23-PO-247
Meo, Antonio	IHC23-PO-182
Mercuri, Bruno	IHC23-PO-260
Mese, Ismail	IHC23-PO-010
Messina, Roberta	IHC23-PO-016
	IHC23-PO-138
	IHC23-PO-242
	IHC23-PO-260
	IHC23-PO-271
	IHC23-PO-273
Messina, Stefano	IHC23-PO-251
Miao, Changhong	IHC23-PO-332
Michels, Lars	IHC23-PO-292
	IHC23-PO-373
Mifsud, Dolores	IHC23-PO-363
Mihovilovic, Marko	IHC23-DP-034
Mikhailyukova, Maria	IHC23-PO-317
Mikkelsen, Christina	IHC23-PO-069
Mikkelsen, Susan	IHC23-PO-069
Min, Chen	IHC23-PO-369
Min, In Kyung	IHC23-PO-047
Minen, Mia T	IHC23-PO-284
Ming, Dong	IHC23-PO-369
Mingjie, Zhang	IHC23-PO-369
Minguez, Ane	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Minota, Karla	IHC23-PO-134
Mitsikostas, Dimos D	IHC23-IND-014
	IHC23-OR-007
	IHC23-PO-221
Mitsufuji, Takashi	IHC23-PO-219
Mitsui, Yoshiyuki	IHC23-PO-066
Miyahara, Junichi	IHC23-PO-244
Miyake, Hitoshi	IHC23-PO-116
Miyazaki, Naoki	IHC23-PO-228
	IHC23-PO-349
Mo, Heejung	IHC23-PO-019
Moavero, Romina	IHC23-PO-098
Mohamed, Samaher Walied	IHC23-PO-218
Moisa, Marius	IHC23-PO-292
Mondel, Prabath	IHC23-PO-203
Monte, Gabriele	IHC23-PO-090
	IHC23-PO-097
	IHC23-PO-098
	IHC23-PO-101
Monteith, Teshamae S	IHC23-PO-293

(continued)

Continued

Author name	Program Codes
Monticone, Sonia	IHC23-PO-090
Montisano, Danilo Antonio	IHC23-PO-117
	IHC23-PO-231
	IHC23-PO-263
Monzen, Tatsuya	IHC23-PO-102
	IHC23-PO-126
	IHC23-PO-331
Moon, Heui-Soo	IHC23-DP-003
	IHC23-OR-008
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	IHC23-PO-020
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	IHC23-PO-243
	IHC23-PO-245
	IHC23-PO-310
	IHC23-PO-327
Moraes Valença, Marcelo	IHC23-PO-172
Moreau, Pascale	IHC23-PO-154
Moreira, Antia	IHC23-DP-015
	IHC23-PO-287
Moreno Ajona, David	IHC23-DP-013
	IHC23-PO-151
	IHC23-PO-257
Morita, Shinji	IHC23-PO-331
Moro, Raúl	IHC23-PO-186
Morollón Sánchez-Mateos, Noemí	IHC23-PO-262
	IHC23-PO-280
Morreale, Cristina	IHC23-PO-090
Morris, Jarrod	IHC23-PO-363
Motah, Mathieu	IHC23-PO-052
Muenzel, E. Jolanda	IHC23-PO-270
Muhsen Al-Khazali, Haidar	IHC23-PO-198
	IHC23-PO-199
Murail, Pauline	IHC23-PO-154
Murakata, Kenji	IHC23-PO-244
Murphy, Brian	IHC23-PO-241
Muthuraman, Muthuraman	IHC23-PO-292
Muñoz, Albert	IHC23-PO-280
Muñoz-Calleja, Cecilia	IHC23-PO-078
Mzuno, Toshiki	IHC23-DP-001
Nabaei, Ghaemeh	IHC23-PO-227
Naber, Willemijn	IHC23-PO-021
Nacca, Raffaella	IHC23-PO-090
Nada, Mona	IHC23-PO-071
	IHC23-PO-096
Nagai, Yoshitaka	IHC23-PO-066
Nagane, Rahul	IHC23-JT-006
Nagaraj, Karthik	IHC23-PO-151
Nagel, Maria Vanesa	IHC23-PO-269
Nagumo, Satoko	IHC23-PO-116
Nagy, Krisztian	IHC23-DP-019
	IHC23-DP-042
	IHC23-PO-282
Nakahara, Jin	IHC23-PO-228

(continued)

Continued

Author name	Program Codes
	IHC23-PO-349
Nakayama, Takeo	IHC23-PO-006
Nakazawa, Tomoko	IHC23-PO-099
Namgung, Jong Young	IHC23-DP-007
Narimatsu, Hiroto	IHC23-PO-009
Nascimento, Thiago	IHC23-PO-191
	IHC23-PO-290
	IHC23-PO-291
Nasergivehchi, Somayeh	IHC23-PO-286
Nattan Souza, Marcio	IHC23-PO-138
	IHC23-PO-212
	IHC23-PO-336
Navratilova, Edita	IHC23-PO-247
Neeb, Lars	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
	IHC23-PO-255
	IHC23-PO-275
Nelin, Igor	IHC23-PO-317
Nežádal, Tomáš	IHC23-DP-019
	IHC23-DP-042
Ng, Gee Jin	IHC23-PO-311
Nguyen, Duc Anh	IHC23-PO-012
Nguyen, Phyong Uyen	IHC23-PO-250
Nicholson, Robert A	IHC23-PO-270
Nickl-Jockschat, Thomas	IHC23-DP-037
Nicolodi, Maria	IHC23-DP-005
	IHC23-PO-144
Nieves, Candela	IHC23-PO-280
Niflioglu, Buket	IHC23-PO-256
Ning, Xiaoping	IHC23-IND-009
	IHC23-IND-014
	IHC23-PO-259
Nisar, Areeba	IHC23-PO-203
Nissilä, Markku	IHC23-DP-016
Njohjam, Mundih	IHC23-DP-021
Novick, Diego	IHC23-IND-013
	IHC23-IND-017
Novitckii, Ivan	IHC23-PO-089
Novoa, Maria	IHC23-PO-328
Nowaczewska, Magdalena	IHC23-PO-353
Nudsasarn, Angkana	IHC23-PO-113
	IHC23-PO-114
Nye, Barbara	IHC23-PO-143
Nørgaard, Ina	IHC23-PO-359
O'Brien, Hope L.	IHC23-IND-004
O'Byrne, Kevin	IHC23-PO-159
O'Daly, Owen	IHC23-PO-178
Obach, Víctor	IHC23-DP-015
	IHC23-PO-150
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	IHC23-PO-279
	IHC23-PO-283
	IHC23-PO-287
Obelitz-Ryom, Karina	IHC23-DP-006

(continued)

Continued

Author name	Program Codes
	IHC23-DP-010
Ocampo-Pineda, Mario	IHC23-PO-199
Oda, Iltsuki	IHC23-PO-066
Oguz, Keriman	IHC23-PO-141
Oh, Ki Chang	IHC23-PO-140
Oh, Kyungmi	IHC23-OR-008
	IHC23-PO-035
Oh, Sun-Young	IHC23-DP-003
	IHC23-PO-243
	IHC23-PO-310
	IHC23-PO-327
Ohtani, Seiya	IHC23-PO-228
Okada, Mariko	IHC23-PO-219
Oksuz, Nevra	IHC23-PO-256
	IHC23-PO-340
Olesen, Jes	IHC23-DP-006
	IHC23-DP-010
	IHC23-PO-069
	IHC23-PO-085
Oliveira, Mariana J	IHC23-PO-281
Olivier, Marina	IHC23-PO-280
Olofsson, Isa Amalie	IHC23-PO-069
Olsen, Michael H	IHC23-PO-239
Omata, Yuko	IHC23-PO-099
Omer, Mohammed	IHC23-PO-351
	IHC23-PO-365
Ong, Jonathan J.Y	IHC23-PO-252
Onishchenko, Kateryna	IHC23-PO-274
Ono, Kaori	IHC23-DP-044
Ordax Díez, Ana	IHC23-DP-017
	IHC23-PO-128
Orlando, Bianca	IHC23-PO-016
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261
	IHC23-PO-273
Orlova, Yulia	IHC23-PO-210
Ornello, Raffaele	IHC23-PO-271
Orsini, Alessandro	IHC23-PO-090
Osada, Takashi	IHC23-PO-320
Ostrowski, Sisse R	IHC23-PO-069
Ota, Kuniko	IHC23-PO-244
Overeem, Lucas Hendrik	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Ozdemir Gultekin, Tugce	IHC23-PO-139
Ozdemir, Asena Ayça	IHC23-PO-118
Ozge, Aynur	IHC23-PO-110
	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-139
	IHC23-PO-256
	IHC23-PO-340
Ozudogru, Seniha	IHC23-PO-377
Ozyalcin, Suleyman	IHC23-PO-110

(continued)

Continued

Author name	Program Codes
Pacheco, Evelyn	IHC23-PO-212
Padovani, Alessandro	IHC23-PO-266
	IHC23-PO-267
Palmieri, Antonella	IHC23-PO-090
Pan, Li-Ling Hope	IHC23-PO-127
	IHC23-PO-188
	IHC23-PO-189
	IHC23-PO-343
Pan, Xiaoping	IHC23-PO-375
Pan, Xin	IHC23-PO-375
Pant, Rashmi	IHC23-PO-008
Panthumjinda, Kammant	IHC23-PO-024
Panto, Akkanat	IHC23-PO-321
Panyarachun, Pariyada	IHC23-PO-321
Papa, Amanda	IHC23-PO-090
Papas, Eric	IHC23-PO-079
Papasavva, Maria	IHC23-PO-081
Papetti, Laura	IHC23-PO-090
	IHC23-PO-097
	IHC23-PO-098
	IHC23-PO-101
Paranavitane, Shiran	IHC23-PO-029
Parikh, Krutika	IHC23-IND-006
	IHC23-IND-012
Parisi, Pasquale	IHC23-PO-090
Park, Bo-yong	IHC23-DP-007
	IHC23-PO-174
Park, Haesuk	IHC23-PO-210
Park, Hong-Kyun	IHC23-DP-003
	IHC23-PO-115
	IHC23-PO-140
	IHC23-PO-243
	IHC23-PO-310
	IHC23-PO-327
Park, Jeong Wook	IHC23-OR-008
	IHC23-PO-011
	IHC23-PO-035
Park, Ji Woon	IHC23-PO-370
Park, Ji-Yun	IHC23-PO-338
Park, Kwang-Yeol	IHC23-OR-008
	IHC23-PO-035
Park, Yeong Jun	IHC23-DP-007
Park, Younjung	IHC23-PO-309
Parsegov, Brynn	IHC23-PO-377
Pascual, Julio	IHC23-PO-073
	IHC23-PO-074
Pascual, Marta	IHC23-PO-073
	IHC23-PO-074
Patel, Dinesh Kumar	IHC23-PO-288
Patel, Niraj	IHC23-IND-017
Pattojoshi, Amrit	IHC23-PO-211
Paul, Kolin	IHC23-DP-028
Pavone, Piero	IHC23-PO-090

(continued)

Continued

Author name	Program Codes
Pearlman, Eric M	IHC23-PO-270
Pedersen, Ole Birger	IHC23-PO-069
Peinado, Manuel	IHC23-PO-279
Pereira, Ana David	IHC23-PO-156
	IHC23-PO-171
	IHC23-PO-173
Pereira, Ricardo	IHC23-PO-289
Peres, Mario	IHC23-PO-015
	IHC23-PO-040
	IHC23-PO-042
	IHC23-PO-131
Pestalozza, Isabella Ferdinanda	IHC23-PO-014
Petelin, Dmitrii	IHC23-PO-058
Petersen, Anja	IHC23-PO-045
Peterson, Zeru	IHC23-DP-037
Petolicchio, Barbara	IHC23-PO-251
Petrušić, Igor	IHC23-PO-176
Petschner, Peter	IHC23-PO-012
	IHC23-PO-013
Pezzini, Alessandro	IHC23-PO-315
Phinyo, Phichayut	IHC23-PO-114
Pichiecchio, Anna	IHC23-PO-194
	IHC23-PO-196
	IHC23-PO-271
Pickering, Rachel	IHC23-PO-303
Pierangeli, Giulia	IHC23-PO-030
	IHC23-PO-249
Pijpers, Judith A	IHC23-PO-076
Pinnaro, MariaStella	IHC23-DP-005
	IHC23-PO-144
Pinto-Pardo, Nicolas	IHC23-PO-154
Pirker-Kees, Agnes	IHC23-PO-190
Planchuelo-Gómez, Álvaro	IHC23-PO-077
	IHC23-PO-186
	IHC23-PO-202
Platho-Elwischger, Kirsten	IHC23-PO-190
Pocock, Kristyn	IHC23-PO-143
Pocora, Maria Magdalena	IHC23-PO-194
	IHC23-PO-196
Poh, Weijie	IHC23-PO-009
Pohl, Heiko	IHC23-PO-292
Pola, Nuria	IHC23-DP-015
	IHC23-PO-279
Polat, Burcu	IHC23-OR-007
	IHC23-PO-139
	IHC23-PO-256
Pongpitakmetha, Thanakit	IHC23-PO-024
Pooja, Mailankody	IHC23-PO-062
Porreca, Frank	IHC23-PO-247
Porta-Etessam, Jesús	IHC23-PO-039
	IHC23-PO-041
	IHC23-PO-262
Portillo, Raquel	IHC23-PO-279
Portuondo, Gustavo	IHC23-PO-269
Posada Cortés, Leidy Milena	IHC23-PO-350
Powers, PhD, Scott W	IHC23-PO-284
Pozo-Rosich, Patricia	IHC23-DP-019
	IHC23-DP-042
	IHC23-IND-017
	IHC23-PO-080
	IHC23-PO-131
	IHC23-PO-229
	IHC23-PO-282
	IHC23-PO-376
Požlep, Gorazd	IHC23-PO-067
Prabhakar, Prab	IHC23-PO-095
Pratiwi, Selviana	IHC23-PO-122
Prchal, Josef	IHC23-PO-377
Proietti Checchi, Martina	IHC23-PO-097
	IHC23-PO-098
	IHC23-PO-101
Proietti, Stefania	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261
	IHC23-PO-273
Puledda, Francesca	IHC23-DP-013
	IHC23-OR-004
	IHC23-PO-095
	IHC23-PO-138
Putortì, Alessia	IHC23-JT-005
Pérez-Pereda, Sara	IHC23-PO-073
Qerimi (Sulstarova), Nensi	IHC23-PO-322
Qerimi, Gjergji	IHC23-PO-322
Qi, Wan	IHC23-PO-369
Qi, Yi	IHC23-PO-175
Qiu, Dong	IHC23-DP-030
	IHC23-PO-179
	IHC23-PO-192
	IHC23-PO-299
Qiu, Enchao	IHC23-OR-011
Qiu, He	IHC23-PO-369
Qiu, Shi	IHC23-PO-375
Qu, Hongli	IHC23-PO-375
Qu, Kang	IHC23-PO-375
Quaife, Matt	IHC23-IND-016
Querzani, Pietro	IHC23-PO-273
Quintana, Simone	IHC23-PO-016
Quintas, Sonia	IHC23-PO-039
	IHC23-PO-041
Qureshi, Ayman	IHC23-DP-025
	IHC23-PO-323
Rabany, Liron	IHC23-IND-015
Radojičić, Aleksandra	IHC23-PO-176
Radović, Mojsije	IHC23-PO-176
Raffaelli, Bianca	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Raggi, Alberto	IHC23-PO-117

(continued)

Continued

Author name	Program Codes
	IHC23-PO-263
Rahimi, Mohammad Dawood	IHC23-PO-360
Rahman, Shafaqat	IHC23-DP-002
	IHC23-OR-001
Rahmanzadeh, Reza	IHC23-PO-199
Raieli, Vincenzo	IHC23-PO-090
Raimondi, Debora	IHC23-PO-271
Raja, Pritam	IHC23-PO-062
Rajapakse, Thiliane	IHC23-PO-250
Rajpal, Naresh	IHC23-PO-146
Rakhmatullaeva, Gulnora	IHC23-PO-145
	IHC23-PO-324
Ramirez Campos, Verena	IHC23-IND-009
	IHC23-IND-014
	IHC23-PO-259
Ramos de Andrade, Juliana	IHC23-PO-172
Ran, Caroline	IHC23-PO-022
	IHC23-PO-044
Ran, Ye	IHC23-PO-034
	IHC23-PO-375
Ranasinghe, Indrachapa	IHC23-PO-346
Ranc, Kristina	IHC23-DP-040
Rancher, Brent	IHC23-PO-241
Ranieri, Angelo	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-251
Rantell, Khadija	IHC23-PO-296
Rao, Renata	IHC23-PO-266
	IHC23-PO-267
Rapoport, Alan M	IHC23-PO-293
Rasmussen, Nadja Bredo	IHC23-OR-002
Rasmussen, Rikke Holm	IHC23-DP-006
Rattanawong, Wanakorn	IHC23-PO-024
	IHC23-PO-027
	IHC23-PO-109
	IHC23-PO-307
	IHC23-PO-321
Raucci, Umberto	IHC23-PO-090
Ray, Jason	IHC23-PO-104
	IHC23-PO-224
	IHC23-PO-225
	IHC23-PO-305
Ray, Sutapa	IHC23-PO-217
Raza, Muhammad Liaquat	IHC23-PO-111
Razeghi Jahromi, Soodeh	IHC23-PO-094
Rea, Brandon	IHC23-DP-037
	IHC23-PO-170
Reale, Antonino	IHC23-PO-090
Recio García, Andrea	IHC23-DP-017
	IHC23-PO-128
	IHC23-PO-262
Recio, Maria	IHC23-PO-279
Reducha, Philip	IHC23-PO-161
Rees, Tayla A	IHC23-DP-020

(continued)

Continued

Author name	Program Codes
	IHC23-DP-032
	IHC23-PO-153
Ren, Zhanxiu	IHC23-PO-375
Renton, Tara	IHC23-PO-300
	IHC23-PO-301
Reuter, Uwe	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Rhyne, Christopher	IHC23-PO-264
Ribeiro, Saulo	IHC23-PO-212
Richer, Lawrence	IHC23-PO-250
Riederer, Franz	IHC23-PO-190
	IHC23-PO-292
Riesco, Nuria	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Riesco, Nurias	IHC23-PO-150
Rimmele, Florian	IHC23-DP-016
Rinalduzzi, Steno	IHC23-PO-251
Riordain, Richeal	IHC23-PO-356
Risau-Gusman, Sebastián	IHC23-PO-202
Rivera-Mancilla, E	IHC23-OR-003
Rivero, Monserrat	IHC23-PO-074
Rizo, Ana	IHC23-DP-015
	IHC23-PO-279
Roa, Javier	IHC23-PO-039
	IHC23-PO-041
	IHC23-PO-041
Robblee, Jennifer	IHC23-PO-217
Robinson, Rebecca L	IHC23-IND-013
Robotti, Micaela	IHC23-PO-014
Rocca, Maria Assunta	IHC23-PO-271
Rodgers, Anthony	IHC23-PO-008
Rodríguez, Margarita	IHC23-PO-186
Rodríguez-Vico, Jaime S	IHC23-PO-039
	IHC23-PO-041
	IHC23-PO-280
Rojo Rello, Silvia	IHC23-DP-017
	IHC23-PO-128
Rollo, Eleonora	IHC23-PO-123
Romozzi, Marina	IHC23-PO-075
	IHC23-PO-123
Roncero, Nuria	IHC23-DP-015
Rong, Qingqing	IHC23-PO-375
Rongfei, Wang	IHC23-PO-369
Rossi, Lucia	IHC23-PO-090
Rossi, Roberta	IHC23-PO-090
Roth-Ben Arie, Zipora	IHC23-IND-009
	IHC23-IND-014
Roxas Jr., Artemio	IHC23-PO-204
Rozen, Todd	IHC23-PO-297
Ruan, Litao	IHC23-PO-193
Rubio, Laura	IHC23-PO-279
Rubio-Beltran, Eloisa	IHC23-DP-036

(continued)

Continued

Author name	Program Codes
	IHC23-PO-159
Ruff, Christian	IHC23-PO-292
Ruibal, Marta	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Ruisanchez, Aintzine	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Russo, Andrew	IHC23-PO-170
Russo, Antonio	IHC23-PO-271
Russo, Marco	IHC23-PO-016
Ryu, Ji-Won	IHC23-PO-106
Sabchez Soblechero, Antonio	IHC23-PO-279
Sacco, Sara	IHC23-DP-019
	IHC23-DP-042
Sacco, Simona	IHC23-PO-271
	IHC23-PO-282
Sadamoto, Yasutaka	IHC23-PO-226
	IHC23-PO-312
Saghir, Khadija	IHC23-PO-344
Sahai-Srivastava, Soma	IHC23-PO-105
Sahbaz, Fatma Gulhan	IHC23-PO-340
Sahin, Aysenur	IHC23-PO-063
Sahin, Gürdal	IHC23-PO-163
	IHC23-PO-233
Saigoh, Kazumasa	IHC23-PO-066
Sakai, Fumihiko	IHC23-IND-001
	IHC23-IND-003
	IHC23-OR-009
	IHC23-PO-102
	IHC23-PO-126
	IHC23-PO-259
	IHC23-PO-331
Salam, Abdul	IHC23-PO-008
Salerno, Antonio	IHC23-PO-251
	IHC23-PO-260
Samarasiri, Udari Tankana	IHC23-PO-339
Samukawa, Makoto	IHC23-PO-066
Sances, Grazia	IHC23-DP-023
	IHC23-JT-005
	IHC23-OR-013
	IHC23-PO-117
	IHC23-PO-194
	IHC23-PO-196
	IHC23-PO-230
	IHC23-PO-352
Sanchez Soblechero, Antonio	IHC23-PO-302
Sandor, Peter	IHC23-PO-292
Sano, Hiromi	IHC23-PO-003
	IHC23-PO-006
Santana dos Reis, Rita	IHC23-PO-172
Santana López, Laura	IHC23-DP-017
	IHC23-PO-128
Santos, Felipe Reinaldo	IHC23-PO-212
Sanz Muñoz, Ivan	IHC23-DP-017

(continued)

Continued

Author name	Program Codes
	IHC23-PO-128
Sara, Yıldırım	IHC23-PO-157
Sarıtaş, Ayşegül Seyma	IHC23-PO-141
Sautter, Carson	IHC23-PO-377
Savasta, Salvatore	IHC23-PO-090
Savitri, Irma	IHC23-PO-122
Sayal, Parag	IHC23-PO-323
Schachter, Daniel C	IHC23-PO-281
Schankin, Christoph	IHC23-PO-190
Schankin, Christopher	IHC23-PO-373
Schenke, Maarten	IHC23-PO-168
	IHC23-PO-169
Schiano di Cola, Francesca	IHC23-PO-016
	IHC23-PO-266
	IHC23-PO-267
Schim, Jack	IHC23-DP-040
Schoenen, Jean	IHC23-PO-292
Schuster, Nathaniel	IHC23-DP-011
Schwedt, Todd J	IHC23-IND-007
Schytz, Henrik Winther	IHC23-PO-353
Schöpfer, Raphaela	IHC23-PO-373
Scott, Peter	IHC23-PO-191
	IHC23-PO-290
	IHC23-PO-291
Scutelnic, Adrian	IHC23-PO-190
Sebastianelli, Gabriele	IHC23-DP-024
	IHC23-JT-004
	IHC23-PO-361
Seget, Nicola	IHC23-PO-361
Seighart, Werner	IHC23-DP-034
Selekler, Macit	IHC23-PO-110
Seminerio, Michael	IHC23-DP-043
	IHC23-IND-001
	IHC23-IND-002
	IHC23-IND-003
	IHC23-PO-132
	IHC23-PO-142
Semprini, Marianna	IHC23-JT-005
Senanayake, Bimsara	IHC23-PO-029
	IHC23-PO-037
	IHC23-PO-313
	IHC23-PO-325
	IHC23-PO-339
	IHC23-PO-346
Seng, Elizabeth	IHC23-DP-043
	IHC23-IND-002
	IHC23-PO-132
	IHC23-PO-142
	IHC23-PO-284
Seo, Jong-Geun	IHC23-PO-035
Serga, Anna	IHC23-PO-317
Sergeev, Alexey	IHC23-PO-058
Serrao, Mariano	IHC23-DP-024
	IHC23-JT-004
	IHC23-PO-361
Servidei, Serenella	IHC23-PO-075

(continued)

Continued

Author name	Program Codes
	IHC23-PO-123
Seshagiri, DV	IHC23-PO-062
Sette, Giuliano	IHC23-PO-014
Severt, Lawrence	IHC23-IND-007
	IHC23-IND-012
Seveso, Greta	IHC23-PO-361
Sexton, Michelle	IHC23-DP-011
Sezgin, Mine	IHC23-DP-009
Sforza, Giorgia	IHC23-PO-097
	IHC23-PO-098
	IHC23-PO-101
Shab-Bidar, Sakineh	IHC23-PO-240
Shafiee Sabet, Mahdi	IHC23-PO-223
Shafiyev, Javid Shafiyev	IHC23-OR-007
Shalaby, Nevin	IHC23-PO-344
Shapiro, Robert E	IHC23-OR-009
	IHC23-DP-043
	IHC23-PO-007
	IHC23-PO-142
	IHC23-PO-270
Sheila, Marianne	IHC23-PO-252
Shemsi (Harizi), Edlira	IHC23-PO-322
Shemsi, Kledisa	IHC23-PO-322
Shen, Yilong	IHC23-IND-008
Shen, Ziyang	IHC23-IND-005
Shengyuan, Yu	IHC23-PO-369
Shibasaki, Yoshiyuki	IHC23-PO-003
Shibata, Mamoru	IHC23-PO-349
Shiina, Tomohiko	IHC23-PO-237
Shimizu, Toshihiko	IHC23-PO-028
Shinomoto, Makiko	IHC23-DP-001
Shmuely, Sharon	IHC23-PO-293
Shubina, Margarita	IHC23-PO-089
Shuhua, Zhang	IHC23-PO-369
Siebert, Anke	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Sierra, Álvaro	IHC23-DP-017
	IHC23-PO-077
	IHC23-PO-128
	IHC23-PO-186
	IHC23-PO-287
Sierra-Mencía, Álvaro	IHC23-PO-262
Silva, A. O. Luciana	IHC23-PO-281
Sincliar, Alexandra	IHC23-DP-036
Singh, Jyotika	IHC23-PO-377
Singh, Ritu	IHC23-PO-264
Sinha, Sanjib	IHC23-PO-062
Siokas, Vasileios	IHC23-PO-081
Sirilertmekasakul, Chananchida	IHC23-PO-321
Sirimaharaj, Nopdanai	IHC23-PO-114
Siyang, Huang	IHC23-PO-369
Sjulstad, Ane Skaare	IHC23-PO-068
Sjöstrand, Christina	IHC23-PO-022

(continued)

Continued

Author name	Program Codes
	IHC23-PO-044
Skliros, Athanasios E	IHC23-PO-103
Skliros, Efstathios A	IHC23-PO-103
Skorobogatykh, Kirill	IHC23-PO-276
Slijepcevic, Mirjana	IHC23-PO-031
Smirnoff, Liza	IHC23-PO-105
Smith, Jonathan H	IHC23-IND-012
	IHC23-PO-282
Smith, Melody	IHC23-PO-241
Smith, Steven M	IHC23-PO-210
Smith, Yolanda	IHC23-PO-290
Smolnikova, Marina	IHC23-PO-089
Snellman, Josefin	IHC23-OR-014
Sofyan, Henry Riyanto	IHC23-PO-122
	IHC23-PO-253
Sohn, Jong-Hee	IHC23-OR-008
	IHC23-PO-035
	IHC23-PO-115
Sokolov, Evgenii	IHC23-PO-058
Sommer, Katherine	IHC23-IND-001
	IHC23-IND-002
	IHC23-IND-003
	IHC23-IND-004
	IHC23-PO-132
	IHC23-PO-264
Song, Tae-Jin	IHC23-DP-003
	IHC23-PO-035
	IHC23-PO-243
	IHC23-PO-310
	IHC23-PO-327
Soontornpun, Atiwat	IHC23-PO-114
Soriano, Joan B	IHC23-PO-078
Sottani, Costanza	IHC23-PO-075
	IHC23-PO-123
Sowers, Levi	IHC23-DP-037
	IHC23-PO-170
Soylu, Kadir Oguzhan	IHC23-PO-164
	IHC23-PO-167
Spano, Giorgio	IHC23-PO-014
Sperling, Bjorn	IHC23-DP-038
	IHC23-DP-040
	IHC23-PO-229
Spingos, Konstantinos C	IHC23-PO-103
Spira, Katherine	IHC23-PO-079
Splendiani, Alessandra	IHC23-PO-271
Srikiatkachorn, Anan	IHC23-PO-372
Srivastava, Pritesh	IHC23-DP-028
Stanyer, Emily	IHC23-DP-036
Stark, Richard J	IHC23-PO-131
	IHC23-PO-305
Stark-Inbar, Alit	IHC23-IND-015
	IHC23-PO-293
Starling, Amaal J	IHC23-DP-038
Stattmann, Miranda	IHC23-PO-316
Stefansen, Simon	IHC23-DP-018

(continued)

Continued

Author name	Program Codes
	IHC23-PO-130
Steinberg, Anna	IHC23-PO-022
	IHC23-PO-044
Steiner, Timothy J	IHC23-DP-018
	IHC23-PO-130
	IHC23-PO-136
	IHC23-PO-137
Steinicke, Maureen	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Stokes, Jonathan	IHC23-IND-012
Straburzyński, Marcin	IHC23-PO-353
Strassman, Andrew	IHC23-DP-041
Straube, Andreas	IHC23-DP-016
	IHC23-PO-255
	IHC23-PO-275
Straube, Jodi	IHC23-PO-241
Strigaro, Gionata	IHC23-PO-182
Students, Istanbul University Department of Gerontology	IHC23-PO-125
Study Group, Head-MENAA	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-294
Stämpfli, Philipp	IHC23-PO-373
Suarez, Antoni	IHC23-DP-015
Suda, Satoshi	IHC23-PO-320
Sufen, Chen	IHC23-PO-369
Sugyama, Hanako	IHC23-PO-244
Suh, Bum Chun	IHC23-PO-245
Sui, Binbin	IHC23-PO-179
	IHC23-PO-180
	IHC23-PO-181
	IHC23-PO-299
Sumelahti, Marja-Liisa	IHC23-DP-016
Sun, Xinyue	IHC23-PO-175
Sun, Yanhui	IHC23-PO-215
Sunwoo, Junsang	IHC23-PO-245
Suppiej, Agnese	IHC23-PO-090
Suwanlaong, Kanokrat	IHC23-PO-265
Suzuki, Keisuke	IHC23-PO-237
Suzuki, Shiho	IHC23-PO-237
Szabo, Edina	IHC23-PO-185
Sztal-Mazer, Shoshana	IHC23-PO-224
	IHC23-PO-225
Sánchez Martínez, Javier	IHC23-DP-017
	IHC23-PO-128
Sánchez-Alonso, Santiago	IHC23-PO-078
Sánchez-Azofra, Ana	IHC23-PO-078
Sánchez-Cerrillo, Ildefonso	IHC23-PO-078
Sánchez-Madrid, Francisco	IHC23-PO-077
	IHC23-PO-078
Sánchez-Soblechero, Antonio	IHC23-PO-039
	IHC23-PO-041
Sørensen, Erik	IHC23-PO-069
Tada, Haruka	IHC23-PO-066

(continued)

Continued

Author name	Program Codes
Tajan, Emilia	IHC23-PO-269
Takahashi, Nobuyuki	IHC23-PO-228
Takahashi, Shinichi	IHC23-PO-320
Takahashi, Yoshiko	IHC23-PO-099
Takemura, Ryo	IHC23-PO-228
	IHC23-PO-349
Takeshima, Takao	IHC23-PO-066
	IHC23-PO-206
	IHC23-PO-244
Takizawa, Tsubasa	IHC23-PO-228
	IHC23-PO-349
Talekar, Kiran	IHC23-PO-203
Talu, Gul Goknel	IHC23-PO-110
Tamba Tolno, Victor	IHC23-PO-368
Tan, Ge	IHC23-PO-207
Tan, Huann	IHC23-PO-300
	IHC23-PO-301
Tang, Hefei	IHC23-PO-179
	IHC23-PO-180
	IHC23-PO-181
	IHC23-PO-299
Tang, Melissa	IHC23-PO-104
Tanprawate, Surat	IHC23-PO-113
	IHC23-PO-114
Tarantino, Samuela	IHC23-PO-097
	IHC23-PO-098
	IHC23-PO-101
Tasillo, Miriam	IHC23-PO-016
Tasma, Zoe	IHC23-PO-153
Tassorelli, Cristina	IHC23-DP-019
	IHC23-DP-023
	IHC23-DP-042
	IHC23-IND-013
	IHC23-JT-005
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	IHC23-PO-230
	IHC23-PO-271
	IHC23-PO-274
	IHC23-PO-352
	IHC23-PO-368
Tatsumoto, Muneto	IHC23-PO-006
	IHC23-PO-237
Taşdelen, Bahar	IHC23-OR-007
Taşdelen, Semih	IHC23-DP-009
	IHC23-PO-344
	IHC23-PO-378
Teekaput, Chutithep	IHC23-PO-114
Tekin, Nil	IHC23-PO-124
	IHC23-PO-125
Temiz, Derya	IHC23-PO-124

(continued)

Continued

Author name	Program Codes
	IHC23-PO-125
Tepe, Nermin	IHC23-PO-139
	IHC23-PO-141
	IHC23-PO-256
	IHC23-PO-340
Tepper, Stewart J	IHC23-DP-038
	IHC23-PO-229
Tereshchenko, Sergey	IHC23-PO-089
Terwindt, Gisela M	IHC23-PO-023
	IHC23-PO-076
	IHC23-PO-200
	IHC23-PO-239
	IHC23-PO-364
Terzaghi, Michele	IHC23-DP-023
Thanprasertsuk, Sekh	IHC23-PO-024
	IHC23-PO-027
	IHC23-PO-109
	IHC23-PO-307
Thiankhaw, Kitti	IHC23-PO-114
Thompson, Amy Claire	IHC23-PO-363
Thuraiaiyah, Janu	IHC23-PO-120
Tilling, Jasmin	IHC23-PO-108
Tockhorn-Heidenreich, Antje	IHC23-IND-016
Togha, Mansoureh	IHC23-PO-094
	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-240
	IHC23-PO-294
Toi, Suzuka	IHC23-PO-126
Tolnai, Daniel	IHC23-PO-198
Tolner, Else A	IHC23-PO-023
	IHC23-PO-168
	IHC23-PO-169
Tomino, Carlo	IHC23-PO-014
	IHC23-PO-016
	IHC23-PO-251
Torelli, Paola	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-261
	IHC23-PO-273
Torphy, Bradley	IHC23-PO-241
Torres-Ferrus, Marta	IHC23-PO-080
Toskich, Beau	IHC23-PO-297
Trabassi, Dante	IHC23-PO-361
Tran, Celia	IHC23-DP-044
Trapali, Myrto	IHC23-IND-016
Travers, Brett	IHC23-PO-135
Trenz, Helen	IHC23-IND-010
	IHC23-IND-011
Triller, Paul	IHC23-PO-048
	IHC23-PO-049
	IHC23-PO-051
Trimboli, Michele	IHC23-PO-260
Trugman, Joel M	IHC23-DP-019

(continued)

Continued

Author name	Program Codes
	IHC23-DP-042
	IHC23-IND-007
	IHC23-IND-012
Tsai, Chia-Lin	IHC23-PO-070
Tsai, Ming-Chen	IHC23-PO-070
Tsang, Benjamin	IHC23-PO-135
Tseng, Chyun-Yea	IHC23-JT-002
Tseng, Hsin-Yi	IHC23-OR-012
Tsukalov, Ilya	IHC23-PO-078
Tu, Yi-Hsien	IHC23-PO-056
Tummanapalli, Shyam	IHC23-PO-079
TURKEN, BEYZA	IHC23-PO-164
Turrini, Renato	IHC23-PO-271
Tutt, Joseph	IHC23-PO-170
Tzeng, Hung-Ruei	IHC23-DP-034
Tzeng, Yi-Shiang	IHC23-PO-088
	IHC23-PO-127
	IHC23-PO-149
Türedi Karabulut, Elif Gözde	IHC23-OR-010
Ullum, Henrik	IHC23-PO-069
Uluduz, Ezgi	IHC23-PO-139
	IHC23-PO-141
	IHC23-PO-256
Uludüz, Derya	IHC23-PO-065
	IHC23-PO-118
	IHC23-PO-129
	IHC23-PO-139
	IHC23-PO-141
	IHC23-PO-256
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	IHC23-PO-368
	IHC23-PO-378
Uludüz, Ezgi	IHC23-PO-065
	IHC23-PO-378
Umashankar, Kandavadivu	IHC23-IND-006
Unal-Cevik, Işın	IHC23-PO-064
	IHC23-PO-118
	IHC23-PO-294
Unt, Triin Helin	IHC23-PO-306
Upton, Thomas J	IHC23-PO-023
Ur Özçelik, Emel	IHC23-PO-344
	IHC23-PO-378
Urani, Alexandre	IHC23-PO-009
Urduri, Nagore	IHC23-PO-279
Ursitti, Fabiana	IHC23-PO-097
	IHC23-PO-098
	IHC23-PO-101
Uruçi, Redon	IHC23-PO-367
Uzhakhov, Alikhan	IHC23-PO-276
Uzun, Sena	IHC23-PO-163
	IHC23-PO-233
Uzunkaya, Ozlem	IHC23-PO-141
Vaghi, Gloria	IHC23-DP-023

(continued)

Continued

Author name	Program Codes
	IHC23-JT-005
	IHC23-PO-117
	IHC23-PO-230
	IHC23-PO-352
Vaiyavuth, Ronnakorn	IHC23-PO-113
	IHC23-PO-114
Valenza, Alessandro	IHC23-PO-014
	IHC23-PO-251
Valeriani, Massimiliano	IHC23-PO-090
	IHC23-PO-097
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	IHC23-PO-101
Vallarino, Carlos	IHC23-IND-013
Valsasina, Paola	IHC23-PO-271
Van de Casteele, Tom	IHC23-OR-002
van den Bogaerdt, Antoon	IHC23-DP-026
	IHC23-OR-003
van den Maagdenberg, Arn	IHC23-PO-168
	IHC23-PO-169
	IHC23-PO-374
van der Arend, Britt W.H.	IHC23-PO-239
	IHC23-PO-364
van der Schoor, Alle G	IHC23-PO-364
van der Weerd, N	IHC23-PO-200
van Harten, T.W	IHC23-PO-200
van Heiningen, Sandra	IHC23-PO-169
van Os, H.J.A	IHC23-PO-200
van Tilborg, Paulien J	IHC23-PO-023
van Veelen, Nancy	IHC23-PO-239
van Zwet, Erik W	IHC23-PO-076
	IHC23-PO-364
Vanacore, Nicola	IHC23-PO-090
Vann, Robert E	IHC23-PO-217
Varnado, Oralee	IHC23-IND-010
	IHC23-IND-011
Varnado, Oralee J	IHC23-IND-016
Varrasi, Claudia	IHC23-PO-182
Vashchenko, Nina	IHC23-PO-276
Velardita, Mario	IHC23-PO-090
Velasco, Fernando	IHC23-DP-015
	IHC23-PO-278
	IHC23-PO-279
Venda Nova, Carolina	IHC23-PO-356
Ventrapragada, Advika	IHC23-PO-007
Vera, Paula	IHC23-PO-077
Vernieri, Fabrizio	IHC23-PO-016
	IHC23-PO-117
	IHC23-PO-231
	IHC23-PO-242
	IHC23-PO-273
	IHC23-PO-282
Verrotti, Alberto	IHC23-PO-090
Versace, Antonella	IHC23-PO-090
Versijpt, Jan	IHC23-PO-272
Vikelis, Michael	IHC23-PO-081

(continued)

Continued

Author name	Program Codes
Vikelis, Michail	IHC23-PO-103
	IHC23-PO-268
Viktrup, Lars	IHC23-IND-010
	IHC23-IND-011
	IHC23-IND-013
	IHC23-IND-016
Vila-Pueyo, Marta	IHC23-PO-080
Villalón, C.M	IHC23-OR-003
Villani, Alberto	IHC23-PO-090
Villar Martínez, María Dolores	IHC23-DP-013
	IHC23-PO-151
Vincent, Arnaud	IHC23-DP-004
Vincent, Maurice	IHC23-IND-013
Visseq, Alexia	IHC23-PO-154
Vivancos, José	IHC23-PO-077
	IHC23-PO-078
Vlachos, George	IHC23-PO-268
Voci, Alessandra	IHC23-PO-098
Voller, Corey	IHC23-PO-274
Vollono, Catello	IHC23-PO-075
	IHC23-PO-123
Voskuyl, Rob	IHC23-PO-168
	IHC23-PO-169
Vu, Khanh	IHC23-PO-250
Vu, Michelle	IHC23-IND-010
	IHC23-IND-011
Vurallı, Doga	IHC23-PO-141
Wada, Naomichi	IHC23-PO-002
Wahib, Sahar	IHC23-PO-071
Waite, Jayme	IHC23-DP-037
	IHC23-PO-170
Waldenlind, Elisabet	IHC23-PO-022
	IHC23-PO-044
Waliszewska-Prosół, Marta	IHC23-PO-353
Walker, Christopher	IHC23-PO-153
Wallace, Mark	IHC23-DP-011
Walsh, Vincent	IHC23-DP-012
	IHC23-PO-087
Wan, Qi	IHC23-PO-375
Wanasuntronwong, Aree	IHC23-PO-372
Wang*, Shuu-Jiun	IHC23-PO-315
Wang, Hao	IHC23-JT-001
	IHC23-PO-152
Wang, Liang	IHC23-PO-175
Wang, Mengya	IHC23-PO-170
Wang, Qinfan	IHC23-PO-175
Wang, Rongfei	IHC23-PO-034
Wang, Shuu-Jiun	IHC23-DP-008
	IHC23-DP-014
	IHC23-DP-039
	IHC23-JT-002
	IHC23-PO-033
	IHC23-PO-056
	IHC23-PO-088
	IHC23-PO-127

(continued)

Continued

Author name	Program Codes
	IHC23-PO-149
	IHC23-PO-177
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	IHC23-PO-189
	IHC23-PO-298
	IHC23-PO-337
	IHC23-PO-343
Wang, Tao	IHC23-PO-165
Wang, Victor	IHC23-PO-015
	IHC23-PO-040
	IHC23-PO-042
Wang, Wei	IHC23-DP-030
	IHC23-PO-179
	IHC23-PO-180
	IHC23-PO-181
	IHC23-PO-299
Wang, Xiaojuan	IHC23-PO-375
Wang, Xiaolin	IHC23-PO-034
Wang, Yen-Feng	IHC23-DP-008
	IHC23-DP-014
	IHC23-PO-033
	IHC23-PO-056
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Wang, Yonggang	IHC23-DP-030
	IHC23-PO-179
	IHC23-PO-180
	IHC23-PO-181
	IHC23-PO-299
Wang, Yu	IHC23-DP-022
Wang, Zhen	IHC23-PO-207
Wantaneeyawong, Chayasak	IHC23-PO-114
Watanabe, Narumi	IHC23-PO-228
	IHC23-PO-349
Watanapa, Nattapat	IHC23-PO-027
Watthanaphothithorn, Shanya	IHC23-PO-372
Weber, Konrad	IHC23-PO-373
Wegener, Susanne	IHC23-PO-316
Wei, Diana Y	IHC23-PO-025
	IHC23-PO-026
Wei, Meng	IHC23-PO-175
	IHC23-PO-193
Weiss, Cordula	IHC23-PO-238
Wellfelt, Katrin	IHC23-PO-022
	IHC23-PO-044
Wen, Bing	IHC23-PO-375
Wermer, M.J.H	IHC23-PO-200
Whichello, Chiara	IHC23-IND-016

(continued)

Continued

Author name	Program Codes
Wiggers, Astrid	IHC23-PO-120
Wijesundara, Devasmitha	IHC23-PO-029
	IHC23-PO-037
	IHC23-PO-325
Wilkins, Arnold	IHC23-PO-277
Williams, Steve	IHC23-OR-004
Wilms, A.E	IHC23-PO-200
Wilson, Lauren	IHC23-IND-006
Winsvold, Bendik	IHC23-PO-069
Wong, Ho-Tin	IHC23-PO-236
Wong, Kai On	IHC23-PO-250
Worm, Jacob	IHC23-PO-353
Wu, Chia-Hung	IHC23-DP-008
	IHC23-PO-177
	IHC23-PO-189
Wu, Hsiu-Mei	IHC23-DP-008
	IHC23-PO-177
Wu, Jr-Wei	IHC23-OR-012
	IHC23-PO-033
Wu, Xiaoyu	IHC23-PO-175
Wu, Yu-Te	IHC23-PO-087
Xiao, Zheman	IHC23-PO-054
	IHC23-PO-362
Xiaolin, Wang	IHC23-PO-369
Xiaoyan, Chen	IHC23-PO-369
Xie, Hongyan	IHC23-PO-375
Xie, Wei	IHC23-OR-005
Xiong, Zhonghua	IHC23-DP-030
Xu, Peng	IHC23-PO-375
Xu, Suiyi	IHC23-PO-046
Xu, Wei xingzi	IHC23-PO-332
Xu, Xiaopei	IHC23-PO-184
Xu, Yanmei	IHC23-PO-034
Xu, Yingying	IHC23-PO-362
XUN, HAN	IHC23-PO-369
Yadav, Ekta	IHC23-PO-248
Yadav, Ravi	IHC23-PO-062
Yalınay Dikmen, Pınar	IHC23-OR-007
	IHC23-PO-063
	IHC23-PO-201
	IHC23-PO-254
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	IHC23-PO-378
Yamagishi, Fuminori	IHC23-PO-002
Yamamoto, Toshimasa	IHC23-PO-219
Yamani, Nooshin	IHC23-PO-213
	IHC23-PO-214
	IHC23-PO-335
Yamato, Kentaro	IHC23-PO-006
Yan, Fanhong	IHC23-PO-034
	IHC23-PO-375
Yan, Lanyun	IHC23-PO-375
Yang, Chunxiao	IHC23-JT-001
	IHC23-PO-152
	IHC23-PO-166
Yang, Fu-Chi	IHC23-PO-070

(continued)

Continued

Author name	Program Codes
Yang, Qian	IHC23-PO-207
Yang, Seonkyeong	IHC23-PO-210
Yang, Xiaosu	IHC23-PO-375
Yang, Ying	IHC23-DP-022
Yanmei, Xu	IHC23-PO-369
Yao, Yuanrong	IHC23-PO-046
Yazıcı Gençdal, Işıl	IHC23-OR-007
	IHC23-PO-334
Yaşar, Hatice Selin Irmak	IHC23-PO-124
	IHC23-PO-125
Ye, Chong	IHC23-PO-193
Ye, Ran	IHC23-PO-369
Yeh, Jiann-Horng	IHC23-PO-087
Yeh, Jiunn-Tyng	IHC23-PO-127
Yemisci, Muge	IHC23-PO-164
	IHC23-PO-167
Yen, Jiin-Cherng	IHC23-JT-002
Yeomans, David	IHC23-DP-033
Yeşilot, Nilüfer	IHC23-DP-009
Yin, Ziming	IHC23-PO-017
	IHC23-PO-034
Yinglu, Liu	IHC23-PO-369
Yokoyama, Masako	IHC23-PO-116
Yokoyama, Ryu	IHC23-PO-219
Yoo, Seung-Hee	IHC23-DP-044
Yoon, Won-Tae	IHC23-PO-245
Youn, Michelle	IHC23-PO-232
Young, William	IHC23-DP-043
	IHC23-PO-142
Yri, Hanne Maria	IHC23-OR-006
Yu, Chia-Chun	IHC23-PO-149
Yu, Jing Jie	IHC23-PO-210
Yu, Shengyuan	IHC23-JT-001
	IHC23-OR-005
	IHC23-OR-011
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Yu, Sung Yun	IHC23-IND-007
Yu, Tingmin	IHC23-PO-375
Yu, Xueying	IHC23-PO-179
	IHC23-PO-180
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	IHC23-PO-299
Yu, Zhe	IHC23-PO-375
Yuan, Hsiangkuo	IHC23-PO-015
	IHC23-PO-040

(continued)

Continued

Author name	Program Codes
	IHC23-PO-042
	IHC23-PO-088
	IHC23-PO-203
Yuan, Ziyu	IHC23-DP-030
	IHC23-PO-179
	IHC23-PO-180
	IHC23-PO-181
	IHC23-PO-299
Yuanrong, Yao	IHC23-PO-369
Yung, Young Bok	IHC23-PO-140
Yılmaz Erol, Tülay	IHC23-PO-053
Yılmaz, Gülcan Göçmez	IHC23-PO-141
Zagami, Alessandro	IHC23-PO-079
Zagar, Anthony J	IHC23-PO-270
Zairinal, Ramdinal Aviesena	IHC23-PO-253
ZAKHAROVA, Nishana	IHC23-PO-064
Zakharyan, Armen	IHC23-PO-270
Zakrzewska, Joanna	IHC23-PO-355
	IHC23-PO-356
Zaletel, Marjan	IHC23-PO-067
Zanandrea, Laura	IHC23-PO-242
Zelaya, Fernando	IHC23-PO-178
Zewde, Yared Z	IHC23-PO-344
Zhan, Cathay	IHC23-IND-005
	IHC23-IND-008
Zhang, Dan	IHC23-PO-375
Zhang, Lvming	IHC23-PO-375
Zhang, Mingjie	IHC23-PO-034
	IHC23-PO-207
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Zhang, Peng	IHC23-DP-030
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Zhang, Pengfei	IHC23-PO-001
	IHC23-PO-007
	IHC23-PO-082
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	IHC23-PO-086
Zhang, Shuhua	IHC23-PO-034
	IHC23-PO-046
Zhang, Victor	IHC23-PO-104
Zhang, Xiaochen	IHC23-JT-001
Zhang, Xinhua	IHC23-PO-375
Zhang, Xue	IHC23-PO-179
	IHC23-PO-180
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Zhang, Xueyan	IHC23-PO-179
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Zhang, Yaqing	IHC23-PO-179
	IHC23-PO-180
	IHC23-PO-181

(continued)

Continued

Author name	Program Codes
	IHC23-PO-299
Zhang, Yixin	IHC23-PO-198
Zhang, Yu	IHC23-PO-362
Zhang, Yuwen	IHC23-PO-332
Zhang, Zihan	IHC23-PO-034
Zhao, Dong	IHC23-PO-034
	IHC23-PO-369
Zhao, Heling	IHC23-PO-375
Zhao, Hongling	IHC23-PO-375
Zhao, Hongru	IHC23-PO-046
	IHC23-PO-375
Zhao, Qian	IHC23-PO-207
Zhao, Wei	IHC23-PO-034
Zhao, Yi Jing	IHC23-PO-252
Zhao, Yixin	IHC23-PO-193
Zhihua, Jia	IHC23-PO-369
Zhong, Qi	IHC23-PO-216
Zhou Chen, Hui	IHC23-DP-027
Zhou, Yanjie	IHC23-PO-054
Zhou, Yue	IHC23-OR-005
Zhu, Hua	IHC23-PO-216
Zhu, Yin	IHC23-IND-005
Zhuang, Zixuan Alice	IHC23-PO-197
Ziming, Yin	IHC23-PO-369
Zoroddu, Francesco	IHC23-PO-251
Zou, Yunjun	IHC23-PO-215
Zubieta, Jon-Kar	IHC23-PO-290
	IHC23-PO-291
Zucco, Maurizio	IHC23-PO-251
	IHC23-PO-260
	IHC23-PO-273
Ávalor, Elena	IHC23-PO-078
Çetingök, Halil	IHC23-PO-124
	IHC23-PO-125
Çetingök, Sera	IHC23-PO-124
Çetingök, Sera Yiğiter	IHC23-PO-125
Çevik, Işıl Ünal	IHC23-PO-129
Çimen Atalar, Arife	IHC23-PO-344
Çimen, Barışcan	IHC23-PO-157
Çoban, Oguzhan	IHC23-DP-009
Öcal, Ruhsen	IHC23-PO-141
Öksüz Gürlen, Nevra	IHC23-PO-057
Öksüz, Nevra	IHC23-PO-061
	IHC23-PO-141
	IHC23-PO-378
Örün, Muhammet Okay	IHC23-PO-141
Özbenli, Taner	IHC23-PO-141
Özdağ Acarlı, Ayşe Nur	IHC23-OR-007
Özdemir, Asena Ayça	IHC23-PO-057
	IHC23-PO-061
Özge, Aynur	IHC23-OR-007
	IHC23-PO-057
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	IHC23-PO-344
	IHC23-PO-378
Özkaya-Sahin, Gülsen	IHC23-PO-233
Özçelik, Emel Ur	IHC23-PO-294
Şahbaz, Fatma Gülhan	IHC23-PO-141
Şirin, Nermin Görkem	IHC23-PO-053

(continued)