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ABSTRACTS

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OP001

Effects of oxytocin receptor antagonization in migraine: A randomized, double-blind, placebo-controlled human provocation study

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Objective: Hormonal phases with a decline in oxytocin (OT) levels are associated with an increased incidence of migraine attacks. Beyond temporal correlations, OT multifaced functions, including analgesic effects, interactions with the CGRP pathway and modulation of the trigeminovascular system further support a potential role in migraine pathophysiology. The aim of this study was to investigate whether inhibition of OT signaling through receptor blockade induces migraine attacks in humans.

Methods: In this randomized, placebo-controlled, double-blind, cross-over study, women with episodic migraine (18-45 years, 1-5 monthly migraine days) and healthy female controls were randomized to receive an infusion of the OT-receptor antagonist atosiban (6.75mg bolus over 1 min + 30.75mg over 1.5 h) or placebo on two experimental days separated by at least one week. All participants were required to undergo continuous hormonal contraception in order to ensure stable estrogen and progesterone levels. The primary endpoint was the difference in the incidence of migraine attacks between atosiban and placebo during the 12-hour post-infusion period.

Results: Twenty women with migraine (27.1 +/- 5.6 years) and 20 healthy controls (25.7 +/- 6.8 years) completed the study. During the 12-hour observation period, 30% of migraine patients experienced migraine attacks after atosiban vs. 20% after placebo (p = 0.51). Headache of any kind was reported by 75% after atosiban vs. 55% after placebo (p = 0.34), with no significant difference in headache intensity over 12h. Healthy controls did not develop migraine but reported headaches in 45% after atosiban vs. 30% after placebo (p = 0.25).

Conclusion: Short-lasting oxytocin inhibition through the OT-receptor antagonist atosiban did not significantly increase the incidence of migraine attacks in women with episodic migraine, although a numerical trend was observed.

OP002

Biochemical profiling and symptomatology of androgen deficiency in males with cluster headache – A prospective case-controlled study

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Objective: Cluster headache (CH) is considered a male-dominated disorder, suggesting a role for androgens in its pathophysiology. We aimed to evaluate hormone profiles in CH

Methods: In this prospective case-controlled study, fasted morning blood samples were collected in 30 males with chronic CH (CCH) and 33 males with episodic CH (ECH, in episode and remission) and in 30 healthy age-matched males(HC). Androgen dysfunction surveys (QADAM,AMS) were collected simultaneously. Steroid hormone profiles were compared between groups: total testosterone(tT) including biochemical hypogonadism(tT≤10.5); hormonal pathways and individual hormones. Regression models were applied with BMI, age and smoking as covariates

Results: Biochemical hypogonadism was observed in 20% of participants with CCH(n=6), 6% with ECH(n=3) and 7% with HC(n=2). AMS and QADAM scores were worse in participants with hypogonadism, in ECH (AMS:β=9.59,p<0.001,QADAM:β=-5.25,p<0.001), and CCH(AMS:β=8.78,p<0.001,QADAM:β=-4.59, p<0.001) compared to HC. Apart from one case, gonadotrophin concentrations were not increased, suggesting a central origin. In the unadjusted model, we observed a trend towards a lower, albeit non statistically significant, mean tT in participants with CCH versus HC (CCH:β=-2.35 nmol/L,p=0.059). In the adjusted model, the differences attenuated, suggesting a strong effect of BMI and age on the mean tT(CCH:β=-0.93 nmol/L,p=0.524;ECH:β=0.55 nmol/L,p=0.674). Measures of hormonal pathways and individual hormones did not differ between groups

Conclusion: Biochemical hypogonadism was observed in 1 out of 5 males with CCH. tT trended to be lower in CCH, but this appeared driven by BMI and age since it attenuated after correction. Androgen deficiency symptoms were more prevalent in CH compared to healthy controls, independent of hypogonadism. Physicians should be aware of potential increased risk and symptoms of (central) hypogonadism in CCH. Further investigation should explore shared underlying mechanisms and tT suppletion in CH

Fig. 1

Table 1. Results of the unadjusted (A) and adjusted (B) linear regression model comparing total testosterone (tT) between participants with episodic (in episode) cluster headache, chronic cluster headache and headache free controls. Covariates were age, BMI and smoking. Reference group is headache free controls (HC).

A: Unadjusted model

	β	95% CI	p-value
CCH	-2.35	-4.79 to 0.09	0.0594
ECH	-0.34	-2.76 to 2.08	0.7787

B: Adjusted model

	β	95% CI	p-value
CCH	-0.93	-3.81 to 1.95	0.524
ECH	0.55	-2.05 to 3.15	0.674
Age	-0.06	-0.12 to 0.00	**0.043***
BMI	-0.40	-0.67 to -0.14	**0.003***
Smoking	-1.06	-3.40 to 1.28	0.371

Fig. 2

Table 2. Raw average levels of individual hormones and unadjusted group comparisons

	Chronic Cluster Headache (N=30)	Episodic Cluster Headache, active (N=32)	Episodic Cluster Headache, remission (N=28)	Healthy Controls (N=30)	P-value group comparisons [a]
tT *nmol/L*	15.3 (± 5.21)	17.3 (± 4.34)	17.22 (± 4.93)	17.65 (± 4.69)	*Table 1*
fT *pmol/L*	309.16 (± 93.69)	323.81 (± 85.71)	332.18 (± 93.78)	328.45 (± 106.96)	0.718, 0.422
SHBG *nmol/L*	34.35 (27.28 – 39.6)	**40.1 (31.75 – 49.55)**	**36.8 (29.58 - 45.25)**	36.65 (30.1 - 51.72)	0.100, **0.008***
AND *nmol/L*	2.78 (2.2 – 4.15)	3.02 (2.6 - 4.5)	2.99 (2.62 - 3.18)	2.8 (2.18 - 3.74)	0.263, 0.722
DHEA *nmol/L*	7.55 (5.03 – 11.27)	9.3 (7.3 - 13.9)	10.4 (7.45 - 12.85)	8.55 (4.78 - 16.12)	0.592, 0.988
DHT *nmol/L*	1.1 (± 0.55)	1.24 (± 0.51)	1.26 (± 0.61)	1.16 (± 0.54)	0.590, 0.204
AMH *µg/L*	5.37 (3.26 - 9.88)	5.46 (2.79 - 6.9)	5.2 (2.84 - 7.11)	5.12 (3.15 - 8.02)	0.836, 0.446
FSH *U/L*	5.3 (4.05 - 7.47)	5.4 (3.25 – 8.55)	4.4 (2.77 - 7.4)	5.05 (3.92 - 7.5)	0.963, 0.319
LH *U/L*	3.8 (2.83 - 5.38)	3.5 (2.5 - 4.3)	3.85 (2.8 - 4.93)	3.8 (2.85 - 5.07)	0.699, 0.303
E2 *pmol/L*	121.7 (± 32.37)	116.71 (± 25.07)	125.75 (± 28.56)	120.8 (± 25.65)	0.757, 0.517
Cortisol *nmol/L*	366.7 (± 126.3)	381.75 (± 113.28)	355.43 (± 102.72)	385.52 (± 106.02)	0.800, 0.512
Inhibin B *ng/L*	232.87 (± 97.36)	236 (± 118.84)	247 (± 121.15)	246.8 (± 116.36)	0.879, 0.580
fTSN/LH *pmol/IU*	86.64 (± 39.69)	96.99 (± 40.55)	93.37 (± 42.1)	89.81 (± 37.45)	0.574, 0.417
fTSN/E2 *pmol/IU*	2.72 (2.01 - 3.16)	2.78 (2.32 - 3.32)	2.45 (2.03 - 3.28)	2.45 (1.99 - 3.77)	0.578, 0.635
InhB/FSH *ng/IU*	44.63 (23.37 - 65.11)	44.73 (18.23 - 76.1)	53.02 (25.62 - 93.01)	47.9 (23.35 - 70.74)	0.966, 0.881
11-KT *nmol/L*	1.33 (± 0.64)	1.37 (± 0.63)	1.44 (± 0.52)	1.27 (± 0.48)	0.811, 0.689
11-KA4 *nmol/L*	0.56 (0.33 - 0.68)	0.64 (0.41 - 0.81)	0.65 (0.49 - 0.72)	0.55 (0.37 - 0.73)	0.449, 0.721
11-OHA4 *nmol/L*	5.56 (4.05- 6.89)	6.43 (3.93 – 9.04)	5.01 (4.44 - 7.53)	5.89 (4.01 - 7.5)	0.666, 0.437
11-OHT *nmol/L*	0.68 (± 0.33)	0.73 (± 0.29)	0.74 (± 0.33)	0.75 (± 0.31)	0.665, 0.671

Serum levels are are depicted as median (IQR) or mean (±SD) depending on distribution.[a] First ANOVA or Kruskall wallis (depending on distribution) p-value for ECH vs CCH vs HC and second p-value for ECH in vs out-episode (paired T test or Wilcoxon). DHEA, DHT, 11OHTSN and 11KetoAND contain samples with values below Lower Limit of Quantification (LLOQ), values of these are calculated as LLOQ/2.

Fig. 3

Table 3. Results of regression models of AMS and QADAM scores compared between subgroups.

A Results of linear regression models ECH, CCH and HC. Reference group is headache free controls (HC).

	β	95% CI	p-value
AMS			
CCH	8.78	4.45 to 13.12	**<0.001***
ECH	9.59	5.69 to 13.50	**<0.001***
Age	0.06	-0.04 to -0.17	0.239
BMI	-0.20	-0.65 to 0.26	0.3888
Smoking	-0.37	-3.84 to 3.09	0.831
Depression symptoms	14.17	10.25 to 18.10	<0.001
QADAM			
CCH	-4.59	-6.97 to -2.22	**<0.001***
ECH	-5.25	-7.39 to -3.11	**<0.001***
Age	-0.08	-0.13 to -0.02	**0.010***
BMI	0.03	-0.21 to 0.28	0.790
Smoking	0.75	-1.15 to 2.65	0.433
Depression symptoms	-6.79	-8.93 to -4.63	**<0.001***

B. Results of linear mixed models compared between in episode and in remission in participants with ECH. Reference group is ECH in remission.

	β	95% CI	p-value
AMS			
ECH, in episode	5.74	2.74 to 8.82	**0.001***
Depression symptoms	9.142	3.91 to 14.38	**0.001***
QADAM			
ECH, in episode	-1.08	-2.68 to 0.51	0.193
Depression symptoms	-6.19	-9.32 to -3.16	**<0.001***

OP003

Non-paralytic botulinum toxin A in trigeminal neuralgia

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Objective: Trigeminal neuralgia (TN) is the most common craniofacial chronic neuropathic pain type and is among the most severe pain types. It manifests as short, electric shock-like pain paroxysms in areas enervated by the trigeminal nerve. Acute treatments are ineffective, and current preventative pharmacotherapies are often limited by poor specificity, inadequate efficacy, and severe side effects. To address these limitations, recombinant botulinum toxin A (BoNT/A) molecules (el-Bitox/A) retaining analgesic but minimal paralytic activity have been developed. This study evaluated el-Bitox/A analgesic efficacy and safety versus native BoNT/A and carbamazepine (CBZ), to the gold-standard treatment, in a TN rat model.

Methods: TN was induced by chronic constriction injury of the infraorbital nerve (IoN-CCI) in male and female rats, and mechanical allodynia was monitored over two weeks using von Frey monofilaments. el-Bitox/A (20 ng) and BoNT/A (5 U) were injected subcutaneously into the ipsilateral cheek one week post-surgery. CBZ (30mg/kg) was given intraperitonially for 7 days and effects assessed after the first dose (acute) and 7 days (chronic). Body weight was monitored as an indirect measure of facial paralysis due reduced jaw strength and impaired food intake.

Results: Mechanical allodynia was reversed by el-Bitox/A and BoNT/A. Acute CBZ had no effect on mechanical allodynia, and only partial reversal was seen after 7 days (n=5–7 per group; P<0.05). BoNT/A, but not el-Bitox/A or CBZ, caused significant weight loss (P<0.05), confirming the non-paralytic profile of el-Bitox/A. Vehicle had no effect in both parameters (n=6 per group).

Conclusion: Both BoNT/A and el-Bitox/more effectively reversed TN-associated hypersensitivity than the gold-standard CBZ. However, BoNT/A had significant side effects that can be avoided by using the non-paralytic el-Bitox/A. These findings highlight el-Bitox/A as a promising, effective treatment option for neuropathic pain.

OP004

Interictal subcortical and cortical anomalies in the sensorimotor pathway of subjects with migraine: A resting state high-density EEG analysis

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Objective: To determine whether the interictal electroencephalographic (EEG) changes observed in subjects with migraine result from aberrant rhythmic pacemaker activity of subcortical or cortical structures within the sensorimotor pathway.
Methods: A resting state 64-channel EEG was recorded in 42 subjects with migraine without aura (MO) during their interictal phase and for comparison in 42 healthy volunteers (HV). The brain activity of four nodes in the sensorimotor pathway (brainstem, thalamus, S1, and M1) was extracted using a functional source separation approach (FSS) with ad-hoc spatial functional constraints. Spectral characteristics and Higuchi's fractal dimension (FD) were examined for each node to estimate the linear and non-linear brain activity and its complexity.
Results: Compared to HVs, subjects with MO had significantly elevated FD values in the brainstem and thalamus in both the left and right hemispheres. No significant differences in FD values were observed between the two cortical nodes (S1 and M1). Additionally, MO showed an increase in delta and a decrease in alpha power spectral density in all four nodes of the sensorimotor system.
Conclusion: Subjects with MO during the interictal phase have alterations in the linear and non-linear functioning of the brainstem and thalamic subcortical nodes in the sensorimotor system. These alterations may be pivotal in the migraine pathophysiology, causing changes in the rhythmic patterns of the cortex.

OP005

Neurofilament light chain and glial fibrillary acidic protein as serum biomarkers of treatment response to CGRP monoclonal antibodies in migraine

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Objective: There is urgent need for biomarkers in migraine. We aimed at investigating the associations of serum -neurofilament light chain (sNfL) and -glial fibrillary acidic protein (sGFAP) with treatment response to Calcitonin Gene-Related Peptide monoclonal antibodies (CGRP mAbs).
Methods: In this prospective observational study, patients with chronic or high-frequency episodic migraine were recruited, before treatment start with CGRP mAbs. sNfL and sGFAP levels were measured at baseline (BL) and month 6 (M6) and were converted to percentiles as previously described. Treatment response was defined as ≥50% reduction in monthly headache days (MHD) at M6 vs. BL. The trajectories of biomarker percentiles were investigated using linear mixed models. The associations of BL-biomarkers with treatment response were analyzed using univariable- and stepwise multivariable logistic regression.
Results: 68 patients (median age:40 years(y), disease duration:17 y, 84% female, 60% chronic, median MHD at BL:18) were included. sNfL and sGFAP levels at BL were not elevated (median percentile of sNfL:39, IQR [19, 61], sGFAP:30, IQR [13, 54]).
At M6, 33/68 (49%) of the patients were responders. Biomarker percentiles did not change over six months (median sNfL at M6:32, sGFAP:33; both p>0.465).
Univariable analysis showed no significant associations between BL sNfL or sGFAP, and treatment response at M6 (p=0.523 and p=0.082, respectively). In the multivariate analysis, higher sGFAP percentile at BL (OR=0.958, 95% CI [0.922, 0.994], p=0.023) and more BL-MHDs (OR=0.839, 95% CI [0.723, 0.972], p=0.020) were associated with lower probability of being a responder.
Conclusion: Higher sGFAP percentiles at baseline were associated with worse response to CGRP-mAbs in the multivariable analysis. While the role of this biomarker in migraine is still under investigation, a potential value in disease phenotyping and prediction of treatment responses seems promising and should be validated in larger cohorts.

OP006

Corneal confocal microscopy reveals nerve fiber laterations in migraine irrespective of subtype or visual hypersensitivity

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Objective: Corneal confocal microscopy (CCM) is a noninvasive ophthalmic imaging technique for evaluating the corneal microstructure, particularly the subepithelial nerve plexus. This dense, dynamic plexus contains small nerve fibers from the ophthalmic branch of the trigeminal nerve. This study aimed to

evaluate corneal nerve alterations in individuals with migraine, including its subtypes and visual hypersensitivity (measured with L-VISS).
Methods: Participants were individuals with episodic (EM) or chronic (CM) migraine, and controls. All subjects underwent CCM, and automated corneal nerve fiber density (ACNFD), length (ACNFL), and branch density (ACNBD) were assessed using the Rostock Cornea Module (Heidelberg Retina Tomograph III). Data were compared with age- and sex-matched healthy volunteers.
Results: Reduced ACNFD, ACNFL, and ACNBD were found in migraine participants compared to controls (all p <.001). No difference was found between EM and CM, and regression analysis showed no significant effect for (inter)ictal visual hypersensitivity.
Conclusion: These findings support the utility of CCM as a sensitive tool for detecting nerve fiber pathology in migraine and highlight its potential in further understanding migraine pathophysiology. The observed nerve changes, present irrespective of migraine frequency status or visual hypersensitivity, suggest a broader role for peripheral nerve dysfunction in migraine beyond sensory hypersensitivity symptoms.

OP007

Breaking the chronic migraine cycle: Semaglutide modulates pain, well-being, and cannabinoid signaling in a preclinical study

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Objective: Chronic migraine (CM) is a disabling neurological disorder that profoundly impairs quality of life. Up to **70%** of patients are **dissatisfied with current prophylactic therapies**. GLP-1 receptor agonists, particularly liraglutide, have shown potential in reducing pain hypersensitivity in preclinical and clinical settings. Chronic migraine has been associated with dysregulation of the endocannabinoid system (ECS), including altered CB1 receptor (*Cnr1*) and endocannabinoid-degrading enzyme (*Faah, Mgll*) expression. We aimed to assess semaglutide"s effects on pain-like behaviour, well-being, and cannabinoid signaling in a mouse model of CM.
Methods: Male and female mice developed a CM-like state through repeated intraperitoneal (*i.p.*) nitroglycerin injections. Semaglutide (subcutaneous) or propranolol (*i.p.*, reference drug) was administered daily over nine days. The orofacial glutamate test (chemical-stimulus evoked facial pain) and the burrowing test (indicative of spontaneous pain and well-being) were used for behavioural evaluation. Brainstem and trigeminal ganglia (TG) samples were collected post-mortem for qPCR analysis of *Cnr1*, *Faah*, and *Mgll* mRNA expression to assess ECS involvement.
Results: Semaglutide significantly reduced glutamate-evoked nociceptive behavior in both sexes, with efficacy comparable to propranolol. However, only semaglutide restored burrowing behaviour in males and females. Molecular analysis revealed sex- and region-specific ESC modulation: in males, semaglutide upregulated *Cnr1* and *Faah* in the brainstem and downregulated *Cnr1* and *Mgll* in the TG; in females, brainstem *Faah* and *Mgll* expression was decreased.
Conclusion: Semaglutide reduced pain-like behaviour comparably to propranolol while also enhancing motivational behavior, suggesting broader benefits for overall well-being. Semaglutide modulated ECS in a sex-specific manner, indicating distinct neurobiological responses in males and females. **These results support semaglutide as a promising candidate for CM therapy**.

Fig. 1

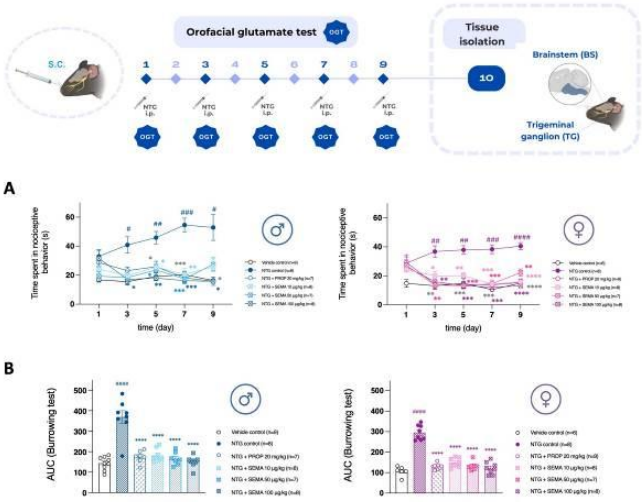


Figure 1. Semaglutide (SEMA) and propranolol (PROP) reduced chemical pain hypersensitivity in male (*blue lines*) and female (*purple lines*) mice with nitroglycerin (NTG)-induced chronic migraine. SEMA and PROP were administered subcutaneously and intraperitoneally, respectively, once daily for nine days. Results are presented as time-course data of the time spent in nociceptive behaviour in seconds (A) and the area under the curve (AUC) data (B) obtained using the orofacial glutamate test. Data were analysed using two-way repeated measures ANOVA followed by Tukey post-hoc test for time-course data (#P < 0.05, ##P < 0.01, ###P < 0.001, ####P < 0.0001, for vehicle vs. NTG control; *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001, for treatment vs. NTG control) and one-way ANOVA followed by Tukey post-hoc test for AUC values (####P < 0.0001, for vehicle vs. NTG control; ****P < 0.0001 for treatment vs. NTG control).

Fig. 2

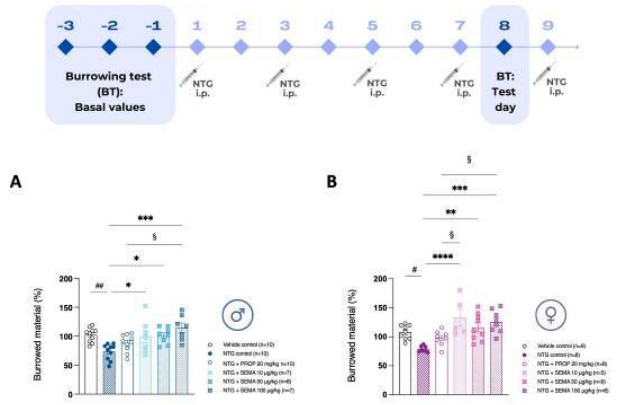


Figure 2. Semaglutide (SEMA) but not propranolol (PROP) improved burrowing behaviour in male (A) and female (B) mice with nitroglycerin (NTG)-induced chronic migraine. SEMA and PROP were administered subcutaneously and intraperitoneally, respectively, once daily for nine days. Results are presented as the amount of burrowed material (%) obtained using the burrowing test. Data were analysed using one-way ANOVA followed by Tukey post-hoc test (#$P < 0.05$, ##$P < 0.01$, for vehicle vs. NTG control; *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$, for treatment vs. NTG control; §$P < 0.05$, for SEMA vs. PROP).

Fig. 3

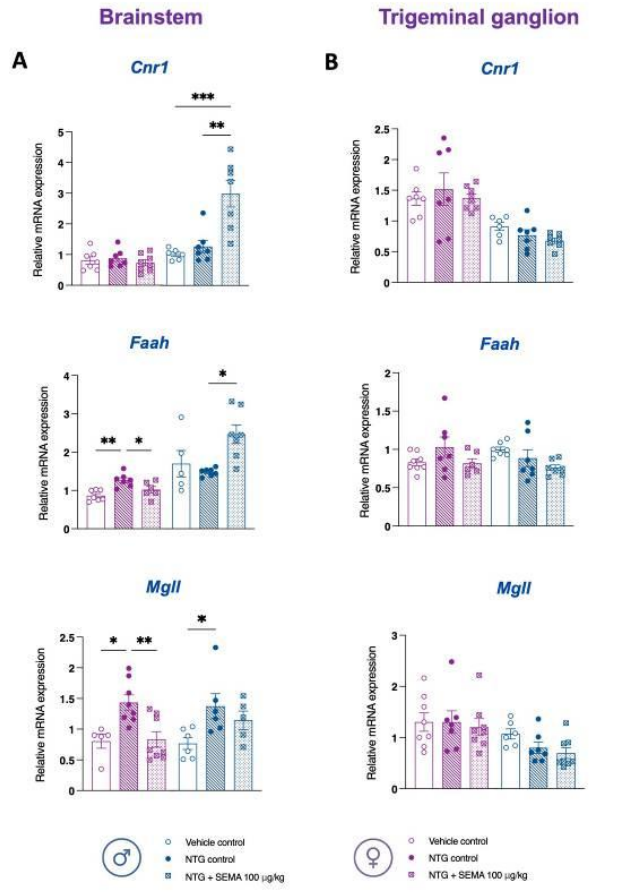


Figure 3. The effects of SEMA on the mRNA expression of *Cnr1*, *Faah* and *Mgll* in the brainstem (A) and trigeminal ganglion (B) of male (*blue lines*) and female (*purple lines*) mice with nitroglycerin (NTG)-induced chronic migraine. SEMA was administered subcutaneously once daily for nine days. Tissues were isolated 10 day upon chronic migraine induction. Data were analysed using one-way ANOVA followed by Tukey post-hoc test (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$).

OP008

Cannabidiol in chronic migraine prevention: Results of a pilot randomized double-blind, placebo-controlled trial

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Objective: To evaluate the efficacy and tolerability of escalating doses of Cannabidiol (CBD) for the prevention of chronic migraine.

Primary objective

To evaluate the change in the average number of migraine days per month with increasing doses of CBD over the 3-month treatment period compared to the placebo group.

Secundary obtective

To assess the evolution of migraine intensity in relation to treatment from baseline and explore the relationship between CBD dose escalation and migraine-free days.

Methods: This study was a randomized, double-blind, placebo-controlled trial for CBD dose escalation, involving 30 patients with chronic migraines, selected according to specific inclusion and exclusion criteria. Elea Laboratory (Argentina) provided the investigational product (CBD) along with a corresponding placebo. All participants were divided into three groups: placebo, CBD at 10 mg/ml, or 20 mg/ml, for a duration of three months.

Results: After three months, CBD 10 mg/ml and CBD 20 mg/ml demonstrated a 68% and 79% reduction in monthly migraine days compared to the placebo group (Fig 1).

Figure 1. Migraine days (mean ± 95% CI) during each 1-month interval. ** P < 0. 05.

After three months, the CBD 10 and 20 mg/ml groups reported that 64% of patients experienced migraine-free days, with the CBD 20 mg/ml treatment showing an increase to 79%. In contrast, the percentage of patients treated with a placebo decreased by 15%, indicating that migraine-free days diminished rather than increased, which is a negative outcome (Fig. 2).

Figure 2. Relationship between CBD dose escalation and migraine-free days

Safety

Somnolence was the most commonly observed side effect during the three treatments.

Conclusion: The results of this study demonstrate that CBD at 10 or 20 mg/ml appears to be effective and well-tolerated for the preventive treatment of chronic

migraine, justifying further studies with a larger population.

Fig. 1

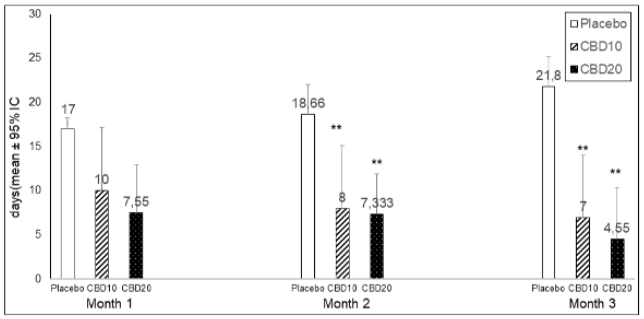
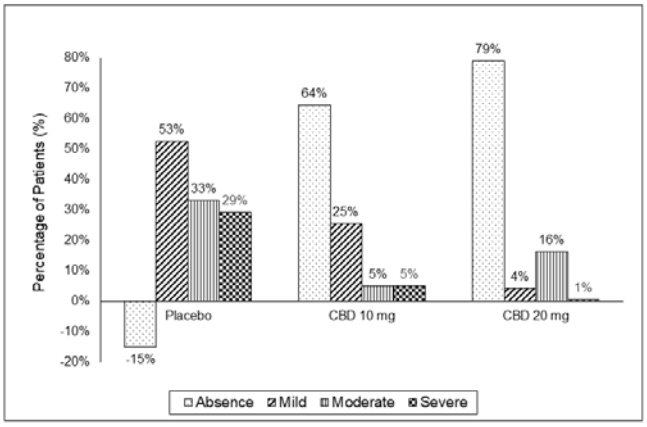


Fig. 2



OP009

Exploring the central effect of anti CGRP-monoclonal antibodies in migraine patients: A resting-state functional MRIstudy

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Objective: While MRI studies have explored brain changes in migraine patients treated with anti-CGRP monoclonal antibodies (mAbs), direct comparisons with untreated patients over time are lacking. We used resting-state functional MRI (RS-fMRI) to compare patients treated with mAbs (mAbs group) to untreated (non-mAbs group), aiming to isolate treatment-specific central effects.

Methods: Forty-eight migraine patients were enrolled: 37 received mAbs and 15 were untreated. Thirty-three matched healthy controls (HC) were assessed at baseline. Clinical and MRI evaluations were performed at baseline and after 3 months (3M). Resting-state functional connectivity (rs-FC) was analyzed using a seed-to-voxel approach based on 11 regions of interest, including cerebellum, periaqueductal gray (PAG), pons, thalamus, hypothalamus, and spinal trigeminal nucleus (STN). Clinical outcomes included monthly migraine days (MMD), acute medication day (AMD) and pills (AMP), pain intensity, disability, headache impact, and cutaneous allodynia.

Results: At baseline, migraine patients showed increased RS FC between the left (L) pons and L frontal gyrus and reduced FC between the cerebellum and right (R) insula compared to HC. Moreover, the mAbs group, characterized by higher MHD, MMD, and AMP, showed reduced RS FC between the L STN and the L cerebellum compared to the non-mAbs group. After 3M, compared to non-mAbs patients, the mAbs group demonstrated greater overall clinical improvement and a significant increase in RS FC between the L STN and L cerebellum, which correlated with decreased migraine frequency.

Conclusion: Patients eligible for mAbs showed altered pain network connectivity, indicating a more severe phenotype. Compared to untreated, mAbs patients had greater clinical improvement and STN network reorganization, supporting central effects beyond the natural disease course. Rs-FC may serve as a biomarker of migraine severity and treatment response.

OP010

Selective reduction of circulating β-CGRP in patients developing de-novo constipation during anti-CGRP antibody therapy

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Objective: To investigate the role of CGRP isoforms in the development of de-novo constipation in migraine patients treated with monoclonal antibodies targeting CGRP (mAb-CGRP).

Methods: We conducted a prospective study in 133 patients diagnosed with high-frequency episodic or chronic migraine. Plasma concentrations of α-CGRP and β-CGRP were measured by enzyme-linked immunosorbent assay (ELISA) at baseline (M0) and three months (M3) after initiating mAb-CGRP therapy. Clinical data, including onset of constipation, comorbidities, and therapeutic response, were collected and analyzed.

Results: De-novo constipation was reported in 12 patients (9.0%) following initiation of mAb-CGRP treatment. Baseline demographics, efficacy parameters, use of concomitant preventive therapies, and most comorbidities did not differ between groups, except for a higher prevalence of anxiety/depression in those with constipation. A significant reduction in α-CGRP levels was observed at three months (M0: 49.5 [IQR 29.2–73.8] pg/mL; M3: 40.5 [20.4–61.0] pg/mL; p < 0.0001), occurring similarly in both groups. While overall β-CGRP levels remained unchanged over the course of treatment (M0: 4.0 [2.1–6.2]pg/mL; M3: 4.3 [2.5–6.0]pg/mL; p=0.574), a selective reduction was observed only in patients who developed constipation (M0: 6.1 [4.7–8.4] pg/mL; M3: 5.0 [3.6–5.7] pg/mL; p=0.034).
Conclusion: This is the first study to demonstrate a selective decrease in β-CGRP in patients with de-novo constipation during mAb-CGRP therapy. The findings support a mechanistic role of β-CGRP antagonism, particularly relevant to gastrointestinal function regulation, in this adverse event, while α-CGRP antagonism appears more closely tied to therapeutic migraine benefit.
This research was supported by grant PMP22/00183.

OP011

Unraveling the spectrum of migraine resistant to Anti-CGRP treatments: Is there a role for the endocannabidiome system?

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Objective: Monoclonal antibodies targeting the CGRP pathway (mAbs) fail in nearly 40% of migraine individuals that may bear a non CGRP-dependent phenotype, potentially attributable to endocannabinoid system (eCBome) dysfunction. Primary aim is to compare eCBome catabolizing enzymes expression of Fatty acid amide hydrolase (FAAH) and Monoacylglycerol lipase (MAGL) between mAbs Responders (RES) and Non-responders (NON-RES). Secondary aims assess differences in other eCBome enzymes (DAGL, NAPE, NAAA), plasma levels of endocannabinoid-associated lipids (AEA, 2-AG, PEA, OEA) and neuropeptides (CGRP, PACAP and VIP).
Methods: We enrolled 59 individuals treated with mAbs (age 43.2 ± 13.2 years), 83.1% females, 34 with high frequency episodic migraine, 25 with chronic migraine, who failed 3.4±1.1 preventive medication classes. NON-RES presented <50% reduction in monthly migraine days in the third month of mAbs compared to baseline. At baseline, we assessed mRNA gene expression (Relative Quantification-RQ) of FAAH and MAGL and eCBOMe enzymes in peripheral blood mononuclear cells and performed plasma quantifications of endocannabinoid-associated lipids and neuropeptides.
Results: Out of the 59 subjects, 45 completed the 3-month follow-up, with 57.8% (n=26) qualifying as RES. MAGL expression was higher in NON-RES (1.97±0.61 RQ) vs. RES (1.58±0.63 RQ, p=0.018). No differences were observed for FAAH (NON-RES 0.75±0.22 RQ vs. RES 0.74±0.25 RQ, p=0.868) and the other eCBome components analyzed. Among neuropeptides, only VIP presented higher plasma levels in NON-RES (151.80±73.33 RQ) vs. RES (91.84±54.89, p=0.031).
Conclusion: NON-RES presented an elevated 2-arachidonoyl glycerol turnover, a key component of the eCBome. This is consistent with previous evidence of an increased MAGL expression in migraine individuals with a severe disease phenotype. Our preliminary findings suggest that a eCBome dysfunction may be pronounced in mAbs NON-RES.

OP012

Alpha-synuclein deficiency attenuates nociceptive signaling in mouse trigeminal afferents relevant to migraine

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Objective: Migraine has been linked to an elevated risk of neurodegenerative disorders, yet the biological mechanisms underlying this association remain unclear. One potential link involves α-synuclein, a neuronal protein encoded by the *Snca* gene, which is essential for synaptic plasticity and neurotransmitter release. While abnormal aggregation of α-synuclein, is a hallmark of Parkinson Disease (PD), its role in pain signalling is poorly understood. Notably, in PD, a very common accompanying symptom is pain, the mechanisms of which are little understood. Interestingly, α-synuclein is a part of neuronal secretory machinery, which is relevant to migraine-related mechanisms of pain, associated with transmitter/neuropeptide release. In this study, we investigated the impact of α-synuclein deficiency on nociceptive signaling in trigeminal meningeal

afferents, a key pathway implicated in migraine pathophysiology.

Methods: Adult C57BL/6JOlaHsd mice (Harlan strain) of both sexes, which carry a chromosomal deletion of the *Snca* gene, served as the experimental group. Age- and sex-matched C57BL/6J mice were used as controls. Electrophysiological recordings of nociceptive spiking activity were obtained from trigeminal meningeal afferents under baseline conditions and following stimulation with 50 mM KCl to assess generalized excitability.

Results: Baseline nociceptive spiking activity was reduced in meningeal afferents of C57BL/6JOlaHsd mice (31 ± 23 spikes/10 min) compared to C57BL/6J controls (997 ± 382 spikes/10 min). Similarly, KCl-induced neuronal excitability of primary afferents was dramatically lower in C57BL/6JOlaHsd mice (64 ± 27 spikes/30 s), representing a 4.7-fold reduction relative to controls (305 ± 63 spikes/30 s).

Conclusion: These findings indicate that α-synuclein deficiency attenuates nociceptive signaling in the trigeminal system, suggesting a previously unrecognized role for α-synuclein in modulating pain pathways associated with migraine.

OP013

Semaglutide mitigates pain hypersensitivity and cognitive dysfunction in a murine model of chronic migraine: Possible role of opioidergic signaling pathways

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Objective: Chronic migraine (CM) is a debilitating headache characterized by persistent pain hypersensitivity and cognitive deficits. Therapeutic strategies targeting both domains remain limited. Preclinical data suggest that GLP-1 receptor agonists (GLP-1 RAs), particularly liraglutide, may alleviate pain in CM. While their procognitive effects are established in other neurological conditions, it is unclear if these benefits extend to CM. We aimed to assess whether semaglutide (a GLP-1 RA) improves pain sensitivity and cognition in a mouse model of CM, focusing on opioidergic signaling and sex differences.

Methods: A CM-like state was induced in C57BL/6 mice of both sexes by repeated intraperitoneal (i.p.) injections of nitroglycerin. Semaglutide (subcutaneous) and propranolol (i.p.; positive control) were administered daily for nine days. Pain hypersensitivity was evaluated using the von Frey test (VFT), and cognitive performance by the novel object recognition test (NORT). Opioidergic involvement was assessed by (1) naloxone (non-selective opioid receptor antagonist) and (2) qPCR analysis of *Glp1r* and *Pomc1* mRNA expression in brainstem and trigeminal ganglia.

Results: Semaglutide dose-dependently reduced both basal and acute mechanical hypersensitivity, with efficacy comparable to propranolol in both sexes (Fig. 1). Unlike the reference drug, semaglutide significantly improved cognitive performance regardless of sex (Fig. 2). Naloxone reduced its antinociceptive effect in the VFT and tended to diminish cognitive benefits in the NORT, indicating opioidergic mediation. In brainstem, both *Glp1r* and *Pomc1* were upregulated in males, while only *Glp1r* was increased in females. No significant changes were detected in trigeminal ganglia (Fig. 3).

Conclusion: Semaglutide mitigated pain hypersensitivity *via* opioidergic pathways and, in contrast to the reference drug, improved cognitive performance in CM mice. These findings support its potential to address both nociceptive and cognitive domains of CM.

Fig. 1

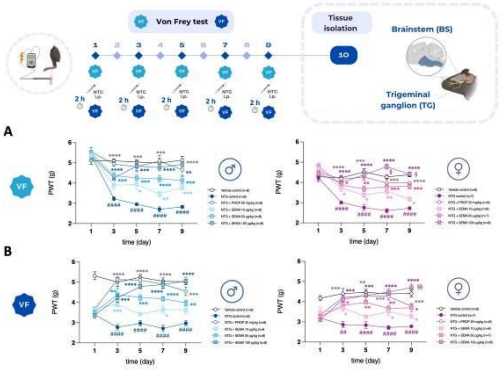


Figure 1. Semaglutide (SEMA) and propranolol (PROP) reduced basal (A) and acute (B) mechanical pain hypersensitivity in male (*blue lines*) and female (*purple lines*) mice with nitroglycerin (NTG)-induced chronic migraine. SEMA and PROP were administered subcutaneously and intraperitoneally, respectively, once daily for nine days. Results are presented as time-course data of paw withdrawal threshold (PWT) obtained using the von Frey test. Data were analysed using two-way repeated measures ANOVA followed by Tukey post-hoc test (###P < 0.001, ####P < 0.0001, for vehicle vs. NTG control; *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001, for treatment vs. NTG control; §P < 0.05, §§P < 0.01, for SEMA vs. PROP).

Fig. 2

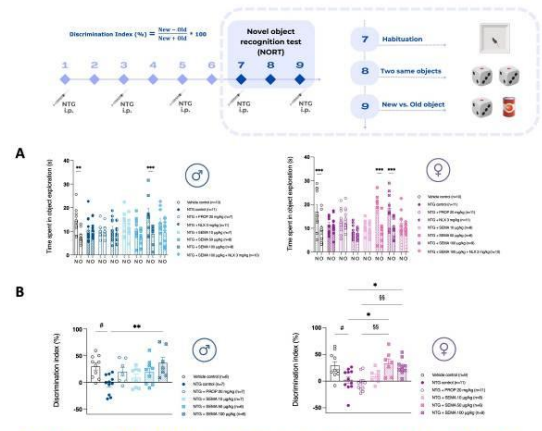


Figure 2. Semaglutide (SEMA) but not propranolol (PROP) improved cognitive performance in male (*blue lines*) and female (*purple lines*) mice with nitroglycerin (NTG)-induced chronic migraine. SEMA and PROP were administered subcutaneously and intraperitoneally, respectively, once daily for nine days. Results are presented the time spent exploring novel (N) and old (O) object (in seconds) and as the discrimination index (DI%) (B) obtained from the novel object recognition test. Data were analysed using two-way ANOVA followed by Tukey post-hoc test for N vs. O object comparison (**P < 0.01, ***P < 0.001) and one-way ANOVA followed by Tukey post-hoc test for DI% (#P < 0.05, for vehicle vs. NTG control; *P < 0.05, **P < 0.01, for treatment vs. NTG control; §§P < 0.01, for SEMA vs. PROP).

Fig. 3

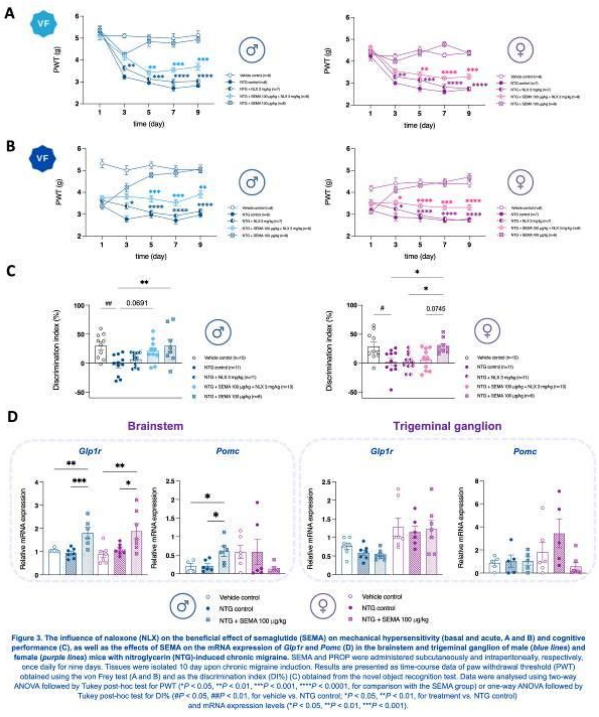


Figure 3. The influence of naloxone (NLX) on the beneficial effect of semaglutide (SEMA) on mechanical hypersensitivity (basal and acute, A and B) and cognitive performance (C), as well as the effects of SEMA on the mRNA expression of *Glp1r* and *Pomc* (D) in the brainstem and trigeminal ganglion of male (*blue lines*) and female (*purple lines*) mice with nitroglycerin (NTG)-induced chronic migraine. SEMA and PRCP were administered subcutaneously and intraperitoneally, respectively, once daily for nine days. Tissues were isolated 10 day upon chronic migraine induction. Results are presented as time-course data of paw withdrawal threshold (PWT) obtained using the von Frey test (A and B) and as the discrimination index (DI%) (C) obtained from the novel object recognition test. Data were analysed using two-way ANOVA followed by Tukey post-hoc test for PWT (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$, for comparison with the SEMA group) or one-way ANOVA followed by Tukey post-hoc test for DI% (#$P < 0.05$, ##$P < 0.01$, for vehicle vs. NTG control; *$P < 0.05$, **$P < 0.01$, for treatment vs. NTG control) and mRNA expression levels (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$).

OP014

Implementation of an occupational health programme for migraine management: Lessons from the workplace MiGRA-Care study

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Objective: Migraine is a leading contributor to productivity loss. Despite international recommendations, occupational health interventions for migraine remain scarce. This study aimed to evaluate preliminary implementation outcomes of Workplace MiGRA-Care, a migraine management programme at work.

Methods: A Type 1 hybrid effectiveness-implementation randomized study was conducted in Portuguese companies with ≥250 employees. The intervention comprised 4 components: (1) training sessions for health professionals, (2) workplace migraine management checklist, (3) digital self-management toolkit, and (4) migraine-specific medical consultation. Participants with self-reported migraine were randomized (1:1) to intervention or control.

Results: Recruitment began in Nov 2023 and lasted 11 months. Of 155 companies identified, 139 were contacted and 56 responded. Following screening, 35 companies attended a project presentation and 11 (8%) adopted the programme. Main reasons for non-participation were insufficient occupational health capacity (n=12; 34%), internal bureaucratic hurdles (n=4; 11%), and cost concerns (n=1; 3%).

One company was national, 7 in northern Portugal and 3 in Lisbon district. Sectors included electric equipment, public administration, communications, transport, social services, food, retail, health, and insurance. 539 workers consented; 371 met eligibility and were randomized. Around 80% were female, 70% had higher education, 80% reported prolonged computer use, over half lacked medical follow-up, and <25% used preventive treatment. In 9 companies, most workers had office roles; 1 company had >70% workers in physical roles, and another >70% workers in customer service. By June 2025, the intervention was completed in 7 companies with 80 consultations over 8 months, 11 participants dropped out and 16 missed appointments.

Conclusion: It is viable to implement a migraine programme at work, despite logistical challenges. The sector diversity and worker profiles support the programme's scalability.

OP015

Comparison of atogepant versus topiramate on cognitive function as assessed by the PROMIS cognitive function abilities subset SF 6a v2.0 for participants requiring preventive treatment for migraine: Results from the head-to-head TEMPLE trial

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Objective: We compared cognitive function as assessed by Patient Reported Outcomes Measurement Information System Cognitive Function (PROMIS-CF) Abilities Subset Short Form 6a version 2.0 between participants receiving either atogepant (ato), an oral calcitonin gene-related peptide receptor

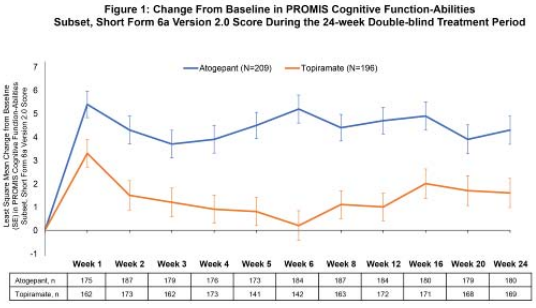
antagonist, and topiramate (topi) for participants requiring preventive treatment for migraine.

Methods: TEMPLE was a 24-week, randomized, double-blind (DB), double-dummy, active controlled trial with a 52-week open-label safety extension to evaluate tolerability, safety and efficacy of ato 60mg once daily (QD) compared to the highest tolerated dose of topi (50, 75, or 100 mg/day) for the preventive treatment of migraine in participants with episodic or chronic migraine. PROMIS-CF score at Week 6 of the 24-week DB treatment period was a hierarchically controlled secondary endpoint and prespecified additional endpoints at other time assessments (Figure 1). PROMIS-CF assesses participant-perceived cognitive deficits, including mental acuity, concentration, verbal and nonverbal memory, verbal fluency, and changes in these cognitive functions in the modified intent-to-treat population (ato n=209; topi n=196) from Week 1 to Week 24. It consists of 6 questions measuring the extent to which cognitive impairment interfered with daily functioning on a scale of "Not at all" to "Very much" over the past 7 days.

Results: At Week 6, ato demonstrated significant improvement in cognitive function compared with topi as assessed by PROMIS-CF score (treatment difference (Δ):5.0 [95% CI: 3.35,6.69], *P*<.0001). As early as Week 1, ato showed nominal improvement in cognitive function compared with topi (Δ: 2.1[0.53,3.65], *P*=.0087) and this improvement was consistent at each time point evaluated through Week 24 (Δ: 2.7[1.00,4.37], *P*=.0018) of the DB treatment period (**Figure 1**).

Conclusion: Ato 60 mg QD demonstrated greater improvements in cognitive function compared with topi through Week 24.

Fig. 1



OP016

Overlap between perceived triggers, premonitory symptoms, and symptom persistence across migraine phases: A REFORM study

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Objective: To evaluate the overlap between common trigger factors and corresponding premonitory symptoms in persons with migraine, and to assess the presence of non-headache symptoms across migraine phases.

Methods: Individuals with migraine were enrolled in this cross-sectional study during September 2020 to June 2022 as part of the prospective, single-center Registry for Migraine (REFORM) study. Data was based on participant recall. The presence of trigger factors, premonitory symptoms, non-headache symptoms during the headache and postdromal symptoms were obtained as part of a semi-structured interview.

Results: Among 632 participants (mean age 44.6 ± 12.0 years; 89% female), the most frequent triggers were sleep disturbances (70.1%), stress (67.7%), and alcohol consumption (59.0%). Common premonitory symptoms included tiredness (39.9%), concentration difficulties (35.0%), and neck pain (33.2%). Significant associations were found between specific triggers and premonitory symptoms: bright light with premonitory photophobia (OR, 2.79; 95% CI, 1.90 to 4.12; $P < 0.001$), loud noise with premonitory phonophobia (OR, 4.26; 95% CI, 2.77 to 6.59; $P < 0.001$), and sleep disturbances with premonitory tiredness (OR, 1.74; 95% CI, 1.15 to 2.64; $P = 0.009$). A positive association was seen between all examined premonitory and postdromal symptom ($P < 0.05$), except for tiredness (OR, 1.51; 95% CI, 0.89 to 2.57; $P = 0.12$).

Conclusion: Our results reveal a notable overlap between specific migraine triggers and corresponding premonitory symptoms, implicating that some perceived triggers could be early signs of an impending attack. Moreover, the continuation of most premonitory symptoms into the postdromal phase suggest that migraine-related symptoms extend across a broader temporal continuum than previously recognized.

OP017

May differential blockade of αCGRP and βCGRP with receptor antagonists underly differences in the efficacy and side-effect profile of anti-migraine drugs?

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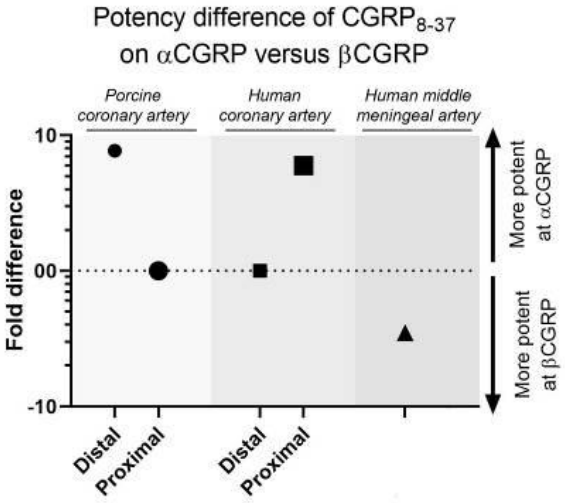
Objective: Data on the effect of CGRP pathway blockers on αCGRP and βCGRP are heterogeneous. We aimed to characterize the blocking effect of the truncated antagonist $CGRP_{8-37}$ in isolated human and porcine arteries across several vascular beds.

Methods: Relaxation responses to αCGRP and βCGRP were measured in the absence or presence of $CGRP_{8-37}$ in porcine coronary arteries (PCA), human coronary arteries (HCA), and human middle meningeal arteries (HMMA).

Results: In distal PCA (n=10–11), αCGRP and βCGRP induced a similar, potent vasodilation (pEC_{50} 8.4±0.4; E_{max} 87±30 and 91±23). In proximal PCA (n=6–7), αCGRP induced stronger vasodilation than βCGRP (pEC_{50} of 8.4±0.9 vs 7.8±0.4, p=0.03; E_{max} of 84±17% vs 67±17%, p=0.0009). $CGRP_{8-37}$ (1 µM) was ~8x more potent at blocking functional responses to αCGRP (pK_B 6.59±0.35) than βCGRP (pK_B 5.71±0.51; p=0.01) in distal PCA (n=6). Surprisingly, no significant blocking effect was observed in proximal PCA (n=5–7). In HCA (n=5-6), 1 µM $CGRP_{8-37}$ did not block relaxation to αCGRP or βCGRP. In proximal HCA, 3 µM $CGRP_{8-37}$ was ~6x more potent at blocking αCGRP (pK_B 6.37±0.70) than βCGRP (pK_B 5.60±0.41; p=0.002), whereas it was equally potent at blocking αCGRP (pK_B 6.06±0.60) and βCGRP (pK_B 6.21±0.33) in distal HCA. In HMMA (n=7), 3 µM $CGRP_{8-37}$ trended towards a ~3x higher potency on βCGRP (pK_B 6.84±0.42) than αCGRP (pK_B 6.39±0.42; p=0.07).

Conclusion: $CGRP_{8-37}$ acts differently in PCA vs HCA and across vascular beds, indicating a system bias that warrants further pharmacological investigation. Mapping αCGRP and βCGRP functional differences upon CGRP receptor antagonism may clarify the efficacy and side-effect profiles of anti-migraine medications.

Fig. 1



OP018

Src family kinases-associated H3K27me3 regulation of C-C motif chemokine ligand 2 (CCL2) gene expression in a rat model of migraine

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Objective: Src Family Kinases (SFK) are critical in neuroinflammation and were implicated in inflammatory gene expression via H3K4me3, a chromatin openness marker, as novel transcriptional regulators in migraine pathophysiology (unpublished). However, the role of repressive histone marks in these conditions remains elusive. This study investigates the involvement of H3K27me3 in CCL2 expression following cortical spreading depression (CSD) and the mechanistic involvement of SFK. Specifically: Examine CCL2 gene level and H3K27me3 enrichment at CCL2 promoter post-CSD; Assess gene levels of the key H3K27me3 histone-modifying enzymes in response to CSD; Determine relationships between H3K27me3 enrichment at CCL2 promoter with CCL2 gene level, SFK activity and H3K4me3 enrichment at the same loci.

Methods: Adult male SD rats were used, with animal procedures approved by the university ethics panel and under national and provincial rules. CSD was induced in the right cerebral cortex using 2 M K^+ for 30 minutes and monitored electrophysiologically. CCL2 and key H3K27me3-modifying enzymes gene levels were assessed via qPCR. The H3K27me3 enrichment at the CCL2 promoter was assessed via Chromatin immunoprecipitation-qPCR. Correlation analyses were subsequently conducted to explore relationships among these molecular factors.

Results: CSD significantly elevated the CCL2 mRNA level and decreased H3K27me3 enrichment at its

promoter. The mRNA level of H3K27me3-modifying enzymes remained unchanged. A negative correlation was found between the reduced H3K27me3 enrichment to the elevated CCL2 gene expression, H3K4me3 enrichment at the same loci and SFK activity, suggesting CSD-induced transcriptional activation of CCL2 is largely associated with chromatin de-repression involving SFK.

Conclusion: CSD reduces the SFK-associated H3K27me3 at the CCL2 promoter, facilitating transcription through chromatin de-repression. The findings bring a new insight into histone modification in migraine-related neuroinflammation.

OP019

RAMP1-dependent hormonal regulation of CGRP and its receptor in the trigeminal ganglion

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Objective: Menstrual migraine (MM) is a debilitating neurological disorder triggered by fluctuations in ovarian hormones, particularly estrogen.This study investigates how sex hormones regulate CGRP-related gene expression in the trigeminal ganglion (TG), with a focus on the receptor activity-modifying protein 1 (RAMP1), using both wild-type (WT) and *Ramp1* knockout (KO) mice.

Methods: We analyzed gene expression in the TG across the estrous cycle and following systemic estrogen or progesterone administration. Expression of *Ramp1*, *Calca* (encoding CGRPα), *Calcrl* (encoding CRLR), estrogen receptors, and related genes was assessed by RT-qPCR. WT and *Ramp1* KO mice of both sexes were used to explore hormone-dependent gene regulation and RAMP1"s functional role.

Results: *Ramp1* expression varied across the estrous cycle, peaking in proestrus and declining in diestrus, inversely correlated with *Calca*. *Calcrl* levels remained unchanged. *Ramp1* expression correlated significantly with *Esr2* (encoding ERβ), suggesting estrogen receptor–mediated regulation. Estrogen treatment upregulated *Ramp1* in both sexes; *Calca* was downregulated in females but upregulated in males. In *Ramp1* KO mice, the cyclical variation of *Calca*, *Ramp2*, and *Ramp3* seen in WT mice was absent, and basal *Calca* expression was elevated in males, indicating that RAMP1 is essential for hormonal regulation of the CGRP system. Additionally, our findings support a role for estrogen-driven epigenetic mechanisms, such as DNA methylation, in the long-term regulation of *Ramp1*.

Conclusion: RAMP1 as a key mediator linking hormonal fluctuations to CGRP signaling in the TG. Hormone-dependent gene expression changes were sex-specific and disrupted in *Ramp1* KO mice, supporting its role in migraine susceptibility. We provide mechanistic insight into hormonal migraine and suggest that both acute hormone signaling and long-term epigenetic regulation shape individual sensitivity to CGRP-based therapies.

OP020

Evidence of mitochondrial dysfunction in hypothalamic neurons in chronic cluster headache: A 7T ^{1}H MR spectroscopy study

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Objective: Understanding hypothalamic neurochemical profile using 7T MR spectroscopy in chronic cluster headaches (cCH).

Methods: In-vivo MR spectra (Figure 1) were acquired at 7T[1] in the hypothalamus(HT) of 11 cCHs(39±11 years) in interictal state and 12 healthy volunteers(HVs)(36±11 years). Ratio concentration of metabolites with respect to total creatine (tCr) were evaluated using LCModel and compared among the two cohorts (Figure 2). Further analyses were performed for glutamate(Glu)/tCr and N-acetyleaspartate(NAA) /tCr in sub-cohort in which age and sex match were achieved (9 cCHs vs HV).

Results: A significant decrease ($p<0.05$) in Glu/tCr was observed in cCH vs HV (Figure 2). Similarly, NAA/tCr significantly decreased in cCH vs HV. These findings are consistent with previous findings [2], and both may be related to neuronal mitochondrial dysfunction[3,4]. In the age and sex matched sub cohorts, cCH still showed a trend in Glu/tCr reduction with respect to the HV (Figure 3), but no for NAA/tCr.

Conclusion: This study demonstrates the ability of MRS to show mitochondrial dysfunction in hypothalamic neurons at ultra-high field.

Figure 1. *In-vivo* MR spectra from hypothalamus

Figure 2. Box plots of metabolite concentrations.

Figure 3. Age & Sex matched data between cCH and HV group for Glu and NAA in HT.

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Fig. 1

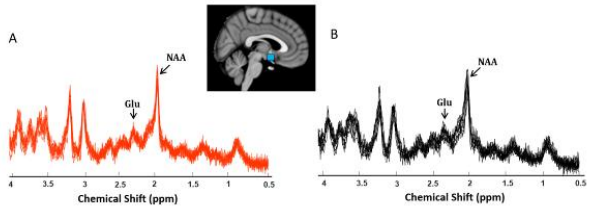


Fig. 2

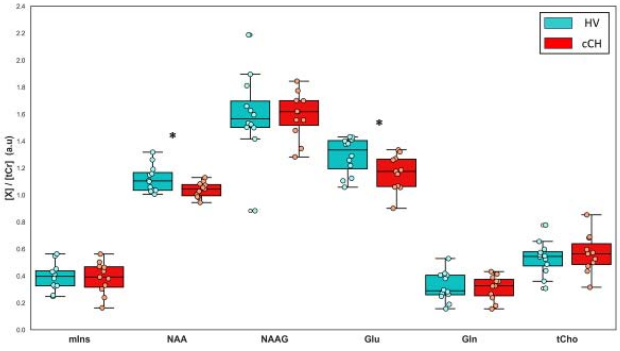
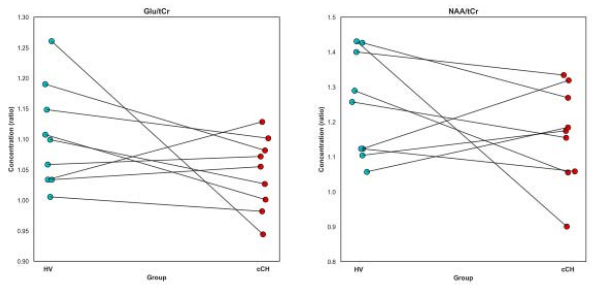


Fig. 3



OP021

Mesocorticolimbic functional connectivity dysregulations in chronic and episodic cluster headache patients

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Objective: CH is a primary headache disorder characterized by short-lasting, strictly unilateral craniofacial pain with autonomic symptoms. Converging evidence suggests that alterations in the hypothalamus and dopaminergic mesocorticolimbic system may contribute to the onset and chronification of pain disorders. To investigate functional connectivity alterations within the mesocorticolimbic system in both episodic (eCH) and chronic (cCH) cluster headache.

Methods: We enrolled 68 adult CH patients (23 cCH, 45 eCH) and 26 healthy controls (CTRL), who underwent 3T resting-state fMRI. Functional data were analysed with CONN toolbox; images of patients with right-sided attacks were flipped to the left. Region of interest (ROI)-to-ROI analyses, with age and sex as covariates, included the following regions: frontal cortex, hippocampus, amygdala, nucleus accumbens, ventral tegmental area (VTA), and hypothalamus. All results were $p<0.05$ FDR-corrected for multiple comparisons.

Results: Both eCH and cCH patients showed significant functional connectivity alterations compared to CTRLs. Specifically, we found i)decreased functional connectivity between the hypothalamus and ipsilateral hippocampus-amygdala complex, ii)increased functional connectivity between the VTA and contralateral hippocampus-amygdala, and iii)decreased functional connectivity between medial frontal areas and bilateral hippocampus-amygdala complex, extending to the orbitofrontal cortex in cCH. No significant differences were observed between eCH and cCH subgroups. Functional alterations were not associated with clinical factors such as disease duration, chronification, or the presence of depressive and anxiety symptoms.

Conclusion: This study confirms disrupted functional connectivity between the hypothalamus and

mesocorticolimbic regions in both CH forms. These alterations may reflect key pathophysiological mechanisms of CH, including its lateralization and chronification.

OP022

Treatment of chronic cluster headache with occipital nerve stimulation: A double-blind, randomized, placebo-controlled clinical trial

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Objective: ccipital nerve stimulation (ONS) has shown promising results in attack prevention in patients with CCH, but evidence from controlled trials is scarce. Conventional (tonic) ONS elicits paresthesia, hampering blinded comparison to placebo. Using paresthesia-free burst ONS, we conducted a randomized, placebo-controlled trial.

Methods: The study is an investigator-initiated, double-blind, randomized, placebo-controlled clinical trial involving patients with CCH. It comprised a four-week baseline, a 12-week trial with transcutaneous electrical nerve stimulation, ONS implantation, a 12-week randomized, double-blind burst ONS treatment period, and a 12-week open-label tonic ONS treatment period. The primary outcome was the proportion of participants reporting a ≥30% reduction in attack frequency in the randomized and open-label trial phases.

Results: Thirty-eight patients underwent ONS implantation and were randomly assigned to burst ONS (n=19) or placebo (n=19). After the randomized trial phase, the proportion of ≥30% responders was 18.81% (95%CI 0.28%-37.87%) in the burst ONS group and 50.02% (95%CI 26.87%-73.09%) in the placebo group. The likelihood of reaching the primary endpoint was 31.20% (95%CI 1.29%-61.23%, p=0.042) higher in the placebo group. After the open-label phase, 42.09% (95%CI 19.91%-64.34%) in the burst ONS group and 51.11% (95%CI 27.32%-74.88%) in the placebo group had ≥30% frequency reduction.

Conclusion: ONS reduced attack frequency but was not superior to placebo. The results indicate that a part of the preventive effect of ONS may be attributed to a placebo response and call for attention to sufficient placebo control when planning further studies.

OP023

Effects of a glucagon like Peptide-1 receptor agonist, semaglutide, combined with hypocaloric meal replacements adjunct to supervised lifestyle change in newly diagnosed idiopathic intracranial hypertension: An open-label randomized controlled trial on weight loss and intracranial pressure

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Objective: Idiopathic intracranial hypertension (IIH) is a neurometabolic disorder in which disease activity is linked to weight change. Rapid pronounced weight loss immediately after diagnosis may benefit clinical outcomes. Glucagon like peptide-1 receptor analogues (GLP1-RA) are promising treatments in IIH.

Methods: This is an open-label randomized controlled trial conducted at two tertiary Danish headache centers. We randomized females with newly diagnosed IIH 1:1 to supervised lifestyle change alone (control) or an adjunct *Very Low-Calorie Diet* (VLCD, 800 kcal daily) combined with weekly injections with a GLP1-RA, Semaglutide (intervention). Co-primary endpoints were reductions in lumbar opening pressure (OP) and BMI after 8 weeks. Secondary endpoints were body composition changes assessed by Dual-Energy X-ray Absorptiometry (DEXA), visual outcomes, and acetazolamide dosage.

Results: We randomized 38 individuals (intervention, n=20; control, n=18,); 34 completed follow-up (intervention, n=19, control, n=15). After 8 weeks, mean (95%CI) BMI was significantly reduced in both groups with a mean (95% CI) between-group difference of -3.9% (-6.4; -1.5, p=.003). OP was equally reduced, both relatively (mean difference 0.6% (-10.4; 11.5), p=.92) and absolutely (mean difference 0 cm

CSF (-5.5; 5.5), p>.99). Total- and truncal fat mass decreased significantly more in the intervention group but was uncorrelated with OP. PMD improved more in the intervention group (mean difference 1.3 ΔdB (95%CI 0.2; 3.5 dB, p=.02). Acetazolamide was equally dosed.

Conclusion: Compared to supervised lifestyle change alone, adjunct Semaglutide combined with a VLCD in newly diagnosed IIH resulted in greater weight and truncal fat mass loss and improvement of visual fields after 8 weeks. Lumbar OP nearly normalized by both strategies. Final conclusions on the eligibility and superiority of GLP1-RA in IIH await effects on headache, quality of life and long-term outcomes.

OP024

Alterations in gut microbiota and the endocannabinoid system in an animal model of chronic migraine

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Objective: The endocannabinoid system (ECs) is a complex cell-signalling system present in the nervous system and gastrointestinal tract. It regulates inflammatory responses and intestinal homeostasis via interactions with the gut microbiota, ultimately influencing brain function indirectly through gut-derived circulating factors and directly via vagus nerve signalling. Increasing evidence suggests a role for ECs in chronic migraine. This study assessed whether gut dysbiosis is associated with ECs alterations, centrally and peripherally, in a chronic migraine-like animal model induced by repeated nitroglycerin (NTG) administration.

Methods: Adult male Sprague-Dawley rats were treated with NTG (5 mg/kg i.p.) or vehicle every two days for nine days (5 injections). On day nine, four hours after the last administration, migraine-like hyperalgesia was tested using the orofacial formalin test. Intestine and trigeminal ganglion were collected to assess ECs gene expression by real-time PCR. Fecal 16S rRNA gene sequencing assessed gut flora alterations.

Results: Chronic NTG administration significantly increased face rubbing time during phase II of the orofacial formalin test, confirming trigeminal hyperalgesia. Microbiota analysis revealed significant beta-diversity differences between NTG and vehicle groups, confirming gut microbial alterations. Moreover, intestinal gene expression showed a significant decrease in monoacylglycerol lipase (MAGL) mRNA, with no changes in fatty acid amide hydrolase, N-acylethanolamine acid amidase, N-acyl phosphatidylcholine phospholipase D, cannabinoid receptor 1, or cannabinoid receptor 2 mRNA expression. Similarly, reduced MAGL mRNA was detected in the trigeminal ganglion of NTG-treated rats.

Conclusion: These findings suggest that microbiota dysbiosis associated with trigeminal hyperalgesia may be linked to altered 2-arachidonoylglycerol metabolism, suggesting a potential role for the gut-brain-endocannabinoid axis in migraine-related pain.

OP025

Identifying candidate molecular biomarkers in idiopathic intracranial hypertension patients

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Objective: Idiopathic Intracranial hypertension (IIH) is a neurological disease associated with obesity and raised intracranial pressure (ICP) often causing severe headaches, visual loss and reduced quality of life. IIH is frequently misdiagnosed, with confirmation requiring invasive lumbar puncture. Monitoring disease progression is also complex, involving repeated visual assessments and sometimes further lumbar punctures. A reliable, non-invasive diagnostic and monitoring tool remains an unmet need. This study aimed to identify candidate serum microRNA (miRNA) markers in adults with active IIH.

Methods: Serum and cerebrospinal fluid (CSF) samples (n=9) were collected from patients with active IIH and 12 months later during disease remission induced by bariatric surgery. RNA was isolated, converted to cDNA and analysed by quantitative polymerase chain reaction (qPCR) using a 40- miRNA panel. Candidate serum miRNAs were also assessed in control participants with obesity and with migraine. Candidate miRNAs identified in patients with active IIH were evaluated against clinical characteristics.

Results: Serum miRNAs (5/40) expression was significantly lower in active IIH patients compared to when in remission. Of these, hsa-miR-16-5p ($p<0.0001$) and hsa-miR-7-5p ($p=0.0032$) were significantly lower in active IIH compared to patients with obesity. hsa-miR-16-5p ($p=0.0354$) and hsa-let-7a-5p ($p=0.0310$) were significantly raised in CSF of patients with active IIH compared to in remission. hsa-miR-16-5p in serum and CSF significantly correlated with ICP ($p<0.0001$, $p=0.046$) and papilledema ($p=0.0346$, $p=0.0241$).

Conclusion: We have identified two potential candidate miRNA biomarkers (hsa-miR-16-5p and hsa-

miR-7-5p) in the serum of patients with active IIH which have a high degree of sensitivity and are associated with clinical measures of disease activity. These results are the first step towards developing a less invasive diagnostic and monitoring biomarker which would lead to a step change in patient care.

OP026

Inflammatory signatures of comorbid episodic migraine and endometriosis: A cytokine-based analysis

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Objective: Migraine and endometriosis are two chronic, often comorbid conditions that significantly affect women"s health.Mounting evidence points to systemic inflammation as a shared pathophysiological mechanism;yet the biological link between them has remained elusive.This study explored inflammatory cytokine profiles in women with migraine, endometriosis, or both,and their association with symptom severity and functional impact.

Methods: We enrolled female patients admitted to the Tor Vergata University Hospital and diagnosed with only episodic migraine,with only endometriosis or with concomitant episodic migraine and endometriosis.Pro-inflammatory cytokines were measured in plasma and correlated with clinical parameters.

Results: Women with episodic migraine showed elevated circulating levels of key pro-inflammatory cytokines, including interleukin (IL)-1β, IL-6, and tumor necrosis factor-alpha (TNF-α), compared to healthy controls.These inflammatory markers were even more pronounced in participants with both migraine and endometriosis, pointing to a synergistic effect of the two conditions on systemic inflammation.IL-1β levels correlated strongly with headache frequency and disability scores, while IL-6 and TNF-α were associated with both migraine severity and pelvic pain.Women with endometriosis alone did not exhibit comparable cytokine elevations, suggesting that inflammation is uniquely amplified in the presence of comorbidity.In parallel, changes in leukocyte distribution, including a higher neutrophil-to-lymphocyte ratio, further supported a state of immune activation exclusive to the comorbid group.

Conclusion: These findings provide the first biological evidence of a shared inflammatory endotype in women suffering from both migraine and endometriosis that may contribute to the increased symptom burden and their comobrbidity, underscoring the need for integrative approaches in diagnosis and management.

Fig. 1

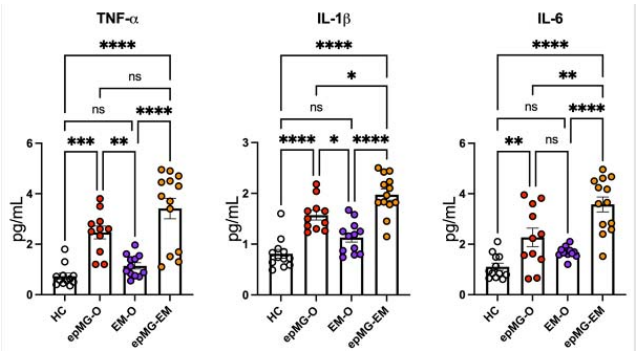
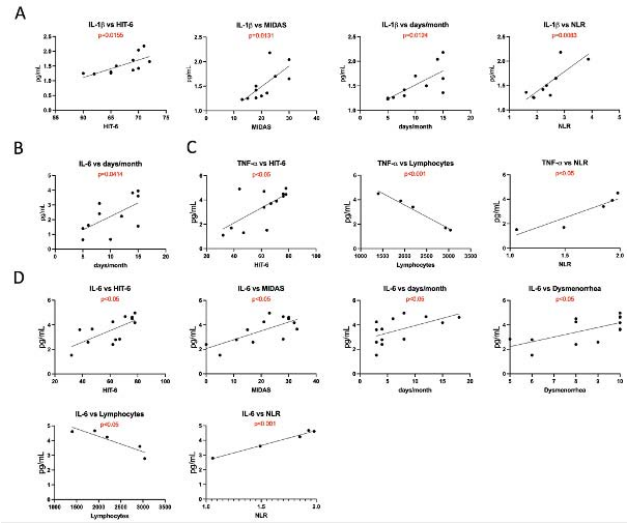


Fig. 2



OP027

Targeting inflammation: The Role of *IL1B* and *NLRP3* genetic variants in migraine susceptibility

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Objective: The role of inflammation in the pathogenesis of migraine is increasingly recognized. Notably, elevated serum levels of the pro-inflammatory cytokine IL-1β have been reported in individuals with chronic migraine. As a key component of the inflammasome, the NLRP3 protein plays a

critical role in activating caspase-1 and regulating IL-1β production. This study aimed to evaluate the role of the rs16944 (*IL1B*) and rs4612666 (*NLRP3*) polymorphisms as potential susceptibility factors for the development of migraines in a Portuguese population.

Methods: A total of 167 individuals diagnosed with migraine and 248 healthy controls were included. The rs16944 and rs4612666 polymorphisms were genotyped by Real-Time PCR methodology.

Results: The rs16944TT (12.0% vs 9.0%, OR [95% CI] = 1.45 [0.737–2.85]) and rs4612666TT (7.2% vs 3.3%, OR [95% CI] = 2.30 [0.905–5.83]) genotypes were more frequent in patients than in controls. However, these differences did not reach statistical significance.

Conclusion: The rs16944TT and rs4612666TT genotype increase, respectively, IL-1β expression and inflammasome activation, contributing to greater pain sensitivity and migraine severity. These preliminary findings support a role for immunogenetic factors - particularly those affecting the IL-1β pathway - in migraine susceptibility. Larger, subtype-stratified studies are warranted to validate these associations and further clarify the inflammatory mechanisms underlying migraine development and progression.

OP028

Profiles of migraine patients treated with triptan: A study based on data from the French nationwide claims database

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Objective: Although recommendations for the diagnosis and management of migraine have been published, it is managed in a very heterogeneous way. Here, we describe the profiles and care pathways of migraine patients treated with triptan in France.

Methods: Retrospective cohort study of migraine patients treated with at least one triptan, identified in the 2/100th French Nationwide claims database (ESND) from 2016 to 2021 and analysed from 2006 to 2022.

Results: Among the 37,884 migraine patients identified, 76% were women and 30% were covered by Universal Complementary Health Insurance. The mean age was 36.6 years at the first triptan. This initial prescription was issued by a general practitioner in 91% of cases and by a neurologist in 4%.

Among patients treated with triptans for less than 4 months (39%), 66% received concomitant analgesics, mainly non-steroidal anti-inflammatory drugs (NSAIDs, 43%), and 18% received weak opioids. In patients treated for more than 4 months (61%), co-dispensing of analgesics was observed in 94% of cases, mainly paracetamol (87%) and NSAIDs (85%), while 51% received weak opioids.

The management of migraine patients evolved following triptan initiation. In the year preceding the first triptan dispensing, NSAIDs were prescribed to 52% of patients, increasing to 89% in the following year. A similar trend was observed for weak opioids (30% before vs. 73% after) and strong opioids (1% before vs. 7% after). Preventive migraine therapies were dispensed to 9% of patients prior to triptan initiation and to 39% thereafter.

The average number of medical consultations also increased: from 5.4 to 6.1 in general practice, from 2.5 to 3.3 in psychiatry, and from 0.3 to 0.5 in neurology. Additionally, the proportion of patients with at least one sick leave increased from 43% to 52% post-initiation.

Conclusion: We highlight here the heterogeneous management of triptan users in France and the change of care pathways after the first triptan dispensing.

OP029

Investigation of the relationship between weather and headache attacks: Smartphone application data analyzed with artificial intelligence

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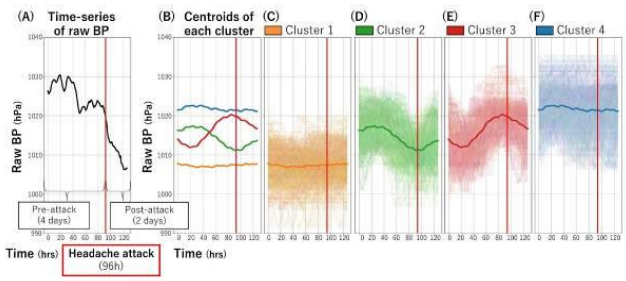
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Objective: To investigate the relationship between weather and headache attacks using big data from smartphone app combined with AI.
Methods: Using data from January to December 2023, we selected users who had used triptans or lasmiditan at least once and recorded headaches on 1–14 days per month, identifying them as having episodic migraine. We applied a generalized linear mixed model (GLMM) to estimate hourly headache occurrences (records/hour) based on various weather variables: barometric pressure (hPa), temperature (℃), humidity (%), precipitation (mm/hour), sunlight duration (hours), wind speed (m/s), the pressure change from 6 hours earlier, and the 6 a.m. barometric pressure on the day of the headache, the following day, and two days later. These variables were selected based on prior research. Additionally, following our previous study, we categorized 6-day time-series barometric pressure patterns (4 days before and 2 days after the headache record) into four types (Types I–IV) using one-to-one Euclidean clustering (Figure 1A-F). Random effects in the model included age, sex, season, time of day, and regional climate classification.
Results: Among the 10,248 users included (321,709 headache records), the average age was 41.2 years (SD 10.8), and 92.5% were female (n = 9,479). The GLMM revealed significant associations between increased hourly headache frequency and multiple weather variables: higher rainfall, longer sunlight exposure, stronger wind, lower barometric pressure compared to 6 hours earlier, and lower pressure at 6 a.m. the following day. Barometric pressure patterns classified as Type I (persistently low), Type II (dropping around the headache), and Type IV (persistently high) were also linked to more frequent headache reports.
Conclusion: This real-world big data analysis demonstrated that several weather conditions—including rain, sunshine, wind, and falling barometric pressure—are significantly related to hourly headache occurrence.

Fig. 1



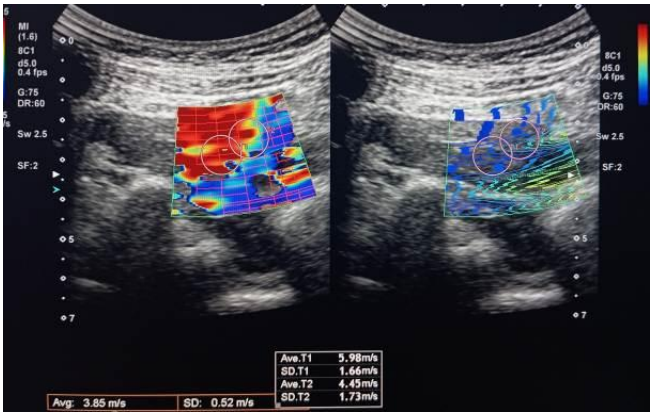
OP030

Ultrasound-guided dry needling of suboccipital muscles: Precision targeting of myodural trigger points and correlated biomarkers in headache disorders

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Objective: Tension-type headaches (TTH) and migraines are often linked to central sensitization and myodural dysfunction. The suboccipital muscles—particularly the obliquus capitis inferior (OI) and superior (OS)—form a functional myodural bridge that influences cerebrospinal fluid dynamics. Tiny myofascial trigger points within these muscles can significantly alter muscle tone and dural mechanics. Precise ultrasound-guided dry needling (US-DN) combined with advanced imaging biomarkers may offer a novel treatment and monitoring approach.
To evaluate the effects of ultra-precise US-DN on headache symptoms, myodural biomechanics, and to explore the correlation between shear wave elastography (SWE) and spinal dural oscillations.
Methods: Sixteen patients (6 migraine, 10 TTH) received US-DN targeting 1–3 mm trigger points in the OI and OS muscles. Needle placement was confirmed with real-time B-mode ultrasound. Muscle stiffness was quantified using SWE with a 2–3 mm ROI. Spinal dural oscillations at C1–C2 were captured via M-mode ultrasonography. Ophthalmic artery Doppler and superb microvascular imaging (SMI) assessed vascular and microvascular changes.
Results: Trigger points within the suboccipital muscles showed markedly increased stiffness on SWE (6 m/s) versus adjacent normal tissue (1–3 m/s). Following pinpoint US-DN, stiffness values normalized to 2–3 m/s, in parallel with a reduction in high-frequency spinal oscillations (from 160–320 Hz to ~80 Hz). This strong correlation suggests SWE and oscillation frequency are reliable, complementary biomarkers of muscle tone and dural stress. SMI revealed no detectable microvascularity in the trigger areas. DN of the OS muscle also reduced referred TMJ-associated migraine symptoms.
Conclusion: SWE and spinal dural oscillations are highly correlated and offer a combined biomarker system to guide and monitor treatment. US-DN represents a precise, personalized approach for managing headaches linked to myodural dysfunction and central sensitization.

Fig. 1



OP031

Tolerability, safety, and efficacy of atogepant versus topiramate in participants requiring preventive treatment for migraine: Results from the head-to-head TEMPLE trial

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Objective: We compared the tolerability, safety, and efficacy between atogepant (ato), an oral calcitonin gene-related peptide receptor antagonist, and topiramate (topi) in participants requiring preventive migraine treatment.

Methods: TEMPLE was a 24-week, randomized, double-blind (DB), double-dummy, active controlled trial with a 52-week open-label safety extension to evaluate tolerability, safety, and efficacy of atogepant 60mg once daily (QD) compared to the highest tolerated dose of topiramate (50, 75, or 100 mg/day) for preventive treatment of migraine in participants with episodic or chronic migraine. The primary endpoint was treatment discontinuation due to treatment-emergent adverse events (TEAEs) in the safety population (ato n=273;topi n=267) during the 24-week DB period. Secondary clinical efficacy endpoints included the proportion of participants with a ≥50% reduction in mean monthly migraine days (MMDs) and change from baseline (CFB) in mean MMDs across Months 4-6 of the DB period in the modified intent-to-treat population (ato n=270;topi n=257).

Results: Atogepant demonstrated superior tolerability compared to topiramate with significantly lower treatment discontinuations due to TEAEs (ato=12.1%; topi=29.6%; RR:0.41[0.28,0.59],*P*<.0001) across 24 weeks. A higher proportion of participants experienced TEAEs with topiramate compared to atogepant (88.8% vs 76.9%). A higher proportion of participants experienced TEAEs related to study treatment with topiramate compared to atogepant (77.9% vs 56.0%).

Atogepant demonstrated superior efficacy compared to topiramate with a significantly greater proportion of participants achieving a ≥50% response (ato=64.1%;topi=39.3%; RR:1.63 [1.37,1.95],*P*<.0001) and a significant mean MMD reduction (ato=-6.27;topi=-4.49; Δ:-1.78[-2.52,-1.04], *P*<.0001) across Months 4-6.

Conclusion: Atogepant 60mg QD demonstrated superior tolerability and efficacy compared with topiramate. Atogepant was generally safe and well tolerated and no new safety signals were identified.

OP032

Atogepant after failure of anti-CGRP monoclonal antibodies in migraine: A multicenter real-world study

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[2]Hospital de Viladecans, Neurology, Viladecans, Spain
[3]Hospital Universitario Fundación Alcorcón, Neurology, Madrid, Spain
[4]Hospital Universitario de la Princesa, Neurology Department, Madrid, Spain
[5]Hospital Universitario San Carlos, Neurology, Madrid, Spain
[6]HCU Lozano Blesa de Zaragoza, Neurology, Zaragoza, Spain
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[8]Hospital Universitario La Paz, Neurology, Madrid, Spain
[9]Hospital Sant Joan Despí, Neurology, Sant Joan Despí, Spain
[10]Hospital Universitario Rio Hortega, Neurology, Valladolid, Spain
[11]Hospital de la Santa Creu i Sant Pau, Neurology,

Barcelona, Spain
[12]Hospital Reina Sofia, Neurology, Tudela, Navarra, Spain
[13]Hospital Universitario Donostia, Neurology, Donostia, Spain
[14]Hospital General Universitario Gregorio Marañón, Neurology, Madrid, Spain
[15]Hospital Universitario de Canarias, Neurology, Santa Cruz de Tenerife, Spain
[16]Albacete Universitary Hospital, Neurology, Albacete, Spain
[17]Vall d'Hebron University Hospital, Neurology Department, Barcelona, Spain
[18]Vall d'Hebron Hospital and Research Institute, Universitat Autonoma de Barcelona, Headache and Neurological Pain Research Group, Barcelona, Spain

Objective: Atogepant has demonstrated efficacy as a preventive treatment for migraine; however, its effectiveness after failure of anti-CGRP monoclonal antibodies (mAbs) remains unstudied. We evaluated its real-world use following mAb treatment failure.
Methods: This was a multicenter (n=17) observational study including patients who initiated atogepant after failing at least one anti-CGRP mAb. Effectiveness, tolerability, and treatment persistence at 3 months were assessed, along with factors associated with treatment response.
Results: A total of 252 patients were included (mean age 48.9 ± 12 years; 83.3% female; 80.6% with chronic migraine and 45.6% with chronic daily headache). In total, 39.7% had failed 1 mAb, 27% had failed 2, 20.2% had failed 3, and 13.1% had failed 4. At baseline, patients had a median of 16 monthly migraine days (MMD), 27 monthly headache days (MHD), and 20 days of acute medication use. At 3 months, response rates were 44.4% (≥30% reduction in MMD), 29.7% (≥50%), and 11.7% (≥75%). Adverse events were reported in 52.5% of patients, most commonly constipation (30%) and nausea (25%). Treatment discontinuation at 3 months occurred in 26.2% of patients (65.1% due to lack of efficacy, 28.8% due to intolerance). The probability of continuing treatment at 180 days was 61% (95% CI: 54%–69%). A higher number of previously failed mAbs was associated with a lower likelihood of response (p=0.02).
Conclusion: Atogepant may be an effective preventive option for patients with migraine after failure of anti-CGRP mAbs, although adverse events are frequent. Effectiveness appears greater in those with fewer previously failed mAbs.

Fig. 1

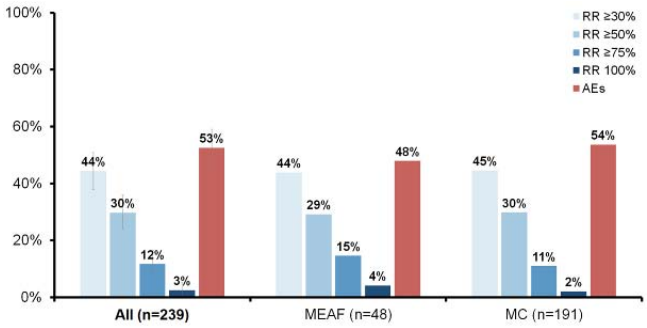


Fig. 2

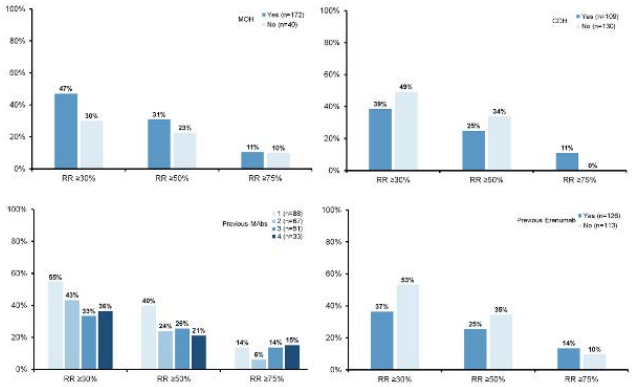
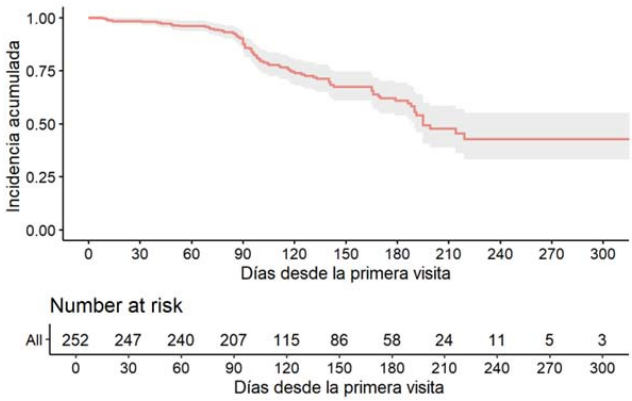


Fig. 3



OP033

Beyond adults: OnabotulinumtoxinA in adolescents with chronic migraine – A tertiary center experience

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Objective: The present study aims to describe the clinical experience with BT-A for the treatment of chronic migraine in adolescents.

Methods: All patients under the age of 18 who received BT-A treatment at the Headache Center of the Bambino Gesù Children"s Hospital between November 2018 and June 2025 were included in this retrospective analysis. BT-A was administered according to the PREEMPT protocol [7]. Collected data included demographic characteristics, number of BT-A injections received, adverse effects, and treatment efficacy. Treatment response was categorized as follows: responders (≥50% reduction in monthly migraine frequency), partial responders (30–49% reduction), and non-responders (<30% reduction).
Results: During the study period, 81 patients received at least one administration of onabotulinumtoxinA (OBT-A). Of these, 67 were females and 14 males, with a mean age of 14.7 ± 1.5 years. The mean disease duration from symptom onset to initiation of OBT-A treatment was 29.3 ± 9.1 months. Prior to starting OBT-A, all patients had attempted at least two prophylactic therapies, and 58.7% discontinued oral treatments due to adverse effects. Concomitant use of other migraine prophylactic medications was permitted.The mean follow-up duration from the first OBT-A administration to the last clinical observation was 17.6 ± 13.7 months (range: 1–48 months). On average, patients received 3.4 ± 3 OBT-A administrations. Nine patients discontinued treatment before completing three administrations due to intolerance to injections.No major adverse events were reported.An initial clinical improvement was observed in 35% of patients after the first administration. By the third administration, 68% of treated patients had shown a therapeutic response. A progressive reduction in migraine frequency was observed with continued OBT-A administration
Conclusion: This case series shows the excellent safe profile and effectiveness of BT-A for preventive treatment of chronic migraine in adolescents.

Fig. 1

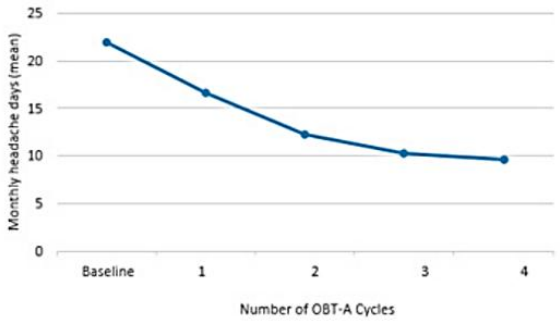
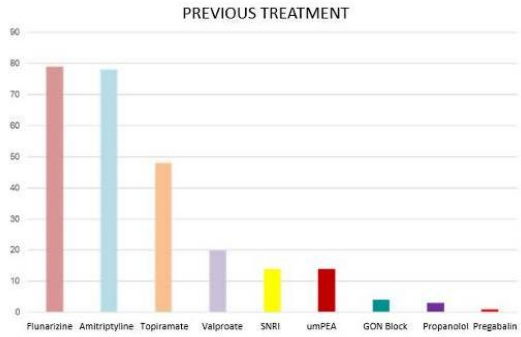


Fig. 2



OP034

Evaluation of the safety and efficacy of ubrogepant in the acute treatment of migraine in patients also taking CGRP-targeting monoclonal antibodies

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Objective: This study evaluated the safety and efficacy of ubrogepant in the acute treatment of migraine in patients also taking calcitonin gene-related peptide (CGRP)-targeting monoclonal antibodies (mAbs) versus those taking ubrogepant alone. Ubrogepant, an oral CGRP receptor antagonist, is effective for acute migraine attacks, while injectable CGRP monoclonal antibodies (CGRP mAbs) serve as preventives. However, limited research has explored their combined use. This study aimed to determine whether ubrogepant remains effective and safe when used alongside CGRP mAbs.
Methods: This was a randomized study conducted at the Chicago Headache Center and Research Institute. A total of 165 participants were assigned to one of four treatment arms: ubrogepant 50 mg or 100 mg, either alone or in combination with a CGRP mAb. Pain freedom, freedom from most bothersome symptom (MBS), and adverse events (AEs) were assessed at multiple time points up to 24 hours post-treatment using participant-reported questionnaires. Statistical analyses included descriptive statistics and chi-square tests, with significance set at $p<0.05$.
Results: The primary outcomes, pain freedom and most bothersome symptom (MBS) freedom at 2 hours, did not significantly differ between the intervention (ubrogepant with CGRP mAb) and control (ubrogepant alone) groups. Secondary endpoints, including sustained pain relief and pain freedom at 24 hours, also showed minimal differences between groups. AE rates were also similar. When compared to the ubrogepant pivotal trial by Dodick, et al (New England Journal of Medicine December 4, 2019) the primary endpoints of pain freedom and freedom from

most bothersome symptom (MBS) at 2 hours in our study exceeded the pain freedom and freedom from MBS results reported by Dodick.

Conclusion: Ubrogepant maintains comparable efficacy and safety profiles regardless of concurrent CGRP mAb use. These findings support its role as an acute migraine treatment for patients already on preventive CGRP mAb therapy.

Fig. 1

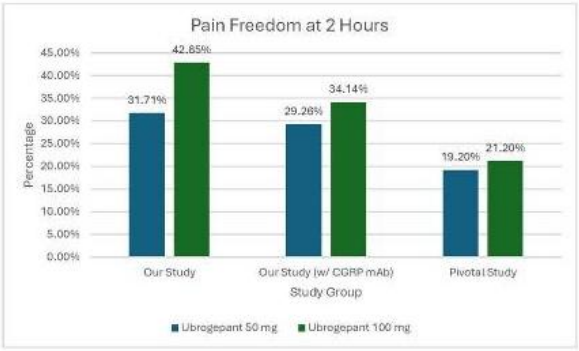
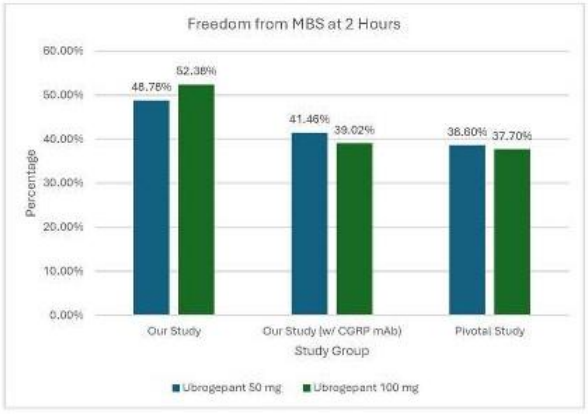


Fig. 2



OP035

Sequential use of OnabotulinumtoxinA and Erenumab in chronic migraine: Real-world report on bidirectional switching

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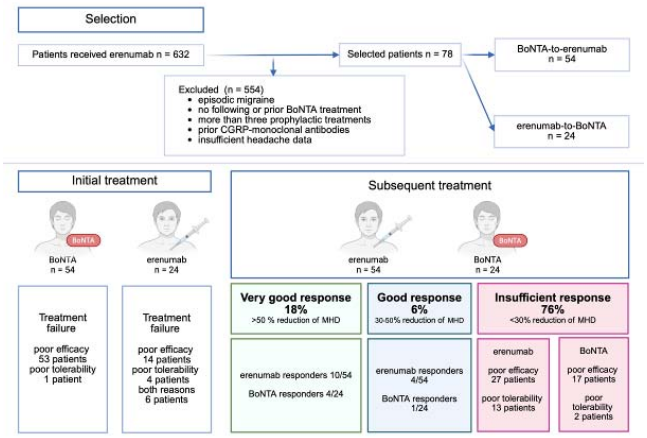
Objective: To investigate the real-world effectiveness of switching between onabotulinumtoxinA and erenumab in patients with chronic migraine who showed inadequate response to their initial preventive treatment. The aim is to provide preliminary evidence to address the current clinical data gap and inform future treatment sequencing strategies.

Methods: This retrospective study included patients with chronic migraine treated at the Headache Center, Charité – Universitätsmedizin Berlin between October 2022 and December 2024. Eligible patients had received both onabotulinumtoxinA and erenumab in sequence, switching due to insufficient efficacy or tolerability. A very good response was defined as a ≥50% reduction in monthly headache days in the third month after the switch.

Results: Out of 632 screened patients, 78 met the inclusion criteria (84.6% female; mean age 43 ± 14 years). Of these, 54 switched from onabotulinumtoxinA to erenumab, and 24 from erenumab to onabotulinumtoxinA. A very good response was observed in 14 patients (17.9%): 10/54 (18.5%) after switching to erenumab and 4/24 (16.7%) after switching to onabotulinumtoxinA.

Conclusion: Sequential preventive treatment with BoNTA and erenumab led to a very good response in about one fifth of patients after initial treatment failure. While these findings suggest a partial overlap in their pathomechanisms, the distinct mechanisms of action may allow for therapeutic benefit in a subset of patients who do not respond to the initial agent. These real-world results support the consideration of treatment switching in clinical practice and highlight the need for prospective studies to identify predictors of response and guide individualized treatment strategies.

Fig. 1



OP036

Toward human-relevant models of migraine: Exploring vascular signaling in endothelial cells

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[3]Delft University of Technology, Microelectronics, Delft, Netherlands
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Objective: The vascular system plays a key role in migraine pathophysiology, though mechanisms remain unclear. The interaction between CGRP, a major migraine mediator, and Piezo1, a mechanosensitive channel, remains unexplored. Human iPSC-derived endothelial cells (hiPSC-ECs) offer a relevant model to study vascular signaling. Focused ultrasound (FUS) is a promising non-invasive neuromodulation tool to study mechanosensitive channels. Using a custom miniaturized FUS generator, we examined Piezo1 responses to ultrasound to explore the role of Piezo1 in migraine-relevant pathways.
Methods: Intracellular calcium (Ca^{2+}) activity was assessed in hiPSC-ECs after stimulation with Yoda1, a Piezo1 agonist, with or without CGRP co-treatment. To investigate downstream effects, we performed immunostaining for paxillin to assess focal adhesion (FA) formation. Separately, we optimized FUS by varying exposure duration (0–5 min) and duty cycle (0.1–100%) at 8.3 MHz and 2.31 MPa, measuring Ca^{2+} influx in Human Umbilical Vein Endothelial Cells (HUVECs).
Results: Sensitizing hiPSC-ECs with CGRP before Yoda1 stimulation significantly enhanced intracellular Ca^{2+} responses compared to either treatment alone or combined acutely, indicating CGRP–Piezo1 crosstalk. This effect was blocked by the CGRP receptor antagonist BIBN4096, confirming specificity. CGRP sensitization also increased the size of paxillin-positive FAs. In contrast, FUS did not activate Piezo1 in HUVECs, likely due to suboptimal acoustic conditions. However, Yoda1-induced activation triggered clear Ca^{2+} responses, confirming Piezo1 involvement.
Conclusion: These findings suggest CGRP–Piezo1 crosstalk in hiPSC-ECs, supporting their use in migraine-related vascular modeling. While FUS did not activate Piezo1 in HUVECs, chemical activation confirmed its Ca^{2+}-dependent role.

OP037

Beyond CGRP receptor blockade: Exploring the mechanisms of traditional migraine prophylactic drugs propranolol and candesartan

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Objective: The mechanisms by which traditional prophylactic medications exert their effects in migraine prevention remain incompletely understood. This study aims to elucidate the underlying mechanisms of two commonly used agents, propranolol and candesartan.
Methods: We examined the mechanisms by which propranolol and candesartan prevent migraine in two experimental models. First, CGRP receptor involvement was assessed using isolated distal porcine (PCA) and human coronary artery (HCA) segments (1–2 mm internal diameter) mounted on a Mulvany myograph system. After precontraction using 30 mM KCl, dose-response curves to αCGRP and capsaicin were obtained in the presence or absence of propranolol and candesartan. Secondly, cortical spreading depression (CSD) susceptibility, representing the pathophysiological basis of migraine aura, was examined using a KCl-induced (1 M) CSD model in rats. In CSD model, topiramate and amlodipine were also studied.
Results: In porcine and human coronary arteries , propranolol and candesartan did not notably shift the dose–response curves of αCGRP-induced vasodilation (pEC50: 8.2±0.63 for PCA; 8.7±0.41 for HCA) at clinically relevant concentrations (20–400 nM for propranolol; 3.3–540 nM for candesartan), nor did they affect capsaicin-induced vasodilation (pEC50: 5.47±0.88 for PCA; 4.46±1.84 for HCA), the latter representing a CGRP-independent pathway. However, candesartan (1 mg/kg/day, 3 weeks) inhibited KCl-induced CSD frequency by 23.81%. Topiramate reduced CSD frequency by 28% at 80 mg/kg and by 30% at 200 mg/kg. In contrast, amlodipine, a calcium channel blocker without migraine prophylactic effects, showed no effect on CSD frequency.
Conclusion: These findings suggest that propranolol and candesartan may not exert their prophylactic effects via direct antagonism of CGRP receptors. Instead, inhibition of CSD may represent a mechanism underlying their prophylactic actions. Their potential presynaptic effects on endogenous CGRP release remain to be investigated.

OP038

The contribution of menstrual migraine to risk for Cardiovascular and Cerebrovascular disease

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Objective: The relationship between migraine and increased risk of cardiovascular and cerebrovascular disease (CVD) is well established, particularly in those with migraine with aura. However, the contribution of menstrual migraine (MM) to CVD risk has not been investigated. We analyzed a large cohort of women with migraine to assess their risk of atherosclerotic CVD events and their connection to menstrual migraine (MM).

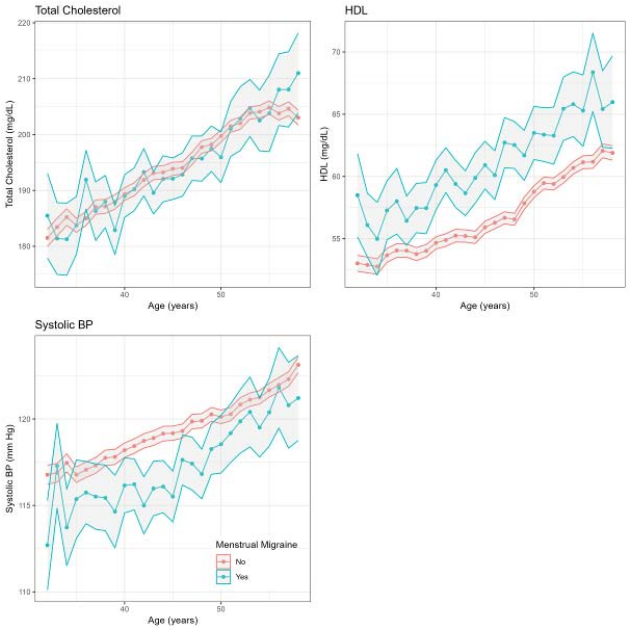
Methods: A cohort of women with at least one migraine ICD diagnostic code since 2008 was identified from the Mayo Clinic Electronic Health Record, and 2013 American College of Cardiology (ACC)/American Heart Association (AHA) atherosclerotic cardiovascular disease (ASCVD) risk scores were calculated. MM was compared to non-MM.

The cohort was stratified into African American (AA) and other individuals, consistent with ACC/AHA model use recommendations. Using the White cohort CoxPH models were fit 1)using only ACC/AHA covariates 2) ACC/AHA covariates plus aura, chronic migraine, and MM. Predictive accuracy of these models was compared to the original ACC/AHA score and each other.

Results: In the full cohort (n=52,153) MM was associated with higher HDL, lower systolic BP and similar total cholesterol vs those without MM at the same age (Fig 1). Those with MM were less likely to have a lifetime ASCVD event (Fisher exact: p<0.001) and were not more likely to have chronic migraine or aura (p= 0.085, p = 0.606) The CoxPH models included 31,963 women and outperformed the existing ACC/AHA score. Adding MM increased the predictive performance of the model (Anova p=0.002). Chronic migraine and aura coefficient were significant(p<0.001) and positive. MM coefficient was significant and negative (p=0.004).

Conclusion: In this cohort of women with migraine, those with a MM diagnosis were less likely to have ASCVD events than those without. MM may represent a migraine subtype with different underlying biological mechanisms and potentially reduced association with CVD risk.

Fig. 1



OP039

Discriminating migraine aura from transient ischemic attack using MRI-based oxygen metabolism mapping

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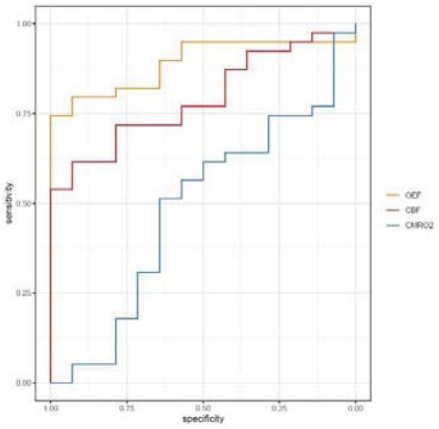
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Objective: Migraine aura is a common acute stroke mimic. Distinguishing between migraine aura (MA) and ischemic stroke or transient ischemic attack (TIA) based solely on clinical presentation can be challenging. Magnetic resonance imaging (MRI) using routine protocols may not definitely differentiate MA from TIA. However, recent advances in the post-processing of dynamic susceptibility-weighted (DSC) perfusion MRI now enables an estimation of cerebral oxygen metabolism. This study aimed to investigate the impact of cerebral oxygen metabolism maps on the differential diagnosis between MA and TIA.

Methods: We performed a retrospective study of patients admitted to the Lyon Stroke Center from the period 2012–2024. Patients who underwent an emergency MRI during initial assessment and received a final diagnosis of either MA or TIA were included.

Results: This study included 53 patients: 39 with a final diagnosis of MA and 14 with TIA. Patients with migraine aura showed significantly higher oxygen extraction fraction (OEF) values within the regions of clinical interest compared to TIA patients. Median OEF change was +14.84% in the MA group versus -1.65% in the TIA group (p<0.001). Cerebral metabolic rate of oxygen (CMRO2) values did not significantly differ between the two groups (p=0.524). Normalized OEF ratio exhibited a significantly higher area the under curve than normalized cerebral blood flow (CBF, p=0.04) and CMRO2 (p=0.001) (figure 1). After adjustment for the time interval from symptoms onset to MRI, OEF remained an independent predictor of migraine aura (odds ratio: 5.43, 95% CI: [1.69, 9.54], p=0.04).
Conclusion: Migraine aura was associated with a focal increase in OEF during the acute phase, that can be captured using routine DSC perfusion MRI.

Fig. 1



OP040
Altered clock function in primary skin fibroblasts cultures derived from cluster headache patients
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Objective: Cluster headache (CH) is the most common form of autonomic trigeminal cephalalgia, and about 2/3 of all patients report symptoms with distinct circadian distribution. Primary skin fibroblasts in culture display robust oscillations in clock gene expression and have been used for investigating the mechanisms of action of drugs targeting the molecular clock. The aim of this study was to investigate the effect of verapamil on molecular clock function.
Methods: We have established primary fibroblast cultures from 14 CH patients and 10 controls. The cells were transfected with a reporter system expressing firefly luciferase driven by BMAL1 promoter, and the bioluminescence signal was monitored continuously for 5 to 10 consecutive cycles using photomultiplier tubes in photon counting mode. Around the time of the second circadian trough in bioluminescence, verapamil (L-type calcium channel blocker; 100 microM) or an equivalent volume of sterile PBS was added to each culture dish. The signals recorded before and after treatment were fitted with sinusoids with exponential decay independently, and the effects of treatment were evaluated as deviations from the signal predicted by baseline parameters.
Results: In fibroblasts isolated from control subjects, PBS treatment re-entrained circadian oscillations in clock gene expression and verapamil treatment led to a more robust re-entrainment associated with faster decay of oscillations in bioluminescence signal. The circadian period was not significantly changed by either treatment. Fibroblasts isolated from CH patients were virtually undistinguishable from controls in baseline conditions. Verapamil treatment resulted in a less robust re-entrainment as compared to controls, and prolonged the circadian period.
Conclusion: Our data points to a less robust molecular clock in primary fibroblasts isolated from CH patients as compared to controls, and verapamil treatment makes cell populations more susceptible to external entrainment.

OP041
Effectiveness of laser acupuncture on sleep quality in patients with chronic migraine: A randomized, sham-controlled, single-blind trial
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Objective: Our published randomized controlled trial (RCT) documented Laser acupuncture (LA) has shown efficacy in migraine prevention. However, its impact on sleep quality in patients with chronic migraine (CM) remains uncertain. This study aimed to evaluate the effectiveness of LA in improving sleep quality among patients with CM.
Methods: From April 2022 to January 2025, patients over 20 years old with CM who received LA as an add-on treatment were included in the experimental group, while the control group received sham treatment using an inactive laser device. Headache improvement was defined as a ≥30% reduction in the number of headache days by week 12 compared to baseline. Both groups were further stratified into subgroups based on whether this threshold was

achieved. The primary outcome was the change in Pittsburgh Sleep Quality Index (PSQI) scores from baseline, assessed monthly. Evaluations were conducted at baseline, week 4, week 8, and week 12.

Results: A total of 76 patients were included in the intention-to-treat (ITT) analysis. At baseline, there were no significant differences in PSQI scores among the four subgroups. The LA & ≥30% reduction group demonstrated a significant improvement in sleep quality, with PSQI scores decreasing from 18.8 ± 6.8 to 15.6 ± 8.2 at week 12 (p = 0.001), and the LA & <30% reduction group also showed improvement (p = 0.038).

Conclusion: LA may have a beneficial effect on sleep quality in patients with CM, particularly among those who experience a ≥30% reduction in headache days. Further large-scale, multi-center studies are warranted to confirm these findings.

Fig. 1

Table. Changes in PSQI Scores Among the Four Groups After Laser Acupuncture or Sham Treatment

PSQI score, mean±SD	Group			
	LA & ≥30% reduction (n=26)	LA & <30% reduction (n=15)	Sham & ≥30% reduction (n=8)	Sham & <30% reduction (n=27)
Baseline	18.8 ± 6.8	15.3 ± 9.5	16.5 ± 8.8	17.3 ± 6.6
4th week	17.8 ± 7.3	14.2 ± 7.8	15.4 ± 9.6	16.1 ± 7.1
8th week	15.9 ± 7.5	14.3 ± 7.8	14.6 ± 9.1	16.7 ± 6.7
12th week	15.6 ± 8.2	16.3 ± 8.2	17.5 ± 7.3	16.3 ± 6.3
p value#	0.001**	0.038*	0.664	0.534

PSQI Pittsburgh Sleep Quality Index
#*p* values based on Friedman test
*p<0.05, **p<0.01.

OP042

White matter tract differences in persistent post-traumatic headache, migraine, and healthy controls: A diffusion tensor imaging study

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Objective: Persistent post-traumatic headache (PPTH) frequently resembles migraine but may involve distinct white matter perturbations. We compared white matter fiber tracts among adults with PPTH, migraine, and healthy controls (HCs).

Methods: This cross-sectional diffusion tensor imaging (DTI) study enrolled adults with PPTH, migraine, and HCs, who underwent a single 3T MRI session. Tract-based spatial statistics quantified white matter integrity. Outcome measures included fractional anisotropy (FA), axial diffusivity (AD), mean diffusivity, and radial diffusivity. Group comparisons used general linear models with threshold-free cluster enhancement and 5,000 permutations. Voxelwise significance was set at $P < 0.05$ after family-wise error correction, adjusting for age and sex. Post-hoc region-of-interest (ROI) analyses explored differences within significant regions.

Results: Imaging data were available from 100 participants with PPTH, 293 with migraine, and 154 HCs. Compared to participants with migraine, those with PPTH exhibited higher FA and AD values in the posterior limb of the internal capsule and superior corona radiata (*PFWE* < 0.05), findings that were further confirmed by post-hoc ROI analysis relative to HCs (both $P < 0.001$). FA values within these tracts were positively associated with monthly migraine-like headache days ($P = 0.043$). In addition, participants with PPTH showed lower AD values within the corpus callosum compared to those with migraine (*PFWE* < 0.05), with similar post-hoc ROI differences relative to HCs ($P = 0.002$). Lower corpus callosal AD values were associated with greater post-concussive symptom severity ($P = 0.036$).

Conclusion: PPTH is associated with distinct white matter alterations involving ascending somatosensory pathways and interhemispheric fibers. These alterations are associated with clinical symptom severity and differentiate adults with PPTH from those with migraine, suggesting trauma-induced maladaptive plasticity.

OP043

The PTHEENOT study: Feasibility of an early, interdisciplinary, non-pharmacological intervention for patients at risk of developing post-traumatic headache

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Objective: To evaluate the feasibility and acceptability of an early interdisciplinary intervention based on cognitive behavioral therapy and graded physical exercise for patients at risk of developing post-traumatic headache (PTH) 2-6 months following mild head trauma.

Methods: This feasibility study evaluated the recruitment, retention, questionnaire comprehension, and the acceptability of a five-week group-based intervention initiated 2-6 months post-injury. The

intervention included psychoeducational sessions, structured physical exercise, peer dialogue, and nursing support. Twelve patients aged 18-60 years (mean age 43), all with mild head trauma, were screened for eligibility. At the time of recruitment, all patients were working. Eight were enrolled in the study: three were on full-time sick leave, three part-time, and two working full-time. Six (75%) completed the intervention; two withdrew due to illness. Data were collected through focus group interviews. A qualitative content analysis was employed to systematically categorize and interpret participants" experiences and evaluate the perceived feasibility and acceptability of the intervention.

Results: Patients expressed high satisfaction with the intervention, valuing structured education, group discussions, and physical activity. Patients reported reduced headache frequency, improved sleep quality, and enhanced coping strategies. Based on patient feedback, nursing sessions were extended from 90 to 120 minutes. A follow-up session was also incorporated to help sustain newly acquired coping strategies. These adjustments will be implemented in the upcoming randomized controlled trial (RCT) design.

Conclusion: The intervention was feasible and well-received, with promising indications of improved headache outcomes and coping abilities. The feasibility study has informed adjustments for the upcoming RCT. Early non-pharmacological interventions may contribute to reducing the risk of developing persistent PTH.

OP044

Kiss1 receptor as a novel target for migraine treatment

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Objective: After puberty, a sharp increase in migraine prevalence is observed, especially in females, suggesting an interaction between the trigeminovascular system (TVS) and the hypothalamic-pituitary-gonadal (HPG) axis. Kisspeptin (KP), a hypothalamic neuropeptide, plays a key role in the onset of puberty. We have previously shown that KP administration sensitizes the TVS. The aim of the present study was to evaluate the expression patterns of the Kiss1 receptor (Kiss1R) in the rodent TVS and to assess the therapeutic potential of blocking Kiss1R with its antagonist p234 in preventing nitroglycerin-induced periorbital mechanical hypersensitivity.

Methods: Adult C57BL6/J mice (n=12) were divided in two cohorts. One cohort was perfused with 4% paraformaldehyde, the trigeminal ganglia and trigeminal nucleus caudalis were isolated, cryosectioned and stained for Kiss1R using tyramide signal amplification. In the second cohort, orofacial mechanical withdrawal thresholds were assessed at baseline and after chronic administration of NTG (10mg/kg) or vehicle (n=5 each), using von Frey filaments. On day 10, thresholds were evaluated after administration of p234 (6nmol/kg) at 60 and 120 minutes.

Results: Kiss1R was widely expressed throughout the trigeminal ganglion and the dorsal horn of the trigeminal nucleus caudalis. Chronic NTG administration significantly reduced mechanical thresholds from day 5 ($P<0.05$). Administration of p234 restored the orofacial mechanical thresholds after 120 minutes, with no statistical difference observed between the NTG and vehicle groups ($P>0.05$).

Conclusion: Our data highlight that KP can modulate trigeminal nociception, aligning with the increased migraine incidence observed after puberty. Targeting the KP signalling pathway may offer a promising therapeutic approach for migraine treatment.

OP045

Distribution of intranasal lidocaine and its effect on electrically-evoked calcium signals in mouse trigeminal ganglion neurons

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Objective: Intranasally (i.n.) applied lidocaine has shown promise in treating postdural puncture headache and has been explored as potential treatment for cluster headache and migraine. However, the mechanisms underlying its analgesic effects remain unclear. This study aimed to determine the concentration of lidocaine reached in relevant tissues after i.n. application and its impact on trigeminal ganglion (TG) neurons.

Methods: We used a mouse model to investigate the distribution of lidocaine (10% w/v) after i.n. application, employing liquid chromatography-mass spectrometry (LC-MS) to measure lidocaine concentrations in various tissues. Additionally, we conducted calcium imaging experiments on acutely

cultured murine TG neurons, using electrical stimulation to assess effects of different concentrations of lidocaine, encompassing the measured tissue concentrations, on neuronal excitability.

Results: Results showed that 30 minutes to 2 hours after i.n. application, lidocaine concentrations ranged from ~2 µM in plasma to ~60 µM in TG. Capsaicin-sensitive TG neurons tolerated repetitive electrical stimulation worse than other neurons and were more readily blocked by 100 µM lidocaine. Furthermore, these neurons displayed sustained increases in calcium signals when exposed to 10 µM lidocaine during repetitive stimulation, which failed to return to baseline levels.

Conclusion: Our findings suggest that micromolar concentrations of lidocaine are reached in brain and TG within 30 minutes to 2 hours after i.n. administration. These low concentrations may selectively affect depolarized trigeminal nociceptors, providing a potential mechanism for anti-headache effects of intranasally applied lidocaine.

OP046

Sexual dimorphism in the clonidine-mediated suppression of trigeminal nociception in wide dynamic range (WDR) neurons

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Objective: Behavioural experiments have shown that male rats are more sensitive to clonidine-induced antinociception than female rats. Interestingly, little is known about how neuronal nociceptive processing at the trigeminal level is affected in females (including the role of the $\alpha_{2A/2B/2C}$-adrenoceptors subtypes involved). Given that trigeminal second-order WDR cells play a crucial processing nociception from peripheral facial areas, this study aimed to investigate the impact of clonidine on the activity of trigeminal WDR cells in male and female rats.

Methods: Extracellular single-unit recordings of trigeminal WDR cells were conducted in anaesthetised Wistar rats and examined in relation to discharges associated with Aδ- and C-fibres. The effect of local clonidine (3.1-31 nmol) on electrical periorbital-evoked firing of WDR cells was recorded. Furthermore, considering that at least three α_2-adrenoceptor subtypes exist (α_{2A}-, α_{2B}- and α_{2C}-adrenoceptors), blockade of these receptor subtypes using BRL 44408 (α_{2A}), imiloxan (α_{2B}), and JP 1302 (α_{2C}) was performed.

Results: Clonidine inhibited neuronal firing associated with Aδ- and C-fibre activation in both sexes. This inhibition was observed in >50 % of the recorded cells. The dose required to induce similar antinociceptive effects was higher in females (31 vs. 10 nmol). Moreover, clonidine-induced inhibition of Aδ- and C-fibre activity was reversed by BRL 44408 in males. In contrast, in females, imiloxan and JP-1302 reversed the clonidine induced inhibition of Aδ- but not C-fibres.

Conclusion: Clonidine-induced WDR antinociception is more pronounced in male than in female rodents. In males, clonidine-induced inhibition of Aδ- and C-fibre discharge relies on α_{2A}-adrenoceptor activation. In females, the activation of $\alpha_{2B/2C}$-adrenoceptors appears to be significant for the inhibition of Aδ-fibre discharge by clonidine, but not for C-fibre discharge, suggesting that other mechanisms or receptors might be involved in females.

OP047

Patterns, efficacy, motivations and impact of therapeutic illicit drug use in cluster headache in the Netherlands: Results from a cross-sectional survey study

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Objective: People with cluster headache (CH) often experience limited efficacy and/or intolerable side effects of conventional treatments. Some turn to illicit drugs, reporting benefits. Existing survey studies lack detailed data on usage patterns, efficacy, motivations and impact. This study aims to address these gaps.

Methods: A cross-sectional survey was conducted among CH patients recruited from two Dutch hospitals and patient organizations. The digital questionnaire covered CH characteristics, demographics, treatment history, attitudes toward drug use and therapeutic use details.

Results: A total of 461 patients were analyzed (56% chronic CH), mean age 53.5±14.0 years. Nearly half (48.2%) reported lifetime drug use. Of these, 26.2% reported therapeutic use, 49.3% recreational use and 24.5% both. Among therapeutic users, the most frequently used substances were psilocybin (63.2%), cannabis (47.4%) and LSD (23.7%). Psilocybin and LSD were mainly used preventively, whereas cannabis was used equally as preventive and acute treatment. Among therapeutic users, preventive efficacy was

reported by 59.3% for psilocybin, 54.9% for cannabis and 60.0% for LSD. In these, reported median attack reduction was 70%, 45%, and 75%, respectively. As acute treatment, 46.4% reported pain reduction with cannabis, describing a median 30% pain reduction with onset after 15 minutes. Therapeutic illicit drug use was most often discontinued because of insufficient efficacy (53.7%) or side effects (25.4%). Most patients reported no impact of therapeutic drug use on work/study, leisure activities or social relationships. When effects were reported, they were positive in ~90% of cases across all domains.

Conclusion: Findings from this survey show that therapeutic illicit drug use is common among Dutch CH patients, especially with psilocybin, cannabis and LSD. The results highlight unmet treatment needs and possible efficacy. This supports the urgency of clinical trials into the potential therapeutic applications of these substances.

OP048

What is a migraine day? Towards a consensus definition both for clinical care and research – A delphi panel-based study

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Objective: Although guidelines for controlled trials have proposed a definition for a migraine day, substantial variability remains across clinical trials, highlighting the lack of a universally adopted definition.

Methods: Through three survey rounds using the Delphi method, a panel of 18 experts evaluated clinical cases to achieve consensus on a standardized definition of a migraine day.

Results: A consensus of more than 70 % was reached on a proposed definition of a migraine day across three distinct situations (1) without acute treatment (2) with acute treatment and (3) in the presence of aura (Table 1).

Conclusion: We would like to propose this definition to the International Headache Society (IHS) for inclusion in the International Classification of Headache Disorders (ICHD). Adoption of this definition could improve consistency in migraine research and clinical documentation, ultimately enhancing comparability across studies and supporting better patient care.

Fig. 1

Table 1: Proposed definition of a migraine day across three distinct situations.

	CRITERIA FOR A MIGRAINE DAY
1. UNTREATED HEADACHE DAY	A headache day can be labelled as a (probable) migraine day when the following criteria are met: - Headache attacks lasting **≥ 4 hours** **AND** - Headache must have at least **two** out of four headache characteristics, regardless of the presence of any associated symptom **OR** - Headache must have at least **one** out of four headache characteristics combined with **one** associated symptom **Headache characteristics:** 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs) **Associated symptoms:** • nausea and/or vomiting • photophobia AND phonophobia
2. TREATED HEADACHE DAY	A headache day can be labelled as a migraine day when the following criterion is met: A headache lasting **≥ 30 minutes**, regardless of drug (class) taken, the presence of any headache characteristic or associated symptom.
3. AURA	A migraine day can be defined as any calendar day on which the following criterion is met: An aura, fulfilling the ICHD-3 criteria for migraine with aura, is experienced regardless of the presence of a headache.

OP049

Steroid hormone dysfunction in female cluster headache patients

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Objective: Previous studies have shown alterations in steroid hormones in male cluster headache patients. This study aimed to examine serum steroid hormone levels in female cluster headache patients relative to healthy controls (n=19), to assess potential endocrine alteration.

Methods: We performed targeted quantitative liquid chromatography tandem mass-spectrometry for 20 steroid hormones (corticosteroids, androgens, progestogens, and estrogens) in serum from adult female cluster headache patients, both chronic (n=28) and episodic (n=23) consisting of 18 paired samples in bout and remission, obtained from the Danish Cluster Headache Biobank in a prospective case-control study.

Results: We found 9 differential steroids in chronic cluster, 8 in episodic in bout and 3 in episodic in remission, compared to controls. The stress hormone cortisol was lower in chronic (P=0.0022) and episodic in bout (P=0.0084). The progestogens pregnenolone and progesterone were lower in chronic (P<0.0001 and P=0.0012) and episodic in bout (P=0.0154 and P=0.0458) however, only pregnenolone was lower in episodic in remission (P=0.0153). The androgens dehydroepiandrosterone (P=0.0311) and androstenedione (P=0.0014) were lower in chronic cluster headache. No differences were found in steroid hormones in the paired analysis between episodic patients in bout and remission.

Conclusion: Female cluster headache patients show a dysregulated steroid hormone profile with corticosteroids and progestogens being lower in the headache state of cluster headache. Furthermore, androgens were lower in chronic cluster headache patients. This highlights potential endocrine involvement in cluster headache and could underly the pathogenesis of cluster headache as well as suggest novel therapeutic pathways.

OP050

Dynamic changes in pain inhibition in episodic and chronic migraine: Evidence of CPM waning

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Objective: More studies are needed to understand pain profiling in migraine. This study aimed to examine the changes in Conditioned Pain Modulation (CPM) along several repetitions across two types of migraine, episodic (EM) and chronic (CM) migraine.

Methods: Fifty-seven migraine patients from the Leiden Headache Center were included: 28 with EM and 29 with CM. CPM was used to study the function of descending pain inhibitory pathways by administering a test stimulus (CPMheat or CPMelectrical) and a conditioning stimulus (cold) at 3 timepoints. Linear mixed effect models were fitted for all patient (migraine overall) and per diagnose (EM vs. CM). Importantly, a subgroup analysis was conducted including patients who demonstrated an effective CPM response at timepoint 1 (T1), to assess possible waning effects over repeated measurements (T2-T3).

Results: In the overall migraine group, CPMheat remained stable across timepoints, with no significant differences between CM and EM groups. Patients with a normal CPM response at T1 showed a significant decline over repeated measurements, notably between T1–T2 ($p = .04$) and T1–T3 ($p < .001$). Age, sex, and stimulus-related factors (test temperature, condition stimulus) did not affect CPM responses. CPMelectrical showed similar patterns, with significant changes from T1 to T2 ($p = .02$) and T1 to T3 ($p < .001$).

Conclusion: The observed waning of CPM suggests that even migraine patients with initially normal pain inhibition may experience progressive reductions in their descending pain inhibitory system over repeated or prolonged pain challenges.

OP051

Epidemiology and journeys of trigeminal neuralgia patients in UK

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Objective: Determine the epidemiology of trigeminal neuralgia, how managed,use of machine learning to determine predictors and potential effects on treatment.

Methods: Data obtained from Clinical Practise Research Datalink kept by the NHS in the UK for a period of 25 years for all patients with Trigeminal neuralgia (TN) an ICD code of G50.0 and control data of patients with other forms of facial pain. These were then analysed by data analysts in consultation with an expert clinician.

Results: Records of 48K TN patients were obtained and 104K control data. The incidence and prevalence were steadily rising till the onset of COVID. Overall prevalence of 0.08% as % of the population.thus 8 in every 10,000 people in UK have TN. The mean

incidence is 0.11 in every 1000 person years. Females were more commonly affected, peak age late 60"s. Distribution was nationwide with most frequently affected group being Caucasian. There was significant co-morbidity with MS. The most frequently used medication was carbamazepine. 10% of patients had some surgical intervention which is considered low and probably related to coding issues. Machine learning established that in patients with TN there was a 16 times increased risk of developing trifascicular heart block.

Conclusion: This data is in keeping with data from the UK disease atlas which suggests that TN may not qualify as a rare disease. There is evidence for increasing neurosurgical management given the potential long term effects of drugs and establishing national multidisciplinary centres to ensure TN patients gain faster access to services. Registries should be set up.

P001

Effectiveness of a mindfulness-based intervention in reducing headache frequency and emotional distress in patients with migraine: A pilot study

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Objective: Migraine is a disabling neurological condition often linked to emotional distress such as anxiety and stress. While medications are standard treatment, mindfulness has emerged as a promising non-pharmacologic approach. This study aimed to assess the impact of an 8-week mindfulness-based group intervention on headache frequency, anxiety, and perceived stress in migraine patients.

Methods: Twenty-eight adults diagnosed with migraine were recruited from a neurology outpatient clinic. Participants attended an 8-week mindfulness-based program adapted from MBSR, led by a clinical psychologist. Headache frequency (monthly headache days), anxiety (GAD-7), and perceived stress (PSS-10) were assessed at baseline and post-intervention. Pre-post differences were analyzed using paired t-tests.

Results: Participants showed a significant reduction in monthly headache days (mean reduction = 3.5 days; $p < .01$), anxiety levels ($p < .01$), and perceived stress scores ($p < .01$). No adverse effects were reported. The program had a high completion rate, with only 11% dropout.

Conclusion: This pilot study suggests that mindfulness may be an effective and well-tolerated intervention for reducing headache frequency and emotional symptoms in migraine patients. Integrating mindfulness into multidisciplinary migraine care may enhance outcomes. Further controlled studies are needed to confirm these preliminary findings.

P002

Low-level 810nm laser acupuncture for chronic migraine patient in change acute headache medication usage days: A follow-up phase of randomized controlled trial

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Objective: Laser acupuncture (LA) has shown efficacy in migraine prevention in our previous published randomized Controlled trial (RCT). Our aim is to verify the efficacy of LA as preventive treatment for chronic migraine (CM) by a follow-up phase of our unpublished RCT (Registration Number: NCT06219694).

Methods: Participants were randomly assigned to either the LA group or the sham treatment group. Both groups received eight treatments over one month, followed by a three-month follow-up period. After six months from the initial treatment, participants in the sham group received open label extension LA treatment, followed by an additional three-month follow-up. LA and open label extension LA were performed by LaserPen-Expert 511A in 810 nm wavelength with an output power density of 5 W/cm^2, with the same acupoint. Each acupoint received 150 mW of output power in continuous mode for 30 seconds, delivering a stimulation energy of 4.5 J. The outcome was the change acute headache medication usage days in 3 months after receiving sham treatment or open label extension LA treatment.

Results: This follow-up phase included 35 patients, 74.3% of whom were female, with a mean age of 43.00 ± 14.28 years and a mean headache duration of 14.71 ± 10.03 years. The acute headache medication usage day in baseline was 9.09 ± 9.56, and before open label extension laser acupuncture was 9.00 ± 9.48, which showed no statistical significant difference (p=0.501). The change acute headache medication usage days compared from baseline till 12 weeks was 0.00 ± 2.17; before open label extension laser to post open label extension laser 12 weeks was -3.94 ± 3.57; showed statistical significant difference (p<0.001).

Conclusion: This follow-up phase of the RCT confirmed that LA is an effective preventive treatment for CM, significantly reducing acute headache medication usage days compared to the sham group.

Fig. 1

Baseline characteristic	Total (n=35)	
	mean	± SD
Age	43.00	± 14.28
Female, n (%)	26	74.29%
Height	162.26	± 8.96
Weight	61.91	± 14.63
BMI	23.36	± 4.28
Headache duration, year	14.71	± 10.03

Fig. 2

Mean ± SD	Baseline (0M)	Before open label extension LA (6M)	*p* value
Acute headache medications usage days per month	9.09 ± 9.56	9.00 ± 9.48	0.501
Wilcoxon Signed Ranks test			

Fig. 3

Mean ± SD	From baseline to 3 months (3M-0M)	From before open label extension LA to 3 months (9M-6M)	*p* value
Change of acute headache medications usage days per month	0.00 ± 2.17	-3.94 ± 3.57	<0.001
Friedman test.			

P003

Impact of toothpaste cessation on migraine frequency and severity: A prospective analysis of pre and post-intervention outcomes

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Objective: Certain ingredients in toothpaste—such as nitrates, fluorides, and essential oils like eucalyptus and camphor—may trigger migraine attacks. We hypothesized that discontinuing toothpaste use could positively impact migraine frequency and severity.

Methods: We prospectively enrolled 100 adult patients meeting ICHD-3 criteria for migraine or probable migraine. Patients with other primary or secondary headache disorders were excluded. Participants discontinued toothpaste use and used only saline water for oral hygiene over four weeks. Headache frequency, duration, intensity (on a 0–10 numerical rating scale), analgesic and balm usage were recorded in a headache diary. Follow-up interviews were conducted in person or by phone. Pre and post-intervention outcomes were compared using paired samples t-test, chi-square, and McNemar tests. Informed consent was obtained from the participants, and institutional ethical clearances were obtained for the study.

Results: The cohort of 100 patients (67% female; mean age 35.9 ± 15.7 years) showed substantial improvement post-intervention. Chronic daily headache prevalence decreased from 57% to 14% (relative risk reduction [RRR] 75%, number needed to treat [NNT] = 3; $p < 0.01$). Combined chronic and high-frequency headache cases dropped from 71% to 22% (RRR 69%, NNT = 2.04). Complete headache freedom was reported by 28% of participants. Headache intensity fell from 8.1 ± 1.5 to 4.44 ± 2.39 ($p < 0.01$). Prophylactic medication use decreased from 20% to 10% (RRR 50%), and analgesic use declined from 9.4 ± 10.5 to 5.5 ± 10.4 days/month ($p = 0.011$). Improvements began within 1–4 weeks and persisted at a mean follow-up of 30 weeks.

Conclusion: Toothpaste cessation may significantly reduce migraine frequency, intensity, and medication use in affected individuals.

P004

Reinforcing the efficacy of laser acupuncture in chronic migraine prevention: An extended patient enrollment study based on an original randomized controlled trial

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Objective: Our previously published randomized controlled trial demonstrated that laser acupuncture (LA) as an add-on preventive treatment for chronic migraine (CM) significantly reduced migraine days and acute headache medication usage (LAFCM trial; ISRCTN11208146). However, headache duration and MIDAS scores showed only numerical improvements at the time of treatment completion. This study aimed to reinforce those findings in an expanded cohort.

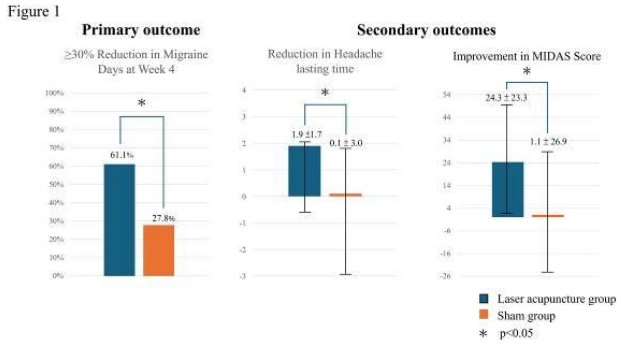
Methods: We enrolled additional patients aged >20 years with CM managed pharmacologically with unsatisfactory effect. Patients were randomly assigned in a 1:1 ratio to receive either low-level 810 nm LA or sham treatment in a single-blind design. All participants completed eight treatment sessions over four weeks. The fourth week, marking the end of the treatment course, was the primary follow-up time point. The primary outcome was ≥30% reduction in migraine days and the secondary outcomes were headache lasting time and migraine disability assessment (MIDAS) score. All outcomes were reported as absolute changes from baseline.

Results: A total of 72 patients (36 patients in each group) were included and baseline characteristics

were similar between trial groups. At the fourth week, the LA group achieved significantly higher rates of ≥30% reduction in migraine days (61.1% vs. 27.8%, p = 0.004), a greater reduction in headache lasting time (1.9 ± 1.7 h vs. 0.1 ± 3.0 h, p = 0.011), and a greater improvement in MIDAS scores (24.3 ± 23.3 vs. 1.1 ± 26.9, p = 0.017) compared to the sham group (Figure 1).

Conclusion: These findings confirm that an 8-session, four-week course of LA as an add-on therapy offers significant preventive benefits for CM patients, including reduced migraine frequency, shorter headache duration, and improved patient outcomes.

Fig. 1



P005

Patient perspectives on physiotherapy interventions for migraine: A pre- and post- intervention qualitative study

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Objective: The aim of this study was to explore expectations and experiences of patients regarding physiotherapy management for migraine.

Methods: Eleven out of 13 participants in a study on physiotherapy management for migraine were interviewed by an independent researcher over phone or videoconferencing using a semi-structured format before and after undergoing two months of physiotherapy treatments that included education, manual therapy and exercise. Over eight hours of interviews were audio-recorded and transcribed. Reflexive thematic analysis identified codes and key themes after five research team meetings

Results: All but one participant reported overall positive experience. Three themes were interpreted. Theme 1 was a gap in migraine management filled by physiotherapy. Participants expressed need for self-management strategies and information from a clinician who had time to understand validate their experience. They wanted assessment and treatment for neck pain and were interested in exploring non-pharmacological treatment. Theme 2 was that many outcomes mattered to patients. Participants had low expectations prior to physiotherapy, but after experiencing physiotherapy, all indicated that short term pain relief was important. Reduced duration, intensity and frequency of neck pain and headache were valued outcomes leading to perceived improved quality of life. Aggravation of symptoms was tolerated if there were immediate gains or clear understanding of why it was necessary. Some participants" main goal was reduced medication use. Long term outcomes were not yet measured but participants expressed feeling positive and empowered. Theme 3 was about accessibility. Participants liked that physiotherapy sessions were longer and more frequent than visits to medical doctors. Exercise prescription and advice needed to be practical and take into account individuals" busy routines.

Conclusion: Patients want physiotherapy incorporated with usual care to improve symptoms and empower self-management.

P006

The efficacy of manual therapy on migraine: A systematic review and meta-analysis

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Objective: This review updates previous evidence to assess the efficacy of manual therapy in managing migraine

Methods: A search in CINAHL, Embase, PubMed, and CENTRAL identified randomized controlled trials (RCTs) from 2017 onward evaluating manual therapy for migraine in adults (≥18 years). Eligible interventions included spinal manipulation, mobilization, or massage, with any control or active comparator. Primary outcomes were migraine days (30 days), pain intensity (VAS 0–10), disability (HIT-6, MIDAS), and adverse events. The review followed PRISMA guidelines.

Results: A total of 501 records were identified, and 6 studies met the inclusion criteria.

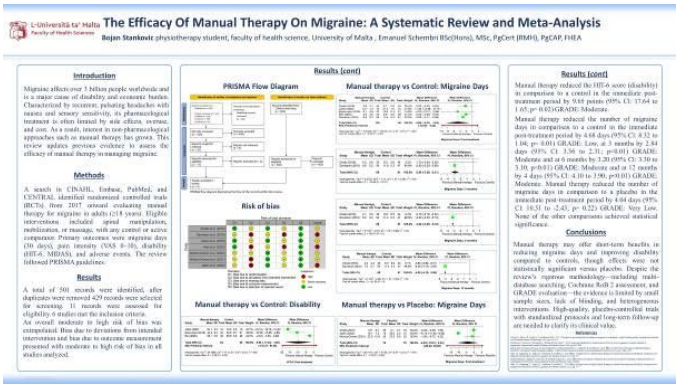
Manual therapy reduced the HIT-6 score (disability) in comparison to a control in the immediate post-treatment period by 9.65 points (95% CI: 17.64 to 1.65; p= 0.02) GRADE: Moderate.

Manual therapy reduced the number of migraine days in comparison to a control in the immediate post-treatment period by 4.68 days (95% CI: 8.32 to 1.04; p= 0.01) GRADE: Low, at 3 months by 2.84 days (95% CI: 3.36 to 2.31; p<0.01) GRADE: Moderate and at 6 months by 3.20 (95% CI: 3.30 to 3.10; p<0.01) GRADE: Moderate and at 12 months by 4 days (95% CI: 4.10 to 3.90; p<0.01) GRADE: Moderate.

Manual therapy reduced the number of migraine days in comparison to a placebo in the immediate post-treatment period by 4.04 days (95% CI: 10.51 to -2.43; p= 0.22) GRADE: Very Low. None of the other comparisons achieved statistical significance.

Conclusion: Manual therapy may offer short-term benefits in reducing migraine days and improving disability compared to controls, though effects were not statistically significant versus placebo. Despite the review"s rigorous methodology—including multi-database searching, Cochrane RoB 2 assessment, and GRADE evaluation—the evidence is limited by small sample sizes, lack of blinding, and heterogeneous interventions. High-quality, placebo-controlled trials with standardized protocols and long-term follow-up are needed to clarify its clinical value.

Fig. 1



P007

Evaluation of a day-clinic intensive program for headache: A study protocol

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Objective: Headaches are a major burden for patients and healthcare systems. At the Headache Outpatient Clinic of Charité – Universitätsmedizin Berlin, an interdisciplinary day-clinic intensive program (IP) is offered to improve care for headache patients. Previous uncontrolled pre-post studies have demonstrated effects of similar programs [1-2], but without direct comparison to outpatient standard care (SC).

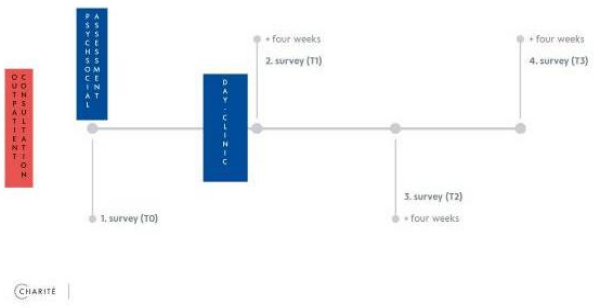
Methods: In a prospective cohort study, two groups are compared: patients participating in a 5-day IP and patients receiving SC. Eligible are patients with ≥5 headache days/month and a diagnosis according to ICD10 (G43: migraine; G44: cluster headache, chronic tension-type headache, medication-overuse headache). Data is collected online via validated questionnaires at four time points (Figure 1: Timeline). Patient-reported outcomes include headache frequency, medication intake, quality of life, general health, psychological distress, pain acceptance, and self-efficacy. Recruitment is planned until summer 2026 with 14 groups of 6 participants each. Accounting for 20% dropout, n=66 is expected for the intervention group. A matched control group (age, sex, headache frequency) of equal size completes identical assessments.

Results: Mixed models with fixed effects for group and time will be used for analysis.

Conclusion: The study will provide evidence on the effectiveness of an interdisciplinary day-clinic approach for headache treatment, aiming to optimize implementation and future treatment guidelines.

1. Gaul C, Brömstrup J, Fritsche G, Diener HC, Katsarava Z. Evaluating integrated headache care: a one-year follow-up observational study in patients treated at the Essen headache centre. *BMC Neurol*. 2011;11(1):124.
2. Rohling S, Funk A, Ruscheweyh R, Schankin C, Straube A, Kamm K. Integrated headache care at the outpatient headache center of the University Hospital of Munich. *Clinical and Translational Neuroscience*. 2018;2(2):2514183X1878684.

Fig. 1



P008

Younger age predicts greater improvement following placebo olfactory training in primary headache disorders

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Objective: Primary headache disorders are highly prevalent and disabling, especially in children, yet treatment options remain limited. Evidence suggests placebo responsivity is higher in younger individuals. This study investigated whether age predicts changes in headache-related disability and frequency following placebo olfactory training, and whether sensory (olfactory) and physiological (pain sensitivity) changes are associated with symptom improvement.
Methods: Data were pooled from two placebo-controlled olfactory training trials in pediatric and adult headache patients. Only participants in the placebo group (N = 73, age 6–55) were included. For 12 weeks, participants used odorless pens at home, believing they contained low-dose scents. Headache frequency and disability (MIDAS/PedMIDAS) were assessed pre- and post-intervention. Sensory outcomes included olfactory threshold and identification (Sniffin" Sticks), and pain sensitivity (QST: mechanical pain threshold and sensitivity). Regression models tested age as a predictor of symptom change, controlling for baseline values. Spearman correlations assessed links between clinical outcomes and sensory/physiological changes.
Results: At baseline, children (<18) reported more headache days and greater disability than adults ($p < .001$; $p = .011$). Overall, 60.3% showed ≥30% reduction in disability, and 37.0% in headache frequency. Age significantly predicted improvement in headache frequency ($\beta = .320$, $p = .008$), with younger patients benefiting more. Of the sensory/physiological measures, only improvement in odor identification correlated with reduced headache frequency ($\rho = –.241$, $p = .040$).
Conclusion: Younger age predicted greater placebo-related improvement in headache frequency. Enhanced odor identification may reflect mechanisms underlying clinical change. These findings highlight the role of developmental and sensory factors in placebo response among headache patients.

P009

Pressure pain threshold response to a maximal cardiopulmonary exercise test in episodic migraine: A pilot study

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Objective: Although exercise is often reported as a possible trigger for migraine attacks, it may also reduce pain through mechanisms such as the release of endorphins and the activation of endogenous pain modulation. This pilot study aimed to investigate changes in pressure pain thresholds (PPT) before and after a single Cardiopulmonary Exercise Test (CPET) in patients with episodic migraine, to explore the potential for exercise-induced hypoalgesia in this population.
Methods: Sixteen adults diagnosed with episodic migraine participated. PPT was assessed bilaterally at the mid-point of the upper trapezius and the tibialis anterior muscles. Measurements were taken three times on each side using a digital pressure algometer (in Newton, N), and the average of both sides was used for analysis. Assessments were carried out before and after a CPET to determine the maximal aerobic capacity.
Results: No significant changes in PPT were found in the upper trapezius (mean difference = 0.4 N; standard deviation (SD) = 4.4 N; $p = 0.702$). In contrast, a significant increase in PPT after the CPET was found on the tibialis anterior muscle (mean difference = -6.4 N; SD: 7.3 N; $p = 0.003$).
Conclusion: A single CPET may induce hypoalgesia in the tibialis anterior muscle in patients with episodic migraine. However, the absence of hypoalgesia in the trapezius - a commonly sensitized area in migraine – suggests that these effects may be site-specific and indicate altered central pain modulation. Although it was not the focus of this study, future research should explore whether changes in PPT following maximal aerobic effort may help predict which patients will tolerate or benefit from exercise-based interventions.

P011

Retrospective analysis of acupuncture for migraine: A 150-patient study demonstrates 35% reduction in attack frequency compared to standard therapy

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Objective: Migraine remains one of the most disabling neurological disorders, with many patients experiencing insufficient relief from pharmacological treatments alone. Acupuncture, as a component of integrative medicine, is increasingly used as an adjunct or alternative strategy, though large-scale clinical data remain limited.

To evaluate the effectiveness of acupuncture in reducing the frequency and severity of migraine attacks in comparison to standard pharmacological therapy

Methods: This retrospective study analyzed clinical records of 150 patients diagnosed with episodic or chronic migraine who underwent acupuncture treatment at a specialized neurology center between 2021 and 2024. Patients were matched with controls who received standard pharmacologic management alone. The primary outcome was the change in monthly migraine days over a 3-month follow-up. Secondary outcomes included intensity (VAS scale) and acute medication usage.

Results: Patients receiving acupuncture experienced a **35% greater reduction in monthly migraine frequency** compared to the standard therapy group ($p < 0.01$). Improvements were also noted in headache intensity and reduced reliance on abortive medications. No serious adverse effects were reported.

Conclusion: This retrospective analysis suggests that acupuncture may offer a significant therapeutic benefit in migraine management, with a marked reduction in attack frequency. Further randomized prospective trials are warranted to confirm these findings and clarify mechanisms of action.

P012

Effects of dry needling of the obliquus capitis Inferior in patients with cervicogenic headache and upper cervical dysfunction: An exploratory randomized sham-controlled trial

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Objective: Cervicogenic headache (CeH) is linked to upper cervical dysfunctions. The obliquus capitis inferior (OCI) muscle may contribute to restricted cervical rotation at the C1-C2 level, altered proprioception and pain. Dry needling (DN) of the OCI is hypothesized to target these dysfunctions.

The aim of this study is to investigate whether a single intervention combining DN and manual therapy (MT) compared to sham needling (SN) and MT, improves C1-C2 rotation, functional, headache-related, and psychological outcomes in a subgroup of CeH patients with a positive cervical flexion-rotation test (CFRT).

Methods: Thirty-four participants were randomly assigned to: (1) DN + MT or (2) SN + MT. The primary outcome was C1-C2 rotational mobility. Secondary outcomes included headache-related parameters (frequency, intensity, duration and perceived effect), functional parameters (cervical mobility, pain pressure thresholds, motor control and proprioception) and psychological parameters (central sensitization, pain catastrophizing, coping strategies and kinesiophobia), outcomes were re-evaluated at one-week follow-up.

Results: Linear mixed-effects models showed a significant and clinically relevant increase for the CFRT, in the DN group compared to the SN group post-intervention (mean difference [MD]: 4,51°; 95% Confidence Interval [CI]: 1,74 ; 7,28), which was maintained at the 1-week follow-up (MD: 5,44° ; 95% CI: 2,55 ; 8,33). No clinically relevant changes were observed in other functional, headache-related or psychological parameters.

Conclusion: Targeting the OCI may be of added value in restoring atlanto-axial dysfunction. While short-term mobility gains were observed, a single intervention appears insufficient to impact other functional or psychological outcomes. Future research involving larger samples should examine DN effects as part of a multimodal treatment with long-term follow-up.

P013

Psychological comorbidities and non-pharmacological treatment strategies in cluster headache: Insights from a qualitative study on patient experiences

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Objective: Cluster headache (CH) is a rare but excruciating neurological condition, often referred to as "suicide headache" due to its extreme pain and associated psychological distress. This study aimed to explore the lived psychological impact of CH and to examine how patients manage these challenges through non-pharmacological means, while identifying gaps in care—particularly those affecting quality of life in- and outside acute attack periods.

Methods: A qualitative study was conducted through semi-structured interviews with individuals diagnosed with CH, recruited via patient networks and social media in the Netherlands. Interviews were audio-recorded, transcribed, anonymized, and analyzed using inductive coding.

Results: Participants (n=18) reported a high prevalence of psychological complaints, notably anxiety (95%), fatigue (72%) and sleep disturbances (55%). CH severely disrupted daily life, with long-term effects on work, relationships and outlook on the future. Psychological distress was not limited to attack periods and lasting fear, exhaustion, and hopelessness extended between attacks. Coping strategies included mindfulness, planning routines, acceptance, and

psychological therapy. Others used sensory tools for pain distraction. Frustration with diagnostic delays, lack of psychological support and poor provider understanding was common.
Conclusion: Cluster headache imposes a sustained psychological burden that persists between attacks, yet current support remains fragmented and insufficient. Systemic changes—such as coordinated care pathways, routine psychosocial screening, and improved provider education—are essential to meet patients"needs. Addressing the patients"quality of life outside of attack periods is crucial for comprehensive, patient-centered CH management.

P014

BioTenCer study: Therapist-independed home-based biofeedback as preventive treatment for tension-type headache

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Objective: To assess the safety and efficacy of Cerebri-TTH, a therapist-independent biofeedback smartphone app, as preventive treatment in adults with frequent or chronic tension-type headache (TTH).
Methods: In this randomized, two-arm, wait-list controlled phase II trial, 300 adults with frequent or chronic TTH are included. After a 4-week run-in period using a daily headache diary, participants are randomized 1:1 to either a 12-week biofeedback app intervention or a wait-list control. The biofeedback is self-administered daily for 10 minutes using wearable sensors that monitor muscle tension, peripheral skin temperature, and heart rate variability. After the main phase, all participants are offered an optional 12-week extension. The primary efficacy endpoint is the change in mean Area-Under-the-headache-Curve (AUC) from baseline to the final 28 treatment days. Safety is evaluated via treatment-emergent adverse events (TEAEs).
Results: Data collection is expected to conclude in autumn 2025. We hypothesize that participants receiving Cerebri-TTH will experience a significant reduction in AUC compared to controls.
Conclusion: If shown to be safe and effective, Cerebri-TTH could represent a scalable, accessible, and non-pharmacological preventive treatment for TTH. Its therapist-independent, home-based format may be especially useful for populations such as pregnant or breastfeeding individuals, who are often restricted from using conventional medications.

P015

Patient experiences and preferences for non-oral acute migraine treatments: A discrete choice experiment

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Objective: The study aimed to examine heterogeneity in patients' preferences for attributes associated with non-oral acute migraine treatments.
Methods: Adult migraine patients who, in the last 3 months, used two or more acute migraine medications and who either had used a non-oral treatment or were not satisfied with their current treatment were recruited in the United States and Germany. Participants completed an online survey with a discrete choice experiment where they were asked to choose between pairs of hypothetical treatments characterised by 8 attributes (pain freedom at 2h, pain relief at 15 minutes (mins), return to normal function at 30 mins, mode of administration, drug- and administration-related side effects, maximum monthly dose, treatment window) in a series of questions. Latent class analysis (LCA) was used to identify unique preference classes. Relative importance (RI) was estimated for each attribute for each class and expressed as a percentage of overall importance of all attributes for the class.
Results: A total of 304 respondents completed the survey (n=152 per country). LCA identified two preference classes of approximately equal size. The most important attribute for Class 1 was mode of treatment administration (RI:30.9%; 95%CI: 20.2-36.5), followed by drug-related side effects (RI:23.6%; 95%CI: 14.2-27.4) and normal function at 30 mins (RI:14.6%; 95% CI:8.8-20.1]. For Class 2, the most important attribute was pain freedom at 2h (RI:33.6%; 95%CI:28.3-36.2) followed by drug-related side effects (RI:19.3%; 95%CI:13.5-22.7) and pain relief at 15 mins (RI:8.6%; 95%CI:13.6; 21.8). Class membership was not explained by observable patient clinical or demographic characteristics.
Conclusion: Respondents differed in their preferences for acute migraine treatment attributes, highlighting the need for patient involvement in treatment decisions. Mode of administration and speed of

response may be the driving factors defining different groups of patients.

P016

Quality of sleep in patients with chronic migraine treated with anti-CGRP monoclonal antibodies

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Objective: Sleep disturbances are common in patients with migraine. Patients with chronic migraine (CM) experience more frequent and severe insomnia symptoms than patients with episodic migraine. We wanted to assess sleep quality (QoS) in patients with CM treated with anti-CGRP monoclonal antibodies (mAbs) during a 6-month follow-up.
Methods: The study included 65 patients who had been diagnosed with CM based on medical history. We collected socio-demographic and clinical data, data about monthly migraine days (MMD), and also used Pittsburgh sleep quality index (PSQI) for assessing QoS. We assessed patients before the start of the treatment (to estimate QoS within 1 month before therapy), 3 months, and 6 months after the start of the prophylactic therapy with mAbs
Results: We noticed a statistically significant difference between the results at these three time points in PSQI scores ($p<0.01$), which was better 3 months and especially 6 months after the therapy was started. Patients with a higher number of MMD, patients with other associated medical conditions (diabetes mellitus, for example), and unemployed patients had higher scores on PSQI ($p<0.05$). A higher number of MMD was an independent predictor of worse PSQI in all three time points.
Conclusion: Lower levels of QoS correlate with worse disease severity and some clinical and socio-demographic variables in CM patients. We found a statistically significant reduction in PSQI scores after the start of prophylactic therapy with mAbs.

P017

Translation and validation of the Dutch Cluster Headache Impact Questionnaire (CHIQ)

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[2]The Migraine Clinic, Amsterdam, Netherlands
[3]Stichting Epilepsie Instellingen Nederland (SEIN), Heemstede, Netherlands

Objective: Cluster headache (CH) can severely impact Quality of Life (QoL). Studies suggest factors beyond attack frequency can affect QoL, indicating the importance of assessing QoL in drug trials. Previously, we translated the Cluster Headache Quality of Life scale (CHQ). This study translated and validated the Cluster Headache Impact Questionnaire (CHIQ), so both questionnaires can be used complementary.
Methods: Patients were recruited from the LUMC-CH database. The TRAP-D method (Translation, Review, Adjudication, Pretesting and Documentation) was used to translate the CHIQ from English to Dutch. The original translation was completed by n=32. Question clarity was discussed in a phone interview. A new group (n=39) completed the revised CHIQ twice (2-day interval) for test-retest validation. Results included internal validity (Cronbach"s Alpha) and reproducibility (Intraclass Correlation Coefficient; ICC). To determine convergent validity (Spearman correlation), all patients completed 3 other questionnaires once – the CHQ, Headache Impact Test (HIT-6) and Hospital Anxiety and Depression Scale (HADS).
Results: 71 patients were included (47% male; 86% chronic CH). One minor change was made to the translation after pre-testing. The CHIQ took a median of 5 minutes (IQR: 4, 9) to complete and most (84%) found it not burdensome at all. Internal validity (Cronbach"s Alpha 0.92) and test-retest reliability (ICC 0.78; 95% CI 0.479, 0.898) were excellent. The mean difference between the 2 CHIQ-assessments was 2.36 ± 4.06. Convergent validity was very strong with CHQ (ρ: 0.86) and HIT-6 (ρ: 0.81), and strong with HADS (ρ: 0.65).
Conclusion: The Dutch CHIQ is a valid, reliable tool for assessing CH's impact on QoL. It aligns with general QoL scales but specifically addresses CH related issues. Its short completion time and negligible burden make it a practical instrument for clinical care and standardized QoL assessment in international trials. Combined, the CHQ and CHIQ offer a comprehensive QoL assessment in CH

P018

The impact of migraine pain intensity on driving behavior: Insights from HIT-6 and self-reported outcomes

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Objective: To evaluate headache characteristics during driving in individuals with migraine and their impact on driving cessation.
Methods: This multicenter, cross-sectional study evaluated consecutive drivers diagnosed with migraine according to the ICHD-3 criteria using a modified 'Driving Habits Questionnaire' and the Headache Impact Test-6 (HIT-6). Migraine characteristics were categorized as follows: migraine with aura (MwA) vs. without aura (MwoA); episodic migraine (EM) vs. chronic migraine (CM); and with vs. without vestibular migraine (VM). We established cut-off points for the HIT-6 score concerning driving cessation due to migraine using Receiver Operating Characteristic (ROC) curves. We employed a Structural Equation Model (SEM) to identify the variables that influence driving cessation.
Results: A total of 1,333 migraine patients (age:37.15±9.69;77.6% female) reported having a driving history. The headache frequency was higher in patients with CM vs. EM (21.78% vs. 9.48%, p<0.001), VM vs. no VM (16.93% vs. 12.86%, p=0.032), but no difference was observed between MaA vs. MwoA (13.54% vs. 12.85%, p=0.639). The severity of pain and HIT-6 scores experienced during driving were higher in patients with MwA, CM, and VM (all, p<0.05). One percent of patients with MwA, 6% of those with CM, and 2% of those with VM ceased driving due to migraine. ROC curves using HIT-6 cut-offs showed a significant impact of migraine severity on driving cessation in different subtypes of migraine, except VM. SEM revealed the differential impact of various factors (e.g., migraine subtypes and severity, accompanying symptoms, driver road condition sensitivity characteristics) on driving cessation.
Conclusion: Patients with chronic migraine and vestibular migraine are more prone to experience headaches during driving. High-severity migraines can be associated with driving cessation. Increased awareness of the impact of migraines on driving is necessary to enhance the functional abilities and quality of life of patients.

Fig. 1

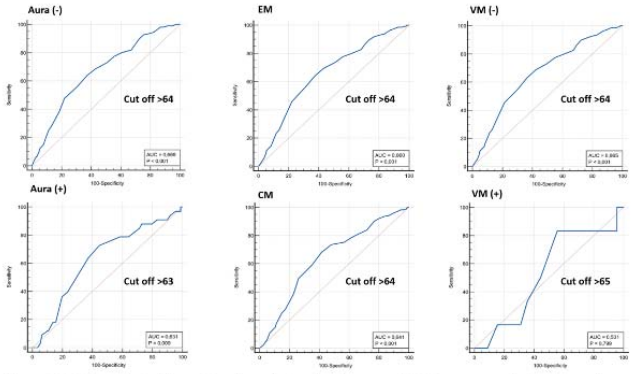


Figure 1: ROC analysis illustrating the relationship between HIT-6 scores and migraine subtypes regarding driving cessation (EM: episodic migraine, CM: chronic migraine, VM: vestibular migraine).

P019

Effect of fasting on migraine patient

A. Hassan[1], *A. Farw*[1], *B. Beriam*[1], *M. Bashir*[1], *Z. AlShebli*[1], *M. Abdelsalhen*[1], *R. Ahmad*[1], *F. Shwaylia*[1], *T. Hashi*[1], *H. Shahrour*[1], *H. Al Sheleh*[1], *M. Aljanahi*[1], *F. Ismail*[1], *A. Hanoun*[1], *W. Elkhhalifa*[1], *A. Mestarihi*[1], *M. Khan*[1], *A. Hassan*[1]
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Objective: Study of the impact of fasting during the holy month of Ramadan on migraine patients.
Methods: This retrospective study included patients diagnosed with migraines. Patients were recruited from the neurology clinic at Tawam Hospital, UAE. Recruitment occurred immediately after Ramadan 2024 to minimize recall bias.
Results: A total of 318 patients were enrolled. The mean age was 39.9 years, 81% female patients. 94% were on prophylactic treatment. In the first 10 days of fasting, headache days increased comparing to the baseline During the last 10 days of Ramadan, there was a significant reduction in migraine days. Headache freedom increased in the second and third periods. The headache severity dropped over time. An interesting finding was that the mean total duration of migraine attacks decreased progressively over the days of Ramadan.
Conclusion: Physicians should educate patients who plan to fast, about the likelihood of increased migraine parameters during the first few days of fasting, followed by a period of stabilization and potential improvement. A window for situational prophylaxis may exist and warrants further controlled study.

Fig. 1

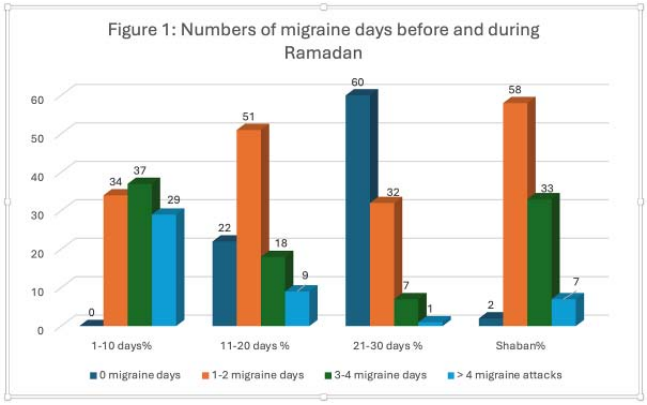


Fig. 2

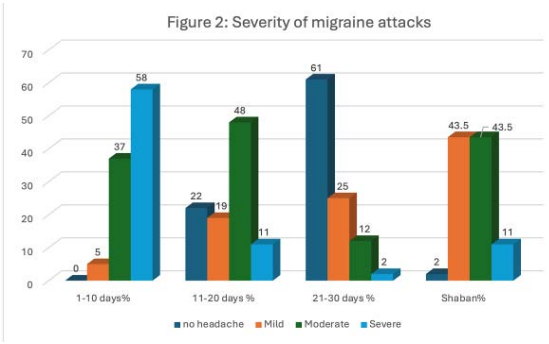


Fig. 3

Table 2: Number of missed days of social activities or working due to migraine attack

Missed days	1-10 days	11-20 days	21-30 days	Shaban
Zero	32	62	89	71
One days	28	23	8	18
Two days	21	11	3	7
Three days	9	3	0	3
Four days	5	1	0	1
Five days	3	0	0	0
Six days	1	0	0	0
Seven days	1	0	0	0

P020

Quality of life changes in cluster headache: Convergent validity, responsiveness and interpretability of the Cluster Headache Quality of life scale (CHQ) as Patient Reported Outcome Measure (PROM)

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Objective: Cluster headache (CH) significantly impacts patients" quality of life (QoL). We aim to validate the CHQ for measuring QoL changes in CH

Methods: In this multicenter prospective observational study participants with chronic CH (CCH) completed the CHQ at a 3-monthly interval alongside headache diaries and general QoL questionnaires (SF-36, HADS & EQ-5D). CHQ"s ability to measure changes was validated in 3 steps:1) convergent validity,2) responsiveness and 3) interpretability. Baseline scores were used for step 1; change scores for step 2 and 3 (Δ baseline - follow up). Twelve correlation hypotheses were formulated and tested for step 1 and 2. Validity was rated by % rejected hypotheses (high:≤25%, moderate:26–50%,poor:≥50%)

Results: For step 1, 117 participants were included; 82 were included for step 2 an 3. At baseline, overall QoL was poor (*CHQ*: 60.9±23.1, *SF-36*: 46.7±19.9) and worse in participants with more intense and frequent CH attacks (>CHQ scores: β=2.92(95% CI 0.91 to 4.93), *P=0.005;* β=0.27(95% CI 0.02 to 0.53), *P=0.033*)Convergent and responsiveness validity was high (≤25% hypotheses rejected). CHQ baseline scores correlated strongly with the HADS, SF36 and EQ-5D (ρ=0.68, ρ=-0.60, ρ=-0.52), but weakly with attack frequency (ρ=0.27). Change scores correlated strongly with HADS and SF36 (ρ= 0.51, ρ= -0.56) and moderately with EQ-5D (ρ= -0.38). Step 3 indicated ≤ –Δ3.5 points change as clinically relevant improvement and ≥ Δ 7.5 points as deterioration.

Conclusion: The CHQ has a high validity to measure (change in) QoL in. CH attack frequency influences QoL, but QoL is stronger correlated with mental health and activity restrictions than attack frequency. Implementing the CHQ may improve understanding of disease burden, enabling more targeted treatment strategies and thus improving overall disease management

Fig. 1

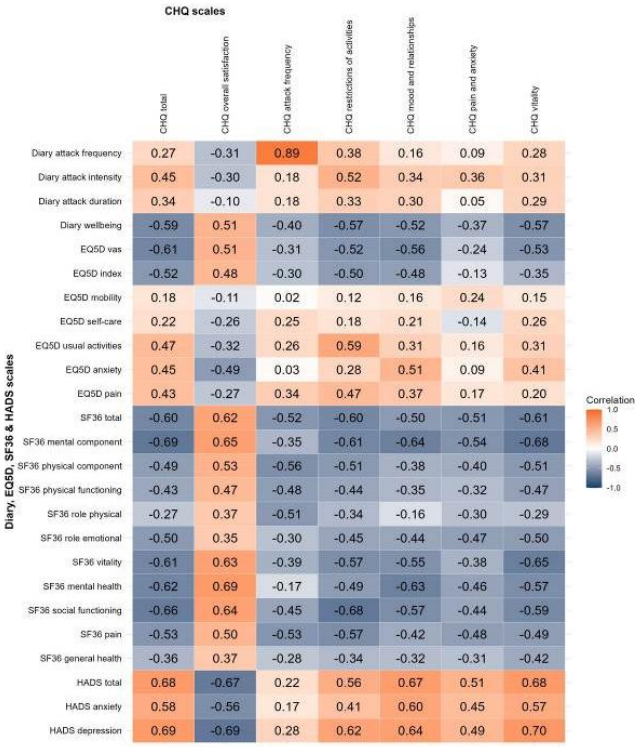


Fig. 2

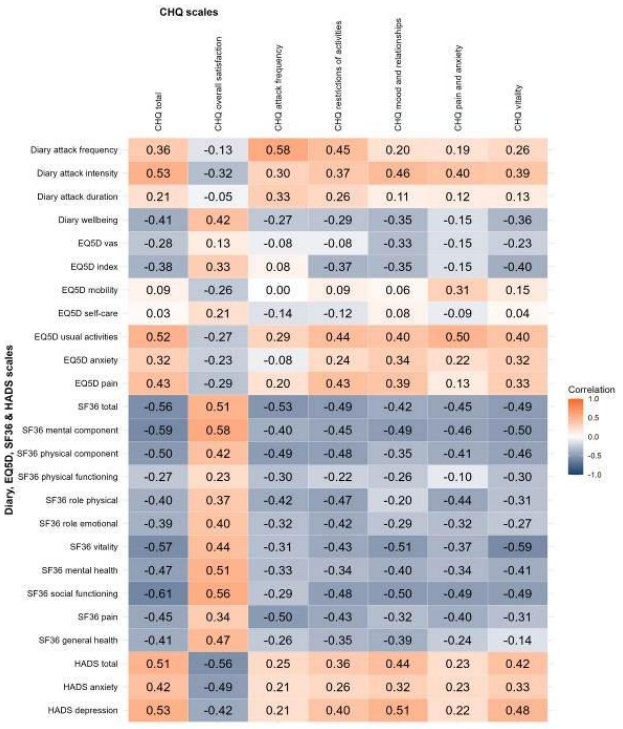


Fig. 3

Table 5. Influence of baseline characteristics on the total score of the CHQ at baseline

	β	95% CI	p-value
Age, *years*	-0.17	-0.50 to 0.12	0.222
Sex, *female*	2.47	-5.50 to 10.45	0.540
Years since diagnosis	-0.00	-0.02 to 0.02	0.888
Comorbid Headache	-3.40	-12.80 to 6.00	0.474
Attack frequency, *weekly*	0.27	0.02 to 0.53	**0.033***
Attack intensity, *scale 0-10*	2.92	0.91 to 4.93	**0.005****
Attack duration, *minutes*	0.01	-0.07 to 0.08	0.871

Results of linear regression to model the influence of baseline characteristics on the total score of the CHQ at baseline. 95% CI: 95% confidence interval. *P < .05, **P<.01, ***P<.001.

P021

Comparison of disability levels between primary and secondary headaches – An online survey in Brazil

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[2]University of Antwerp, Antwerp, Belgium

[3]Furtwangen University, Freiburg, Germany

Objective: To verify the impact and disability between primary (PH) and secondary headaches (SH), using the Headache Impact Test-6 (HIT-6) and the Headache Disability Index-Brazil (HDI) questionnaires.

Methods: This cross-sectional online survey included headache sufferers in Brazil between Feb/2022 to Dec/2024. Participants were recruited via a tertiary hospital with a headache clinic and on social media. Self-reported data included headache diagnosis, monthly frequency and intensity (0-10). Diagnoses were categorized as PH or SH per ICHD-III. All participants completed the HIT-6 and HDI. HIT-6 disability was classified as: little/no impact (<49), some (50–55), substantial (56–59), and severe (60–78). HDI categories were based on sample percentiles: mild (<40.0), moderate (40.1–82), and severe (>82).

Results: Among 541 participants, 466 (86.1%) had PH and 75 (13.9%) SH. SH patients were older (42.7 ± 12.7 vs. 37.0 ± 10.6 years, p=0.001), however, they did not differ regarding the frequency (15.7 ± 12.3 vs. 11.7 ± 9.1 days/month, p=0.067), and the intensity of headache (7.3 ± 2.3 vs. 7.9 ± 1.8, p=0.102). There were no differences on HDI scores (61.5 ± 25.1 vs 54.7 ± 28.6, p=0.032) and HIT-6 scores (p=0.055) between PH and SH. In the HIT-6, PH had a higher prevalence of severe impact (85.2% vs. 70.7%; p = 0.001), whereas SH had a higher prevalence of little to no impact (9.3% vs. 1.9%). Regarding HDI, SH had a higher proportion of mild disability (41.3% vs. 22.7%; p = 0.001), while PH had a higher proportion of moderate disability (57.3% vs. 36.0%).

Conclusion: There were no differences in total impact or disability scores between primary and secondary headache subgroups. However, a higher proportion of individuals with primary headaches reported severe impact on both the HIT-6 and HDI questionnaires. This highlights the burden that these disorders impose on patients' daily functioning. Nevertheless, these data should be interpreted with caution due to the difference in sample size between the groups.

P022

Psychometric evaluation of HALT and HURT in European Portuguese-speaking patients with migraine

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[2]MiGRA Portugal - Portuguese Migraine and Headache Patients' Association, Lisbon, Portugal
[3]University of Algarve – ESGHT, Research Centre for Tourism, Sustainability and Well-Being (CinTurs), Faro, Portugal
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[5]Hospital da Luz, Lisbon, Neurology, Lisbon, Portugal
[6]Universidade Católica Portuguesa, Center for Interdisciplinary Research in Health, Lisbon, Portugal

Objective: Headache-Attributed Lost Time (HALT) and Headache Under-Response to Treatment (HURT) were developed by Lifting The Burden global campaign against headache. Although translated into European Portuguese, their psychometric properties had not been validated. This study aimed to assess the reliability, construct and criterion validity of HALT and HURT in Portuguese patients with migraine.
Methods: A cross-sectional study recruited two cohorts: adults with self-reported migraine (validated by ID-Migraine) completed an online survey disseminated through a patients" association in 2024; patients with clinically confirmed migraine completed a paper survey in a headache clinic in 2021–2022. Surveys contained HALT-90, HURT, mMIDAS, and EQ-5D-3L. Analyses included Cronbach"s alpha, inter-item and item-total correlations, principal component analysis, subgroup sensibility, criterion validity, and floor/ceiling effect assessment.
Results: This study included 295 individuals, 253 with self-reported diagnosis and 42 with clinically confirmed diagnosis. HALT showed good reliability α=0.75, with item-total correlations above 0.35. It demonstrated construct validity with a unidimensional structure (51.13% explained variance); correlated strongly with mMIDAS (r=0.81) and moderately with EQ-5D-3L (r=-0.50). HURT showed moderate reliability α=0.65, improving to 0.74 excluding two items on adverse events and diagnosis understanding. These items had low item-total and negative item-item correlations. HURT showed a three components structure (63.31% explained variance); moderate correlations with mMIDAS (r = 0.63) and EQ-5D-3L (r=-0.30). Both tools were sensible to clinical severity (higher scores in chronic migraine, medication overuse, or 4+ prior preventives). No floor or ceiling effects were found.
Conclusion: European Portuguese versions of HALT and HURT show satisfactory psychometric properties. Both are valid and reliable for assessing headache burden and treatment response in clinical and research settings.

P023

Investigation of the pain reduction and migraine-associated symptoms in the treatment of migraine attack in a real-world setting of Austrian patients after the introduction of Sumatriptan 85mg/Naproxen-Natrium 500mg combination tablet

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Objective: The purpose of this case series was to assess the pain reduction and tolerability of sumatriptan/naproxen combination in the treatment of acute migraine attack.
Methods: Primarily we looked at the headache reduction indicated by the reduction of moderate or severe headache pain to mild or no pain. In addition, the attenuation of migraine-associated symptoms—including nausea, photophobia, phonophobia, fatigue, and neck pain—was evaluated at 1, 2, and 24 hours post-administration. The extent of headache relief, the improvement in associated symptoms, and treatment tolerability were assessed using a patient-reported outcomes in our questionnaire. Data from 20 patients were analysed.
Results: At 1 hour post-administration, 65% of patients reported a reduction in migraine headache intensity. By 2 hours, 70% were either pain-free or experienced substantial relief. After 24 hours, this figure increased to 90%. Despite initial improvement, 15% of patients required a second dose of sumatriptan/naproxen within 24 hours due to migraine recurrence. The frequency of associated symptoms—including nausea, photophobia, and phonophobia—was also reduced. Adverse events were uniformly mild, transient, and well tolerated across the study population.
Conclusion: Sumatriptan 85mg/Naproxen Natrium 500mg combination tablet was effective and generally well tolerated in the treatment of our patients presenting with migraine headaches. These data provide insights into real-word utilisation of the new combination tablet Sumatriptan 85mg/Naproxen Natrium 500mg in the treatment of acute migraine attacks.

P024

Regimen and associated factors of preventive migraine medication discontinuation: A retrospective study at a tertiary headache center in a lower-middle-income country

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Objective: One of the most common problems in migraine treatment is the discontinuation of preventive medications, especially due to intolerance and poor efficacy. This study presents a retrospective analysis of Thai patients at a tertiary care-based headache center in Thailand, focusing on treatment patterns of migraine prophylaxis over six months.
Methods: We conducted a retrospective electronic medical record (EMR) review of migraine patients who attended the headache clinic at King Chulalongkorn Memorial Hospital between December 2020 and July 2024. Patients diagnosed with migraine and with at least six months of follow-up data and complete EMR data were included in the study. Medication prescription status and treatment regimens were recorded. The primary outcome was the discontinuation of any migraine preventive medication during follow-up visits. A multivariable Cox regression model, adjusted for sex, age, and diagnosis, was used to explore baseline factors associated with the termination of migraine prophylactic drugs.
Results: Among the 100 eligible patients (mean age [SD]: 39.6 [14.4] years; 87.0% female), 41% discontinued at least one medication. The highest discontinuation rates were observed with serotonin norepinephrine reuptake inhibitors (SNRIs) at 53.8%, calcium channel blockers (CCBs) at 37.5%, and beta-blockers (BBs) at 25.6%. Notably, no patients discontinued calcitonin gene-related peptide monoclonal antibodies (CGRP mAbs) (**Figure 1**). Patients using CGRP mAbs at baseline had a significantly higher discontinuation rate of at least one other oral preventive drug compared to those not using CGRP mAbs: 31.7% vs. 25.4% at month 3, and 55.4% vs. 33.4% at month 6 (p = 0.04) (**Figure 2**).
Conclusion: In this study, nearly half of the participants discontinued at least one preventive medication within six months. CGRP mAbs was the only class of preventive migraine medication that was not terminated and were also associated with a higher rate of discontinuation of other preventive medications.

Fig. 1

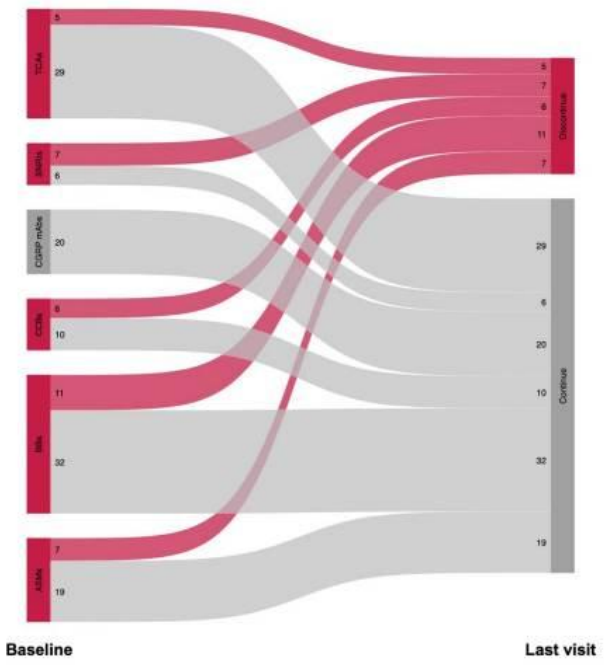
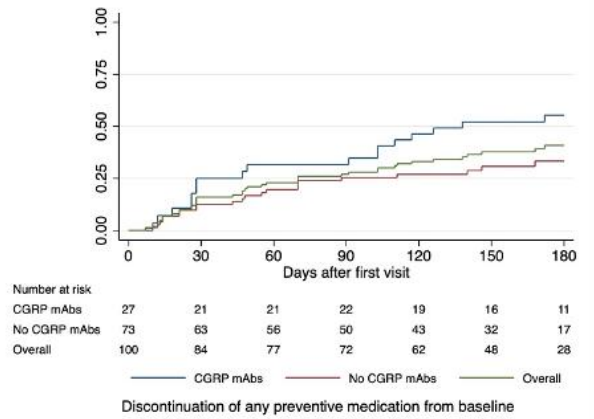


Fig. 2



P025

Impact of the number of previous triptans trialed on triptan effectiveness, tolerability, and healthcare resource use: Multicountry results from the CaMEO-I study

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[5]MIST Research, Wilmington, NC, United States
[6]Albert Einstein College of Medicine, Department of Neurology, New York, NY, United States
[7]Cote d'Azur University, Pain Department and FHU InovPain, Nice, France
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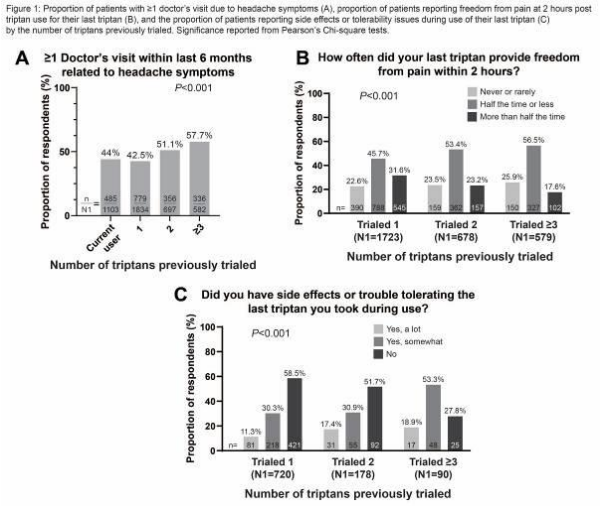
Objective: Triptan use can be associated with suboptimal efficacy and adverse events leading to high discontinuation rates. The International Headache Society has recently outlined trying 3 triptans before concluding non-response to the class [1]. Here, we evaluated the impact of the number of triptans trialed on triptan effectiveness, tolerability, and healthcare resource use in the Chronic Migraine Epidemiology and Outcomes-International (CaMEO-I) study cohort.

Methods: CaMEO-I was a cross-sectional web-based survey conducted in 2021-2022 in the US, UK, France, Germany, Japan, and Canada. Patients with ICHD-3 migraine were stratified by history of current use or previous trialing of 1, 2, or ≥3 triptans. Associations between number of triptans trialed and the number of doctor's visits related to headache symptoms, the proportion of patients reporting freedom from pain within 2 hours of triptan use, and the proportion reporting triptan tolerability issues during use were assessed. Chi-square linear trend tests for categorical variables were conducted.

Results: Of 4216 respondents, 26% (1103) were current triptan users, 43% (1834) trialed 1, 16% (697) trialed 2, and 14% (582) trialed ≥3 triptans. In the last 6 months of current users or those who trialed 1, 2, or ≥3 triptans, 44.0%, 42.5%, 51.1%, and 57.7% had ≥1 doctor's visit concerning their headache (P<0.001, Figure 1) respectively. Of 2980 patients who had previously trialed 1, 2, or ≥3 triptans, the proportion reporting that their last triptan provided freedom from pain at 2 hours more than half the time was 31.6%, 23.2%, and 17.6% (*P*<0.001), respectively. Of patients who previously trialed 1, 2, or ≥3 triptans, the proportion reporting any tolerability issues with their last triptan increased from 41.5%, to 48.3%, to 72.2% (*P*<0.001), respectively.

Conclusion: Trialing multiple triptans is associated with increased number of doctor's visits and decreased effectiveness and tolerability among patients with migraine.1 Ornello et al. *Cephalalgia* 2025;45(4)

Fig. 1



P026

CGRP monoclonal antibodies for migraine and the risk of adverse pregnancy outcomes: Women's Headache Health – A nationwide registry-based cohort study from 2018 to 2022

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Objective: To assess whether exposure to CGRP mAbs is associated with adverse pregnancy outcomes compared to a control group of pregnant women with chronic migraine not receiving preventive medical treatment.

Methods: This population-based study included pregnancies among women with chronic migraine registered in the nationwide Medical Birth Registry of Norway from 2018 to 2022, identified through reimbursement records for CGRP mAbs within five years prior to pregnancy (n=607). Pregnancy exposure to CGRP mAbs was defined as at least one prescription or hospital injection occurring between three months before the last menstrual period and delivery (n=75).

The controls were determined by the absence of any migraine preventive prescriptions in this period (n=237). Risk ratios (RRs) for pregnancy complications in CGRP mAbs users compared to controls were estimated using log-binomial regression with overlap weighting to adjust for potential confounders.

Results: After the overlap weighting adjustment, baseline characteristics were balanced between groups. The mean maternal age was similar (CGRP mAbs: 31.5±4.0; controls: 31.5±4.2), as was nulliparity (47.9%), obesity before pregnancy (12.2%), triptan use (69.4%), and migraine with aura (36.7%) in both groups. Compared to controls, CGRP mAbs users had adjusted RRs of 4.24 (95% confidence intervals (CI): 1.02, 17.58) for hypertensive disorders during pregnancy and 6.16 (95% CI: 1.08, 34.88) for preeclampsia (Figure 1). The risks of premature labor and low birth weight were 1.19 (95% CI: 0.36, 3.87) and 1.48 (95% CI: 0.09, 23.53)

Conclusion: Our findings cannot rule out a possible increased risk of hypertensive disorders and preeclampsia during pregnancy associated with the use of CGRP mAbs during pregnancy compared to controls. However, confidence intervals were wide, and the risk of other pregnancy complications was not increased.

P027

Preventive migraine treatment in patients under 25: A 24-month observational study on adherence, therapeutic switching, and prescription determinant factors

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Objective: This retrospective study examined migraine patients under 25 to assess patterns in oral and anti-CGRP monoclonal antibody (mAb) prescriptions, follow-up adherence, and monthly migraine day (MMD) trends. It aimed to identify factors linked to follow-up dropout, mAb use, and migraine worsening

Methods: The study included 383 patients (77.8% female; mean age: 20.8) followed at the Headache Center of Fondazione Policlinico Campus Bio-Medico. Non-migraine headaches were excluded. In patients with >8 MMDs, mAb efficacy was defined as a ≥50% MMD reduction (RR50). Logistic regression and chi-square tests identified predictors of dropout, mAb prescription, and response.

Results: At baseline, patients reported 10.9 MMDs. NSAIDs were the most used acute treatment (75.7%); triptans were underused (5.7%). Preventive therapy had never been used by 62.2%, and only 18.1% had tried one regimen. Common comorbidities were neuropsychiatric and gynecological. Photophobia and stress were the most reported symptom and trigger, respectively. After initial evaluation, 85.4% were prescribed preventives—mainly tricyclic antidepressants (29.2%) and nutraceuticals (21.4%). Over time, oral preventives declined, while mAbs and botulinum toxin remained stable. Shorter migraine history and fewer baseline MMDs were associated with follow-up dropout ($p<0.01$). mAb use for ≥6 months increased RR50 odds (OR 2.51; $p=0.01$), with better response in males (OR 0.443 for females; $p=0.035$). Early mAb initiation led to greater MMD reductions, though some residual disease remained

Conclusion: This young migraine cohort showed a high disease burden and comorbidities. Milder cases were less likely to maintain follow-up. Early mAb use was more effective, especially in females, though late initiation yielded similar residual MMD levels to oral therapies.

P028

Does heterogeneity in patient population, study design, and endpoint definitions affect indirect comparisons of acute migraine treatments? A methodological assessment

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Objective: Indirect treatment comparisons (ITCs) can be used to summarize and compare results across studies, based on the assumption that the placebo response adjusts for differences among studies. We sought to identify factors that influence heterogeneity in an ITC of acute treatments for migraine and to determine if adjustment for those factors influences the results.

Methods: A review of recently published ITCs was conducted, followed by a thorough examination of individual studies. We focussed on a recently published ITC [1] based upon a comprehensive evidence base, publicly available details of analyses and the decision to analyse treatments individually (rather than at the class level).

Results: Review of individual studies found substantial heterogeneity across trials, including differences in: pain intensity of treated migraine attacks, patterns of prior/concomitant migraine medication use, co-

primary endpoint designation, and tools used to capture them (paper diaries or e-diaries). Despite the substantial heterogeneity observed no attempts to control for systemic differences were identified in the main analyses of published ITCs [1-5].
Extension of the analyses conducted by Karlsson et al [1] demonstrated an approximate doubling of placebo response rate over the review period, consistent with Thokagevistk et al. [6] who reported changes in the relative effect of sumatriptan over time.
Conclusion: ITCs of acute migraine trials, sometimes conducted decades apart, acknowledge heterogeneity but did not attempt to statistically adjust for it. More sophisticated analytical approaches are needed to obtain unbiased and reliable estimates of indirect comparative effectiveness.

P029

Fear of movement in patients with episodic and chronic migraine: Adaptation of the tampa kinesiophobia scale for headache to Turkish culture, validity and reliability study – Preliminary results

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Objective: This study aimed to evaluate the validity and reliability of the Tampa Kinesiophobia Scale for Headache (TKS-H) in chronic migraine (CM) and episodic migraine (EM) patients.
Methods: Exploratory Factor Analysis (EFA) was performed to evaluate construct validity. Internal consistency was assessed using Cronbach"s alpha, and test-retest reliability via Intraclass Correlation Coefficient (ICC). Pearson correlation was used to assess relationships with headache intensity (Numeric Rating Pain Scale) (NRPS), Migraine Disability Assessment (MIDAS), Headache Impact Test-6 (HIT-6), and Hospital Anxiety and Depression Scale (HADS).
Results: A total of 178 patients (CM:105; EM:73) participated. The means in EM and CM were as follows, respectively. NRPS: 6.02 (1.86) / 7.45 (2.23), TKS-H: 58.91 (11.3) / 63.84 (12.54), MIDAS:62.47 (6.77) / 58.48 (55.29); HIT-6:62.47 (6.77) / 64.78 (5.62); HADA: Anxiety-8.79 (4.38) / 9.82 (4.59), Depression-8.29 (4.26) / 8.61 (4.44). The scale had excellent internal consistency in both CM (α=0.926) and EM (α=0.915). Test-retest reliability was high (ICC=0.926 for CM, n=35; ICC=0.915 for EM, n=21). EFA revealed a stable six-factor structure explaining 70% of the variance in both groups. Factors: Neck-all body movement-triggered anxiety, physical activity beliefs, exercise avoidance attitudes, sensory-trigger awareness, social attitudes toward exercise, and ambiguous item loadings. In the CM, TKS-H was correlated with HIT-6 (r = .454, p < .000); anxiety (r = .432, p < .000) and depression (r = .398, p < .000), (MIDAS) (r = .244, p = .012), NRPS (r = .205, p = .036). In the EM, TSK-H was correlated with HIT-6 (r = .602, p < .000), MIDAS (r = .341, p = 0.03), anxiety (r = .345, p = 003), and depression (r = .307, p =.008), NRPS (r = .233, p = .047).
Conclusion: The TKS-H is a valid and reliable tool for assessing physical activity-related beliefs in patients with both EM and CM.

Fig. 1

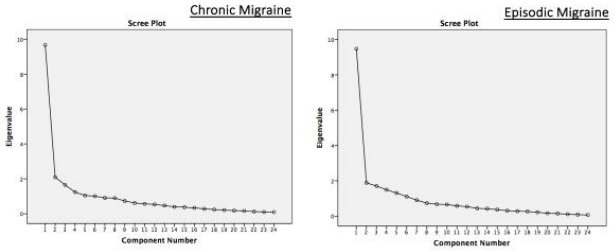


Figure. Scree Plots for chronic migraine and episodic migraine.

P031

How preventive migraine regimens influence CGRP mAb initiation: Insights from a headache clinic in Thailand

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Objective: While calcitonin gene-related peptide monoclonal antibodies (CGRP mAbs) are effective for migraine management, their use in low- and middle-income countries is limited by cost and accessibility. This study explored factors associated with CGRP mAb initiation using real-world data from Thailand.
Methods: Data were retrospectively collected from participants attending the headache specialist clinic at King Chulalongkorn Memorial Hospital, a tertiary teaching hospital in Bangkok, Thailand, between December 2020 and July 2024. Those diagnosed with migraine and had at least six months of follow-up data were included in the analysis. A multivariable Cox regression model, adjusted for sex, age, and diagnosis, was used to explore baseline factors associated with CGRP mAb initiation during the follow-up period.
Results: Among 80 participants included in the analysis, 71 (88.8%) were female with a median (IQR) age of 40.0 (28.4–51.9) years; 42 (52.5%) had episodic migraine and 38 (47.5%) had chronic migraine. Commonly used preventive medications included beta blockers (BBs) (46.2%), tricyclic antidepressants (TCAs) (35.0%), and antiseizure medications (22.5%). During a total follow-up of 11,554 person-days, 16 participants (20.0%) initiated CGRP mAbs at a median of 44.5 days (IQR 23.5–109). In the adjusted model, BB use (adjusted odds ratio [aOR] 0.23, 95% CI 0.07–0.82, *p*=0.02) and TCA use (aOR 0.17, 95% CI 0.04–0.76, *p*=0.02) were associated with a lower likelihood of CGRP mAb initiation. Post hoc analysis further demonstrated that BB use was significantly associated with a lower likelihood of discontinuing any preventive medications prescribed at the first visit (aOR 0.36, 95% CI 0.15–0.88, *p*=0.03).
Conclusion: In this real-world study, the use of BBs or TCAs as part of the preventive regimen at the first visit was associated with a lower likelihood of initiating CGRP mAbs. BB use was also associated with greater persistence in the use of preventive medications during follow-up.

P032

Clinical and therapeutic profiles of patients with chronic daily headache in a tertiary headache center

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Objective: To characterize patients diagnosed with chronic daily headache (CDH) and describe their clinical features, comorbidities, and responses to treatment.
Methods: We performed a retrospective review of consecutive patients who fulfilled International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria for CDH and were seen at a tertiary headache clinic between 2018 and 2024. Demographic, clinical, and therapeutic variables were analyzed with descriptive statistics and non-parametric tests.
Results: Ninety-five patients were included (mean age ± SD, 48.8 ± 17.4 years; 80 % women). Headache onset occurred before age 50 in most cases. Psychiatric comorbidities were present in 45 %, sleep disorders in 28 %, and other chronic pain conditions in 39 %. More than one-third (36 %) had two or more chronic comorbidities. Continuous daily pain was reported by 48 %, and 54 % met criteria for medication-overuse headache (MOH). The most common CDH subtypes were chronic tension-type headache (33.7 %), chronic migraine (32.6 %), and new daily persistent headache (21.1 %). Additional neuroimaging (other than TC) was obtained in 47.4 % of patients. Preventive therapy was initiated in 90.5 %, most frequently with antidepressants (49.5 %). A ≥50 % reduction in headache frequency or intensity was achieved in 48.4 % of treated patients. By 12 months, 63 % had tried at least one preventive agent. Adverse events occurred in 28 %, and drug intolerance led to discontinuation in 16 %. Only 10.5 % of patients were discharged after their first visit.
Conclusion: Patients with CDH referred to a tertiary center often have multiple comorbidities, high rates of medication overuse, and significant psychiatric burden. Despite extensive therapeutic trials, only about half attain a meaningful clinical response, underscoring this population's complexity and treatment resistance.

P033

Atogepant reduce psychological dependence to acute treatments evaluated with the Leeds dependence questionnaire (LDQ): A prospective observational study

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Objective: This study aimed to assess whether preventive treatment with atogepant reduces psychological dependence on acute migraine medications, using the Leeds Dependence Questionnaire (LDQ), in a real-world migraine population. Secondary objectives included evaluating associations between LDQ score changes and clinical outcomes such as acute medication use and monthly headache days (MHDs), and the influence of medication overuse (MO) and psychiatric comorbidities.

Methods: We conducted a prospective observational study in 43 migraine patients (69.8% chronic migraine; 67.4% with MO) treated with atogepant 60 mg daily for 12 weeks. LDQ scores were measured at baseline and week 12. Monthly headache days, acute medication numbers (AMNs), and days of use (AMDs) were recorded. A linear mixed-effects model was used to assess LDQ score changes over time, adjusting for MO status, MOH diagnosis and psychiatric comorbidities.

Results: The LDQ total score significantly decreased from 7.95 ± 5.79 to 6.42 ± 5.08 (mean change –1.53; p = 0.032). Three LDQ items, loss of control, compulsive use, and psychological distress, showed significant improvement. Mixed-effects modeling confirmed a significant effect of treatment (p = 0.022), independent of MO status or psychiatric conditions. LDQ changes did not correlate significantly with AMNs, AMDs, or MHDs.

Conclusion: Atogepant significantly reduced psychological dependence on acute migraine medications in a real-world setting. This effect was independent of MO or psychiatric comorbidities and not directly related to medication intake reduction. These findings suggest preventive therapy may improve behavioral dimensions of migraine and support the use of LDQ in routine clinical care.

Fig. 1

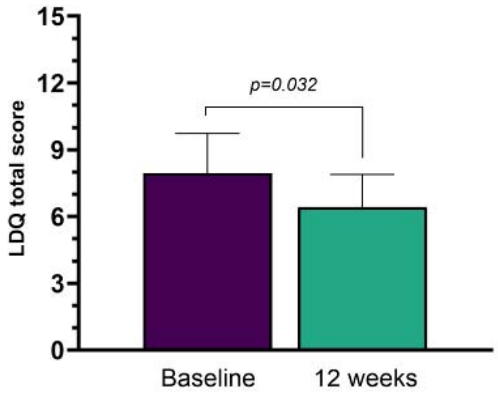
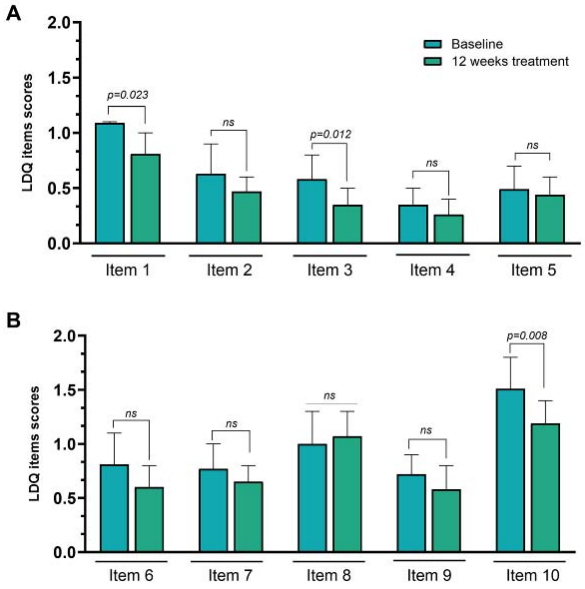


Fig. 2



P034

Protective effect of headache in patient with aneurysmal subarachnoid hemorrhage

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Objective: Thunderclap headache is one of the most common symptoms among patients with aneurysmal subarachnoid hemorrhage (aSAH). It may be caused by inflammation of brain arteries, irritation of the meninges by blood, intracranial pressure changes, and possibly neuropathic factors. We aimed to explore a connection between headache and the clinical course of aSAH.

Methods: The study included medical records of 421 patients with aSAH divided into two groups: 1) with headache at admission and 2) without headache. The following methods were used for statistical analysis: Chi-square test-test, binomial logistic and linear regression.

Results: Surprisingly, no statistically significant association was found between headache and meningeal signs (Chi-square test=0.217; df=1; p=0.642). However, patients presenting with headache had significantly lower odds of developing paresis (OR=0.175; CI=0.097–0.313; p<0.001), a presence of Babinski sign (OR=0.139; CI=0.077–0.25; p<0.001), and oculomotor dysfunction (OR=0.271; CI=0.148–0.498; p<0.001). Headache at admission also correlated with milder clinical severity on the modified WFNS scale (OR=0.052; CI=0.028–0.096; p<0.001), shorter duration of lumbar drainage placement (p<0.001), and a 64.6% reduction in mortality risk (OR=0.354; CI=0.202–0.621; p<0.001).

Conclusion: Headache at admission in patients with aSAH was associated with a more favourable clinical course. The presence of headache correlated with significantly lower odds of paresis, Babinski sign, and oculomotor dysfunction. Additionally, headache was associated with lower WFNS severity scores, shorter lumbar drainage duration, and reduced mortality risk.

P035

Positive ANA screening in headache patients rarely an indicator of autoimmune disease

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Objective: To evaluate whether ANA testing in hospitalized adults with headache helps identify underlying rheumatologic disease. We assessed its diagnostic yield and explored clinical and laboratory predictors of autoimmune diagnoses in this setting.

Methods: We performed a retrospective cohort study of 539 adults hospitalized for headache at Sheba Medical Center (2007–2022), all of whom underwent ANA testing. Patients were stratified by ANA result, and data on demographics, ANA titers/patterns, CRP levels, and confirmed rheumatologic diagnoses were extracted. Statistical tests included chi-square, t-tests, and multivariate analyses.

Results: Among 539 patients, 244 (45.3%) had a positive ANA. Rheumatologic diagnoses were confirmed in 52 (9.6%), more often in ANA-positive patients (16.4% vs. 4.1%, $p<0.001$). ANA-positive patients were older (median 47.4 vs. 40.1 years, $p<0.01$), more likely female, and had higher titers. Homogeneous and mixed patterns were more common in rheumatologic cases; unrecognized patterns predominated in non-rheumatologic ones. CRP levels showed no significant group differences, though vasculitis and GCA cases had markedly elevated CRP (mean 52.7 mg/L). Figure 1 demonstrates a clear age gradient across rheumatologic diagnoses, with the highest mean age seen in vasculitis patients (64.8 years). Figure 2 illustrates elevated CRP levels specifically among patients with vasculitis, in contrast to SLE and non-rheumatologic groups.

Conclusion: Despite association with autoimmune disease in select cases, ANA testing in headache admissions has low overall yield. Most ANA-positive patients lacked a rheumatologic diagnosis. A targeted, symptom-based approach—guided by age, sex, titer, .and pattern—is recommended

Fig. 1

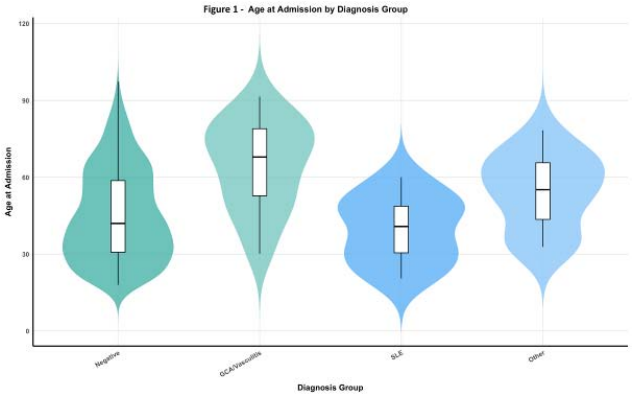
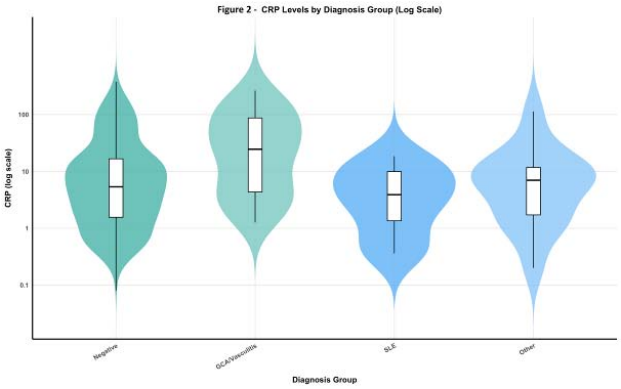


Fig. 2



P036

Early treatment with atogepant improves sleep quality without sleep-related adverse events: A prospective observational study

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Objective: Calcitonin gene-related peptide (CGRP), a key player in migraine pathophysiology, also influences sleep regulation. While CGRP monoclonal antibodies have shown mixed effects on sleep, no study to date has evaluated the impact of gepants on sleep quality.This study assessed whether atogepant, recently approved for migraine prevention, affects

sleep quality and sleep-related adverse events in real-world settings.

Methods: We conducted a prospective, observational, single-center study including 43 migraine patients (69.8% with chronic migraine). All received atogepant 60 mg/day for potentially 12 weeks. Sleep quality was assessed using five validated questionnaires (PSQI, AIS, Bergen, ESS, ISI) at baseline and at follow-up. Migraine frequency, disability (MIDAS, HIT-6), allodynia (ASC-12), acute medication use, and adverse events (AEs) were also recorded.

Results: Atogepant significantly improved sleep quality with PSQI scores decreased from 9.6 to 8.2 (p=0.002), improvements in AIS (p=0.014) and Bergen scores (p=0.046). Sleep duration was the only PSQI subdomain with a statistically significant change. No differences were found in ESS or ISI scores. Notably, no patients reported sleep-related AEs such as somnolence, nightmares, or vivid dreams. Psychiatric comorbidities were associated with poorer baseline sleep but did not influence the magnitude of improvement. Prior anti-CGRP failure predicted a lesser sleep benefit. Finally, migraine burden improved across all evaluated migraine-related variables.

Conclusion: Atogepant improved subjective sleep quality without causing sleep-related adverse events, supporting its role in comprehensive migraine management, particularly in patients with disrupted sleep.

Fig. 1

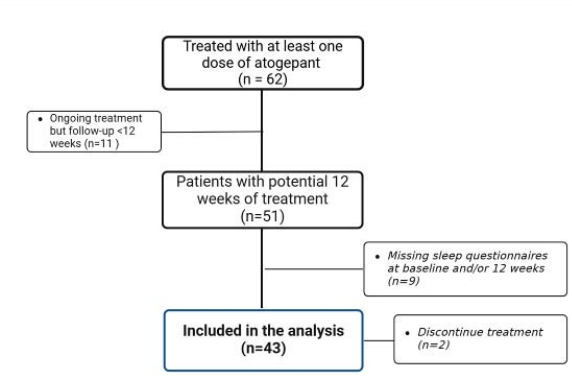


Fig. 2

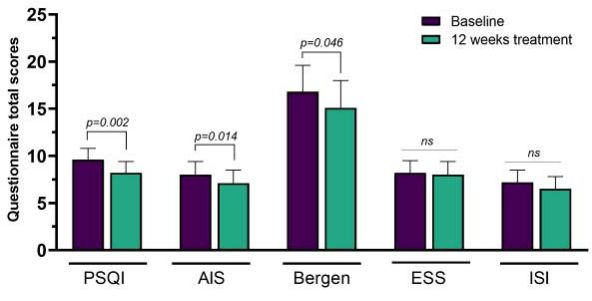
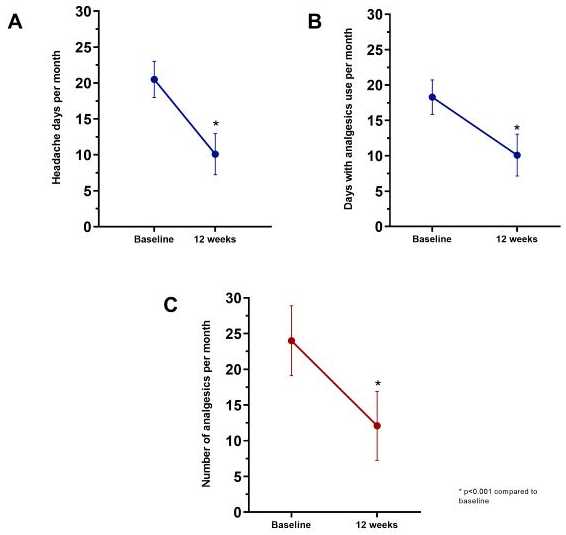


Fig. 3



P037

Relationship between cycling of traditional oral generic preventive medications and patient-reported outcomes: Multicountry results from the CaMEO-I study

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Objective: Oral generic preventive medications (OGPMs) are often associated with suboptimal efficacy, contraindications, or side effects, leading to high discontinuation rates and cycling through additional OGPMs. We evaluated the relationship between the number of traditional OGPMs taken and patient-reported outcomes among Chronic Migraine Epidemiology and Outcomes-International (CaMEO-I) study respondents from non-US countries.

Methods: CaMEO-I was a cross-sectional, web-based survey conducted in 2021–2022 in Canada, France, Germany, UK, Japan and US. Respondents with ICHD3 migraine were stratified by self-reported history of ever using 1, 2, or ≥3 OGPMs; those using targeted preventive medication(s) were excluded. Associations between OGPM use and migraine related disability (MIDAS), cognitive impairment (Migraine Cognitive Impairment Questionnaire, MCIQ), migraine specific quality of life (MSQ), allodynia (ASC-12), and functional disability (FDS) were assessed. Linear trend

tests using chi-square for categorical and ANOVA for continuous variables were conducted.

Results: Among all non-US respondents, 14% (1711/12088) used at least 1 OGPM. Of these, 46% used 1 (780/1711), 19% used 2 (329/1711), and 35% (602/1711) used ≥3 OGPMs. Cycling through OGPMs was associated with greater moderate to severe disability on MIDAS (1: 61%, 2: 65%, ≥3: 67%; *P*=.013), increased proportion of respondents above the median score on MCIQ (1: 62%, 2: 69%, ≥3: 71%, *P*<.001) and reduced MSQ role function restrictive domain scores (mean [SD] 1: 54 [22], 2: 49 [22], 3: 47 [21]; *P*<.001). Associations between cycling OGPMs and decreased MSQ role function preventive and emotional function domains, and increased allodynia were also observed.

Conclusion: Cycling through OGPMs was associated with greater migraine related disability, cognitive impairment, and decreased quality of life in respondents with migraine from non-US countries.

P038

Patient-reported outcomes in the ContemporAry ProspecTive understanding of migraine real-world evidence (CAPTURE) study

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Objective: To evaluate changes from baseline through Month 12 in patient-reported outcomes (PROs) among participants in the ContemporAry ProspecTive Understanding of Migraine Real-world Evidence (CAPTURE) study.

Methods: CAPTURE is a 2-year, international, prospective, longitudinal, observational study of disease burden and treatment patterns among patients with migraine currently consulting at specialty clinics who were ≥18 years, had a migraine diagnosis for ≥1 year, used ≥1 migraine medication, and experienced ≥4 MHDs over the last 3 months. Participants were stratified by headache frequency during a 30-day screening: 4–<8 MHDs (Cohort 1), 8–<15 MHDs (Cohort 2), and ≥15 MHDs (Cohort 3). Change from baseline was assessed using a mixed-effects model for repeated measures.

Results: The study population (*N*=555; Cohort 1=139, Cohort 2=251, Cohort 3=165) was >83% female and >94% White, with a mean age of 41.4-43.0 years old. The figure shows that modest changes from baseline on the Headache Impact Test-6 were observed in all cohorts (Cohort 1: -3.18 [95% CI −4.58, −1.79], Cohort 2: -4.04 [95% CI −5.44, −2.63], Cohort 3: -2.33 [95% CI −3.84, −0.82]). The table shows that most PROs (MSQv2.1, WPAI, HAD-S and MIBS-4) improved at Month 12, but the magnitude of change was not clearly associated with baseline migraine frequency.

Conclusion: This snapshot analysis suggests that, when completed, CAPTURE will define a clearer picture of the evolution over time of different PROs in different migraine frequency subgroups. Other prognostic factors will be studied per protocol.

Fig. 1

Change From Baseline in Patient-Reported Outcomes at Month 12 in the CAPTURE study (N=555)[a].

	Cohort 1: 4–<8 MHDs N=139			Cohort 2: 8–<15 MHDs N=251			Cohort 3: ≥15 MHDs N=165		
		Change from baseline[b]			Change from baseline[b]			Change from baseline[b]	
	n	Mean (SD)	LSM (SE), 95% CI	n	Mean (SD)	LSM (SE), 95% CI	n	Mean (SD)	LSM (SE), 95% CI
MSQv2.1, Role Function-Restrictive									
Month 3	123	3.79 (21.712)	5.15 (2.167), 0.86, 9.43	225	2.83 (20.374)	4.78 (1.843), 1.16, 8.41	149	5.09 (19.613)	4.71 (2.151), 0.47, 8.96
Month 6	117	6.32 (22.421)	7.94 (2.229), 3.58, 12.35	206	6.44 (26.488)	7.55 (1.890), 3.83, 11.27	138	7.39 (21.146)	7.21 (2.199), 2.87, 11.55
Month 12	79	6.69 (21.831)	9.00 (2.235), 4.57, 13.43	141	8.97 (22.283)	10.00 (2.053), 5.95, 14.04	82	6.32 (19.54)	7.75 (2.996), 3.02, 12.48
WPAI %[c]									
Work time missed (Absenteeism)									
Month 3	71	4.59 (9.942)	−0.80 (1.443), −3.61, 2.01	146	2.49 (19.560)	2.11 (1.767), −1.26, 5.48	83	−2.53 (26.486)	−0.67 (2.720), −6.06, 2.75
Month 6	66	2.51 (9.766)	−2.54 (1.441), −5.41, 0.33	126	0.24 (13.699)	0.00 (1.267), −2.49, 2.49	77	−3.51 (28.89)	−2.25 (2.919), −8.04, 3.55
Month 12	46	5.13 (11.314)	0.34 (1.858), −3.39, 4.08	84	4.95 (10.1)	−0.96 (1.380), −3.71, 1.80	44	−0.46 (19.593)	−2.21 (3.071), −9.37, 3.95
Impairment while working (Presenteeism)									
Month 3	71	1.97 (31.651)	4.11 (3.398), −2.65, 10.87	144	0 (28.136)	−1.78 (2.836), −7.33, 3.82	78	−5.96 (28.166)	−3.29 (3.760), −10.79, 4.22
Month 6	66	−6.06 (31.471)	0.44 (3.491), −6.50, 7.37	125	−0.16 (27.997)	−1.98 (2.923), −7.75, 3.80	72	−4.86 (29.802)	−3.17 (3.698), −10.52, 4.18
Month 12	46	1.74 (30.28)	1.61 (4.275), −6.95, 10.17	84	−8.21 (30.897)	−7.87 (3.881), −14.51, −1.24	43	1.86 (31.187)	1.64 (4.748), −7.83, 11.12
Overall impairment									
Month 3	71	2.1 (32.605)	3.12 (3.626), −4.09, 10.34	144	1.35 (30.222)	−1.03 (3.088), −7.14, 5.04	78	−3.24 (30.597)	−1.33 (3.929), −9.13, 6.46
Month 6	66	−7.01 (31.979)	−2.11 (3.686), −9.44, 5.21	125	−0.48 (28.625)	−2.13 (3.189), −8.26, 4.01	72	−5.08 (31.692)	−2.46 (3.952), −10.32, 5.39
Month 12	46	0.79 (33.656)	0.18 (4.590), −9.01, 9.37	84	−7.65 (32.147)	−8.16 (3.823), −15.53, −0.79	43	1.7 (32.63)	2.55 (5.056), −7.54, 12.65
Activity impairment due to migraine									
Month 3	81	−4.32 (36.108)	−1.42 (3.554), −8.47, 5.64	163	+0.86 (26.138)	−1.58 (2.510), −6.53, 3.38	88	−3.35 (25.666)	−2.84 (3.423), −9.61, 3.93
Month 6	73	4.36 (30.918)	−4.09 (3.277), −10.60, 2.43	144	−1.23 (27.681)	−2.31 (2.629), −7.50, 2.87	84	−1.79 (30.366)	−1.27 (3.615), −8.43, 5.89
Month 12	51	1.37 (30.985)	−2.76 (4.094), −10.95, 5.44	95	+0.89 (31.74)	−9.34 (3.072), −15.41, −3.26	47	−2.13 (27.529)	−1.13 (4.156), −9.42, 7.16
HAD-S[d]									
Total score									
Month 6	118	−0.86 (6.830)	−1.17 (0.698), −2.54, 0.21	209	−0.32 (6.398)	−0.85 (0.643), −2.12, 0.41	137	−1.82 (7.507)	−1.80 (0.871), −3.52, −0.08
Month 12	70	−1.46 (6.565)	−1.92 (0.759), −3.43, −0.41	143	−1.27 (6.723)	−1.62 (0.703), −3.00, −0.23	81	−0.27 (6.904)	−0.84 (0.965), −2.75, 1.07
Anxiety									
Month 6	118	−0.52 (3.431)	−0.82 (0.339), −1.50, −0.08	209	+0.21 (3.707)	−0.58 (0.363), −1.30, 0.13	137	−0.35 (3.987)	−0.76 (0.462), −1.67, 0.15
Month 12	70	−0.91 (3.913)	−1.25 (0.426), −2.09, −0.40	143	−0.63 (3.914)	−0.84 (0.402), −1.63, −0.04	81	−0.17 (3.787)	−0.43 (0.513), −1.45, 0.58
Depression									
Month 6	118	−0.34 (3.580)	−0.39 (0.385), −1.15, 0.38	209	−0.09 (3.564)	−0.29 (0.340), −0.98, 0.39	137	−1.07 (4.419)	−1.05 (0.469), −2.02, −0.09
Month 12	70	−0.34 (3.245)	−0.68 (0.410), −1.50, 0.13	143	−0.64 (3.682)	−0.79 (0.377), −1.54, −0.03	81	−0.10 (4.003)	−0.45 (0.544), −1.52, 0.63
MIBS-4									
Month 3	123	−0.21 (3.124)	−0.31 (0.312), −0.93, 0.30	220	−0.29 (3.258)	−0.46 (0.293), (−1.04, 0.11	149	0.3 (3.289)	0.30 (0.368), −0.42, 1.02
Month 6	117	−0.15 (3.289)	−0.30 (0.330), −0.95, 0.35	206	−0.48 (3.520)	−0.64 (0.330), −1.28, −0.03	138	−0.08 (3.647)	−0.06 (0.382), −0.81, 0.70
Month 12	79	−0.62 (2.83)	−0.92 (0.329), −1.57, −0.27	142	−0.89 (3.323)	−0.93 (0.326), −1.57, −0.29	82	−0.37 (3.145)	−0.21 (0.472), −1.02, 0.61

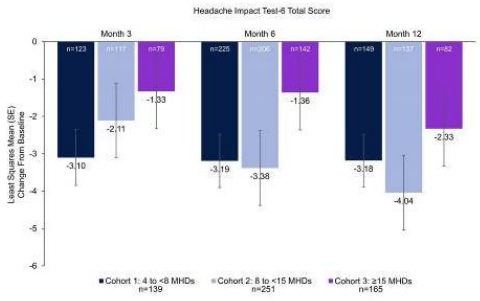
CAPTURE=ContemporAry ProspecTive Understanding of Migraine Real-world Evidence; SD=standard deviation; MHD=monthly headache day; LSM=least squares means; SE=standard error; CI=confidence interval; MSQv2.1=Migraine-Specific Quality-of-Life Questionnaire, WPAI=Work Productivity and Activity Impairment Questionnaire: Migraine, HAD-S=Hospital Anxiety and Depression Scale, MIBS-4=Migraine Interictal Burden Scale.

[a]Among participants who met inclusion/exclusion criteria with evaluable MRD data at screening and enrollment for ≥12 months or completion of the Month 12 visit.

[b]Assessed using a mixed-effects model for repeated measures, with baseline score, sex, age, and baseline weight as a covariate, visit as fixed factors, and baseline-by-visit as interaction terms, with an unstructured covariance matrix.

Fig. 2

Change From Baseline on the Headache Impact Test-6 Over 12 Months in the CAPTURE Study (N=555).



P039

Multiparametric psychological profile of children and adolescents with headache disorders: Assessing disease burden, quality of life, and behavioral parameters

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Objective: Pediatric headaches can lead to significant impairment in daily life, reducing health-related quality of life and limiting participation in school, leisure activities, or sports. There is an increased risk of chronification, particularly in cases of frequent pain and unfavorable individual or psychosocial factors. To investigate relevant psychological factors over the disease course, standardized assessment tools are essential.

Methods: Data from 316 pediatric headache patients (mean age 12.57±3.11 years; 190 female) collected in 2017-2023 were analyzed. Three main dimensions were assessed: 1) disease burden (daily life impairment) using PedMIDAS, 2) health-related quality of life using KINDL, and 3) behavioral aspects using CBCL/6-18R and YSR/11-18R.

Results: Patients with chronic headache (n=121) based on ICHD3 showed: 1) significantly higher PedMIDAS scores ($p<0.001$), 2) significantly lower KINDL scores (total and dimension scores: $p<0.001$-$p=0.016$) and 3) significantly higher CBCL (Total Score $p=0.042$) and YSR scores (Internal Score $p=0.039$) compared to patients with episodic headache (n=175). No significant differences were found between patients with migraine and those with tension-type headache. Detailed results will be presented at the time of the conference.

Conclusion: Children with chronic headache experience a greater burden compared to those with episodic headache in terms of daily functioning, health-related quality of life (including physical and mental well-being, self-esteem, and peer relationships), and behavioral parameters—regardless of headache type according to the IHS classification.

P040

Elevated symptoms of burnout in a cluster headache cohort

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Objective: People with cluster headache suffer daily headache attacks of extreme intensity during active bouts. The attacks, which commonly occur at night, greatly impact sleep and quality of life for those affected. Symptoms of burnout are categorized as a depletion of a person''s energy reserves, affecting daily functioning, and may occur in any context of life. We hypothesize that the symptoms of cluster headache increase the risk for burnout during active bouts.

Methods: To investigate the extent of burnout in a Swedish cluster headache cohort, 701 study participants with cluster headache were invited to answer the Shirom-Melamed Burnout Questionnaire. Scores for burnout were compiled and compared between study participants in active bout and remission using logistic regression. Additionally, in-depth analysis of clinical characteristics was performed with the aim of identifying risk factors for burnout.

Results: A total of 284 individuals with cluster headache were included in the final analysis. Symptoms of burnout were commonly observed in people with cluster headache. In an active bout, 67.6% (n = 50) of the study participants scored above 3.75, which is indicative of having a risk for burnout, as compared to 39.5% (n = 83) of the study participants in remission. Regression analysis further showed that symptoms of burnout decrease with the number of years since the last active bout. Female study participants were at higher risk for burnout than males.

Conclusion: We observed a high degree of symptoms of burnout people with cluster headache, especially in active bout. These data suggest that the risk for symptoms of burnout is substantial in cluster headache and should be assessed when managing cluster headache patients in the healthcare system.

P041

A rare case of spontaneous intracranial hypotension complicated with intracranial hypertension

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Objective: Can intracranial hypertension complicate spontaneous intracranial hypotension (SIH)?

Methods: We report the case of a 27-year-old woman who presented to our department for an unusual headache**.**

Results: In June 2019, she presented to the Headache Emergency department for postural headache after a moderate cranial trauma. Brain MRI confirmed signs of SIH, and the spinal MRI found an anterior epidural fluid collection at C6-T1 **(Fig.1).** An epidural blood patch(EBP) was performed one month after symptom onset, resulting in initial improvement. However, due to a recurrence of postural headache, a second EBP was performed 2 months later. The patient experienced resolution of orthostatic headaches but continued to report headaches during forward-bending movements. Brain MRI performed in 2022 revealed indirect signs of SIH, and the spinal MRI still found anterior epidural fluid collection.

In 2023, she presented with an unusual headache that persisted while lying down, accompanied mainly by tinnitus in the left ear. An AngioCT revealed a diminution of the transvers sinus, and a lumbar puncture found an opening pressure of 35 cmH20. No other abnormalities were found in her MRI **(Fig.2.)**, and no papillary oedema was found. We later understood that the patient was using retinoids to treat eczema. The patient was advised to discontinue retinoids and was started on acetazolamide. Due to a favorable outcome, normal opening pressure and ophthalmologic examination the treatment was stopped after two months. The patient continues to experience headaches when leaning forward, with recurrent signs of SIH on brain MRI, and a persistent anterior epidural collection on spinal MRI. Due to pregnancy, the search for a dural leak and consideration of surgical treatment have been delayed.

patient gave her informed consent to publish their details

Conclusion: We report a rare case of spontaneous intracranial hypotension (SIH) complicated by secondary intracranial hypertension attributed to retinoid therapy for eczema.

Fig. 1

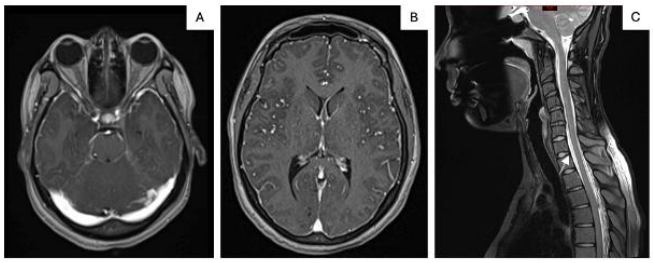


Fig.1. A: MRI: Axial section – venous distention sign. B: MRI T1 Gadolinium – pachymeningeal enhancement; C: MRI - Sagittal section – anterior epidural fluid collection at C6-T1 level

Fig. 2

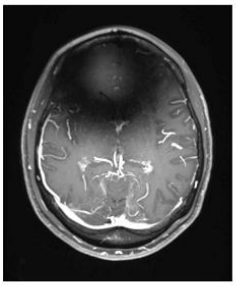


Fig.2. Cerebral MRI – axial section T1 gadolinium – diminution of the transverse sinus. The image shows artifacts due to the dental braces.

P042

Pain catastrophizing in chronic migraine patients receiving eptinezumab treatment

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Objective: This study aimed to evaluate changes in pain catastrophizing over time, from baseline to 9 months, in migraine patients undergoing Eptinezumab treatment.

Methods: The Pain Catastrophizing Scale (PCS) was used to assess 34 patients undergoing treatment with Eptinezumab at the Headache Center of the Carlo Besta Neurological Institute in Milan. This instrument was administered and explained during a regularly scheduled visit.

Results: Participants had a mean age of 46.97 years (median: 49.5, SD: 12.3), and included 33 females and 1 male. Eight patients dropped out due to adverse events. Although baseline scores did not always reach the clinical significance cut-off (>30), a high level of Pain Catastrophizing was observed (median PCS tot = 22, SD = 8.24), mainly driven by high scores in Helplessness (12 ± 3.77) and Rumination (10 ± 4.07). Magnification is lower at baseline (median: 1.5, SD: 1.42). The comparison at T9 was conducted only for a subset of 16 patients who have completed the follow-

up thus far. A significant reduction in the total PCS score was observed (T0 = 19.5 ± 7.93 vs T9 = 12 ± 10.17), with marked decreases in Helplessness (T0 = 11 ± 4.10 vs T9 = 6 ± 4.30) and Rumination (T0 = 8.5 ± 3.84 vs T9 = 6.5 ± 5.13). While PCS scores showed a downward trend by T9, it is also important to consider the high standard deviations across scores, which highlight considerable inter-individual variability.

Conclusion: Baseline Pain Catastrophizing levels in our sample of chronic migraine patients were close to the upper limit of the normal range. This supports the tendency of these patients to experience intrusive thoughts, persistent worry, and feelings of Helplessness, which amplify the subjective experience of pain. By 9 months, significant improvements were observed in overall catastrophizing, particularly in Helplessness & Rumination subscales. These findings emphasize the need to study psychological factors, given their potential impact on the progression and outcomes of migraine treatment.

P043

An assessment of patient characteristics and treatment satisfaction in short-term and long-term prevention users of rimegepant utilizing a cross-sectional, observational online survey in the United States

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Objective: Rimegepant (RIM) is approved for both acute and preventive migraine treatment. RIM may provide patients a flexible option for short-term prevention (STP) when appropriate, beginning treatment during periods of increased risk for an attack and discontinuing when the period resolves. This study describes clinical characteristics and treatment satisfaction of STP and long-term prevention (LTP) users of RIM.

Methods: This cross-sectional survey was administered online to US adults with migraine who initiated RIM for ≥3 months and used RIM within 30 days before the survey. Demographics, migraine history, and Treatment Satisfaction Questionnaire for Medication (TSQM-9) score were assessed between mutually exclusive groups of RIM users based on an applied hierarchy. STP users used RIM to prevent attacks for a time-limited period when headache avoidance was important. LTP users used RIM regularly (every other day) without breaks to prevent/reduce the severity or frequency of attacks.

Results: There were 152 STP and 83 LTP RIM users (64% and 80% female) with a median age of 45 years (**Table**). STP vs LTP users reported a median duration of migraine diagnosis of 5 vs 10 years and a median of 5 vs 6 days of migraine and 6 vs 10 days of headache in the past month. Both STP and LTP RIM users were satisfied with their current treatment regimen to manage migraine (**Figure**, median TSQM-9 global satisfaction score: 71.4 per group), with the highest score for the convenience domain (77.8 vs 83.3, P=0.061), suggesting that patients were most satisfied with this aspect.

Conclusion: STP and LTP RIM users had similar demographics and clinical characteristics. STP users had fewer headache/migraine days vs LTP users in the past month. Patients using RIM had high levels of treatment satisfaction, regardless of regimen, supporting the value of both treatment approaches. Further research is needed to evaluate the benefits of the dosing and treatment flexibility provided by RIM.

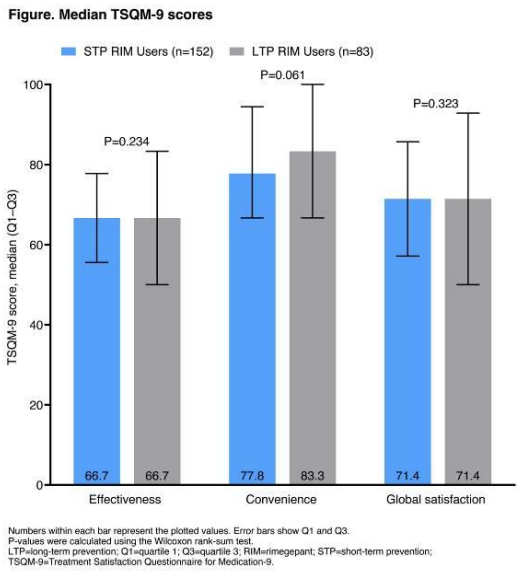
Fig. 1

Table. Demographics and clinical characteristics

	STP RIM users n=152	LTP RIM users n=83	P value[a]
Age, median (Q1, Q3), y	44.5 (37.0, 51.0)	45.0 (39.0, 55.0)	0.311
Gender, n (%)			
Male	54 (35.5)	17 (20.5)	0.018
Female	98 (64.5)	66 (79.5)	-
Race, n (%)			
White	126 (82.9)	70 (84.3)	0.776
Black	18 (11.8)	13 (15.7)	0.408
Asian	2 (1.3)	1 (1.2)	1.000
American Indian/Alaska native	1 (0.7)	2 (2.4)	0.285
Native Hawaiian/Other Pacific Islander	1 (0.7)	0	1.000
Other	8 (5.3)	0	0.053
Comorbidities, n (%)[b]			
Anxiety	91 (59.9)	48 (57.8)	0.761
Depression	69 (45.4)	43 (51.8)	0.347
Cluster headache	55 (36.2)	24 (28.9)	0.260
Allergies/hay fever	40 (26.3)	35 (42.2)	0.013
Disease history			
Time since first migraine diagnosis, median (Q1, Q3), y	4.8 (2.4, 16.5)	9.8 (3.3, 24.8)	0.057
Days of headache in the past 30 days, median (Q1, Q3), d	6.0 (4.0, 12.0)[c]	10.0 (6.0, 15.0)[c]	0.005
Days of migraine in the past 30 days, median (Q1, Q3), d	4.5 (2.0, 9.0)[d]	6.0 (3.0, 10.0)[d]	0.094
Treatment history, n (%)			
Previously taken preventive treatment	65 (42.8)	40 (48.2)	0.424
Current acute treatment			
Rimegepant	115 (75.7)	40 (48.2)	<0.001
Sumatriptan	32 (21.1)	24 (28.9)	0.176
Taking >1 acute treatment	18 (11.8)	8 (9.6)	0.607
Time since first RIM use, median (Q1, Q3), y	2.1 (1.2, 2.8)	2.3 (1.3, 3.4)	0.196

[a] P-values were calculated using Chi-square, Fisher exact, or Wilcoxon rank-sum test, as appropriate.
[b] The 4 most common comorbidities are listed.
[c] STP RIM users (n=142), LTP RIM users (n=80).
[d] STP RIM users (n=138), LTP RIM users (n=79).
LTP=long-term prevention; Q1=quartile 1; Q3=quartile 3; RIM=rimegepant; STP=short-term prevention.

Fig. 2



P044

Real-world characteristics and treatment experience of patients using rimegepant for short-term prevention and acute treatment of migraine: Results from a cross-sectional survey in the US

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Objective: Rimegepant (RIM) is approved for both acute and preventive migraine treatment. Thus, RIM may potentially provide patients a flexible option for short-term prevention (STP), before migraine onset in anticipation of and during exposure to known triggers/situations. This study assessed patient characteristics and treatment experience among STP and acute treatment (AT) users of RIM.

Methods: A cross-sectional survey was administered online to United States adults with migraine who initiated RIM for ≥3 months and used RIM within 30 days before the survey. Patient-reported outcomes (PROs) were evaluated between mutually exclusive groups of RIM users based on an applied hierarchy: STP users (used RIM to prevent attacks for a time-limited period, when headache avoidance was important) and AT users (used RIM to stop, relieve, or lower symptoms when an attack occurs).

Results: Of 152 STP and 190 AT RIM users (median age 45 vs 44 years, P=0.832), 64% vs 80% were female (P=0.001) (**Table**). Median migraine history was 5 (STP users) vs 11 (AT users) years. STP users reported fewer median days of headache (6 vs 10 days) and migraine (5 vs 6 days) in the past month vs AT users. Many STP and AT users scored ≥3 in the global anxiety disorder-2 (58 vs 52%) and patient health (48 vs 42%) questionnaires (**Figure 1A**). Moderate/maximal symptom control with their current migraine treatment was reported by 52% of STP vs 71% of AT users (**Figure 1B**). Both groups had high treatment satisfaction (**Figure 1C**, median score STP vs AT users, TSQM-9 global satisfaction 71 vs 71; P=0.626), with highest satisfaction in the convenience domain (78 vs. 83; P=0.215).

Conclusion: Most patients using RIM for STP or AT reported high levels of treatment satisfaction and moderate/maximal control of migraine symptoms. The findings further support the clinical benefits of RIM for the AT of migraine, with similar benefits perceived when used for STP. Further study is needed to explore PROs among RIM users.

Fig. 1

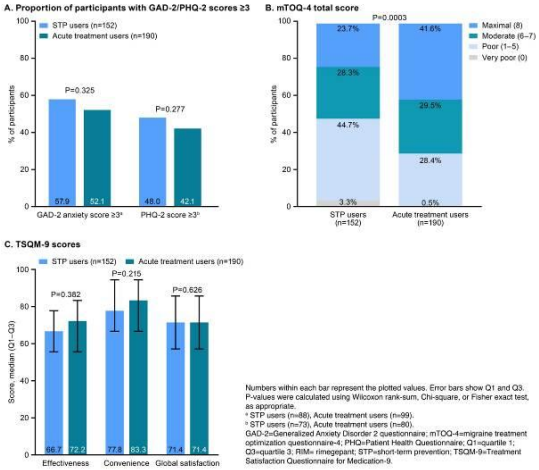


Fig. 2

Table. Demographics and clinical characteristics

	STP RIM users n=152	AT RIM users n=190	P-value[a]
Age, median (Q1, Q3), y	44.5 (37.0, 51.0)	44.0 (36.0, 53.0)	0. 832
Gender, n (%)			
Male	54 (35.5)	37 (19.5)	0.001
Female	98 (64.5)	152 (80.0)	-
Non-binary	0	1 (0.5)	-
Race, n (%)			
White	126 (82.9)	159 (83.7)	0.846
Black	18 (11.8)	24 (12.6)	0.825
Asian	2 (1.3)	1 (0.5)	0.587
American Indian/Alaska native	1 (0.7)	6 (3.2)	0.137
Native Hawaiian/Other Pacific Islander	1 (0.7)	1 (0.5)	1.000
Other	8 (5.3)	10 (5.3)	1.000
Comorbidities, n (%)[b]			
Anxiety	91 (59.9)	117 (61.6)	0.747
Depression	69 (45.4)	100 (52.6)	0.183
Cluster headache	55 (36.2)	56 (29.5)	0.188
Allergies/hay fever	40 (26.3)	68 (35.8)	0.061
Insomnia	39 (25.7)	57 (30.0)	0.375
Sleep apnea	37 (24.3)	53 (27.9)	0.458
High cholesterol	35 (23.0)	57 (30.0)	0.148
Disease history			
Time since first migraine diagnosis, median (Q1, Q3), y	4.8 (2.4, 16.5)	11.4 (3.2, 25.4)	0.005
Time since first migraine experience, median (Q1, Q3), y	11.5 (5.0, 26.3)	19.8 (5.8, 31.4)	0.011
Days of headache in the past 30 days, median (Q1, Q3), d	6.0 (4.0, 12.0)[c]	9.5 (5.0, 15.5)[c]	0.001
Days of migraine in the past 30 days, median (Q1, Q3), d	4.5 (2.0, 9.0)[d]	6.0 (3.0, 9.0)[d]	0.093
Treatment history, n (%)			
Current acute treatment			
Rimegepant	115 (75.7)	190 (100.0)	<0.001
Sumatriptan	32 (21.1)	29 (15.3)	0.165
Taking >1 acute treatment	18 (11.8)	31 (16.3)	0.241
Previously taken preventive treatment	65 (42.8)	147 (77.4)	<0.001
Time since first RIM use, median (Q1, Q3), y	2.1 (1.2, 2.8)	1.7 (1.0, 2.7)	0.190

[a] P-values were calculated using Chi-square, Fisher exact, or Wilcoxon rank-sum test, as appropriate.
[b] The comorbidities occurring in ≥25% of participants in each group are listed.
[c] STP RIM users (n=142), AT RIM users (n=184).
[d] STP RIM users (n=138), AT RIM users (n=182).
AT=acute treatment; Q1=quartile 1; Q3=quartile 3; RIM=rimegepant; STP=short-term prevention.

P045

Real-world patient satisfaction and effectiveness of ubrogepant and atogepant for migraine in Israel: Interim analysis of COBRA study

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Objective: To evaluate patient-reported satisfaction and effectiveness of ubrogepant (UBRO) and atogepant (ATO) for migraine in real-world settings in Israel.

Methods: Interim analysis (April 25, 2025) of an ongoing 3-month prospective, observational, multi-center study (NCT05827887). Eligible patients received ATO for prevention or UBRO for acute therapy per clinical decision. UBRO patients completed a 30-day headache e-diary to document drug efficacy. A follow-up visit was held after 3 months for all patients. Primary endpoint: proportion of patients who were extremely satisfied or satisfied at month 3. UBRO secondary endpoints: pain freedom (PF) and pain relief (PR) at 2 hours post-dose, and change from baseline (CFB) in MTOQ-6 score. ATO secondary endpoints: CFB in monthly headache days (MHD), monthly acute medication use days (AMD), and HIT-6 score. Additional endpoint: proportion of patients achieving ≥50%, ≥75%, and 100% reductions in MHD at month 3.

Results: 52 UBRO and 43 ATO patients (**Table 1**) received ≥1 dose. Effectiveness was analyzed for 49 UBRO and 41 ATO patients who reported satisfaction. Satisfaction at month 3 was reported by 59.2% of UBRO and 63.4% of ATO patients. **In the UBRO cohort**, the mean proportions of treated attacks with PF or PR at 2 hours post-dose were 24.1% and 53.0%, respectively. **In the ATO cohort**, significant reductions of mean MHD (from 16.7 to 10.6 days, p <0.001) and AMD (from 12.7 to 8.8 days, p <0.05) were observed at month 3 (**Table 2**). Additionally, 56.1%, 34.1% and 9.8% of the ATO patients experienced ≥50%, ≥75% and 100% reductions in MHD, respectively. Adverse events were reported in 12.6% overall (**Table 3**).

Conclusion: In this real-world study**,** UBRO for acute therapy and ATO for prevention of migraine demonstrated patient satisfaction and effectiveness.

Acknowledgements

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Fig. 1

Table 1. Baseline Demographic and Disease Characteristics

	Overall N=95	Atogepant N=43	Ubrogepant N=52
Age (Years)	45.1 (13.9)	44.1 (12.4)	45.9 (15.2)
Sex, n (%)			
Female	79 (83.2%)	33 (76.7%)	46 (88.5%)
Male	16 (16.8%)	10 (23.3%)	6 (11.5%)
Ethnicity, n (%)			
Jewish	91 (95.8%)	41 (95.3%)	50 (96.2%)
Arabic	3 (3.2%)	1 (2.3%)	2 (3.8%)
Other	1 (1.1%)	1 (2.3%)	0 (0.0%)
Body Mass Index (Kg/m²)	24.2 (4.0)	24.6 (4.0)	23.8 (4.0)
Disease Duration (years)	17.7 (14.5)	20.2 (14.1)	15.7 (14.6)
Migraine type, n (%)			
Episodic	37 (38.9%)	9 (20.9%)	28 (53.8%)
Chronic	58 (61.1%)	34 (79.1%)	24 (46.2%)
Prior exposure to migraine acute treatments, n (%)	87 (91.6%)	39 (90.7%)	48 (92.3%)
Prior exposure to triptans	67 (70.5%)	25 (58.1%)	42 (80.8%)
Prior exposure to migraine preventive treatments , n (%)	69 (72.6%)	38 (88.4%)	31 (59.6%)
Prior exposure to CGRP mAbs	27 (28.4%)	21 (48.8%)	6 (11.5%)
No. headache days during the last 30 days	14.5 (8.8)	16.5 (8.6)	12.8 (8.7)
No. of acute medication use days during the last 30 days	11.9 (7.9)	12.7 (8.2)	11.2 (7.7)

Data represent mean (SD) unless otherwise indicated.

Fig. 2

Table 2. Secondary Efficacy Endpoints

Atogepant cohort					
Characteristic	Baseline N = 41	Visit 2 (month 3) N = 41	Difference[1]	95% CI[1, 2]	p-value[1]
Headache days during last 30 days	16.7 (8.8)	10.6 (10.4)	-6.1	-9.1, -3.1	<0.001
acute medication use days during last 30 days	12.7 (8.3)	8.8 (9.8)	-3.9	-7.8, -0.10	0.045
HIT-6 Score	69.3 (6.1)	60.0 (12.2)	-9.3	-13, -6.0	<0.001
HIT-6 responders (≥5 points decrease from baseline), n (%)		24 (58.5%)			
Ubrogepant cohort - 30-day e-diary analysis (N=34)[3]					
Proportion of headaches with pain freedom 2 hours post dose per participant (%)				24.1 (29.6)	
Proportion of headaches with pain relief 2 hours post dose per participant (%)				53.0 (38.8)	
Proportion of headache days treated with UBRO per participant (%)				60.0 (27.4)	
Proportion of headaches that required a 2nd dose of UBRO per participant (%)				11.8 (19.2)	
Ubrogepant cohort – Visit 2 (Month 3) analysis					
Characteristic	Baseline N = 49	Visit 2 (month 3) N = 49	Difference[1]	95% CI[1, 2]	p-value[1]
MTOQ-6 Score	15.7 (4.6)	19.2 (4.8)	3.5	1.9, 5.1	<0.001

Data represent mean (SD) unless otherwise indicated.
[1]Paired t-test
[2]CI = Confidence Interval
[3]Includes participants who reported at least 7 days (not necessarily consecutive) in their e-Diary, took Ubrogepant at least once during the 30-day period and completed satisfaction questionnaire at visit 2.

Fig. 3

Table 3. Adverse Events and Tolerability

	Overall N = 95	Atogepant N = 43	Ubrogepant N = 52
Any adverse event (AE)	12 (12.6%)	8 (18.6%)	4 (7.7%)
Any serious AE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Any treatment-related AE*	9 (9.5%)	7 (16.3%)	2 (3.8%)
Any AE leading to discontinuation	3 (3.2%)	2 (4.7%)	1 (1.9%)
Deaths	0 (0.0%)	0 (0.0%)	0 (0.0%)

Data are n (%)
* Assessed by the investigator

P046

Retrospective study of trigeminal neuralgia: Analysis of 100 episodes managed in the emergency department

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Objective: To analyze the diagnostic and therapeutic approach in patients presenting with suspected trigeminal neuralgia at the Emergency Department of the Salamanca University Hospital Complex

Methods: A retrospective observational study was conducted between May 2023 and March 2025, including patients discharged from the Emergency Department with a diagnosis of trigeminal neuralgia. Clinical and demographic variables were collected. We analysed the treatments administered in the emergency setting, subsequent referrals for specialist follow-up, treatment response, and the complementary tests performed

Results: A total of 100 episodes of trigeminal neuralgia were analyzed, corresponding to 74 patients, with a mean age of 57.6 years (64% female). Neurology was consulted in 41% of cases. The most frequently prescribed treatment by neurologists was lacosamide, with a pain relief rate of 84.6%, whereas emergency physicians predominantly administered paracetamol, NSAIDs, and opioids. Among patients without a prior diagnosis, only half were referred for neurological assessment, with the diagnosis being

confirmed in 50% of these cases. Brain MRI was performed in 44% of patients, revealing a neurovascular conflict in 18% of those scans. Only four cases underwent microvascular decompression surgery.

Conclusion: Trigeminal neuralgia poses a significant challenge in the emergency setting, with considerable heterogeneity in both its diagnostic and therapeutic management, and a high proportion of initial diagnoses not subsequently confirmed. This study underscores the importance of neurological assessment in the emergency department and the need for close follow-up to optimize symptom control

P047

No changes in blood pressure assessed with the 24-hour Holter monitoring in patients treated with anti-CGRP monoclonal antibodies: A prospective observational study (SAFHYPER)

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Objective: To assess early changes in blood pressure (BP) after initiating anti-CGRP/R mAbs in patients with episodic migraine using 24-hour Holter monitoring.

Methods: We conducted a prospective, single-center, real-world study including 20 patients with episodic migraine treated with anti-CGRP/R mAbs. Participants underwent 24-hour Holter BP monitoring before treatment and four weeks after the first injection. Primary outcome was the change in mean systolic BP (SBP). Secondary outcomes included changes in diastolic BP (DBP), differential BP, diurnal/nocturnal values, heart rate (HR), and dipping patterns.

Results: Mean 24-hour SBP and DBP showed non-significant reductions after treatment (−2.4 mmHg and −1.8 mmHg, respectively). No significant changes were found in diurnal BP, while a trend toward improved nocturnal BP control and increased frequency of physiological dipping patterns was observed (from 45% to 85%). HR remained unchanged. No adverse events were reported.

Conclusion: Anti-CGRP/R mAbs did not significantly alter 24-hour BP in the early treatment phase in patients with episodic migraine. These findings support the short-term cardiovascular safety of anti-CGRP/R mAbs, though further studies with larger cohorts and longer follow-up are warranted.

Fig. 1

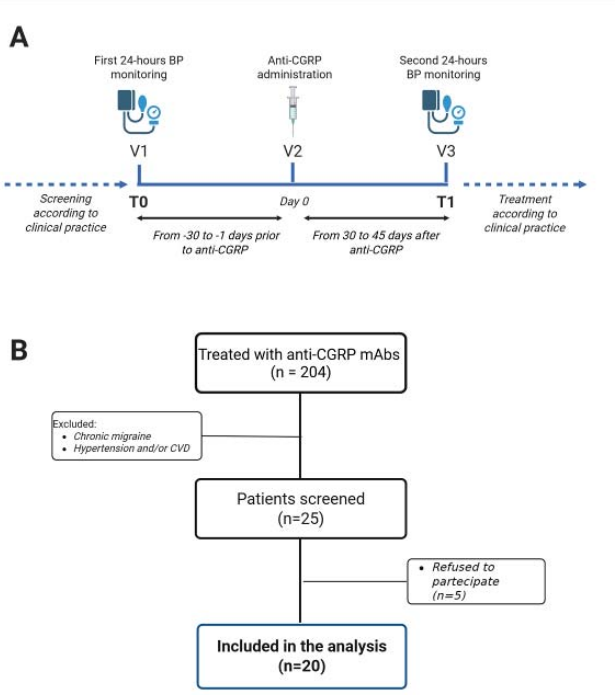


Fig. 2

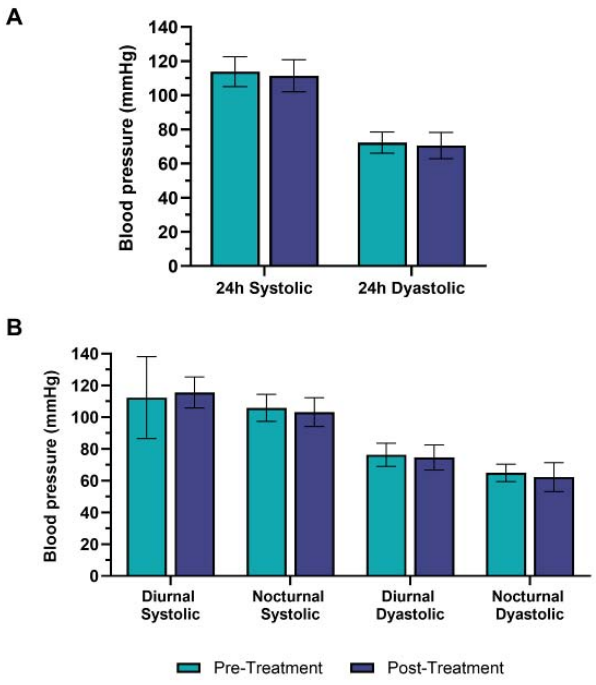
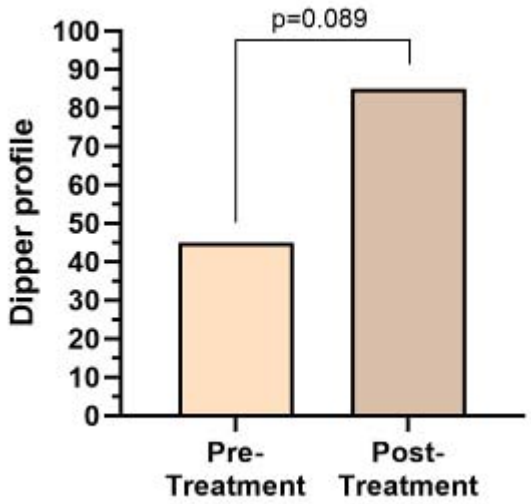


Fig. 3



P048

An observational prospective study assessing the effectiveness of eptinezumab as a preventive treatment for migraine in a real-world setting in Spain: Interim results from the RELEASE study

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Objective: The RELEASE study aims to evaluate the real-world effectiveness of eptinezumab, complementing evidence from randomized controlled trials.

Methods: This observational, non-comparative, prospective study includes participants receiving eptinezumab for migraine prevention under routine clinical practice in Spain. It is part of a global umbrella design, involving a series of local studies, each conducted in a participating country. Data is collected from medical records, a patient application, and an electronic diary (eDiary), as well as during infusion-related site visits at baseline and after 3, 6, and 12 months of treatment. This early analysis included participants enrolled before March 1, 2025, with at least one follow-up measurement of the primary outcome (change from baseline in monthly migraine days [MMDs]). Follow-up measurement was defined as completing the eDiary on at least 14 out of 28 days in any month post-baseline.

Results: Seventy-five participants were included in this early analysis. Mean (±SD) age was 45 (±9) years, and 69/75 (92%) were females. Fifty-four of 75 (72%) participants had chronic migraine, and 44/75 (59%) received other anti-CGRP(s) before eptinezumab. At Month 3, 46% (n=33/71) and 32% (n=23/71) of participants experienced ≥30% and ≥50% MMD reduction, respectively. The change from baseline in MMDs was particularly pronounced in participants naïve to anti-CGRP(s) at the time of eptinezumab initiation. Additionally, significant reduction was observed in HIT-6 total score at Month 3 (change from baseline: –4.65; 95% CI: –6.17, –3.12; $p<0.01$; n=57). Six-month data for participants achieving this milestone will be presented in the poster.

Conclusion: This early analysis showed the effectiveness of eptinezumab for migraine prevention in a real-world setting in Spain.

P049

Consistency of effect of rimegepant as an acute treatment for migraine attacks: Data from a prospective, real-world study

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Objective: This prospective, real-world study aimed to evaluate the consistency of rimegepant's efficacy as an acute treatment for migraine across three separate attacks among Chinese patients

Methods: This was a single-arm, prospective, real-world study (NCT05709106). Adults diagnosed with migraine (with or without aura) in accordance with the International Classification of Headache Disorders, 3rd Edition (ICHD-3) and prescribed rimegepant as part of the routine treatment were screened for this study. Eligible patients were instructed to use a digital platform to record their pain intensity, functional ability, and accompanying symptoms at predefined time points during three migraine attacks. In this report, percentages of participants achieving pain freedom, freedom from the most bothersome symptom (MBS) and normal function at 2 h post-dose were evaluated for each attack and in ≥2/3 attacks.

Results: A total of 89 patients were included in the analysis, with a mean (SD) age of 43.2 (12.3) years. And the mean (SD) number of monthly migraine days (MMDs) was 13.2 (8.7). Compared with pre-dose level, the percentages of participants achieving pain freedom, MBS freedom and normal function at 2 h

post-dose were 37.2%, 65%, and 56%, respectively, in the first attack **(Table 1)**. Notably, rimegepant demonstrate evident and consistent efficacy across all three attacks. In the second attack, the corresponding percentages were 42.4%, 56.4%, and 46.4%, while in the third attack, they were 42.5%, 71.1%, and 51.8% **(Table 1)**. Additionally, 35.8% of participants achieved pain freedom at 2h post-dose in ≥2 of 3 attacks, 65% achieved MBS freedom, and 50% achieved normal function **(Table 1)**.

Conclusion: These results confirm the good real-world efficacy of rimegepant and further demonstrate consistency of response across multiple attacks.

Fig. 1

Table.1 Percentages of participants achieving pain freedom, MBS freedom, normal function at 2h post-dose across three attacks and in≥2/3 attacks.

Outcomes	1st attack n/N (%)	2ed attack n/N (%)	3rd attack n/N (%)	⩾2/3 attacks n/N (%)
Pain freedom [a]	32/86 (37.2)	36/85 (42.4)	37/87 (42.5)	29/81 (35.8)
MBS freedom [b]	26/40 (65)	22/39 (56.4)	27/38 (71.1)	13/20 (65)
normal function [c]	29/52 (56)	26/56 (46.4)	29/56 (51.8)	18/36 (50)

MBS, most bothersome symptom.
[a] Among participants with pain at pre-dose
[b] Among participants with MBS at pre-dose
[c] Among participants with functional disability at pre-dose

P050

Insomnia and sleep quality in patients with treatment-resistant chronic migraine

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Objective: Treatment-resistant chronic migraine (TRCM) is a complex condition often complicated by sleep disturbances, which exacerbate disability and reduce quality of life. Standardized assessments of sleep comorbidities in this population remain limited.
To evaluate sleep disorder prevalence in TRCM patients refractory to ≥3 oral preventives and botulinum toxin using validated scales.

Methods: This prospective observational study included 164 adults with TRCM (mean age 48.3 years, 86.5% women) from our headache unit. Sleep quality, insomnia, and daytime sleepiness were assessed via Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and Epworth Sleepiness Scale (ESS). Clinical and demographic variables, including prior Botox use (37.3% discontinued, 7.5% naïve) and concurrent anti-CGRP monoclonal antibodies (most patients), were analyzed descriptively.

Results: Poor sleep quality (PSQI >5) affected 77%, excessive daytime sleepiness (ESS >10) 21%, and clinically significant insomnia (ISI ≥15) 95%. Functional impairment was notable: 60% reported work/social difficulties (PHQ-9), with 37% describing severe limitations. Comorbid sleep disorders were rare: obstructive sleep apnea (3%), restless legs syndrome (12.5%), and sleepwalking (2.4%). Antidepressant use was reported in 33.3% of cases.

Conclusion: Sleep disturbances, particularly insomnia, are highly prevalent in TRCM, despite low rates of other sleep disorders. The high rates of functional impairment and antidepressant use highlight the need for integrated psychiatric and sleep-focused interventions in this population.

P051

Consistency of response to rimegepant for the acute treatment of migraine: A population and participant-level analysis of a prospective real-world observational study (CONFIDENCE)

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Objective: Evaluate the real-world consistency of response to rimegepant (RIM) 75 mg for the acute treatment of migraine.

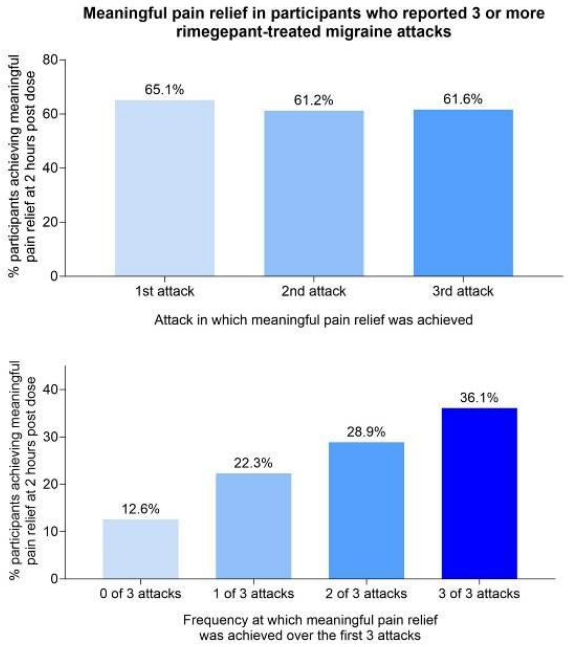
Methods: A prospective observational study in the Migraine Buddy® app among adults with 3–14 headache days in the prior 30 days. Participants completed a baseline survey, a 28-day diary, and a study completion survey through a custom app interface. Analyses assessed RIM response at the population (i.e. % treated attacks achieving a positive response) and participant level (i.e. % participants achieving a positive response in ≥2 of their first 3 treated attacks). A positive response was defined as meaningful pain relief within 2hrs post-dose, a meaningful improvement in function within 2hrs post-dose, or satisfaction/extreme satisfaction with attack treatment (all as determined by the participant).

Results: Overall, 66.2% (2169/3276) of recorded migraine attacks were treated with RIM. The 416/429 enrolled participants who reported ≥1 RIM-treated

attacks had a mean (SD) age of 39.6 years (10.9), 86.1% were female, and 90.4% White. Most participants had a high headache frequency (median 8 [IQR: 5, 10] headache days in the past 30 days), moderate to severe disability (MIDAS score ≥11 in 89.9%), and used preventive treatment (84.1%). Among RIM-treated attacks, 61.3% achieved a meaningful pain relief and 57.6% meaningful improvement in function within 2hrs post-dose; satisfaction/extreme satisfaction with treatment was reported in 68.4% of attacks. Among the 349 participants with ≥3 RIM-treated attacks, 65.0% achieved meaningful pain relief within 2hrs in ≥2 of their first 3 attacks (Figure), 59.6% a meaningful improvement in function within 2hrs in ≥2 of their first 3 attacks, and 73.9% satisfaction/extreme satisfaction with treatment in ≥2 of their first 3 attacks.

Conclusion: In this real-world study, the response to RIM for the acute treatment of migraine was consistently favorable at the population level and in individual participants. NCT06467370

Fig. 1



P052

Prospective, real-world evidence of meaningful pain relief, return to function, and satisfaction among patients with migraine on acute rimegepant treatment alone or with concomitant preventive migraine medication

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Objective: This analysis of a prospective, observational, real-world study (NCT06467370) assessed the effectiveness of acute rimegepant (RIM) treatment in patients with migraine across 4 subgroups: 1) no concomitant preventive medication (RIM-only); 2) oral migraine preventive medications (OMPMs), 3) onabotulinumtoxinA (BTX) and 4) anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs).

Methods: Adults with 3–14 headache days and in the prior 30 days and planning to use RIM over the next 30 days were enrolled via the Migraine Buddy® app. No study treatment was provided. Patients completed a baseline questionnaire, Day 2–29 daily assessment reports, and a Day 30 questionnaire. Analyses included the proportion of patients achieving a response in at least 66.7% of the first 10 RIM-treated attacks for meaningful pain relief (MPR) or return to function (RTF) within 2 and 4 hours, or being satisfied/extremely satisfied with RIM across different domains.

Results: Responses from 416 patients (RIM-only [*n*=66] or RIM with OMPMs [*n*=69], BTX [*n*=140], or anti-CGRP mAbs [*n*=141]) who used RIM to treat ≥1 migraine attack were analyzed. At baseline, most patients reported moderate to severe migraine-related disability (RIM-only [90.9%] or RIM with OMPMs [94.2%], BTX [92.9%], or anti-CGRP mAbs [84.4%]). MPR ranged from 44.7%–65.2% and 78.7%–83.3% for 2 and 4 hours, respectively; RTF ranged from 39.7%–68.2% and 68.8%–84.8% for 2 and 4 hours, respectively (Figure). Overall satisfaction with RIM ranged from 55.3%–77.3% (Figure). Across all endpoints, response was highest in "RIM-only" subgroup and lowest in the "anti-CGRP mAbs" subgroup.

Conclusion: Patients treating migraine attacks with RIM, independent of preventive treatment use, reported meaningful pain relief, a return to normal function, and high satisfaction. It is unclear if the differences between the subgroups is based on selection bias or if there is a difference in acute RIM effectiveness with prevention use.

Fig. 1

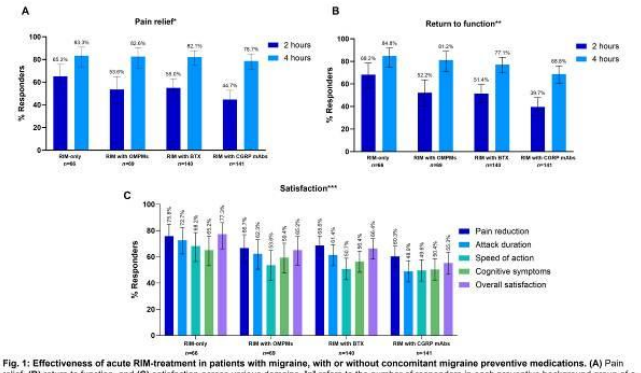


Fig. 1: Effectiveness of acute RIM-treatment in patients with migraine, with or without concomitant migraine preventive medications. (A) Pain relief, **(B)** return to function, and **(C)** satisfaction across various domains. "n" refers to the number of responders in each preventive background group of a total of 416 patients with at least one RIM-treated attack. Analyses included the proportion of responders achieving a response in at least 66.7% of attacks in up to 10 RIM-treated attacks. Data are represented as mean (%) with 95% CI.
* When the level of headache pain reduces to a degree that is meaningful to the patients, along with or prior to pain freedom.
** Improvement in functioning to perform daily activities using functional disability scale.
*** Includes responses in which patients indicated they were satisfied or extremely satisfied.
BTX, botox; CGRP, anti-calcitonin gene-related peptide; CI, confidence interval; mAbs, monoclonal antibodies; OMPMs, oral migraine preventive medications; RIM, rimegepant.

P053

Efficacy of atogepant on migraine headache severity in episodic migraine stratified by patient impression of disease improvement: A post-hoc analysis of the 12-week ADVANCE and 52-week open-label trials

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Objective: Evaluate the impact of atogepant (Ato) on frequency and pain severity of moderate to severe monthly migraine headache days (MHDs), categorised by Patients' Global Impression of Change (PGIC) response.

Methods: This post-hoc analysis included participants with episodic migraine receiving atogepant from the ADVANCE study, a 12-week phase 3 trial, or a separate 52-week open label (OL) trial. PGIC responders rated improvement as "Much better" or "Very much better". Headache pain intensity was recorded daily using a 3-point severity scale (mild–severe). We assessed the change from baseline (CFB) in mean moderate to severe MHDs and the CFB in mean pain severity of MHDs, including resolved MHDs (score=0 if MHDs reduced post-baseline). Analysis of ADVANCE conducted without multiplicity control used a mixed-effects model for repeated measures to report nominal P values for the least squares mean difference (LSMD) CFB between Ato 60 mg once daily (QD) and placebo (Pbo).

Results: PGIC responders in ADVANCE had a CFB in mean moderate to severe MHDs (**Figure 1A**) of -3.49 days for Pbo and -4.60 days for Ato (LSMD [95%CI]: -1.15 [-1.64, -0.66]; P < 0.001) at Week 12. In the OL trial, PGIC responders showed a 52-week CFB of -4.61 days. ADVANCE PGIC non-responders (**Figure 1B**) had reductions of -1.17 days for Pbo and -1.74 days for Ato (LSMD: -0.26 days [-1.17, -0.66]; P = 0.5803). Ato non-responders in the 52-week OL trial showed a CFB of -2.10. PGIC responders (**Figure 2A**) had a CFB in mean severity scores of -1.19 for Pbo and -1.52 for Ato in ADVANCE participants (LSMD: -0.37 [-0.50, -0.23]; P < .0001), and -1.66 in Ato OL trial participants. PGIC non-responders (**Figure 2B**) had a CFB in mean severity scores of -0.51 for Pbo and -0.73 for Ato in ADVANCE (LSMD: -0.15 [-0.33, 0.03]; P = 0.1087), and -1.01 in the OL trial.

Conclusion: Ato 60 mg QD showed greater reductions in both frequency and severity of MHDs in PGIC responders relative to Pbo.

Fig. 1

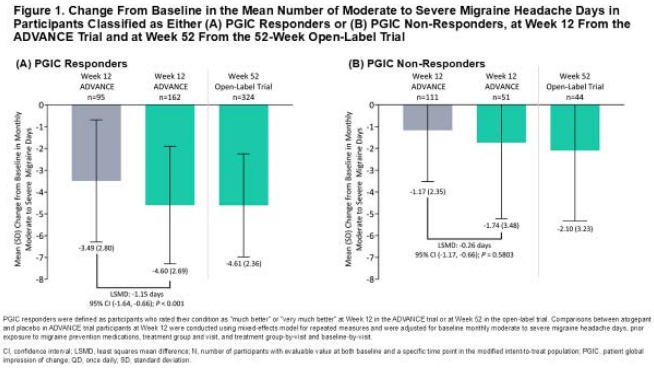
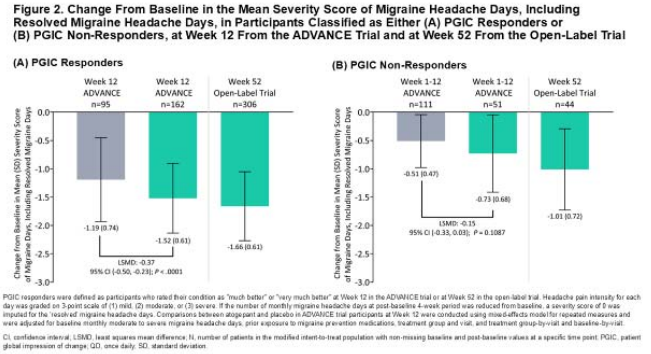


Fig. 2



P054

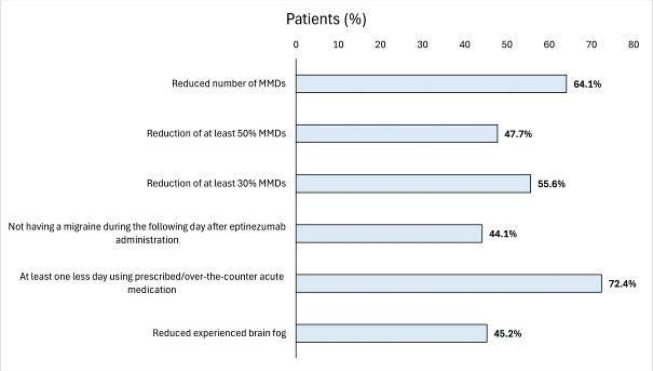
Effectiveness and satisfaction with eptinezumab for the preventive treatment of migraine in patients under routine clinical practice in Spain: EPIC study

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[3]Lundbeck Spain, Barcelona, Spain

Objective: To describe the perceived effectiveness and satisfaction of neurologists with eptinezumab as a migraine preventive treatment in routine clinical practice, and to analyze the sociodemographic and clinical profiles of patients.
Methods: National, observational, study based on aggregated data from patients with high-frequency episodic migraine (HFEM) or chronic migraine (CM), through a structured questionnaire specifically developed for this study and addressed to neurologists.
Results: Forty neurologists participated in the study. According to their responses, 83% of patients treated with eptinezumab were female, 67.5% were 40-49 years old, and time since HFEM and CM diagnosis was 8.8 and 12.2 years, respectively. Treated patients had previously received ≥3 preventive therapies without response and most (>50%) had previously tried other anti-CGRP. Common comorbidities included anxiety (50.9%), depression (42.9%) and inflammatory conditions (21.0%). After eptinezumab, 47.7% and 55.6% of patients experienced a reduction of ≥50% and ≥30% in monthly migraine days (MMDs), respectively, and 45.2% reduced brain fog (Fig 1). Symptomatically, neurologists reported that 70.5% and 61.3% experienced less severe attacks and faster relief, respectively. Almost all (97.5%) neurologists observed fewer migraine-related emergency visits/hospitalizations. Additionally, neurologists reported that 58.1% of patients demonstrated enhanced social/family functioning and 58.6% work/academic productivity, and 71.5% expressed convenience regarding infusions after starting treatment with eptinezumab. Neurologists' overall satisfaction with eptinezumab reached 8.9/10.
Fig 1. Treatment effectiveness
Conclusion: Eptinezumab is perceived by neurologists as a highly effective treatment reducing MMDs, severity and frequency of symptoms and visits to the emergency room or hospitalizations in patients with HFEM and CM in a real-world setting, which results in improved patients' quality of life.

Fig. 1



P055
Evaluation of real-world effectiveness of acute migraine treatment: Results from DREAM, a nationwide population study on 58,000 people
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Objective: What is the effectiveness of acute migraine treatments and impact on return to normal function reported by patients in Denmark?
Methods: The nationwide DREAM (Danish REgistry Analyses of Migraine) study combined data from Danish national health registers with a survey consisting of 87 questions on experience with acute and preventive migraine medications. All Danish residents ≥ 18 years having redeemed a triptan prescription or diagnosed with migraine (ICD-10: G43) between Jan 2021 – Dec 2023 were invited. With the European Headache Federation consensus statement on effective treatment of acute migraine medication in mind, we evaluated the effectiveness of acute treatments to treat the most recent migraine attack (any severity, ≤3 months prior) defined as: 1) pain freedom or pain relief within 2h, lasting at least 24h, 2) no or minimal migraine accompanying symptoms within 2h, 3) no side effects. As return to normal function is a goal of acute treatment and important to patients we asked respondents about their ability to return to normal function at 2h after taking medication.
Results: Of the 144,323 people invited, 58,317 (40%) responded, of which 50,857 reported having a migraine diagnosis from a physician (migraine population (MP), 83% women, mean age 50.0). Of the 38,981 people in the MP treating a migraine attack

within 3 months, only 14,021 (36%) reported effective treatment, with only 8,422 (60%) of these returning to normal function within 2h

Conclusion: Only about 1 in 5 people treating a migraine attack achieved both effective treatment and the ability to return to normal function at 2h, indicating that the majority of patients using acute treatments still experience a significant burden from migraine and could benefit from strategies for treatment optimization.

P056

Migraine related sick leave among people with effective treatment of migraine: Results from DREAM, a nationwide population study

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Objective: What is the impact of acute migraine treatment on days of sick leave reported by patients in Denmark?

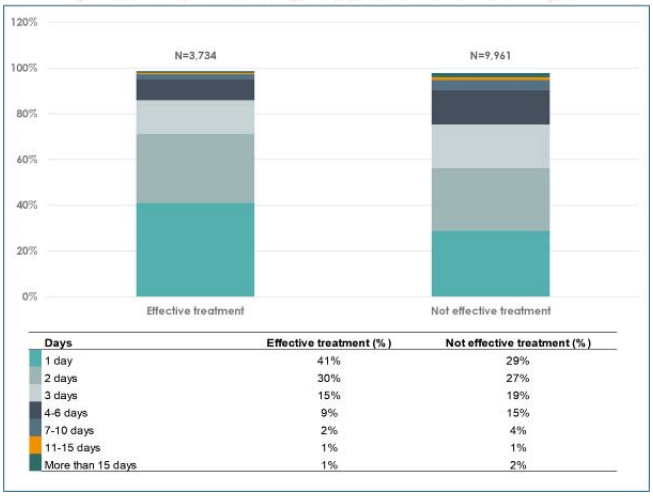
Methods: In the DREAM (Danish REgistry Analyses of Migraine) study an electronic survey was sent to all Danish residents ≥18 years having redeemed a triptan prescription or being diagnosed with migraine (ICD-10: G43) between Jan 2021 – Dec 2023. With the European Headache Federation consensus statement on effective treatment of acute migraine medication in mind, we defined effective acute treatment of the most recent migraine attack (any severity, ≤3 months prior) as: 1) pain freedom or pain relief within 2h, lasting at least 24h, 2) no or minimal migraine accompanying symptoms within 2h, 3) no side effects. Self-reported days of sick leave due to migraine were analysed for people with migraine who are employed or in education stratified by effective or not effective treatment of their most recent migraine attack.

Results: Among 58,317 respondents there were 26,472 people (84% women) with a migraine diagnosis, who were employed or in education, and had treated a migraine attack within 3 months. Of these, 13,695 (52%) had at least one day of sick leave due to migraine during that time. Of the 9,550 people with effective treatment, 3,734 (39%) reported at least one day of sick leave due to migraine, and of 16,922 people without effective treatment, 9,961 (59%) reported at least one day of sick leave due to migraine, p<0.001. The distribution of days of sick leave of people with and without effective treatment is presented in Figure 1.

Conclusion: People with migraine reporting effective treatment of their most recent migraine attack had significantly fewer days of migraine related sick leave than people without effective treatment, suggesting an important benefit of optimized treatment to patients and society. However, the substantial migraine related sick leave reported by people with effective treatment warrants reconsideration of patients" treatment goals.

Fig. 1

Figure 1: Distribution of days of sick leave due to migraine for people with and without effective treatment of migraine



Days	Effective treatment (%)	Not effective treatment (%)
1 day	41%	29%
2 days	30%	27%
3 days	15%	19%
4-6 days	9%	15%
7-10 days	2%	4%
11-15 days	1%	1%
More than 15 days	1%	2%

P057

Burden of self-reported migraine in the Pfizer Ireland workforce – A cross-sectional study

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Objective: To estimate the prevalence and evaluate the impact of migraine on workplace productivity among employees of Pfizer Ireland.

Methods: An online anonymous survey was administered to all Pfizer Ireland employees between February and March 2025 to collect data on demographics, migraine history and work productivity. Participants with self-reported migraine were assessed using the ID-Migraine™ screening tool (MST) and further completed the Work Productivity and Activity Impairment (WPAI-migraine) questionnaire to quantify productivity impact of migraine.

Results: Of 6,517 Pfizer Ireland employees, 1,131 (17.4%) participants completed the survey, with 51.4% being male, and 56.3% being 30 to 49 years of age. The prevalence of self-reported migraine was 33.1%

(*N*=374), and 38.6% (*N*=437) based on the MST. Episodic and chronic migraine were reported by 71.4% and 7.5% participants with self-reported migraine, respectively. Amongst those with self-reported migraine, 160 (42.8%) participants indicated that their migraine was self-diagnosed, while 214 (57.2%) stated that a clinician made the diagnosis. Work time loss (absenteeism) due to migraine was reported by 37/345 (10.7%) of participants with self-reported migraine, resulting in mean of 17.5% (SD 23.0) of time missed/week; impairment while working (presenteeism) due to migraine was reported by 185/345 (53.6%) resulting in a mean of 28.4% (SD 17.2) of work productivity impairment/week. Overall, participants with self-reported migraine had a mean work productivity loss and activity loss in the past 7 days of 16.1% (SD 20.4) and 26.4% (SD 30.4), respectively.

Conclusion: The migraine prevalence among Pfizer employees was higher than the observed globally, probably as employees with migraine felt more engaged to participate in the study. Migraine impairs work productivity for most migraine sufferers, highlighting a need for support and treatment optimization, benefiting both individuals and the organization.

P058

Chronic migraine progression and persistence: Results from the chronic migraine epidemiology and outcomes (CaMEO) study

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Objective: Migraine progression is typically defined by the episodic (EM) to chronic migraine (CM) transition, precluding progression of CM. Using the CaMEO study, we evaluated 2 different definitions of migraine disease progression, based on changes in either monthly headache days (MHDs) or in Migraine Disability Assessment Scale (MIDAS) scores.

Methods: The CaMEO Study (NCT01648530) was a longitudinal web-based survey, evaluating migraine disease state every 3 months for up to 1 year in a representative sample of people with migraine (US population). Eligible respondents met an ICHD-3 definition for CM at baseline and provided assessments at baseline, 3, 6, 9 and/or 12 months. Disease progression was defined as an increase of ≥5 MHDs or ≥5 MIDAS points from baseline to any follow-up timepoint; persistence required maintaining progression at subsequent timepoints for ≥6 months. External validators included the Migraine Specific Quality of Life Questionnaire (MSQv2.1), a depression screener (PHQ-9), and an anxiety screener (GAD-7).

Results: 342 eligible respondents with CM had a baseline median of 19.3 (Q1-15.9, Q3-21.7) MHDs and a median MIDAS score of 30.0 (Q1-13, Q3-65). 16.4% (n=56) of respondents progressed based on an increase of ≥5 MHDs, and 27.2% (n=93) based on an increase of ≥5 MIDAS points. In total, 34.5% (n=118) of respondents progressed and 7.3% (n=25) progressed and persisted based on ≥1 of these 2 disease progression definitions. The subgroup with disease progression demonstrated lower quality of life on MSQv.2.1 and higher rates of depression (PHQ-9) and anxiety symptoms (GAD-7).

Conclusion: CM is a sometimes-progressive disorder. Novel definitions of progression characterize the disease state dynamics of people with CM, underscoring the need for CM treatment optimization.

P059

Real-world evaluation of rimegepant usage and switch patterns in a single tertiary headache center

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Objective: To characterize real-world usage and switch patterns of acute and preventive rimegepant at Jefferson Headache Center (JHC).

Methods: A retrospective study (IRB# iRISID-2024-1646) was conducted at JHC. Patients visit data and medication order data were extracted and cleaned from the electronic health records. Adult migraine patients who were prescribed rimegepant between January 2020 and May 2025 were included. Non-JHC orders were excluded. Data are presented descriptively.

Results: Among 2,786 patients receiving rimegepant prescriptions, 8,808 orders were documented (Table 1). Figure 1 illustrates the monthly utilization of rimegepant with/without onabotulinumtoxinA or other CGRP mAbs. The majority (91.1%, n=2,541) received acute rimegepant, with 45.1% having concurrent preventive CGRP mAbs. Of 540 preventive rimegepant users, 316 were CGRP-naïve at JHC and 337 remained on rimegepant at last JHC visits. 295 patients had prescriptions for both acute and preventive rimegepant. Preventive switches involving rimegepant occurred in 322 patients: 236 switched from other CGRP preventives to rimegepant, 218

switched from rimegepant to another CGRP preventive, and 38 experienced >1 rimegepant switches to/from others. When switching to rimegepant, prior CGRP preventive use duration was a median of 258 (123–516) days, with rimegepant use of 181 (87–315) days. Among those switches, galcanezumab (93) and fremanezumab (60) were the most common immediate prior CGRP preventives. When switching from rimegepant, rimegepant use duration was a median of 123 (70–255) days, with the next CGRP preventive use of 234 (154–429) days. Among those, there were 80 switches to atogepant and 59 to fremanezumab.

Conclusion: Real-world data demonstrate rimegepant's versatility as both acute and preventive therapy. Its dual indication enables flexible dosing strategies, serving as a preventive for CGRP-naïve patients and as an effective CGRP preventive option within treatment algorithms.

Fig. 1

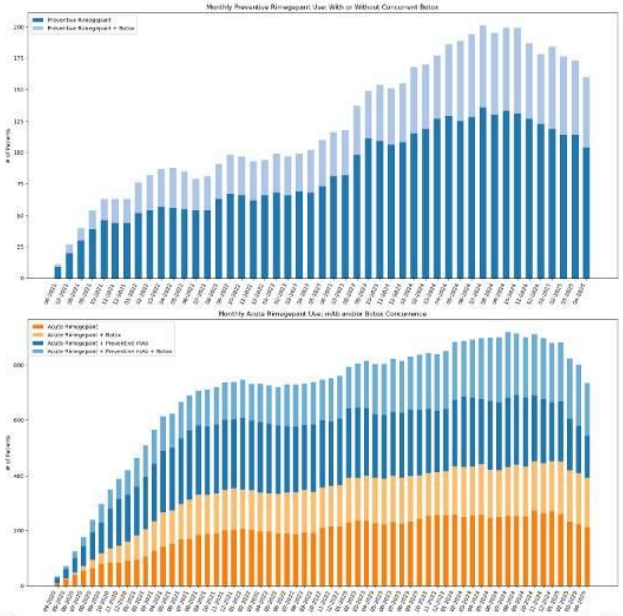


Figure 1. A) Preventive rimegepant monthly utilization on rimegepant alone (dark blue) and with concurrent OnabotulinumtoxinA (light blue) **B)** Acute rimegepant monthly utilization on rimegepant alone (orange), with concurrent Botox only (peach), with a concurrent CGRP mAb (dark blue), or with both a preventive mAb and Botox (light blue).

Fig. 2

Table 1. Baseline demographics and comorbidities of patients prescribed rimegepant

Demographics	All patients	Acute-only (PRN)	Preventive-only (EOD)	Acute & Preventive
# of patients (%)	2,786	2,246 (80.6%)	245 (8.8%)	295 (10.6%)
Age	46.0 ± 14.7	46.3 ± 14.7	44.1 ± 15.4	45.5 ± 14.4
Female	83.9%	83.8%	83.3%	84.8%
BMI at index date	28.3 ± 7.1	28.4 ± 7.3	27.7 ± 6.7	27.9 ± 6.6
Prior CGRP mAb exposure at JHC	51.7%	55.8%	28.6%	40.2%
Headache Diagnoses[a]				
History of chronic migraine	89.6%	91.6%	75.5%	86.5%
History of MOH	11.6%	11.8%	6.5%	14.2%
History of other headache diagnosis (excluding MOH)	21.4%	21.0%	23.7%	22.0%
Comorbidities[a]				
Anxiety/depression	34.1%	35.2%	23.3%	34.8%
Chronic pain	13.2%	12.7%	14.3%	16.6%
Hypertension	9.2%	9.6%	6.5%	7.8%
Obesity	9.7%	10.3%	4.9%	9.5%
Obstructive sleep apnea	2.5%	2.5%	2.4%	2.0%

[a]Based on visit diagnosis (≥2 occurrences).

P060

Clinical outcomes in the contemporary prospective understanding of migraine real-world evidence (CAPTURE) study

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Objective: To evaluate longitudinal changes in monthly headache days (MHDs), monthly migraine days (MMDs), and acute medication use among individuals with migraine in the ContemporAry ProspecTive Understanding of Migraine Real-world Evidence (CAPTURE) study.

Methods: CAPTURE is a 2-year, international, prospective, longitudinal, observational study of disease burden and treatment patterns among patients with migraine currently consulting at specialty clinics. Participants aged ≥18 years with a migraine diagnosis for ≥1 year who used ≥1 migraine medication and experienced ≥4 MHDs in the 3 months before screening were stratified by headache frequency during 30-day screening: 4–<8 MHDs (Cohort 1), 8–<15 MHDs (Cohort 2), and ≥15 MHDs (Cohort 3). Change from baseline was assessed using a mixed-effects model for repeated measures.

Results: The population (N=555; Cohort 1=139, Cohort 2=251, Cohort 3=165) had a mean age of 41.4-43.0 years and was >83% female and >94% White. Over the 12-month period, participants in Cohorts 2 and 3 showed substantial reductions in MHDs, MMDs, and acute medication use days. The percentages of participants who were in the same cohort at baseline and Month 12 were 34% (17/50) for Cohort 1, 41.4% (41/99) for Cohort 2, and 55% (33/60) for Cohort 3. Many (36% [18/50]) Cohort 1 participants experienced <4 MHDs at Month 12.

Conclusion: The CAPTURE study demonstrates improved migraine frequency and reduced acute medication use over 12 months, particularly among participants with higher baseline headache frequencies. These findings underscore the clinical value of longitudinal real-world observational data in

guiding therapeutic expectations and management strategies for migraine.

Fig. 1

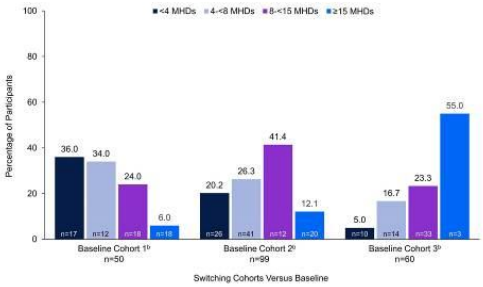
Change in Monthly Migraine Days From Baseline Through Month 12 in the CAPTURE Study (N=555)[a]

	n	Baseline Mean (SD)	Visit Mean (SD)	Change From Baseline[b]		
				Mean (SD)	LS Mean (SE)	95% CI
4 to <8 MHDs						
Baseline	139	4.08 (1.929)	—	—	—	—
Month 3	97	3.99 (2.000)	4.07 (3.359)	0.07 (2.961)	−0.02 (0.397)	−0.80, 0.77
Month 6	71	3.88 (1.981)	3.83 (3.392)	−0.06 (3.494)	−0.29 (0.444)	−1.18, 0.59
Month 9	67	3.89 (1.927)	3.82 (3.424)	−0.08 (3.356)	−0.12 (0.477)	−1.07, 0.83
Month 12	50	3.80 (1.895)	3.51 (3.072)	−0.30 (3.250)	−0.19 (0.512)	−1.21, 0.82
8 to <15 MHDs						
Baseline	251	7.67 (2.992)	—	—	—	—
Month 3	180	7.71 (2.874)	7.45 (5.316)	−0.26 (5.012)	−0.80 (0.534)	−1.85, 0.26
Month 6	139	7.50 (2.782)	6.29 (4.525)	−1.21 (4.447)	−1.42 (0.544)	−2.49, −0.34
Month 9	116	7.89 (2.802)	6.39 (4.796)	−1.51 (4.831)	−1.70 (0.555)	−2.79, −0.60
Month 12	99	8.12 (2.559)	6.66 (4.552)	−1.45 (4.513)	−1.78 (0.554)	−2.88, −0.69
≥15 MHDs						
Baseline	165	16.29 (6.572)	—	—	—	—
Month 3	120	16.11 (6.255)	13.16 (7.402)	−2.95 (6.561)	−2.48 (0.867)	−4.19, −0.77
Month 6	91	16.03 (6.504)	13.03 (7.863)	−3.00 (7.276)	−1.93 (0.931)	−3.77, −0.09
Month 9	81	15.55 (6.201)	12.82 (7.923)	−2.73 (7.239)	−2.47 (0.965)	−4.38, −0.56
Month 12	60	15.16 (6.600)	12.20 (8.092)	−2.96 (7.565)	−2.20 (1.026)	−4.23, −0.17

CAPTURE=ContemporAry ProspecTive Understanding of Migraine Real-world Evidence; SD=standard deviation; MHD=monthly headache day; LS=least squares; SE=standard error; CI=confidence interval.
[a]Among participants who met inclusion/exclusion criteria with evaluable MHD data at screening and enrollment for ≥12 months or completion of the Month 12 visit.
[b]Assessed using a mixed-effects model for repeated measures, with baseline score, sex, age, and baseline weight as a covariate, visit as fixed factors, and baseline-by-visit as interaction terms, with an unstructured covariance matrix.

Fig. 2

Switching Between Cohorts From Baseline to Month 12 in the CAPTURE Study (N=555)[a]



CAPTURE=ContemporAry ProspecTive Understanding of Migraine Real-world Evidence; MHD=monthly headache day.
[a]Among participants who met inclusion/exclusion criteria with evaluable MHD data at screening and enrollment for ≥12 months or completion of the Month 12 visit.
[b]Participants missing due to inevaluable electronic diary data or non-completion of electronic diary data for ≥15 days of the 30-day assessment period: Cohort 1 (n=89), Cohort 2 (n=152), Cohort 3 (n=105).

P061

Fremanezumab helps in long-term migraine prevention in children – Real-world evidence

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Objective: There is a significant need for effective and well-tolerated medicines in the prevention of migraine in children. The purpose of this retrospective study is to evaluate the safety and effectiveness of fremanezumab in real world setting.

Methods: The study population consists of 18 patients who had participated in a clinical trial investigating the safety, tolerability, and efficacy of fremanezumab, and who demonstrated clinical benefit. Effectiveness was evaluated using the pedMIDAS disability scale and changes in the number of headache days. Safety was assessed through adverse effectsand changes in laboratory tests (serum chemistry, hematology, and coagulation) or ECG. A physical examination was performed at every third injection.

Results: The mean age of participants was 14.6 years (11.7 to 17.7 years). Of these, ten were females. Half of the children had episodic migraine, and the remaining with chronic migraine. The number of fremanezumab injections received varied from 12 to 36, with monthly injections of 225mg. AEs were reported in 13 patients (72%). These included redness, swelling or pain at the injection site and were not considered as clinically significant. No severe adverse effects were reported. No clinically significant findings were noted in ECGs, laboratory values, or during physical examinations. Two participants discontinued the treatment due to lack of efficacy. Quality of life improved by at least one pedMIDAS grade in 14 participants, deteriorated in one, and remained unchanged in 3 participants. Mean total PedMIDAS-score changed from 67.9 at baseline to 50.6 at follow-up (p=0.134) and the mean reduction was 17.3 points. The mean number of headache decreased from 15.3 to 9.8 days in the latest recording (p=0.027), mean reduction of 5.5 days.

Conclusion: Fremanezumab showed a favourable safety profile and was associated with clinically meaningful reductions in headache frequency in children and adolescents with migraine in a real-world setting.

P062

False non-responders to anti-CGRP monoclonal antibodies: A real-world analysis beyond migraine frequency reduction

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Objective: To explore clinical outcomes in patients with migraine treated with anti-CGRP monoclonal antibodies (mAbs) who did not meet formal response criteria at six months but continued therapy, and to assess whether alternative markers of benefit support treatment continuation beyond frequency reduction.

Methods: This was a retrospective observational study of prospectively collected data from a multicentre headache unit. Patients with migraine who initiated anti-CGRP mAbs and, at six months, failed to meet institutional reimbursement criteria (≥50% reduction in monthly migraine days [MMD], or ≥30% MMD reduction plus ≥1-point HIT-6 improvement), but continued treatment, were included. Outcomes included headache frequency,

intensity, analgesic use, disability, and patient-reported global impression of change, assessed through diaries and validated questionnaires.

Results: Of 415 patients starting mAbs, 106 (25.5%) were non-responders at month 6 but continued treatment. Among them, 91.5% showed improvement in at least one domain. Common benefits included MIDAS improvement (60.2%), PGIC ≥5 (54.5%), HIT-6 reduction (44.1%), resolution of medication overuse headache (46.4%), conversion from chronic to episodic migraine (41.2%), and ≥50% reduction in severe intensity days (29.3%). Among 82 patients who continued to month 12, 18.3% eventually met reimbursement criteria, suggesting delayed benefit.

Conclusion: A significant proportion of patients classified as non-responders at six months experience clinically meaningful improvements in other domains. These findings underscore the importance of a multidimensional assessment of treatment response to avoid premature discontinuation of potentially beneficial therapies.

Fig. 1

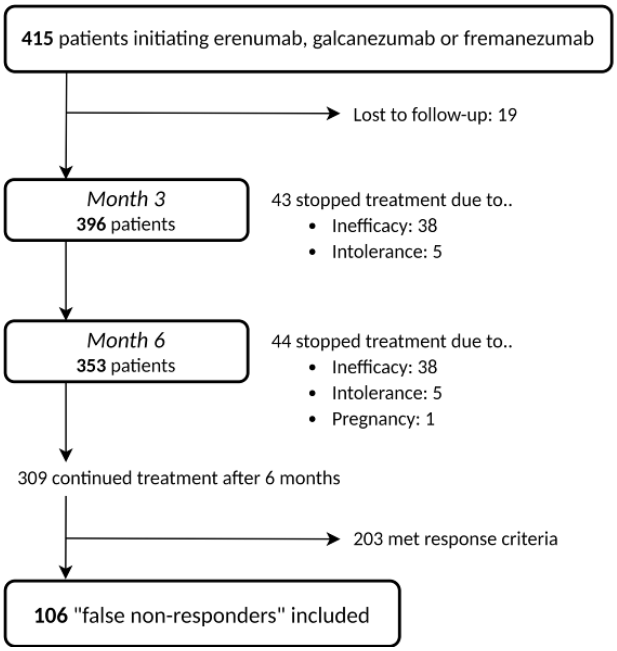
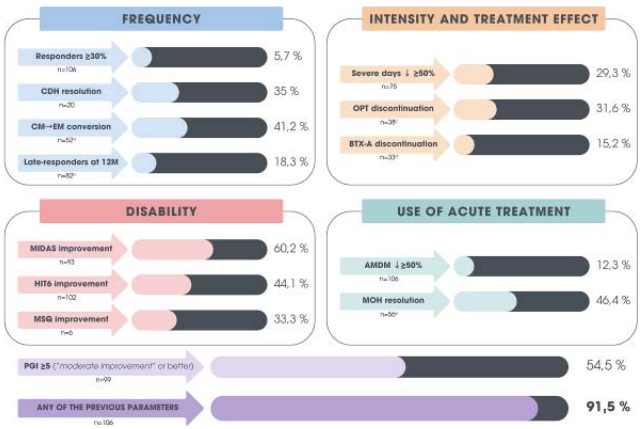


Fig. 2



P063

The PopHEAD study: Prevalence of headache disorders in Norway, results from a population based cross-sectional study

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Objective: Reliable prevalence estimates of headache disorders are essential for public health planning. Despite previous large-scale studies, there is a lack of validated and up-to-date prevalence estimates from population-representative populations in Europe. Here, we aimed to estimate the one-year prevalence of the major headache disorders in Norway using a validated diagnostic tool.

Methods: PopHEAD is a population-based Norwegian cross-sectional study. A random sample of 28,753 individuals aged 18–70 years was invited to complete a digital version of the Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire, adapted and translated into Norwegian and later validated. Headache diagnoses were made using a standardized algorithm based on International Classification of Headache Disorders (ICHD-3) criteria. Prevalence estimates were calculated as crude proportions with 95% confidence intervals and sequentially adjusted for age and sex, measurement error and selection bias.

Results: A total of 8,265 participants (3,344 men and 4,921 women; mean age 47.3 years) responded. The crude one-year prevalence was 29.6% for migraine (36.5% in women, 19.4% in men), 52.7% for Tension type headache (TTH) (51.4% in women, 54.6% in men), and 5.1% for medication overuse headache (MOH) (6.5% in women, 3.1% in men). After adjusting

for age, sex, measurement error, and selection bias, the final estimated prevalence was 20.3% for migraine, 47.9% for TTH, and 5.9% for MOH. Migraine prevalence estimates were higher among participants with lower income and education, while TTH estimates were higher in those with higher socioeconomic status. MOH prevalence was highest in participants aged 26–45 and those with lower education.

Conclusion: The PopHEAD study provides updated, validated and bias-adjusted prevalence estimates for migraine, TTH and MOH in the Norwegian adult population. These data may inform health resource allocation for headache management in similar populations.

P064

Identifying risk markers for high likelihood of triptan-refractory migraine among first-time users: A real-world retrospective cohort study

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Objective: The European Headache Federation defines triptan-refractory status as failure of ≥3 triptans, including ≥1 subcutaneous formulation. We aimed to identify patients with high probability of triptan-refractory migraine, and to assess clinical features that may have predicted treatment refractoriness.

Methods: This retrospective cohort study utilized deidentified data from the second-largest healthcare provider in Israel and identified members aged ≥21 years with first triptan dispensation during 2012-2022. Users were classified as "presumed triptan-refractory migraine" if they used and discontinued ≥3 different generic triptan ingredients. Delivery system was not regarded due to the low prevalence of use with subcutaneous formulations in Israel. Conversely, users were classified as "presumed non triptan-refractory migraine" if they used 1/2 generic ingredients regardless of discontinuation status, or they used 3 generic ingredients without discontinuation. Stepwise logistic regression was used to identify predicting features for triptan-refractory migraine.

Results: We identified 1303 (3%) patients with presumed triptan-refractory migraine and 39994 (97%) with presumed triptan non-refractory migraine. Compared to individuals aged 26-35 years, younger patients (20-25 years) had a 30% higher probability of experiencing triptan refractory migraine. Conversely, older patients showed decreased probability: 30% lower among patients aged 46-55 years and 64% lower among patients aged 56 years and older. Female sex, medium-high socioeconomic status, prior diagnosis of irritable bowel syndrome and overactive bladder were associated with an 19%, 35%, 33% and 55% higher probability of triptan refractory migraine, respectively.

Conclusion: This study estimate that approximately 3% of treated patients develop triptan-refractory migraine with a predominance of young females from medium-high socioeconomic status. Further studies are warranted

P065

Triptans treatment patterns among first-time users: A real-world retrospective cohort study

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Objective: Migraine is a prevalent and debilitating neurological disorder with substantial impact on an individual quality of life and on the healthcare system. Triptans have been established as the standard of care for moderate-to-severe acute migraines for over two decades. This study aims to evaluate real-world triptan treatment patterns.

Methods: This retrospective cohort study utilized deidentified data from the second-largest healthcare provider in Israel and identified members aged 21 years or older who had a first triptan dispensation between 2012 and 2022 (i.e., index-date). The end of follow-up was December 2023. Triptan discontinuation was defined as the absence of additional dispensations between the last dispensation date (plus 90 days) and the end of follow-up, except where treatment cessation was due to contraindications. Time to discontinuation was analyzed using the Kaplan-Meier method.

Results: We identified 41,297 adults with a first triptan dispensation (median age at index-date: 38.4 years [inter-quartile range: 28.2,48.0], 75.6% females). Among those, 28,920 (70%) discontinued their triptan use with median time to discontinuation of 7.8 months (95% CI: 7.2-8.4). After excluding 19904 (48%) with only a single dispensation, 12,185 out of 21,393 individuals (56.9%) discontinued use, with an overall median treatment time of 4.6 years (95% CI: 4.5-4.7). Approximately 25% of triptan users purchased more than one generic ingredient and 14.8% more than two.

Conclusion: This study indicates a high discontinuation rate. This may suggest potentially suboptimal response or tolerability issues with the current standard of care.

P066

Do migraine and tension-type headache affect cardiac structure and function? Findings from the HUNT population-based study

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Objective: To evaluate whether primary headache disorders, especially migraine and tension-type headache (TTH), are associated with alterations in cardiac structure and function.
Methods: We analyzed data from the HUNT4 study (2017-2019), a population-based cohort study in Norway. Of 5,752 individuals aged ≥20 years randomly selected for echocardiography, 2,039 participants with complete headache and echocardiographic data were included. Individuals with prior stroke, myocardial infarction, or heart failure were excluded. Headache types were classified using validated questionnaires. Cardiac structure and function were assessed by echocardiography. Associations were analyzed using adjusted linear regression models.
Results: Among 2,039 participants, two third were women and under 65 years. Compared to those without headache, individuals with migraine (n=150) and TTH (n=286) had 4-15% and 4-8% smaller cardiac volumes, respectively. Adjusted β-coefficients for left ventricular end diastolic volume were -2.62 (95% CI, -7.01 to 1.76) for migraine, -4.04 (95% CI, -6.87 to -1.20) for TTH, and -1.29 (95% CI -5.23 to 2.63) for unclassified headaches. Stroke volume was numerically lower in migraine (-1.56 ml) and TTH (-1.76 ml), with greater but non-significant reductions in men (-2.48 ml for migraine; -3.46 ml for TTH). Diastolic early mitral inflow (E-wave) was lower in the migraine (-2.24, 95% CI -5.24 to 0.76), but this also did not reach statistical significance. Myocardial and tricuspid regurgitation velocities did not differ between the headache groups.
Conclusion: Our findings suggest a potential association between TTH and subclinical changes in left ventricular volumes. Further studies are needed to confirm these observations and explore their clinical relevance.

P067

Tolerability sof witch from erenumab to fremanezumab in adults with chronic migraine

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Objective: Although erenumab and fremanezumab are effective for migraine prevention, it remains unclear whether patients who experience adverse events (AEs) on erenumab can tolerate fremanezumab. Erenumab targets the calcitonin gene-related peptide (CGRP) receptor, while fremanezumab targets the ligand. Despite this distinction, switching treatment due to AEs is often not reimbursed, based on the assumption of class-wide intolerance. This study evaluated tolerability of switching from erenumab to fremanezumab in patients with chronic migraine who experienced AEs on erenumab.
Methods: We analyzed data from patients with chronic migraine who discontinued erenumab due to AEs and subsequently received at least three months of fremanezumab. AEs were recorded before and after switching.
Results: In total, 94 patients (median age: 50 years) were included. Hereof, only 29 (31%) patients experienced treatment-emergent AEs after switching. Constipation was the most common AEs on erenumab (n=74, 79%), which reduced to only 12% (n=9) of patients after switching to fremanezumab. No patients discontinued fremanezumab during the study period due to AEs.
Conclusion: Switching from erenumab to fremanezumab due to adverse events was well-tolerated, particularly among patients with erenumab-induced constipation. These findings support the clinical utility of switching therapies based on tolerability issues and highlight the importance of individualized strategies in migraine management.

P068

Real-world effectiveness of eptinezumab in migraine patients with prior preventive migraine treatment failures: Preliminary results from a general neurology unit in Greece

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Objective: To evaluate the real-world effectiveness of eptinezumab for migraine prevention in a hospital-based setting.

Methods: This retrospective observational analysis included 25 adult patients with migraine who received at least one dose of eptinezumab 100 mg. Effectiveness was assessed by changes in Monthly Migraine Days (MMDs), ≥50% and ≥75% Migraine Responder Rates (MRRs), reduction in average pain severity, resolution of the Most Bothersome Symptom (MBS), days of acute medication use, and Patient-Reported Outcomes (HIT-6 and MIDAS).

Results: Patients had a mean migraine history of 26 years, 10 MMDs at baseline, average pain severity of 8/10, and used acute medication on 9 days/month. Prior treatments included traditional preventives (68%), botulinum toxin (56%), while 60% were anti-CGRP naïve. Mean baseline HIT-6 and MIDAS scores were 65 and 77, respectively, indicating severe impact and disability. By day 15, 96% of patients reported clinical improvement. At day 30, 92% experienced significant improvement or resolution of their MBS, with pain being the most frequently reported. Mean MMDs decreased from 10 to 2, and pain severity from 8 to 4. At 3 months, benefits were sustained: patients reported 3 MMDs, pain severity of 4/10, and acute medication use on 3 days/month. Overall, 88% of patients achieved a ≥50% response at 3 months.

Conclusion: Eptinezumab demonstrated rapid and sustained effectiveness in reducing migraine frequency, severity, and associated disability in a real-world clinical setting. Improvements were reported by the majority of patients within 15 days of treatment initiation and were maintained over the first 12 weeks.

P069

Final Italian analysis of the PEARL study: 24 months of fremanezumab treatment on quality-of-life outcomes

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Objective: The impact of migraine extends beyond headache frequency, affecting various domains of an individual"s life, including their ability to work, socialize, and perform daily living activities, particularly for those with chronic migraine (CM). In this sub-analysis of the 24-month, prospective, observational Pan-European Real Life study (PEARL; EUPAS35111), we assessed the effectiveness of fremanezumab on quality-of-life outcomes in a cohort of adult participants with episodic migraine (EM) or CM treated in Italy according to routine clinical practice.

Methods: Participants were enrolled across 30 headache centers in Italy. Endpoints included: the proportion of participants reaching ≥50% reduction from baseline in Migraine Disability Assessment (MIDAS) score, mean change from baseline in MIDAS and 6-Item Headache Impact Test (HIT-6) scores, all measured at Months 12 and 24, and the proportion of participants with CM reverting to EM by Month 24.

Results: In total, 354 participants were enrolled from Italian centers and included in the effectiveness analysis. In participants with data available, 75.0% (EM, 78.7%; CM, 73.2%) at Month 12 (n=288) and 66.7% (EM, 73.3%; CM, 63.3%) at Month 24 (n=45) reached a ≥50% reduction in MIDAS score. Improvements in MIDAS scores were observed at Month 12 (mean change from baseline −68.4 [EM, −52.0; CM, −76.4]), and at Month 24 (mean change from baseline −78.5 [EM, −63.0; CM, −86.0]), both in participants with EM and CM. Impact of headache, assessed by HIT-6 score, reduced at Month 12 (mean change from baseline −11.1 [EM, −10.7; CM, −11.2]), and Month 24 (mean change from baseline −13.0 [EM, −13.3; CM, −12.9]). In total, 71.9% of participants with CM at baseline had reverted to EM at Month 12 (0–7 monthly migraine days [MMD], 53.1%; 8–14 MMD; 18.8%), and by Month 24, the proportion was 86.7% (0–7 MMD, 66.7%; 8–14 MMD; 20.0%).

Conclusion: Fremanezumab treatment was associated with improvements in MIDAS and HIT-6 scores over 24 months in participants with EM and CM.

P070

The prevalence and characteristics of interictal headaches in people with cluster headache

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Objective: Cluster headache (CH) patients often report interictal headaches (IH). Due to relatively limited knowledge on IH, we aimed to explore their prevalence and characteristics in CH.

Methods: All 912 CH patients in our database were invited to complete a single e-survey on their CH attacks (CHA) and, if present, IH (headache between CHA, not better explained by another ICHD-3 diagnosis). We distinguished 2 IH patterns: continuous pain (shadow headache; SH) and short-lasting pain (shadow attack; SA). Participants rated impact on quality of life (QoL; 10-point scale) for each headache subtype. Descriptive statistics and logistic regression were performed.

Results: 529 patients completed the survey. 275 (53%) reported one or both IH types (SH: n=134 [25%]; SA: n=191 [36%]). IH prevalence was higher in women (β=1.53; 95% CI 1.00-2.32; *P*=.05) and those with self-reported comorbid primary headaches (β=3.57; 95% CI 2.20-5.93; *P*<.001), and lower with increasing age (β=0.971; 95% CI 0.96-0.987; *P*<.001). Headache characteristics differed in SH and SA vs CHA (Fig. 1). SH and SA were more often bilateral (38% & 37% vs 1%), frontal and occipital (44% & 56% vs 24%; 43% & 55% vs 14%) instead of orbital (49% & 35% vs 82%), all *P*<.001. SH and SA were dull/nagging (46% & 43%) rather than stabbing in CHA (87%), less severe (NRS 5 [IQR 4-6] vs 9 [9-10]) and less often accompanied by autonomic symptoms and restlessness (28% & 29% vs 96%; 33% & 33% vs 92%), all *P*<.001. SH and SA impacted QoL less than CHA (5 [IQR 3-7] and 4 [2-6] vs 8 [6-9]). In the SH group, 25 (19%) used analgesics ≥10 days/month (excluding triptans taken for CHA).

Conclusion: The presentation of IH is less distinct than CHA, though some patterns were found. While SH may indicate medication overuse headache in some, in our cohort most used analgesics <10 days/month. We propose both IH forms are part of the CH phenotype. The high prevalence and moderate impact on QoL highlight the need to recognize IH. Our findings can aid physicians to identify IH.

P071

Evaluation of crystal-clear days in migraine patients receiving CGRP monoclonal antibodies

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Objective: To identify the number of crystal-clear days (CCD; defined as "days without headache and having minimal or no migraine symptoms") in chronic migraine (CM) patients using CGRP monoclonal antibodies (CGRP-mAbs) and to observe changes during the treatment period.

Methods: Out of 378 migraine patients referred to the Headache Center at the Department of Neurology, University of Campania "Luigi Vanvitelli," between February and August 2023, 277 CM patients were identified. Data from a six-month follow-up were analyzed. All patients underwent extensive interviews to examine clinical parameters of disease severity, such as migraine days per month (MMD), average migraine pain intensity, attack duration, and the number of CCD per month

Results: Among the 277 CM patients, 222 (80.1%) did not present any CCD per month. After the first, third, and sixth months of treatment, a significant reduction in patients without CCD was observed (34.30%, 25.27%, and 21.66% respectively, compared to 80.14% at baseline) (p<0.001). This was paralleled by a reduction in the frequency of attacks (10.78, 8.39, and 7.44 MMD respectively, compared to 22.08 at baseline) (p<0.001), pain intensity (6.54, 5.82, and 5.30 on the NRS respectively, compared to 9.13 at baseline) (p<0.001), and attack duration (7.93, 6.52, and 6.30 hours respectively, compared to 17.60 at baseline) (p<0.001).

Conclusion: CM is a debilitating neurological disorder that affects 1% to 2% of the globalpopulation. Interictally, migraineurs have an enduring predisposition to attacks and abnormalities in cortical processing, supporting the hypothesis that migraine is a chronic disorder with episodic manifestations. Moreover, migraine-free days do not necessarily indicate symptom-free days.Treatment with CGRP-mAbs resulted in a dramatic improvement not only in the frequency of attacks but also in migraine symptoms during the interictal period. Further studies are needed to investigate predictive factors of this response.

P072

Treatment patterns in the ContemporAry ProspecTive Understanding of migraine Real-world Evidence (CAPTURE) study

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Objective: To describe patterns of medication use for migraine over the first 12 months of the ContemporAry ProspecTive Understanding of Migraine Real-world Evidence (CAPTURE) study.
Methods: CAPTURE is a 2-year, international, prospective, longitudinal, observational study of disease burden and treatment patterns among patients with migraine currently consulting at specialty clinics. Participants aged ≥18 years with a migraine diagnosis for ≥1 year who used ≥1 migraine medication and experienced ≥4 MHDs in the 3 months before screening were stratified by headache frequency during 30-day screening: 4–<8 MHDs (Cohort 1), 8–<15 MHDs (Cohort 2), and ≥15 MHDs (Cohort 3). Assessments were current migraine treatment(s)/duration, new treatment(s), changes in current treatment, switching (initial-subsequent/monotherapy-combination therapy), and acute medication overuse.
Results: The population (N=555; Cohort 1=139, Cohort 2=251, Cohort 3=165) was aged 41.4-43.0 years, >83% female, and >94% White. The percentage of participants who switched from initial treatment to subsequent treatment and from monotherapy to combination therapy was generally low (<8%), being higher for acute medications (≤7.9%) than for preventive medications (≤6.0%). A substantial decrease from baseline in the percentage of overusers at Month 12 was observed in Cohorts 2 and 3: 19.1% to 8.1%, and 63.0% to 31.7%, respectively. Overuse occurred in <6% of participants in Cohort 1.
Conclusion: Through Month 12, acute medication overuse decreased in both Cohorts 2 and 3, being more marked in the latter. Cohort 2 switched more frequently preventive treatments. These snapshot findings suggest that the completed CAPTURE study may provide novel insights into migraine treatment patterns, helping to characterize migraine burden.

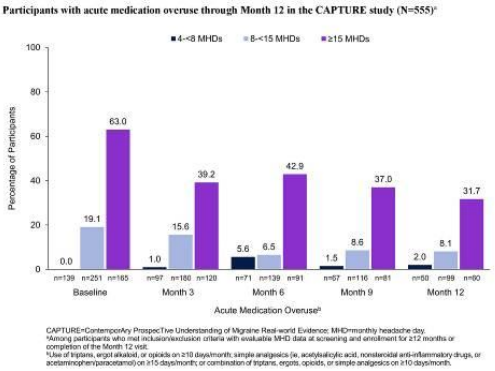
Fig. 1

Switching of initial migraine treatments among CAPTURE participants at Month 6 and Month 12 (N=555)[a]

	4–<8 MHDs N=139	8–<15 MHDs N=251	≥15 MHDs N=165
Acute, n (%)			
Initial treatment to subsequent treatment			
Month 6	5 (3.6)	8 (3.2)	8 (4.8)
Month 12	5 (3.6)	10 (4.0)	13 (7.9)
Monotherapy to combination therapies			
Month 6	5 (3.6)	18 (7.2)	6 (3.6)
Month 12	6 (4.3)	19 (7.6)	11 (6.7)
Preventive, n (%)			
Initial treatment to subsequent treatment			
Month 6	3 (2.2)	9 (3.6)	7 (4.2)
Month 12	4 (2.9)	15 (6.0)	8 (4.8)
Monotherapy to combination therapies			
Month 6	1 (0.7)	7 (2.8)	3 (1.8)
Month 12	2 (1.4)	12 (4.8)	4 (2.4)

CAPTURE=ContemporAry ProspecTive Understanding of Migraine Real-world Evidence; MHD=monthly headache day.
[a]Among participants who met inclusion/exclusion criteria with evaluable MHD data at screening and were enrolled for ≥12 months or had completed the Month 12 visit.

Fig. 2



P073

Use of eptinezumab in refractory chronic migraine: Real-world experience from the Glasgow headache service

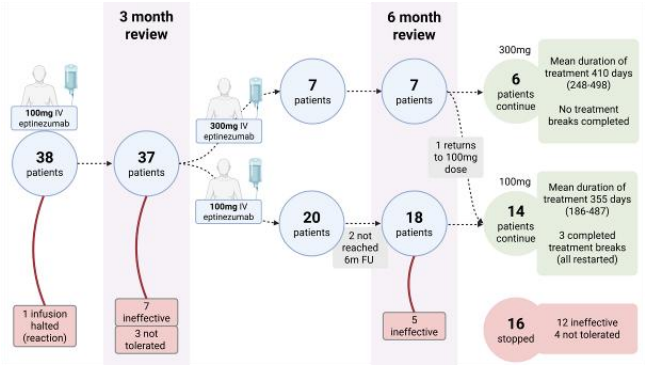
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Objective: Eptinezumab is an intravenously administered monoclonal antibody (MAb) targeting the calcitonin gene-related peptide (CGRP) ligand. We report our experience using eptinezumab in a cohort of patients with refractory chronic migraine.
Methods: We retrospectively reviewed medical records and headache diaries for 38 patients who received eptinezumab in our service between October 2023 and February 2025. All patients received 100mg eptinezumab initially, some patients later received 300mg. Monthly (28 day) headache diaries were collected at baseline and over 2-3 months post-treatment. Headache days (HD) were classified as severe (SHD) if the average pain rating (numeric rating scale) was 7 or greater. Monthly HDs and SHDs were averaged over the available follow up period. Treatment response was defined as a 30% reduction in HDs or a 50% reduction in SHDs compared to baseline.
Results: All patients had tried or had contraindications to at least 6 preventative treatment classes; 97% had previously received CGRP targeting treatment; 97%

had previously received botulinum toxin; and 71% met the European Headache Federation definition of refractory migraine. Complete headache diary data was available for 33 patients: at 2-3 months follow up after 100mg IV eptinezumab, 18 (55%) met criteria for a positive response. Mean reduction in HDs was 5.1 (95% confidence interval [CI] 3.0-7.1), and in SHDs was 5.6 (95% CI 3.4-7.7). 27 patients (71%) continued eptinezumab after the initial 3-month trial. 20 received further doses of 100mg, whilst 7 received the 300mg dose. At the time of review, 22 patients remained on treatment (mean duration 348 days, range 95-498 days).

Conclusion: Eptinezumab appears to be a reasonable treatment option in refractory migraine, even after poor response to prior CGRP-targeting treatment. Our study has limitations; most significantly its retrospective and uncontrolled nature and the lack of headache diary data after 3 months to corroborate reported longer-term response.

Fig. 1



P074

Use of eptinezumab or an alternative subcutaneous CGRP-targeting monoclonal antibody after non-response to two prior CGRP targeting treatments: A real-world observational evaluation

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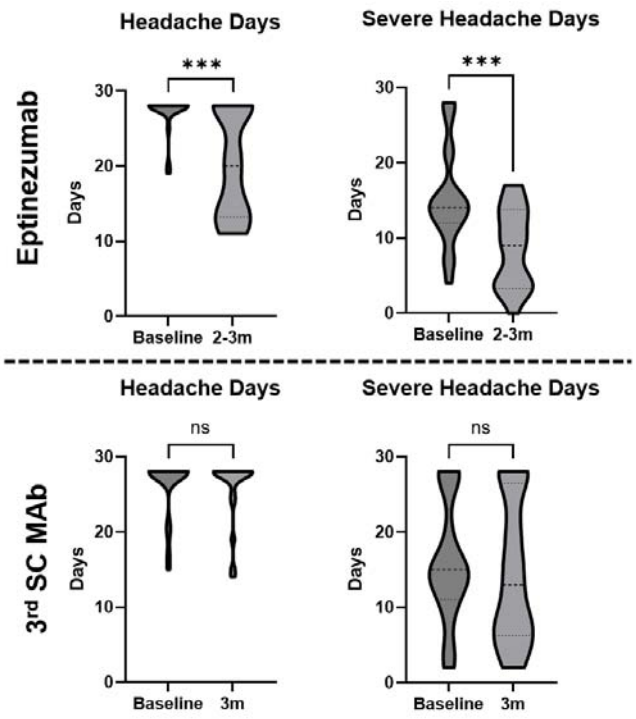
Objective: Multiple treatments targeting the calcitonin gene-related peptide (CGRP) pathway have been developed for the preventative treatment of migraine. Real world data suggest that an alternative CGRP targeting treatment can be effective if a patient does not respond to a first. We present our experience comparing the use of eptinezumab, an intravenously administered monoclonal antibody (MAb) targeting CGRP, or an alternative subcutaneous (SC) CGRP-MAb after failure of 2 prior CGRP targeting treatments.

Methods: We identified 43 patients who had received a third CGRP-MAb after non-response to 2 prior CGRP targeting treatments; 22 received a third SC MAb (11 galcanezumab, 10 fremanezumab and 1 erenumab) and 21 received eptinezumab. Their medical records and headache diaries were retrospectively reviewed. Monthly headache diaries were collected at baseline and 3 months post-treatment. Headache days (HD) were classified as severe (SHD) if the average pain rating was 7 or greater. Treatment response was defined as a 30% reduction in monthly HDs or a 50% reduction in SHDs.

Results: Patients receiving eptinezumab or a third SC MAb had no significant differences in age, gender, baseline HDs/SHDs, number of prior preventative treatment trials or medication overuse. Complete headache diary data were available for 19 patients in each group. 12/19 (63%) met criteria for positive response with eptinezumab; 6/19 (32%) met criteria for positive response with a third SC MAb. Reduction in HDs after treatment was 7.0±1.4 (mean±SEM, $p<0.01$) with eptinezumab and 0.4±0.6 ($p=0.54$) with a third SC MAb. Reduction in SHDs after treatment was 6.6±1.5 ($p<0.01$) with eptinezumab and 1.9±1.8 ($p=0.29$) with a third SC MAb.

Conclusion: After non-response to 2 CGRP targeting treatment, eptinezumab resulted in a significant reduction in HDs/SHDs. Use of a third SC MAb did not result in a significant reduction in HDs/SHDs, with lower overall positive response rates. Our evaluation is limited by its uncontrolled, observational nature.

Fig. 1



P075

Associations between headache prevalence and use of conventional and heated tobacco products and

passive smoking: A cross-sectional study based on the Japan 'Society and New Tobacco' Internet Survey (JASTIS)

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Objective: Heated tobacco products (HTPs) are novel nicotine delivery systems that heat tobacco leaves without combustion. While the association between conventional cigarette smoking and headache disorders has been well documented, evidence regarding HTP use remains limited. This study aimed to examine whether HTP use is associated with the prevalence of chronic headaches in a large Japanese cohort.
Methods: We utilized data from the Japan "Society and New Tobacco" Internet Survey (JASTIS), a nationally representative, ongoing internet-based cohort initiated in 2015 to monitor trends in tobacco product use. Participants were recruited from a panel of over 2 million individuals. In the 2025 wave, 23,228 respondents with complete and valid data were included from the initial 28,000 participants. Headache prevalence was assessed by the question, "Have you experienced headaches in the past year?"—with responses of "occasionally" or "frequently" categorized as positive. Multivariable logistic regression was used to adjust for demographic, socioeconomic, lifestyle, and clinical variables.
Results: Current (OR: 1.71; 95% CI: 1.44–2.03) and former (OR: 1.54; 95% CI: 1.37–1.73) cigarette smokers showed significantly increased odds of reporting headaches. Current HTP users also demonstrated a modest but significant association (OR: 1.15; 95% CI: 1.01–1.32). Additionally, 16% of participants reported experiencing headaches following passive exposure to cigarette or HTP smoke.
Conclusion: Current and former use of conventional cigarettes was significantly associated with increased headache prevalence, and a smaller yet significant association was observed for HTP use. These findings suggest that, despite perceptions of reduced harm, HTPs may still contribute to headache development through exposure to nicotine and other volatile compounds.

P076

Healthcare professionals' opinions on the role of physical therapy in the management of headache diagnoses: An international survey

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Objective: Physical therapy (PT) is commonly adopted as a non-pharmacological treatment for headache diagnosis; however, there are no commonly accepted PT practices. This study aimed to explore healthcare

professionals views and clinical use of PT in headache treatment.

Methods: An international online survey was distributed to healthcare professionals working in the headache field. The survey inquired about professionals' attitudes toward PT recommendations, preferred approaches, and patient selection criteria.

Results: A total of 84 healthcare professionals completed the survey, primarily neurologists (n=67, 79.7%) and physiotherapists (n=8, 9.5%). Thirty-three (49.2%) neurologists occasionally and 4 (50%) physiotherapists very frequently recommended physiotherapy (PT) methods (Table 1). Thirty-one (46.2%) neurologists referred patients to physiotherapists specialized in headaches. PT was most commonly recommended for chronic migraine (n=62, 73.8%), chronic tension-type headache (n=74, 88%), and cervicogenic headache (n=75, 89.2%). Twenty-six (30.9%) professionals used specific criteria for referral, such as neck pain, trigger points, posture disorders, or special populations (e.g., elderly, pregnant women, children). Over half (n=52, 61.9%) reported not conducting specific evaluations before recommending PT. Manual therapy (n=61, 72.6%) and exercises (n=74, 88%) were the most recommended methods. Misuse often involved incorrect application techniques (n=52, 61.9%). Fifty-two (61.90%) professionals had neurologist-physiotherapist collaboration in their institutions. Most professionals (n=72, 85%) emphasized the need for more clinical research, and 78 (92.8%) supported specialized PT training on headache management (Table 2).

Conclusion: PT is preferred for headaches. However, there are deficiencies in structured protocols and multidisciplinary collaborations. Education, guidelines, and research should be increased to improve PT approaches in the treatment of headaches.

Fig. 1

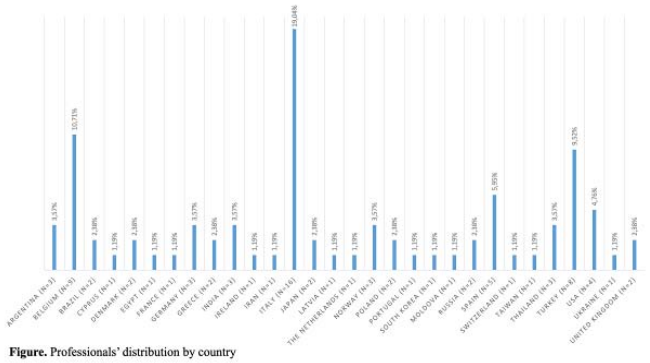


Figure. Professionals' distribution by country

Fig. 2

Table 1. Professionals information and PT recommendations

Professionals n (%)	Years of Professional Experience n (%)	How Often Do You Recommend Physical Therapy to Your Patients? n (%)	Do You Refer Your Patients to Specific Physical Therapists Who Work in the Headache Field? n (%)
Neurologist: n=67 (79.7%)	<6 years: n=11 (16.4%) 6-10 years: n=13 (19.4%) >10 years: n=43 (64.1%)	Very Frequently: n=18 (26.8%) Occasionaly: n=33 (49.2%) Rarely: n=16 (23.8%)	Yes: n=31 (46.2%)
Physiotherapist: n=8 (9.5%)	<6 years: n=1 (12.5%) 6-10 years: n=1 (12.5%) >10 years: n=6 (75%)	Very Frequently: n=4 (50%) Occasionaly: n=3 (37.5%) Rarely: n=1 (12.5%)	Yes: n=7 (87.5%)
Physiatrist: n=1 (1.1%)	>10 years: n=1 (100%)	Occasionaly: n=1 (100%)	Yes: n=1 (100%)
Internal Medicine Physician: n=2 (2.3%)	>10 years: n=2 (100%)	Very Frequently: n=1 (50%) Rarely: n=1 (50%)	Yes: n=1 (50%)
Family Physician: n=1 (1.1%)	>10 years: n=1 (100%)	Rarely: n=1 (100%)	Yes: n=1 (100%)
General Practitioner - PhD Fellow: n=1 (1.1%)	<6 years: n=11 (16.4%)	Occasionaly: n=1 (100%)	Yes: n=1 (100%)
Nurse: n=1 (1.1%)	>10 years: n=1 (100%)	Occasionaly: n=1 (100%)	No: n=1 (100%)
Pharmacologist: n=2 (2.3%)	6-10 years: n=1 (50%) >10 years: n=1 (50%)	Occasionaly: n=1 (50%) Rarely: n=1 (50%)	No: n=2 (100%)
Exercise Physiologist: n=1 (1.1%)	>10 years: n=1 (100%)		Yes: n=1 (100%)

PT: Physical Therapy; Very Frequently: >70% individuals with headache, Occasionaly: 30-70%, Rarely: <30%

Fig. 3

Table 2. Answers to survey questions

Items	n (%)	Other Answers
Headache Diagnostic Groups for Which PT is Recommended	Episodic migraine: n=38 (45.2%) Chronic migrainc: n=62 (73.8%) Episodic tension-type headache: n=45 (53.5%) Chronic tension-type headache: n=74 (88%) Cervicogenic headache: n=75 (89.2%) Trigeminal-autonomic cephalalgias: n=6 (7.1%)	
Presence of specific criteria when referring appropriate patients to PT	Yes: n=26 (30.9%)	If Yes: -Neck pain-stiffness-limited movement, -Trigger points in pericranial/cervical muscles, -Postural disorders, -Elderly, pregnant women and children who cannot receive pharmacological treatment
Existence of specific tests or evaluations performed before referring patients to PT	Yes: n=32 (38%)	
Existence of local guidelines/recommendations/operative procedures, including physical therapy, for the treatment of patients with headache disorders in the centres	Yes: n=19 (22.6%)	
Additional frequently recommended PT methods	Manual therapy (mobilization, massage, osteopathy...): n=61 (72.6%) Exercise (neck stabilization, aerobic exercise, yoga, pilates, shoulder exercises, scapular correction exercises...): n=74 (88%) Electrotherapy (TENS, ultrasound...): n=29 (34.5%)	Other -Patients education -Dry needling
The frequency of patients stopping PT	Very frequently: n=20 (23.8%) Occasionally: n=49 (58.3%) Rarely: n=15 (17.8%)	
The reasons of patients stopping PT	Lack of effectiveness therapy?: n=58 (69%) Adverse events: n=10 (11.9%) Costs: n=47 (55.9%)	Other -Lack of free time -Insurance limitations -Compliance problem
Examples of misuse of PT	Aggressive manual therapy during an acute migraine attack: n=42 (50%) Physical therapy performed with incorrect techniques: n=52 (61.9%) Not considering the patient's migraine type and comorbidities: n=43 (51.1%) Practices not based on scientific evidence: n=50 (59.5%)	
Existence of neurologist-physiotherapist collaboration in institutions	Yes: n=52 (61.9%)	
Suggestions for increasing the effectiveness of PT in the field of headache	More clinical studies should be conducted: n=72 (85.7%) Physiotherapists should be given special training on headaches: n=78 (92.8%) Patients should be better informed about physical therapy: n=66 (78.5%)	Other -Communication between neurologists, family physicians and physiotherapists should be improved, -Neurologists should have more knowledge about PT practices -Evidence-based guidelines for PT should be developed

PT: Physical Therapy, TENS: Transcutaneos Nerve Electric Stimulation

P077

"*Migraine and I*" – Small project for big changes?

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Objective: Migraine is one of the most common neurological conditions and one of the leading causes

of disability among working-age population. Only minority of patients are receiving proper care. The aim of our project *"Migraine and I"* was to enhance the knowledge of medical students about migraine and to identify migraine enthusiasts among them who could deepen their understanding and subsequently educate their peers.

Methods: Neurological team, consisted of two neurologist and three neurology residents, have designed five short lectures about migraine. Topics have covered the burden of migraine, pathophysiology, clinical picture, differential diagnosis and approach to a patient with migraine. Participating medical students completed pre - and post - lecture questionnaires and knowledge tests to assess learning outcomes.

Results: Thirty students (79% of them were female), that had already finished a neurology course, have attended our lectures. Baseline knowledge was limited, with an average correct response rate of 29.9%. Following the lectures series, this rate significantly increased to 60%. Students were very satisfied with the lectures; 86.7% of them rated lectures as great. Six highly motivated students joined our team to continue lecturing and participating in various migraine-related initiatives.

Conclusion: Extracurricular lectures can greatly improve the knowledge about migraine among young future doctors, but the problem is the lack of interest for them. Only 13% of students who were invited have attended lectures. Finding the way how to attract much more students would make a difference. Nevertheless, working in small, motivated groups has proven to be highly effective and productive.

P078

AI-powered simulated patients with automated feedback for enhancing headache history-taking skills: A convergent mixed-methods study

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Objective: Headaches are a common but diagnostically challenging, relying heavily on patient history. However, medical students often struggle due to limited case exposure and feedback. This study evaluated the feasibility and effectiveness of an AI-powered simulated patient (AISP) chatbot in enhancing history-taking and clinical reasoning skills for three primary headache disorders, migraine, tension-type, and cluster headaches, among medical students in Faculty of Medicine, Chulalongkorn University.

Methods: We developed a custom AISP platform with automated, rubric-based feedback on three headache cases. Third-year medical students participated in this mixed-methods experimental study, which included a 1-week self-study and pre-test OSCE, a 1-week washout, and a 1-week AISP practice followed by post-test OSCE. Changes in OSCE and CRI_HT scores and user satisfaction (via the Chatbot Usability Questionnaire, CUQ) were assessed. Focus group discussions (FGDs) explored three key areas: (1) learning enhancement, (2) system limitations, and (3) future implementation. Qualitative data were analyzed thematically.

Results: Twenty-five medical students participated (92% male), with a mean age of 20.7 years (SD=0.5). OSCE scores improved by 22.5 points ($p<0.001$, $d=1.93$), and CRI-HT scores improved by 8.8 points ($p<0.001$, $d=1.81$) (Fig. 1). CUQ results indicated high usability. Most students gave positive feedback on the app, highlighting its user-friendliness, informative content, and ease of use. Some, however, noted the the app felt overly robotic. FGDs revealed three key themes (Fig. 2): (1) enhanced learning through convenience, structured format, and repetitive practice; (2) realistic interactions with technical and soft-skill limitations; and (3) suggestions for broader case variety and curriculum integration.

Conclusion: AISPs with automated feedback show strong potential as scalable tools for improving clinical skills in headache education and may effectively complement traditional teaching.

Fig. 1

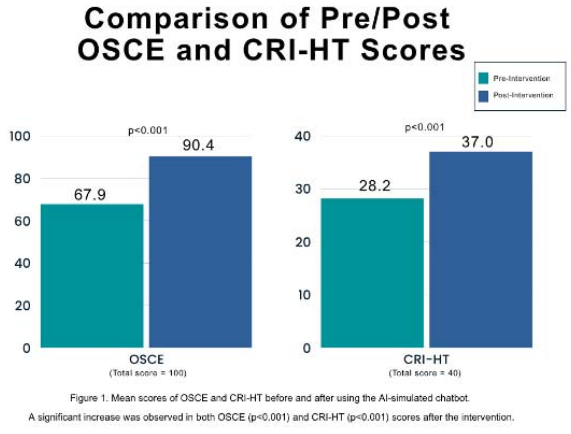
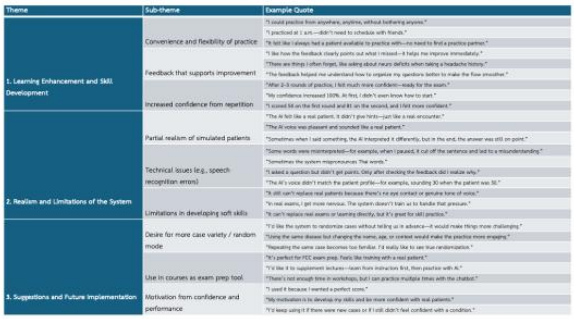


Figure 1. Mean scores of OSCE and CRI-HT before and after using the AI-simulated chatbot.
A significant increase was observed in both OSCE ($p<0.001$) and CRI-HT ($p<0.001$) scores after the intervention.

Fig. 2

Figure 2.Themes, sub-themes, and example quotes from students' reflections on using the AI-simulated patient chatbot, highlighting learning benefits, system limitations, and suggestions for improvement.



Theme	Sub-theme	Example Quote
1. Learning Enhancement and Skill Development	Convenience and flexibility of practice	"I could practice from anywhere, anytime, without bothering anyone." "I practiced at 1 a.m.—didn't need to schedule with friends." "It felt like I always had a patient available to practice with—no need to find a practice partner."
	Feedback that supports improvement	"I like how the feedback clearly points out what I missed—it helps me improve immediately." "There are things I often forget, like asking about neuro deficits when taking a headache history." "The feedback helped me understand how to organize my questions better to make the flow smoother."
	Increased confidence from repetition	"After 2–3 rounds of practice, I felt much more confident—ready for the exam." "My confidence increased 100%. At first, I didn't even know how to start." "I scored 66 on the first round and 81 on the second, and I felt more confident."
2. Realism and Limitations of the System	Partial realism of simulated patients	"The AI felt like a real patient. It didn't give hints—just like a real encounter." "The AI voice was pleasant and sounded like a real patient." "Sometimes when I said something, the AI interpreted it differently, but in the end, the answer was still on point."
	Technical issues (e.g., speech recognition errors)	"Some words were misinterpreted—for example, when I paused, it cut off the sentence and led to a misunderstanding." "Sometimes the system mispronounces The words." "It asked a question but didn't get points. Only after checking the feedback did I realize why." "The AI's voice didn't match the patient profile—for example, sounding 30 when the patient was 50."
	Limitations in developing soft skills	"It still can't replace real patients because there's no eye contact or genuine tone of voice." "In real exams, I get more nervous. The system doesn't train us to handle that pressure." "It can't replace real exams or learning directly, but it's great for skill practice."
3. Suggestions and Future Implementation	Desire for more case variety / random mode	"I'd like the system to randomize cases without telling us in advance—it would make things more challenging." "Using the same disease but changing the name, age, or context would make the practice more engaging." "Repeating the same case becomes too familiar. I'd really like to see true randomization."
	Use in courses as exam prep tool	"It's perfect for FCE exam prep. Feels like training with a real patient." "I'd like it to supplement lectures—learn from instructors first, then practice with AI." "There's not enough time in workshops, but I can practice multiple times with the chatbot."
	Motivation from confidence and performance	"I used it because I wanted a perfect score." "My motivation is to develop my skills and be more confident with real patients." "I'd keep using it if there were new cases or if I still didn't feel confident with a condition."

P079

Improving headache care through specialized education

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Objective: Headache disorders affect 40% of the global population but remain underdiagnosed and untreated due to limited specialist access. This gap highlights the need for structured educational programs to improve healthcare professionals' skills in headache diagnosis and management. We aimed to explore the impact of an academic master's program on graduates' careers, work status, and educational needs.

Methods: In this observational cross-sectional study performed between July and September 2024, 88 Master of Headache Disorders (MHD) graduates from the University of Copenhagen were invited to complete an anonymous online survey assessing career impact and educational needs.

Results: 80 graduates (91% response rate) across cohorts from 2018 (MHD1) to 2024 (MHD4) were analyzed, representing 36 countries; 63% were female, and 43% aged 35-44 Before enrollment, the majority held bachelor"s or master"s degrees, predominantly in neurology (48%), nursing (13%) and physiotherapy (8%). Post-graduation, 69% of respondents remained active in headache care, while 90% shared headache knowledge regularly (38% every month and 24% weekly). Additionally, 96% reported career advancement and 47% experienced a salary increase. The master"s thesis led to a clinical or research study, with 7% of them published and 23% planning publication.

Conclusion: The survey findings provide empirical evidence that structured headache education among healthcare professionals is associated with sustained engagement in headache care, enhanced professional career trajectories, and improved dissemination of headache-related knowledge among peers. Despite limited long-term data, our results highlight the need for accessible headache education programs to mitigate the global burden of headache disorders. Further research should evaluate the long-term clinical impact.

P080

The regional outreach programme of the International Hadache Society (IHS): A WHO-IGAP oriented program to improve access to care for headache patients in sub-Saharan Africa

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Objective: The WHO Intersectoral Global Action Plan highlights the need to scale up neurological services. In sub-Saharan Africa (SSA) primary care services are the only healthcare providers available for patients with neurological conditions, including headache. Despite being one of the most disabling conditions, headache remains underdiagnosed and poorly managed due to insufficient training

Methods: The IHS, through its Regional Outreach Programme (ROPE), partnered with the Disease Relief through Excellent and Advanced Means (DREAM) program to deliver two structured in-person teaching and training courses in Blantyre, Malawi (2022 and 2025). These courses provided local primary care operators, especially non-physician clinicians (NCP), with practical skills in the diagnosis and management of primary and secondary headaches. Local field-based mentorship periods, along with a "train-the-trainer" model, were an essential part of the program. To assess the effectiveness of the educational intervention, pre- and post-training evaluation test regarding different domains of headache medicine was administered

Results: Across both editions, 64 experienced NCPs (55% rural-based) without neurology training attended. Five 2022 trainees became 2025 lecturers, joining IHS neurologists from Italy and Ghana. Pre-course evaluations revealed major knowledge gaps across all domains. Final scores in 2025 were significantly higher than those in 2022 (median 63.6% vs 50%, p=0.017). Largest improvements were seen in neurological exam, diagnosis, and management (+17–20%, fig1) compared to the pre-course assessment

Conclusion: The training output indicates that partnerships between international scientific societies and established local healthcare programs facilitate effective task shifting among primary healthcare

providers. This helps to bridge the huge diagnostic and treatment gap for headaches in SSA. ROPE represents a successful, replicable model for improving access to care for people with headaches in underserved regions

Fig. 1

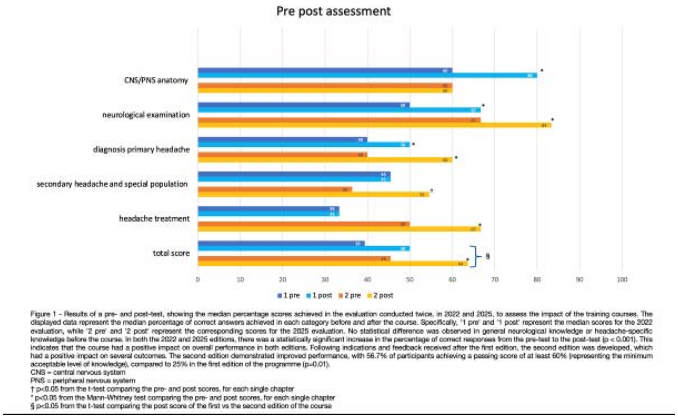


Figure 1 – Results of a pre- and post-test, showing the median percentage scores achieved in the evaluation conducted twice, in 2022 and 2025, to assess the impact of the training courses. The displayed data represent the median percentage of correct answers achieved in each category before and after the course. Specifically, '1 pre' and '1 post' represent the median scores for the 2022 evaluation, while '2 pre' and '2 post' represent the corresponding scores for the 2025 evaluation. No statistical difference was observed in general neurological knowledge or headache-specific knowledge before the course. In both the 2022 and 2025 editions, there was a statistically significant increase in the percentage of correct responses from the pre-test to the post-test ($p < 0.001$). This indicates that the course had a positive impact on overall performance in both editions. Following indications and feedback received after the first edition, the second edition was developed, which had a positive impact on several outcomes. The second edition demonstrated improved performance, with 56.7% of participants achieving a passing score of at least 60% (representing the minimum acceptable level of knowledge), compared to 25% in the first edition of the programme ($p=0.01$).
CNS = central nervous system
PNS = peripheral nervous system
† $p<0.05$ from the t-test comparing the pre- and post scores, for each single chapter
* $p<0.05$ from the Mann-Whitney test comparing the pre- and post scores, for each single chapter
§ $p<0.05$ from the t-test comparing the post score of the first vs the second edition of the course

P081

Development and evaluation of a behavioral training program for the reduction of migraine attacks in patients in the primary care setting

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Objective: According to the AWMF (German Society for Neurology) guidelines for the treatment and prophylaxis of migraine, patients with frequent migraine attacks with pronounced symptoms should be offered not only medication-based migraine prophylaxis but also behavioral modification training. The goal was to reduce the frequency of migraine attacks per month.

Methods: Based on the recommendation of the guidelines, a training system for behavior modification was designed. Psychological methods such as education, self-observation, relaxation techniques, mindfulness, endurance sports, as well as recommendations for low-sugar, low-fat and ketogenic diets and the reduction of processed foods were implemented.The program was evaluated in patients who had been in neurological treatment for 3 years or more and who had established medication-based migraine prophylaxis. The patients received the training using information resources. The evaluation was based on a questionnaire that included, among other things, acceptance, teaching quality and motivation, as well as the frequency of migraine attacks.

Results: The process evaluation shows a high level of acceptance and a measurable effect in terms of extrinsic and intrinsic motivation for the training material. The frequency of migraine attacks was reduced from 4-6 times a month to 1-3 times a month three months after the start of the program. 40% of the subjects stated that they no longer had migraine attacks three months after using the program and training material.

Conclusion: The recommendations of the information tool were understandable and could be implemented. The psychological methods for self-observation and mindfulness, endurance sports and the nutritional recommendations could be implemented. The questionnaire was partly considered too extensive. The program is an effective tool for learning behavior modification for migraine as an accompanying measure to medication-based prophylaxis.

Fig. 1

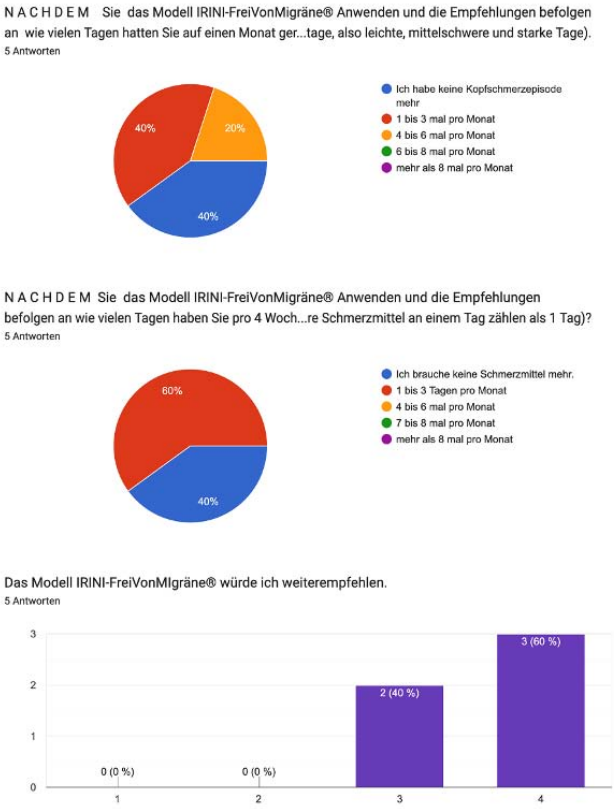
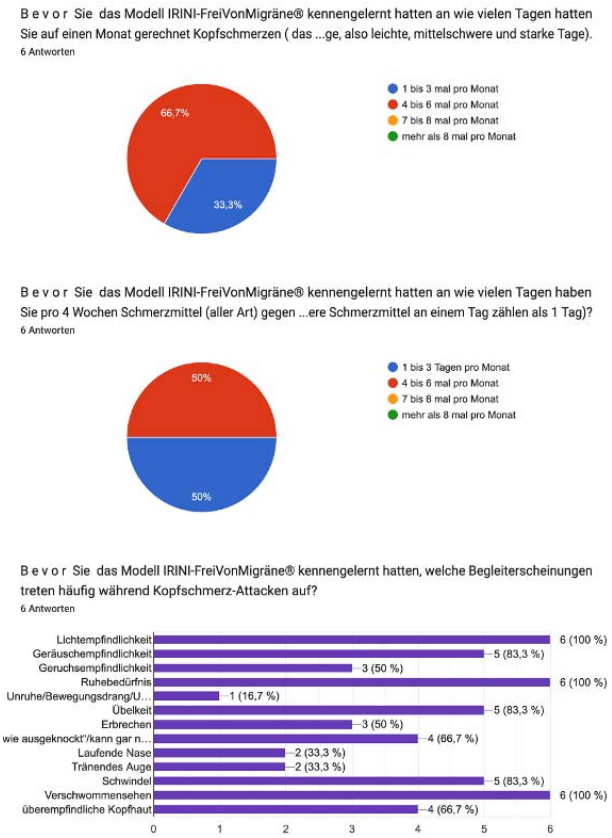


Fig. 2



P082

What patients want: A qualitative study on an information resource on migraine

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Objective: The aim of this study was to explore patient preferences and perspectives on a migraine information resource to be used in clinical settings.

Methods: Seven individuals with migraine participated in two-hour focus groups to refine a digital information resource they received during participation in a study on individualized physiotherapy management. A physiotherapist experienced in managing patients with headache facilitated discussion regarding content, format and delivery of information. The sessions were audio-recorded and transcribed. Reflexive thematic analysis was performed to refine codes and interpret key themes from the data.

Results: Four themes were interpreted. Theme 1 was that the science mattered. Participants wanted evidence-based, neuroanatomical and physiological information to explain what migraine is, why they experience those symptoms, and how to self-manage. Theme 2 was validation. Knowledge of migraine enabled self-compassion, reflection and acceptance which led to better self-management strategies such as pacing, exercise and stress relief. External validation from others through sharing of knowledge further encouraged these strategies. Theme 3 described tailoring of information for the population and the individual. This meant that the clinician delivering information needed a thorough understanding of each patient"s experiences and circumstances so as to individualise content, delivery and pacing of information. Theme 4 was empowerment and positivity: it relates to the positivity participants wanted projected by the information and the empowerment they gained from it. Participants wanted migraine described as a condition that can be managed and quality of life improved, not a "disability". Knowledge gave a sense of control. Self-management strategies with personal relevance were empowering.

Conclusion: Patients want scientific, validating, positive and relatable information that will empower self-management in migraine.

P083

Coping and pain catastrophizing in migraine patients and their mothers: A comparison between mothers with and without migraine

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Objective: We aimed to:1) explore coping strategies and pain catastrophizing in children and their mothers, and their association with (a) headache frequency and (b) pain intensity; 2) compare coping and catastrophizing between patients and mothers (with and without migraine), analyzing relationships across subscales.

Methods: We included 166 children (m.a 12.2 ± 2.6 years) with migraine, and their mothers. Patients were categorized by:1) daily,high and low frequency; 2) severe and mild pain intensity; and 3) children of mothers with and without migraine. Pain catastrophizing was assessed using the PCS/PCS-C (Pain Catastrophizing Scale/Child), while coping strategies were evaluated using the PPCI (Children's Coping Strategies to Physical Pain) and the CSQ-R-I (Coping Strategies Questionnaire-Revised, Italian version).

Results: Children with daily headache showed higher scores in "Total PCS-C" (0.038) and "Helplessness"

(0.015). Their mothers showed higher scores in "Self-Statement" (0.050). Mothers of children with severe pain had higher scores in "Magnification" (0.011) and lower scores in "Ignoring Pain Sensations" (0.029). Children of migraine mothers had higher "Problem Solving" scores (0.047). No significant differences were observed between mothers with and without migraine, but "Magnification" in non-migraine mothers correlated with children's "Rumination"(0.049), "Helplessness"(0.028), and "Catastrophizing"(0.009).

Conclusion: Children with daily headache exhibit greater pain catastrophizing and helplessness. Migraine severity is linked to maladaptive coping strategies in mothers, which, in non-migraine mothers, correlate with similar maladaptive strategies in their children. While no significant differences were found between mothers with and without migraine, children of migraine-affected mothers showed a greater tendency toward problem-solving, suggesting adaptive traits that may be learned or inherited.

P084

Factors impacting the telephone follow-up response rate in patients with migraine without aura: A cross-sectional study of 1299 females

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Objective: The out-of-hospital management is important for migraine treatment. Telephone follow-up is the commonly used. The study aims to explore the factors impacting the response rate of telephone follow-up in migraineurs.

Methods: After 1299 female patients with migraine without aura (MwoA) from the headache outpatient database were followed, demographic factors, call time, call day, and headache-related factors were analyzed.

Results: Among the 1299 eligible female patients with MwoA, 821 (63.2%) responded (positive response, PR), and among them, 204 (24.8%) contacted us initiatively after follow-up (feedback response, FR). Age<45, calling in the morning, and nonthrobbing headache were factors related to PR. Multivariate logistic analysis showed that age<35 (OR 1.480), 35≤age<45 (OR 1.466), call in the morning (OR 1.487), headache course≥6 years (OR 1.363), and no aggravation by activity (OR 1.525) were related to PR. The analysis of factors influencing FR indicated that age<40, high education level, age at onset<25, and more accompanying symptoms were related to FR. The multivariate analysis suggested that living in a first-tier city (OR 1.981), age at onset<25 (OR 1.498,), and age<40 (OR 1.531) were related to FR.

Conclusion: Age, headache course, call time and headache-related factors influenced the response rate for migraineurs. Patients living in first-tier cities had a stronger desire to establish regular contact with headache experts and participate in follow-up. Age, follow-up time, city of residence, and statement in advance should be considered to design a personalized follow-up plan.

P085

Comparison of pain characteristics and activity patterns in migraine patients with and without cervical dysfunction – A descriptive preliminary study

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Objective: This study aimed to compare pain characteristics and activity patterns in migraine patients with and without cervical dysfunction.

Methods: A total of 88 individuals diagnosed with migraine were included and classified into two groups based on cervical dysfunction status: Cervical Dysfunction group (CD group; n = 45; median age: 24.0 [IQR: 18.0–50.0]) and Non-Cervical Dysfunction group (Non-CD group; n = 43; median age: 21.0 [IQR: 18.0–50.0]). Cervical dysfunction was assessed using the Cornell Musculoskeletal Discomfort Questionnaire. Pain characteristics (frequency, intensity, duration) over the past month were recorded. Activity patterns were evaluated with the Patterns of Activity Measure-Pain, including Avoidance, Overdoing, and Pacing subscales.

Results: The pain frequency was significantly higher in the CD group compared to the Non-CD group (p = 0.015). However, no statistically significant differences were found between groups for pain intensity (p = 0.516) and duration (p = 0.166). Overdoing scores were significantly higher in the CD group (p = 0.008), while Avoidance (p = 0.844) and Pacing (p = 0.933) scores showed no significant differences (Fig 1).

Conclusion: These findings suggest that although pain intensity and duration were similar between groups, increased headache frequency and higher Overdoing scores in the CD group may reflect a maladaptive pain response. Evaluating cervical musculoskeletal involvement appears relevant in migraine care. Recognizing pain activity patterns -especially Overdoing- can guide patient education and self-management approaches. Supporting patients in modifying these behaviors may help reduce pain intensity and enhance functional outcomes. Future

research should explore how such strategies can be effectively integrated into clinical practice.

Fig. 1

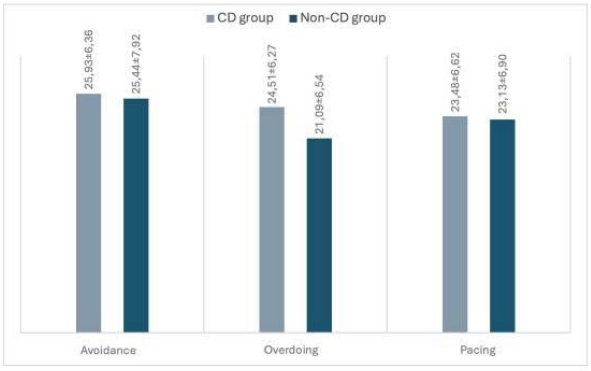


Fig 1. Comparison of Patterns of Activity Measure-Pain scores between groups

P086

Understanding patient perceptions of migraine provocation models: A call for awareness and ethical engagement

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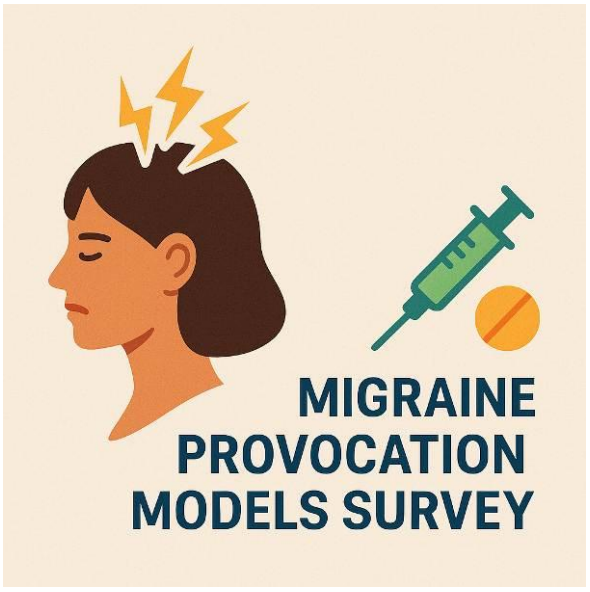
Objective: Human provocation models are a cornerstone of migraine research, enabling the study of pathophysiological mechanisms and the identification of novel therapeutic targets. However, these studies involve the intentional induction of migraine attacks, which may raise ethical concerns. Despite their widespread use in countries like Denmark, little is known about how patients perceive these models or whether cultural differences affect their acceptance. This study aimed to explore and compare the perspectives of Danish and Italian individuals with migraine regarding provocation models.

Methods: We conducted a cross-sectional online survey among Danish and Italian individuals with migraine, using Facebook-based recruitment (Figure 1). A total of 268 Danes and 146 Italians responded to a questionnaire exploring awareness, attitudes, ethical concerns, willingness to participate, trust in researchers, and preferences for alternative research approaches.

Results: Awareness of provocation models was significantly higher in Denmark (28%) than in Italy (2%). Despite limited prior knowledge, participants recognized the scientific value of such studies. Key concerns included the risk of severe migraine attacks, inadequate pain relief, and long-term effects. Willingness to participate was conditional, and ethical acceptability was recognized when strict guidelines were followed. Notably, Danish respondents expressed greater trust in researchers, while Italian respondents showed stronger preference for alternative research methods.

Conclusion: This study reveals a need for better patient education and communication around provocation studies. Addressing ethical concerns is critical not only to facilitate research participation, but also to reduce stigma and build public trust.

Fig. 1



P087

Stigma in migraine: Preliminary results from the Studio Emicrania Maugeri (SEM) project

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Objective: We assessed the experience of stigma related to migraine in healthcare workers using the Migraine-related Stigma (MiRS) scale [1].

Methods: The Studio Emicrania Maugeri (SEM) is an observational study aimed at evaluating the prevalence and characteristics of migraine among healthcare workers. Maugeri is a healthcare organization comprising 25 clinical sites in Italy. All the employees (4050 persons) were invited to answer to an anonymous web questionnaire about headache. Participants who consented and reported experiencing headaches at least once per year completed the Italian Version of the "ID Migraine" [2] for migraine screening, and a literal translation of the MiRS questionnaire to evaluate the frequency of experienced migraine-related stigma.

Results: A total of 783 persons answered the questionnaire, of which 363 with a positive migraine screening completed the MiRS questionnaire. The majority of respondents (57%) reported experiencing stigma rarely or sometimes, while 33% reported never experiencing stigma. However, a notable proportion

(10%) reported experiencing some kind of stigma often or very often.
Conclusion: These preliminary results confirm the importance of addressing stigma in migraine and suggest the need for targeted interventions to reduce its impact in occupational settings even among healthcare workers.

P088

Assessing migraine awareness in adolescents: Insights for developing preventive and educational programs

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Objective: The aim of this study was to assess the level of awareness about migraine among high school students, to explore the potential impact of preventive and educational interventions in this population.
Methods: A 20-item questionnaire was developed, covering four domains: disease knowledge, stereotypes and stigma, impact on quality of life, and use of healthcare resources. It was administered to 63 fourth-year students from a high school in Rome. Responses were analyzed using descriptive statistics.
Results: The student population comprised 38 males and 25 females, aged 17–18 years. Most students (88.9%) recognized characteristic migraine symptoms, including nausea, vomiting, photophobia and phonophobia. However, only 25.4% identified migraine as a brain disorder and 46% expressed uncertainty about its curability. Regarding stereotypes, 87.3% rejected the idea that "all headaches are the same". Nevertheless, many still perceived absenteeism from school (44.5%) or social events (30.2%) due to migraine attacks as excessive. More than half (55.6%) reported concern that their pain might not be taken seriously, and 20.6% anticipated difficulties in discussing it with others. Concerning healthcare, 71.4% acknowledged the risk of medication overuse, while 33.3% considered diagnostic imaging necessary to confirm a migraine diagnosis, reflecting partial and sometimes distorted views of clinical management.
Conclusion: This study highlights existing gaps in migraine knowledge among adolescents, alongside persistent stereotypes and stigma that may hinder appropriate healthcare use. These findings underscore the importance of implementing preventive and educational programs in schools to enhance awareness and promote healthier behaviors. Limitations include the exploratory nature of the study and the lack of formal validation of the questionnaire, which calls for further research to refine the assessment tools and confirm these preliminary results.

P089

Awareness of medication overuse headache in Hungary: Survey among pharmacists and the general population

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Objective: Although medication overuse headache (MOH) represents a significant burden, awareness of the condition remains limited worldwide. Pharmacists may play a role in counselling patients about appropriate medication use, yet their level of knowledge on MOH has not been comprehensively evaluated.
Methods: Our objective was to assess the knowledge of MOH among pharmacists and the general population in Hungary using an online survey about MOH.
Results: The pharmacist survey was completed by 116 pharmacists (76.7% female) working in Hungarian community pharmacies. The majority (62.1%) reported being asked for advice about headache at least daily. However, 41.4% had never heard of MOH. Among those familiar with the condition, most (80.9%) had learned about it during university studies or continuing education. Regarding medications associated with MOH, the most frequently recognized was non-steroid anti-inflammatory drugs (NSAIDs, 88,8%), only 23,3% mentioned that triptans could be overused. In the general population survey, 579 volunteers (75% female) participated. Only 25.2% had ever heard of MOH, and 70% were unaware of which analgesics could contribute to its development. Among those who were aware that analgesics could cause headaches, 48.2% had learned about it through healthcare education or work, 25.3% via media, and only 21.8% had heard about it from a pharmacist. This percentage is still higher than the proportion informed by their physician (17.1%).
Conclusion: Awareness of MOH in Hungary is insufficient among both pharmacists and the general population. Although pharmacists showed higher awareness than general population, substantial knowledge gaps remain. Most pharmacists would suggest patients to ask headache specialists" help,

highlighting their pivotal role in early detection. Targeted educational programs for pharmacists, as well as public health campaigns, are essential to improve prevention and reduce the burden of MOH. Funding: EKOP-2025-624, Anna Richter Award, Hungaropharma Scholarship

P091

Eptinezumab reduced patient-reported disease burden in patients with chronic migraine and medication-overuse headache: 24-week results from the RESOLUTION trial

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Objective: To evaluate the 24-week impact of eptinezumab versus placebo on electronic patient-reported outcomes (ePROs) in adults with chronic migraine (CM) and medication-overuse headache (MOH) who received patient education.

Methods: The phase 4 RESOLUTION trial (NCT05452239) included a 12-week double-blind placebo-controlled period and 12-week open-label extension (OLE). Adults (18–75 yrs) with CM and MOH (excluding opioid-overuse headache) were randomized 1:1 to the IV eptinezumab 100mg or placebo group at baseline, both preceded by a brief educational intervention on MOH. All participants received eptinezumab 100mg at the end of Week 12. Secondary endpoints included ePROs assessed at Weeks 4, 12, and 24: Headache Impact Test, Migraine-specific Work Productivity and Activity Impairment questionnaire (Weeks 12 and 24 only), modified Migraine Disability Assessment, Migraine-Specific Quality-of-life questionnaire v2.1, EQ-5D visual analogue scale, Hospital Anxiety and Depression Scale, and Treatment Satisfaction Questionnaire for Medicine.

Results: Of 608 randomized participants, 593 were treated in the OLE period; 584/593 (98.5%) completed the trial. Baseline ePRO scores indicated moderate to severe disease burden. During the placebo-controlled period, eptinezumab was associated with greater improvements than placebo at Weeks 4 and 12 in headache-related life impact, migraine-related disability, overall and migraine-specific quality of life, and work productivity and activity impairment, and resulted in higher treatment satisfaction. During the OLE period, participants who received a second eptinezumab infusion had sustained improvements, and those who switched from placebo to eptinezumab treatment achieved similar improvements by Week 24.

Conclusion: In participants with CM and MOH who also received patient education, eptinezumab resulted in greater improvements than placebo at Weeks 4 and 12 across ePROs. Similar improvements were seen in both groups at Week 24 after open-label eptinezumab treatment.

P092

Efficacy and safety of eptinezumab in adults with chronic migraine and medication-overuse headache: 24-week results of the RESOLUTION trial

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Objective: To evaluate the 24-week efficacy and safety of eptinezumab in adults with chronic migraine (CM) and medication-overuse headache (MOH) who also received patient education.
Methods: RESOLUTION was a phase 4 clinical trial (NCT05452239) including a 12-week double-blind placebo-controlled period and 12-week open-label extension (OLE). Adults (18–75y) with CM and MOH (excluding opioid-overuse headache) were randomized (1:1) to IV eptinezumab 100mg or placebo. All received a brief educational intervention about MOH before infusion. All received eptinezumab 100mg at Week 12. Measures for primary and key secondary endpoints (all met with eptinezumab *vs* placebo within Weeks 1–12) were captured during the OLE period: changes from baseline in monthly migraine days, monthly headache days, monthly days with acute headache medication use, and average daily pain, and participants no longer meeting CM/MOH thresholds. Safety was assessed via treatment-emergent adverse events (TEAEs).
Results: Of 608 participants randomized at baseline, 593 (98%) were treated with eptinezumab in the OLE period; 584/593 (98%) completed the trial. Across endpoints, improvements observed during the placebo-controlled period were sustained during the OLE period for participants initially treated with eptinezumab, with similar levels of improvement gained for those started on placebo. The proportion of participants with TEAEs in the OLE period was similar between eptinezumab–eptinezumab and placebo–eptinezumab groups (30% *vs* 34%). Few TEAEs led to withdrawal (<2%) or infusion interruption (<1%).
Conclusion: In adults with CM and MOH who received patient education in the RESOLUTION trial, eptinezumab treatment resulted in early (Weeks 1–4) improvements in disease burden *vs* placebo that were consistent over Weeks 1–12. Improvements were sustained following a second eptinezumab infusion (Weeks 13–24), with similar improvements observed in participants started on placebo then treated with eptinezumab. No new safety signals were identified.

P093

The Nordic Chronic Migraine trial of CGRP monoclonal antibody and onabotulinumtoxin a dual therapy – A randomized-controlled double-blind trial (NorMig)

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Objective: There is tremendous evidence demonstrating the efficacy of calcitonin gene-related peptide monoclonal antibodies (CGRP mAbs) in migraine patients. However, patients with chronic migraine considered as responders may still experience substantial disease burden.
For this patient group, a combination of CGRP mAbs and onabotulinumtoxin A, might be beneficial. Although there are real-world data supporting this combination therapy, evidence from randomised controlled trials is lacking.
The aim of the NorMig trial is to assess the efficacy of dual therapy with CGRP mAbs and BTA compared to

single therapy with CGRP mAbs in chronic migraine patients.

Methods: NorMig is an ongoing randomized placebo-controlled, double-blind multi-centre phase III trial of CGRP mAbs and onabotulinumtoxin A versus treatment with CGRP mAbs+placebo in patients with chronic migraine. The trial is conducted in compliance with Guidelines of the International Headache Society for controlled trials of preventive treatment in chronic migraine.

Primary outcome is the reduction of Monthly Migraine Days over 12 weeks of treatment with the study medication.

Patients with chronic migraine aged 18-70 years with indication for CGRP mAbs or onabotulinumtoxin A and no previous use of CGRP mAbs or onabotulinumtoxin A are included after 4-week baseline registration.

Results: The trial has started at Norwegian sites and is planned to be extended to centres in the Nordic countries to reach the sample size of 450 patients. Updated numbers of inclusions will be presented at the congress.

Conclusion: The NorMig trial has the potential to change current treatment practice for chronic migraine and reduce migraine related disability.

Fig. 1

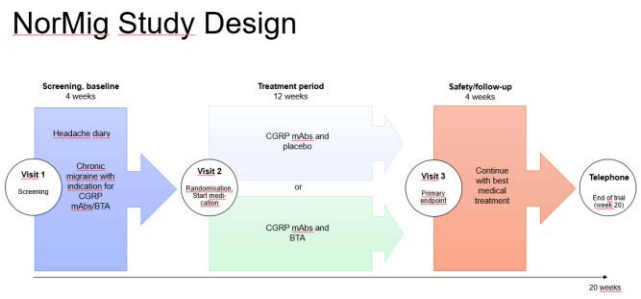
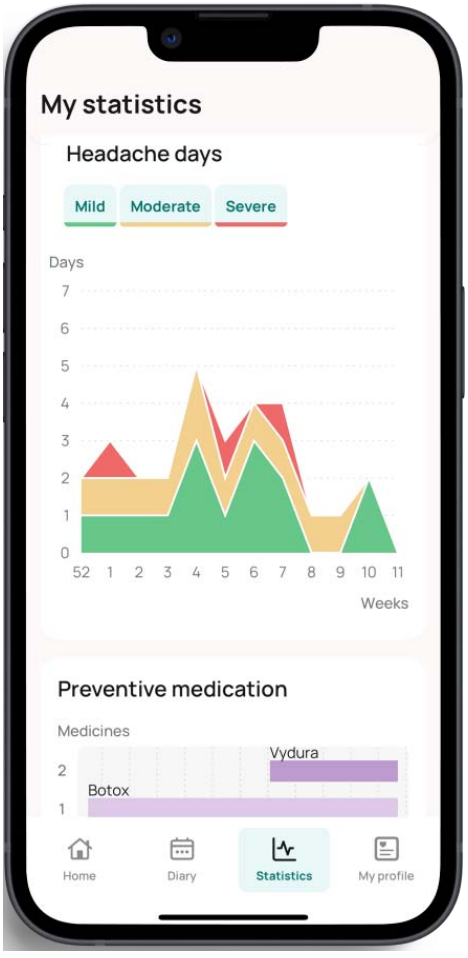


Fig. 2



Fig. 3



P094

Eptinezumab reduced acute medication use in participants with chronic migraine and medication-overuse headache: 24-week results from the RESOLUTION trial

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Objective: To evaluate the 24-week impact of eptinezumab on acute headache medication use in adults with chronic migraine (CM) and medication-overuse headache (MOH) who also received patient education.

Methods: The phase 4 RESOLUTION trial (NCT05452239) included a 12-week double-blind placebo-controlled period and a 12-week open-label extension (OLE) period. At baseline, adults (18–75y) with CM and MOH were randomized 1:1 to IV eptinezumab 100mg or placebo; all participants received a brief educational intervention on MOH before infusion. At the end of Week 12, all participants received eptinezumab 100mg. Key secondary endpoints included change from baseline in monthly days with acute medication use (Weeks 1–4 and 1–12) in the full analysis set (FAS; placebo-controlled). In the OLE population, endpoints included change from baseline in number of monthly days with acute medication use, triptan use, and non-opioid analgesic/NSAID use (4- and 12-week intervals). Inferential statistics for the FAS and descriptive statistics for the OLE population were used.

Results: Participants randomized: n=608; treated at baseline: n=604; FAS: n=602; treated/analyzed in OLE period: n=593; completed the trial: n=584. Baseline mean monthly acute medication days: 20.1 across arms (FAS). 535/604 (89%) participants took triptans and 487/604 (81%) took non-opioid analgesics/NSAIDs during screening. Eptinezumab was more favorable than placebo in reducing monthly acute medication days, particularly triptan days (Weeks 1–4 and 1–12, $p<0.01$ all comparisons). During the OLE period, improvements were sustained for those continuing eptinezumab, and those started on placebo achieved similar changes from baseline as those continuing eptinezumab.

Conclusion: In participants with CM and MOH who also received patient education at baseline, eptinezumab resulted in greater reductions than placebo in acute medication use over Weeks 1–12. Similar reductions from baseline were seen in both arms during open-label eptinezumab treatment (Weeks 13–24).

P095

Efficacy and safety of combination of anti-CGRP monoclonal antibodies and onabotulinumtoxinA in chronic migraine treatment: A systematic review and meta-analysis

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Objective: Migraine is a common, disabling disorder with CGRP as a key therapeutic target. OnabotulinumtoxinA, which inhibits CGRP release from unmyelinated C nociceptive fibers, and anti-CGRP monoclonal antibodies (mAbs), which selectively block CGRP-receptor interaction at meningeal vessel walls, peripheral sites and along Aδ fibers offer preventive options for chronic migraine (CM). While combining may improve outcomes, their interaction—additive or synergistic—remains unclear. This systematic review and meta-analysis assesses current evidence on their combined use for CM prevention and treatment.

Methods: Following PRISMA 2020, PubMed, ProQuest, Lancet, EBSCO, and ClinicalTrials.gov were searched (past 10 years). Eligible randomized and observational studies reported monthly migraine days (MMD), monthly headache days (MHD), and adverse events. Pooled analyses employed random-effects models; risk of bias was assessed with RoB 2.0/ROBINS-I and funnel plot, and GRADE analysis was done independently.

Results: 5 studies (n=615, all with diagnosis of CM) were included, comparing three combination regimens to onabotulinumtoxinA monotherapy. Erenumab + onabotulinumtoxinA showed significant reductions in MHD (-5.53 days; 95% CI: -7.76, -3.30; p<0.00001, low certainty) and MMD (-4.42 days; 95% CI: -6,28, -2.56; p<0.00001, low certainty) compared to onabotulinumtoxinA alone. Galcanezumab + onabotulinumtoxinA yielded borderline significant MHD reduction (-5.30 days; 95% CI: -10.54, -0.06; p=0.05, low certainty) compared to onabotulinumtoxinA alone. Safety profiles were favorable with no serious adverse events reported.

Conclusion: Combining anti-CGRP mAbs with onabotulinumtoxinA appears to be a promising approach for CM prevention. Although current safety data are limited, the reported adverse events have generally been mild. Further research is needed to establish its safety, efficacy, and optimal protocols in episodic and chronic migraine populations.

Fig. 1

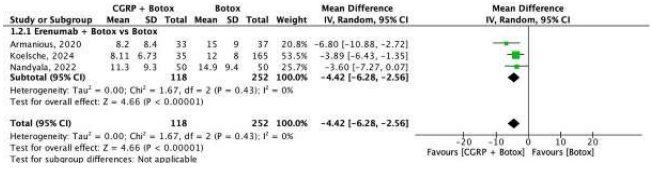


Fig. 2

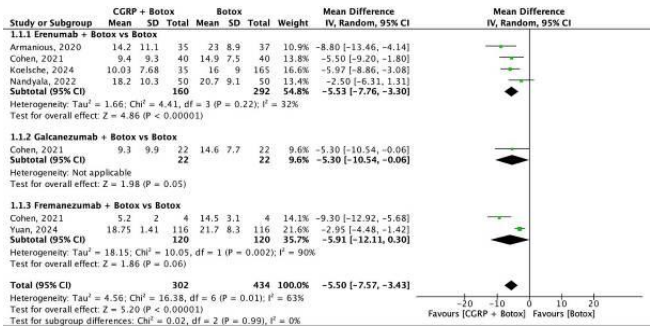
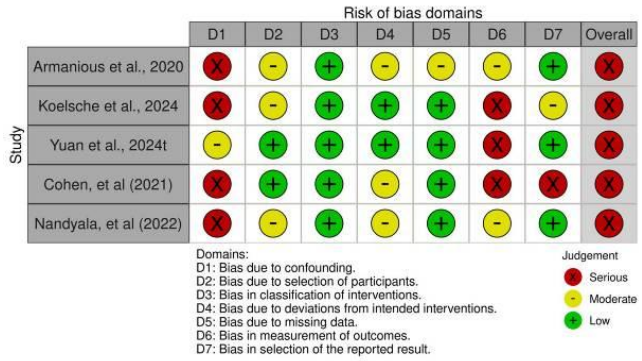


Fig. 3



P096

Association between the clinical profile of patients with trigeminal neuralgia and treatment resistance: Case series analysis

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Objective: Is There an Association Between the Clinical Profile of Patients with Trigeminal Neuralgia and Treatment Resistance?

Methods: This retrospective study included all patients diagnosed with Trigeminal Neuralgia (TN) seen at the Headache Outpatient Clinic of Hospital Egas Moniz between January 2024 and April 2025. A total of 51 patients met the inclusion criteria. Demographic, clinical, and imaging data were collected. Statistical analysis was conducted using IBM SPSS version 29.0. Non-parametric tests were applied because the variables had a non-normal distribution. Treatment resistance was defined as the use of three or more medications.

Results: The sample consisted of 66.7% female patients, with a mean age at symptom onset of 60.2 ± 17.0 years. MRI was performed in 35 patients, with abnormalities detected in 65.7% of cases. No significant associations were found between MRI findings and the side or location of pain, neurological signs, disease relapse, botulinum toxin usage, or surgical interventions. TN was classified as classical (40%), idiopathic (50%), and secondary (10%). The average number of medications prescribed was 2.7 ± 1.3. There was no significant association between the number of drugs and disease duration or age at symptom onset. Although the number of medications did not differ significantly across TN subtypes, patients with secondary TN tended to require more medications (mean: 4.3). In a small subgroup (n = 3), satisfactory pain control was achieved using lacosamide in combination with another medication.

Conclusion: In patients with TN, no clinical or imaging variables were significantly associated with treatment resistance. These findings suggest that standard clinical characteristics may not fully explain therapeutic response, emphasizing the need for individualized treatment strategies and further research into predictive biomarkers. Preliminary observations also support further investigation of lacosamide as a potential first-line treatment option."

P097

Evaluating the efficacy of combined treatment in patients with Persistent Idiopathic Facial Pain (PIFP)

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Objective: Persistent idiopathic facial pain (PIFP) (previously known as atypical facial pain) is characterized by persistent facial and/or oral pain in the absence of a neurologic deficit. Due to the lack of the large-scale multi-center randomized control trials, current guidlines for the treatment regimen are limited in terms of evidence quality. Our main goal was to assess the effectiveness of the combined treatment with antidepressant and an antiseizure medication, based on patient feedback collected during clinical follow-up.
Methods: A retrospective analysis was conducted on 9 patients meeting diagnostic criteria for PIFP. Clinical data that included initial symptoms on the admission, prior medical history, prescribed treatments and therapeutic responses were reviewed. All patients received combinations of medications targeting neuropathic pain and musculoskeletal tension, antidepressants (e.g., duloxetine, venlafaxine), anticonvulsants (e.g., carbamazepine, gabapentin) and COX-2 inhibitors.
Results: Most patients reported partial or significant symptom relief with combination therapy (n=6; ~67%) The most consistently effective regimens involved duloxetine or venlafaxine combined with carbamazepine or gabapentin. Symptom patterns varied, including hemifacial pain, burning sensations, periorbital pain, and jaw tightness. Some patients had comorbid conditions such as migraine, bruxism, or post-COVID syndromes (n=3). Neuroimaging was largely unremarkable, except in one case suggesting a possible neurovascular conflict. Treatment response often required dose titration.
Conclusion: Combined pharmacological approaches targetting both neuropathic and affective components may provide meaningful symptom control in PIFP.

P098

Trigeminal neuralgia secondary to posterior fossa arteriovenous malformation and hydrocephalus: A diagnostic and therapeutic challenge

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Objective: Classical trigeminal neuralgia typically results from neurovascular compression at the root entry zone of the trigeminal nerve, most commonly by the superior cerebellar artery (SCA). Although rare, the concomitant presence of a posterior fossa arteriovenous malformation (AVM) can underlie this condition, adding diagnostic and therapeutic complexity.
Methods: Clinical case
Results: A 32-year-old woman presented with paroxysmal facial pain in the right V3 territory, described as brief, electric shock-like episodes triggered by touch, chewing, and speech, with progression to eight daily episodes within one month. Neurological examination revealed macrocephaly, inattention, gaze-evoked horizontal nystagmus, generalized hyperreflexia, and broad-based gait.
Brain CT showed hydrocephalus with sulcal effacement. CT angiography revealed a large posterior fossa AVM (Spetzler-Martin grade V) centered in the superior vermis. MRI confirmed compression of the right trigeminal nerve by an ectatic SCA and periventricular edema due to chronic hydrocephalus. Angiography identified multiple arterial feeders (SCAs, PICAs) and venous aneurysms causing brainstem molding.
Carbamazepine 200 mg every 8 hours led to full pain resolution within 48 hours. Due to its size and complexity, the AVM was deemed inoperable. The clinical picture was attributed to decompensation of chronic hydrocephalus, and placement of a ventriculoperitoneal shunt resulted in marked improvement of gait and balance. Three months post-discharge, medical therapy was successfully withdrawn.
Conclusion: This case illustrates a rare presentation of trigeminal neuralgia secondary to a large posterior fossa AVM, associated with decompensated chronic hydrocephalus. Although there was a favorable response to initial medical and surgical management, the case underscores the need for careful consideration of alternative therapeutic strategies should symptoms recur in a patient with an inoperable AVM.

P099

Predictive factors of response to anti-CGRP monoclonal antibodies in patients with multiple sclerosis

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Objective: The study aimed to investigate the predictive factors of response to Calcitonin gene-related peptide (CGRP)–targeted therapies in patients with migraine and multiple sclerosis (MS).
Methods: This retrospective, multicenter study (17 Italian MS centers) included patients with MS treated with anti-CGRP monoclonal antibodies (mAbs) or gepants, combined with disease-modifying treatments (DMTs), on a stable DMT regimen for at least three months before the anti-CGRP targeted therapy initiation and a minimum follow-up period of three months for the concomitant treatment. Collected MS data included age at onset, prior and current DMT, EDSS score, MRI activity, and clinical relapses. Collected migraine data included monthly headache days (MHDs) before and at last follow-up, disease duration, age at onset, type, and duration of anti-CGRP mAb treatment. A multivariate linear regression model was then used to examine the associations between predictor variables and treatment response (MHD delta from baseline to last follow-up).
Results: Of the 47 patients included (mean age±SD 42.86±9.68 years, 87% females), 87% had relapsing MS, and 13% had progressive MS. Mean MS age onset was 28.33±9.11 years while mean migraine age onset was 19.04±8.12 years. At baseline, the mean MHDs was 20.5±7.05. Mainly used DMTs were ocrelizumab (25.5%), natalizumab (19.1%), and dimethyl fumarate (17.0%), while anti-CGRP treatments included anti-CGRP mAbs (95%) and atogepant (5%). The mean interval between DMT initiation and anti-CGRP therapy was 53.33± 40.81 months. Baseline MHD positively predicted treatment response (β = +0.894, p< 0.01), indicating that patients with a higher initial migraine burden experienced a greater reduction in MHDs. Conversely, longer MS duration was linked to reduced benefit (β=–0.749, p=0.02).
Conclusion: We confirm the safety of combined DMT and CGRP treatments in patients with both conditions. Timely and tailored therapy should be planned early in MS disease course to achieve the best outcomes.

P100

Super-refractory cerebrospinal fluid hypotension headache: A case report

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Objective: Dural tears/subarachnoid-venous communications may cause cerebrospinal fluid hypotension (CSFH). Though rarely severe, extreme measures with anecdotal evidence may sometimes be needed.
Methods: Case-report
Results: A 74-year-old woman with no trauma history had acute intense orthostatic headache. Brain CT revealed pachymeningeal enhancement and bilateral 10mm subdural effusions. She was given paracetamol, caffeine and fluids. MRI revealed C6-7, D3, D8-11, L3 and S1-2 spinal nerve root cysts. Poor response prompted lumbar blood patch (BP). Confusion and obtundation were noted even prior, followed by coma in the subsequent hours. A 2nd CT showed convexity effusion enlargement and de novo 9mm falcine hemorrhage with cerebellar tonsil herniation. She was ventilated after antiseizure therapy failed. EEG showed diffuse slowing. Trendelenburg positioning and vigorous L3-4 intrathecal saline administration were tried after demonstrated negative pressure upon subarachnoid space catheterization, with marked consciousness improvement in 48h. Upright headache recurred, however, and CT myelography showed an active D11 CSF leak and distant bilateral kidney enhancement, suggestive of a CSF-venous fistula. A 2nd dorsal BP was performed. However, prostration ensued so more fluid was instilled at the catheter site, and digital subtraction myelography revealed another major lumbar CSF leak at the

catheter placement site. It was surgically closed, a new catheter was placed at L2 with maintained 30cmH2O pressure post-fluids, and a final target epidural patch was done to the high-flow CSF from a mixture of iodine contrast, autologous blood and fibrin glue. The patient regained full consciousness and tolerated progressive standing, headache-free.

Conclusion: This case highlights the complex management of BP-refractory CSFH. Coma precipitated intrathecal fluid reposition, which is rarely reported but may have allowed our patient time for further investigation, though with complications, before definite leak closure.

P101

Middle meningeal artery lidocaine infusion for refractory migraine: First case report in Portugal

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Objective: Refractory migraine is a disabling and hard-to-treat condition. Middle meningeal artery (MMA) lidocaine infusion may be a treatment option.

Methods: Case report.

Results: A 42-year-old man with episodic migraine since the age of 20 developed chronic daily bifrontal headaches, pressure-like, associated with photophonophobia, kinesiophobia, and anorexia. The condition was further complicated by medication-overuse headache, resulting in multiple hospital admissions.

Various pharmacologic classes were tried without benefit: antihypertensives and calcium channel blockers (propranolol, candesartan, flunarizine), antiepileptics (valproic acid, topiramate, oxcarbazepine), antidepressants (amitriptyline, nortriptyline, venlafaxine, fluvoxamine, sertraline, clomipramine), other preventives (prednisolone, oxitriptan, melatonin), cycles of botulinum toxin (PREEMPT protocol), monoclonal antibodies (galcanezumab, fremanezumab, erenumab), and atogepant.

At the time of the procedure, the patient was on eptinezumab 100 mg and botulinum toxin every three months but continued to have daily headaches, with severe intensity and reliance on eletriptan for acute relief. A selective lidocaine infusion into both middle meningeal arteries was performed under angiographic guidance resulting in immediate and sustained reduction in headache intensity, fewer migraine days, and decreased eletriptan use. HIT-6 score improved from 67 to 55 at 30-day follow-up. MIDAS assessment will be more informative after longer follow-up. No adverse events occurred.

Conclusion: MMA lidocaine infusion has been described in few cases, and this is, to our knowledge, the first reported in Portugal. It constitutes an invasive therapeutic approach that should be considered only as a rescue option for carefully selected patients with severely refractory migraine. Further studies and long-term follow-up are needed to assess efficacy and safety.

P102

Combining anti-CGRP antibodies with atogepant: Safety and efficacy in a patient cohort

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Objective: Atogepant is reimbursed by the Portuguese National Health Service since January 2025. This study aims to assess safety and efficacy of combined treatment with anti-CGRP monoclonal antibodies (mAbs) plus atogepant in patients with migraine.

Methods: We reviewed a prospective, standardized database of migraine patients treated with a combination of anti-CGRP monoclonal antibodies (mAbs) and atogepant at our tertiary hospital between January and June 2025. Clinical data were collected at baseline and three months after initiation of the combined treatment.

Results: Among 27 patients (26 women; mean age 45.9 ± 1.4 years), the average number of prior oral preventive treatments was 4.3 ± 0.3. All had previously received botulinum toxin (7 continued it). Treatments included erenumab (n=1), fremanezumab (n=11), galcanezumab (n=6), and eptinezumab (n=9). At three months, improvements were observed in monthly migraine days (mean 12.6 ± 7.8 vs. 9.5 ± 7.5; $p = 0.044$), but not in headache days (mean 17,3 ± 8.9 vs. 14.9 ± 9.9; $p = 0.053$), or HIT-6 (mean 64,9 ± 6,1 vs 62,5 ± 5,7, $p = 0.197$). Regarding safety, one patient who initiated atogepant and subsequently added eptinezumab reported new-onset asthenia. Among the 26 patients who added atogepant to an ongoing mAb, 9 reported new adverse events: constipation (n=2), asthenia (n=2), nausea (n=2), somnolence (n=2), insomnia (n=1) and weight gain (n=1). No serious adverse events were reported.

Conclusion: In this real-world cohort, combining anti-CGRP mAbs with atogepant appears to be safe and may offer additional benefit.

P103

Real-world evidence of monoclonal antibodies use in refractory migraine patients on polytherapy: Insights from a headache center

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Objective: Preventive polytherapy is often used in refractory migraine, despite limited evidence and potential drug interactions. We aimed to examine the impact of initiating monoclonal antibodies (MAbs) on polytherapy migraine regimens.
Methods: Prospective cohort study, at a single headache center, targeting individuals with a >1 prophylactic treatment failure (TF) in the past 5 years. Statistical analysis performed with SPSSvs.26 (significance value <0.05).
Results: Of the 144 patients (n=133, 91.7% females; mean age: 43.8±11.5years), 58.3% (84) had episodic migraine. The median number of TF pre-MAbs was 5.0 (IQR=[3.0-6.0]); 66.7% had ≥4TF. On inclusion (M0), preventive polytherapy was being used in 51.4% [74; 63.5% (47) with 2 prophylactics, 31.1% (23) 3, and 4.1% (3) ≥4 simultaneously]. The median duration of MAbs treatment was 12.0[5.0-22.0] months, with an effective therapeutic response of 76.4% (110). At months 3 (M3), 6, and 9 the number of individuals with ongoing oral preventives decreased (M0=3.58>M6=2.70>M9=2.55; at M6, 19 have stopped all oral preventives). Further reduction in MHD (M0=12.0[8.7-18.0] vs. M3=5.3[3.3-10.0], p<0.001), pain intensity (7.5[6.5-8.0] vs. 5.0[4.0-7.0], p<0.001) and monthly rescue medications days (10.0[7.7-15.0] vs. 4.5[2.0-7.9], p<0.001) at M3. In the responders" group, using Ranks" average, there was a reduction in the number of visits to the emergency room (M0=1.56 vs. M3=1.45, p=0.003) and absences from work (M0=0.6[0.0-4.0] vs. M3=0.0[0.0-0.0], p<0.001) at M3.
Conclusion: In this sample, MAbs proved to have beneficial effects not only by diminishing the necessity for preventive polytherapy in patients with refractory headache but also by ameliorating the impact and disability associated with migraine.

P104

Clinical outcomes of botulinum toxin type A in chronic migraine: Real-world data from Unidade Local de Saúde de Trás-os-Montes e Alto Douro

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Objective: Chronic migraine is a disabling neurological disorder defined by ≥15 headache days per month. OnabotulinumtoxinA is the first neurotoxin specifically approved for its prophylaxis. This study aimed to evaluate clinical outcomes in patients with chronic migraine treated with botulinum toxin type A at a regional tertiary center (Unidade Local de Saúde Trás-os-Montes e Alto Douro), focusing on changes in headache frequency, severity, and tolerability.
Methods: A retrospective review was conducted of adults diagnosed with chronic migraine who received botulinum toxin type A injections for prophylaxis from 2019 to April 2025. Data collected included baseline and post-treatment monthly headache days, migraine severity, and adverse events.
Results: Forty-five patients (mean age 48.3 years, 84.4% women) were included. Eighteen (40%) remain on regular treatment; among those who discontinued, the main reason was lack of clinical benefit (59.3%), while 22.2% improved and no longer met criteria for treatment. Among ongoing patients, the mean treatment duration to date was 2 years and 3 months. Of these, 83.3% reported a reduction in monthly headache days, ranging from 3 to over 13 fewer days per month. Only one patient reported a mild, self-limited adverse event following treatment. Notably, 35.6% of patients were simultaneously or sequentially treated with anti-calcitonin gene-related peptide monoclonal antibody or calcitonin gene-related peptide receptor antagonist, which, according to real-world and retrospective data, can provide additional reductions in monthly migraine days when compared to monotherapy, likely due to their complementary mechanisms of action within the trigeminovascular system.
Conclusion: These findings are consistent with randomised trials and meta-analyses, which show a reduction of headache days per month and significant improvements in severity and disability scores, with a favourable safety profile.

P105

Analysis of the influencing factors of treatment efficacy and poor prognosis after comprehensive management of patients with moderate to severe migraine disability

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Objective: To evaluate the efficacy of a comprehensive management plan for patients with moderate to severe disabilities in migraine, explore

factors affecting poor prognosis, and provide a basis for optimizing treatment strategies.

Methods: Data from 164 migraine patients from September 2022 to September 2024 were collected, and the Migraine Disability Assessment (MIDAS) questionnaire was used to divide them into no or mild impairment group (MIDAS≤10) and moderate to severe impairment group (MIDAS>10). This study mainly included 98 patients with moderate to severe disabilities. After a 6-month intervention, patients were divided into a good prognosis group (MIDAS≤10) and a poor prognosis group (MIDAS>10). For patients with poor prognosis explore the factors that affect poor prognosis.

Results: After comprehensive management, MIDAS, MoCA, GAD-7, PHQ-9, PSQI, HIT-6, SF-36, P<0. 05. The results of multiple logistic regression analysis showed a significant correlation between multiple factors and poor prognosis in migraine patients. In terms of age, PHQ-9, HIT-6, SF-36, P<0. 05.

Conclusion: The comprehensive management plan has significant therapeutic effects on patients with moderate to severe disabilities in migraine. Age, PHQ-9, HIT-6, and SF-36 are independent influencing factors for poor prognosis.

P106

Octreotide in the management of pharmacoresistant idiopathic intracranial hypertension: A case report

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Objective: Idiopathic Intracranial Hypertension (IIH) is a condition with unknown pathophysiology, involving factors such as obesity, growth hormone (GH) production, increased cerebrospinal fluid (CSF) production, and impaired reabsorption, which lead to symptoms like headache and visual acuity loss. First-line pharmacological treatment includes acetazolamide, a carbonic anhydrase inhibitor that reduces CSF production, along with topiramate or diuretics. Alternatives include GLP-1 receptor analogs, 11B-HSD1 inhibitors, and octreotide.

Methods: We present the case of a 34-year-old obese woman diagnosed with IIH, treated with furosemide and topiramate, with poor response and limiting side effects. She refused a ventriculoperitoneal shunt, so treatment with octreotide was started at 0.2 mg/24h for 5 days, then 20 mg/month for 6 months.

Results: Octreotide acts as a somatostatin receptor agonist in the choroid plexus, decreasing CSF production and inhibiting GH and IGF-1. One month after treatment initiation, clinical improvement and resolution of papilledema were observed, which persisted after discontinuing treatment at 6 months.

Conclusion: Treatment-refractory IIH presents a therapeutic challenge. Octreotide is a promising alternative with favorable outcomes, expanding therapeutic options for this condition.

P107

Inhaled Acetylsalicylic Acid (ASA) reaches therapeutic blood levels and effectively blocks cyclooxygenase enzymes

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Objective: ASA has antithrombotic and analgetic effects, however when administered orally exhibits numerous gastrointestinal side effects, which limits the dose. Orally inhaled ASA avoids these side effects and utilizes the lung as a safe route of administration. While the GI side effects can also be avoided with intravenous (i.v.) administration, inhaled ASA would allow for flexible self-treatment by the patient, at home or on the road. The purpose of this study was to compare the PK of different inhaled doses of ASA to i.v. administration.

Methods: In a multiple cross-over study in healthy subjects, pharmacokinetics and pharmacodynamic effects of inhaled ASA, applied with a newly developed mesh inhaler device (ASCOT® inhaler), were investigated and compared to ASA i.v. In total, 16 healthy subjects received 4 different single doses of inhaled ASA (250 mg, 500 mg, 750 mg at 87.5 mg/mL) and one intravenous dose of ASA (500 mg at 87.5 mg/mL) in a randomized 4-times cross-over design. In a separate study part, 500 mg ASA at 158.7 mg/mL were inhaled by 12 subjects. Blood levels of ASA and salicylic acid (SA), as well as Thromboxane B2 (TxB2) were measured over a period of 24 hours post-dose.

Results: Inhalation was safe and well tolerated. Measured PK profiles showed a good dose-exposure relationship. Typical adverse events observed, such as coughing or sore throat, were mainly mild and dependent on the dose and the inhaled concentration of ASA. Pharmacokinetic analyses showed a rapid bioavailability of 62% of the delivered dose. The decrease in TxB2 levels with inhalation was similar to i.v. treatment 30 min post-dose. This effect remained even after 24 hrs.

Conclusion: Inhaled ASA is safe, and the PK data supports the approach. The rapid and consistent decrease of TxB2 levels point towards a similar beneficial effect on pain compared to the standard i.v.

treatment. Further studies should be carried out in patients to confirm the initial results.

P108

Use of mediation modeling to examine the relationships among treatment with rimegepant, headache pain severity, and functional disability in patients with migraine

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Objective: To estimate the extent to which rimegepant-mediated reductions in pain intensity contribute to improvements in physical functioning during the acute phase of migraine.

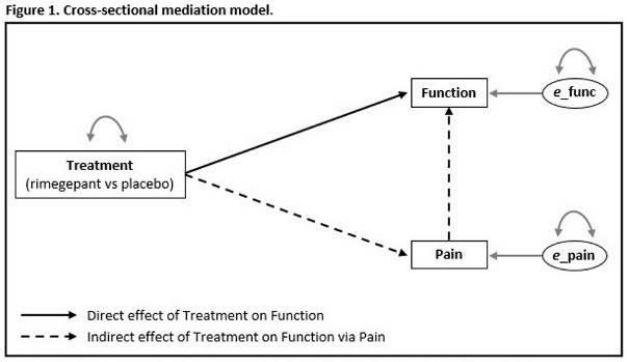
Methods: Data were pooled from 4 placebo-controlled trials of rimegepant 75 mg for the acute treatment of migraine (NCT03235479, NCT03237845, NCT03461757, NCT05399459). Participants rated current pain and functional disability on 4-point scales prior to dosing and from 15 min to 48 h post dose. A cross-sectional mediation model including variables for pain, function, and treatment (rimegepant or placebo; Figure 1) was run separately at each timepoint. Based on results of cross-sectional modeling, a longitudinal pseudo-steady state mediation model was constructed to estimate relationships between variables using all available data during the period when all processes in the model were considered to have achieved and maintained equilibrium. The pseudo steady-state model assumed relationships between variables were the same at all timepoints.

Results: Across all studies, participants (N = 3975) were mostly female (77.4%–88.7%) and mean age was 40.2–41.6 years. Cross-sectional models (N = 3441–3834 across time points) indicated that the period represented by measurements at 3, 4, 6, and 8 h can be considered as a pseudo-steady state period for a mediation model representing interrelationships among pain, function and treatment. The pseudo steady-state model (N = 3281) incorporated all available data from 3, 4, 6, and 8 h post dose (**Figure 2**) and estimated that 76.1% of the effect of treatment on function is mediated indirectly via improvements in pain, with 23.9% representing a direct effect (representing all other effects/mediators not included in the model; **Figure 3**).

Conclusion: The effect of rimegepant on functioning was largely mediated through reductions in pain intensity during the acute migraine attack phase. Approximately one-quarter of the improvement in functioning was mediated through factors other than pain intensity.

Fig. 1

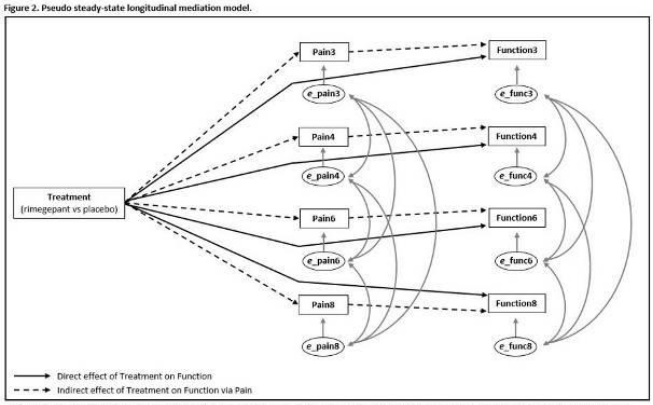
Figure 1. Cross-sectional mediation model.



Treatment is a binary variable: rimegepant (value of 1) or placebo (value of 0). Function represents functional disability (rated on a scale of 0 = normal, 1 = mildly impaired, 2 = severely impaired, 3 = requires bedrest). Pain represents headache pain severity (rated on a scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe). *e_*pain and *e_*func represent error terms. Curved 2-headed arrows pointing to the same variable represent variance.

Fig. 2

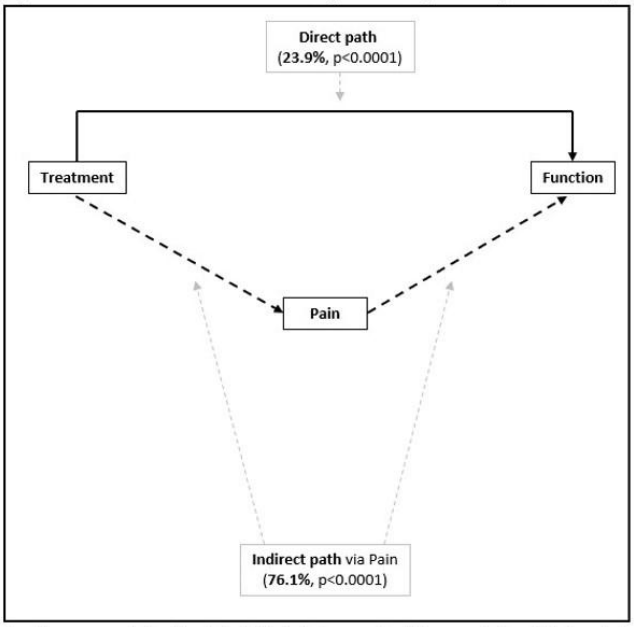
Figure 2. Pseudo steady-state longitudinal mediation model.



Treatment is a binary variable: rimegepant (value of 1) or placebo (value of 0). Function3, 4, 6, and 8 represents functional disability at 3, 4, 6, and 8 h post dose, respectively (rated on a scale of 0 = normal, 1 = mildly impaired, 2 = severely impaired, 3 = requires bedrest). Pain3, 4, 6, and 8 represents headache pain severity at 3, 4, 6, and 8 h post dose, respectively (rated on a scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe). *e_*pain and *e_*func represent error terms. Curved 2-headed arrows pointing to the same variable represent variance. Curved 2-headed arrows pointing to different variable represent covariance.

Fig. 3

Figure 3. Estimated direct and indirect effects (pseudo steady-state longitudinal model).



Function represents functional disability (rated on a scale of 0 = normal, 1 = mildly impaired, 2 = severely impaired, 3 = requires bedrest). Pain represents headache pain severity (rated on a scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe).

P109

Trigeminal neural and hemifacial spasm – An uncommon association

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Objective: To describe a case of concurrent trigeminal neuralgia and hemifacial spasm caused by trigeminal neurovascular contact and to discuss the underlying pathophysiological mechanisms.
Methods: Patient gave their consent to publish their details in an open access journal.
A 61-year-old female presented with a 3-year history of recurrent electric shock-like pain attacks in the left hemiface, along the maxillary and mandibular trigeminal nerve branches' distribution. The pain usually lasted a few seconds and recurred multiple times a day. Some episodes were triggered by talking and touching the face.
Results: The neurological examination showed a left-sided hemifacial spasm. The MRI showed a point of contact with the anterior inferior cerebellar artery in the prepontine cistern. The patient started eslicarbazepine acetate 400 mg as a single daily dose, titrated to 800 mg, and the trigeminal neuralgia attacks were markedly reduced. She was referred to a Neurosurgery consultation, but surgical options were deferred due to marked clinical improvement with medical treatment. The hemifacial spasm was successfully treated with botulinum toxin injections every 6 months.
Conclusion: This case underscores the rare co-occurrence of trigeminal neuralgia and ipsilateral hemifacial spasm, with evident vascular compression of the trigeminal nerve but no identifiable facial nerve compression. These findings support the hypothesis that facial nerve hyperactivity may result from aberrant activation of the trigemino-facial reflex pathway, even without direct anatomical compression.

Fig. 1



P110

What happens to bone in chronic migraine patients after one year of anti-CGRP therapy? A prospective study of bone metabolism markers and densitometric parameters

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Objective: CGRP is a known modulator of bone homeostasis. We prospectively investigated the evolution of bone metabolism and density in chronic migraine patients during their first year of monoclonal anti-CGRP antibody (mAb-CGRP) treatment.
Methods: Sixty (60) patients with chronic migraine were recruited. Biochemical markers of bone formation (P1NP) and resorption (CTX) were measured at baseline (M0), three (M3), and twelve (M12) months after starting mAb-CGRP therapy. Scans were performed at M0 and M12 at lumbar spine, femoral neck, and total hip to determine the bone mineral density (BMD). T-scores were calculated for all sites. Analyses were stratified by menopausal status.
Results: P1NP levels showed a non-significant downward trend over time (M0: 40.4 [32.7–59.5] µg/L; M3: 38.8 [28.2–51.7] µg/L, $p > 0.999$; M12: 37.8 [29.7–51.1] µg/L, $p > 0.999$). Similarly, CTX levels remained unchanged (M0: 0.324 [0.254–0.446] pg/mL; M3: 0.322 [0.228–0.443] pg/mL, $p > 0.987$; M12: 0.278 [0.200–0.483] pg/mL, $p > 0.999$). Lumbar spine bone mineral density significantly declined after one year (M0: 0.979 [0.897–1.041] g/cm²; M12: 0.949 [0.873–1.014] g/cm², $p = 0.001$), with a corresponding decrease in lumbar T-scores (M0: –0.9 [–1.6–0.0]; M12: –0.9 [–1.6–(–0.3)], $p = 0.003$). When stratified by menopausal status, this decline remained significant only among postmenopausal women ($n = 23$; $p = 0.004$ for bone mineral density, $p = 0.005$ for T-score). No significant changes were observed at femoral neck or hip sites.
Conclusion: One year of mAb-CGRP treatment may negatively affect bone formation, particularly in postmenopausal women with chronic migraine. While no significant alterations were observed in biochemical markers, bone density findings suggest localized bone loss at the lumbar spine. These preliminary results underscore the importance of bone health surveillance and preventive strategies in women receiving long-term anti-CGRP therapies.

Work supported by grants PI21/00532 and PMP22/00183.

P111

Bone metabolism alterations in women with chronic migraine eligible for anti-CGRP therapy: A comorbidity worth monitoring

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Objective: To evaluate bone metabolism in women with chronic migraine (CM) eligible for monoclonal anti-CGRP antibody (mAb-CGRP) treatment, compared to age- and sex-matched healthy controls (HC)

Methods: Before initiating mAb-CGRP therapy, biochemical assessments were performed in 97 women with CM and 111 HC, including serum levels of calcium, vitamin D, parathyroid hormone (PTH), and bone turnover markers, procollagen type 1 N-terminal propeptide (P1NP) and C-terminal telopeptide of type I collagen (CTX). Densitometries were conducted at lumbar spine, femoral neck, and total hip to determine bone mineral density (BMD) and T-scores. Trabecular bone score (TBS) was also calculated. Prevalence of osteoporosis was derived from T-Scores

Results: Women with CM had significantly lower serum calcium (9.5[9.2–9.8]mg/dL vs 9.7[9.4–9.9]mg/dL; p=0.001) and vitamin D levels (20[14–25]ng/mL vs 26[20–30]ng/mL; p<0.001) compared to HC. Bone turnover markers showed numerically reduced values in CM patients: P1NP (39.7[32.0–60.0] vs 44.8[35.1–58.9] µg/L; p=0.119) and CTX (0.339[0.257–0.537] vs 0.360[0.250–0.500] pg/mL; p=0.890), but did not reach statistical significance. However, CM patients exhibited significantly lower TBS (1.3[1.2–1.4] vs 1.4[1.3–1.5]; p<0.001), femoral BMD (0.708[0.608-0.795] vs 0.770[0.710–0.860]g/cm²; p<0.001), femoral T-score (–1.3[–2.1–(–0.5)] vs –0.8 [–1.2–0.0]; p<0.001), hip BMD (0.843 [0.744–0.929] vs 0.880[0.800–0.970]g/cm²; p=0.015), and hip T-score (–0.8[–1.6–(–0.2)] vs –0.5[–1.2–0.2]; p=0.022). The proportion of osteoporosis showed numerical differences althpuh it did not achieve statistical signifance (CM: 23.7% vs HC: 13.5%; p=0.057).

Conclusion: Women with CM eligible for mAb-CGRP therapy present with relevant bone metabolism alterations before treatment initiation. These findings highlight the need for routine skeletal health assessment and preventive care strategies in this population, especially in those at risk of osteoporosis.

Supported by PI21/00532 and PMP22/00183

P112

Increased integration and synergy in EEG- and fNIRS-based data in migraine patients after a three-month treatment with galcanezumab: Relations with long-term clinical outcome

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Objective: Galcanezumab (GCA) is a well-tolerated monoclonal antibody developed for migraine prophylaxis. This study further explores GCA-induced central changes by investigating the metabolic-electrical brain interaction and network properties.

Methods: We employed a multimodal approach combining electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS), along with high-order connectivity analysis obtained using Partial information Decomposition (PID), and explored the relationship between neurophysiological measures and long-term clinical effects of GCA in 20 patients under GCA therapy . Clinical outcomes were reassessed after one year of treatment (1Y). Ten healthy controls also underwent EEG/fNIRS recordings. EEG and fNIRS signals were analyzed and harmonized. We computed global network properties including strength, global efficiency, clustering coefficient, sinergy and redundancy.

Results: For both EEG and fNIRS data, we found lower strength and clustering coefficients in patients than in controls at all time points $(p<0.05)$, with no differences between time points. Global efficiency significantly increased in patients at 3M, reaching levels comparable to those of the control group. PID on fNIRS data showed an overall increase in redundancy and synergy after treatment $(p<0.05)$. For both EEG and fNIRS data, synergy and global efficiency at 3M significantly correlated with clinical indicators at 1Y, including the Migraine Disability Assessment and the number of acute medications/month $(p<0.05)$.

Conclusion: The results support the hypothesis of specific anti-nociceptive GCA effects associated with increased integration in functional and electrical brain connectivity, and also indicated that EEG/fNIRS synergy analysis may serve as a potential predictive factor of GCA-related clinical improvement.

Fig. 1

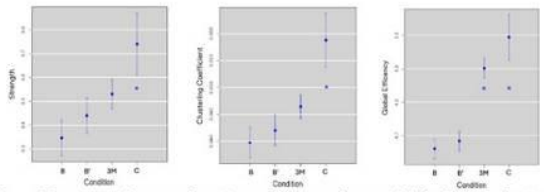


Fig . Mean strength, mean clustering coefficient and mean global efficiency obtained from EEG networks of the occipital brain area for the different conditions, B, B', 3M and normal controls (C), in the theta frequency band. Significant results of the Wilcoxon rank-sum test are indicated with the blue stars.

Fig. 2

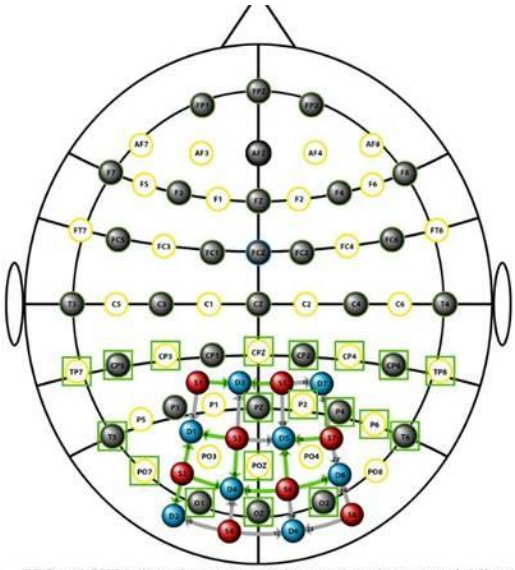


Fig EEG and fNIRS channels, in green, with a significantly statistical difference between B and $3M$.

Fig. 3

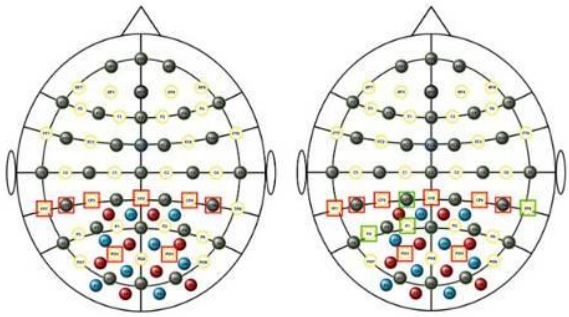


Fig 8. Clusters of EEG channels built on Synergy levels in B and $3M$. In green are highlighted the channels gained in $3M$ with respect of B.

P113

Synergistic antimigraine effects of lisinopril and memantine associated with an improved therapeutic index

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Objective: Despite available treatments, many migraine patients experience suboptimal response or tolerability issues. Combining agents with complementary neurological and vascular mechanisms may offer improved outcomes in preventive therapy. This study evaluated the pharmacodynamic interaction between lisinopril and memantine, both of which have shown efficacy in randomized controlled trials and are used off-label for migraine prophylaxis.

Methods: The efficacy of lisinopril and memantine, administered alone and in combination (1:1 dose ratio), was tested in two rat models of migraine involving chronic trigeminovascular sensitization: (1) partial infraorbital nerve ligation (pIONL) and (2) repetitive dural inflammatory soup infusion (rDISI). Orofacial or periorbital tactile allodynia was measured using von Frey filaments. Additionally, pharmacodynamic interactions on blood pressure and heart rate were assessed in awake, unrestrained rats via cardiovascular telemetry. Dose–response curves were generated and compared.

Results: In the pIONL model, both drugs reversed allodynia in a dose-dependent manner, while the combination produced a five-fold leftward shift in the dose–response curve, indicating synergy. In the rDISI model, lisinopril reversed allodynia in a dose-dependent manner, whereas memantine alone had only minimal effect. However, when co-administered, memantine markedly potentiated the effect of lisinopril, enabling a ten-fold dose reduction. Cardiovascular telemetry confirmed lisinopril's expected effects: blood pressure reduction and dose-dependent reflex tachycardia. Memantine had no cardiovascular effects and did not alter lisinopril's profile in combination.

Conclusion: Lisinopril and memantine exhibit strong pharmacodynamic synergy in migraine models without adverse or amplifying cardiovascular effects. This combination may offer enhanced efficacy with a favourable side effect profile, supporting its potential utility in migraine prophylaxis.

P114

Atogepant demonstrates greater improvement in function using the activity impairment in migraine-diary (AIM-D) during interictal days: Post-hoc analysis from the PROGRESS chronic migraine trial

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[5]Mayo Clinic, Scottsdale, AZ, United States

Objective: The interictal phase, the period between migraine attacks, is linked with symptoms that negatively impact daily functioning. This post-hoc analysis evaluates the impact of atogepant(ato) on interictal days using daily diary data from the Activity Impairment in Migraine-Diary(AIM-D).

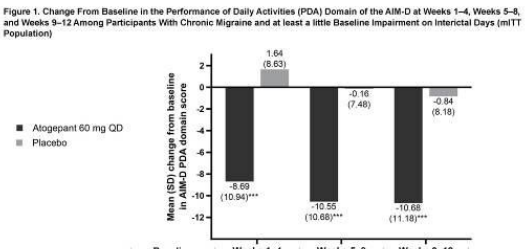
Methods: PROGRESS, a phase 3, multicenter, randomized, double-blind, placebo(pcb)-controlled, parallel-group trial enrolled patients with ≥1-yr history of chronic migraine(CM). After a 4-wk screening period, adults with CM were randomized to receive ato 30mg twice daily, ato 60mg once daily(QD), or pbo for 12wks. AIM-D consists of 11 items across two domains: Performance of Daily Activities(PDA) and Physical Impairment(PI). Domain scores are converted to a 0–100 point scale, with higher values indicating greater burden.

This analysis focused on participants receiving ato 60mg QD or pbo. Each day in baseline and double-blind treatment periods was classified into 1 of 4 categories: headache(HA) day, premonitory(day preceding a HA day), postdromal(day following a HA day), or interictal(all other days). For each participant, mean AIM-D domain scores were calculated per four category during the 4-wk baseline, and in each of the 4-wk epochs that constitute the double-blind treatment phase. Change from baseline was computed for patients who reported impairment at baseline (here we report results for interictal days). All *P* values were computed using t-tests and are nominal.

Results: On interictal days, ato 60mg QD resulted in significant (*P*<0.001) reductions from baseline in PDA scores (-8.69, -10.55, -10.68) vs pbo (1.64, -0.16, -0.84) in weeks 1–4, 5–8, and 9–12, respectively (**Fig 1**). Results for PI scores were similar, with patients taking ato 60mg QD reporting significant reductions (*P*<0.001) from baseline (-8.12, -9.73,-8.89) vs pbo (1.61, 1.08, 1.33) in weeks 1–4, 5–8, and 9–12, respectively (**Fig 2**).

Conclusion: Ato 60mg QD may reduce interictal burden and minimize the disruptive effects of migraine between attacks.

Fig. 1

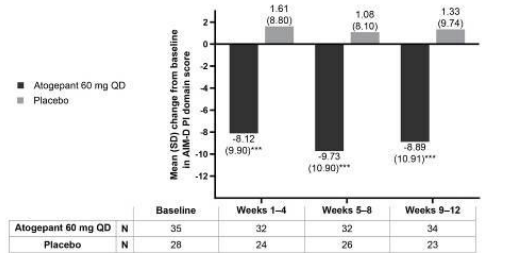


		Baseline	Weeks 1–4	Weeks 5–8	Weeks 9–12
Atogepant 60 mg QD	N	38	35	35	36
Placebo	N	32	29	31	26

Figure 1. Change From Baseline in the Performance of Daily Activities (PDA) Domain of the AIM-D at Weeks 1–4, Weeks 5–8, and Weeks 9–12 Among Participants With Chronic Migraine and at least a little Baseline Impairment on Interictal Days (mITT Population)

AIM-D, Activity Impairment in Migraine Diary; mITT, modified intent-to-treat; QD, once daily; SD, standard deviation; N, number of eligible participants with >0 baseline AIM-D PDA domain score on interictal days; ***, nominal *P* value<0.001. Participants reported mean (SD) baseline AIM-D PDA scores of 12.78 (11.23) and 7.95 (6.62) in the atogepant and placebo groups, respectively. Participants in the atogepant group had mean (SD) interictal days of 3.8 (2.5), 10.3 (6.8), 13.3 (7.5), and 13.6 (8.2) at baseline, weeks 1–4, 5–8, and 9–12, respectively. Participants in the placebo group had mean (SD) interictal days of 4.0 (2.1), 5.5 (4.5), 7.2 (5.6), and 9.3 (5.5) at baseline, weeks 1–4, 5–8, and 9–12, respectively. This analysis was conducted in the mITT population, which included all randomized participants who received ≥1 dose of treatment, had evaluable baseline data, and ≥1 evaluable 4-week period of postbaseline data.

Fig. 2



		Baseline	Weeks 1–4	Weeks 5–8	Weeks 9–12
Atogepant 60 mg QD	N	35	32	32	34
Placebo	N	28	24	26	23

Figure 2. Change From Baseline in the Physical Impairment (PI) Domain of the AIM-D at Weeks 1–4, Weeks 5–8, and Weeks 9–12 Among Participants With Chronic Migraine and at least a little Baseline Impairment on Interictal Days (mITT Population)

AIM-D, Activity Impairment in Migraine Diary; mITT, modified intent-to-treat; QD, once daily; SD, standard deviation; N, number of eligible participants with >0 baseline AIM-D PI domain score on interictal days; ***, nominal *P* value<0.001. Participants reported mean (SD) baseline AIM-D PI scores of 12.84 (8.98) and 7.82 (6.39) in the atogepant and placebo groups, respectively. Participants in the atogepant group had mean (SD) interictal days of 3.8 (2.4), 11.4 (7.2), 13.0 (7.8), and 12.7 (7.8) at baseline, weeks 1–4, 5–8, and 9–12, respectively. Participants in the placebo group had mean (SD) interictal days of 3.9 (1.9), 5.8 (4.6), 6.6 (5.4), and 8.7 (4.9) at baseline, weeks 1–4, 5–8, and 9–12, respectively. This analysis was conducted in the mITT population, which included all randomized participants who received ≥1 dose of treatment, had evaluable baseline data, and ≥1 evaluable 4-week period of postbaseline data.

P115

The chronopharmacology of atogepant in migraine prevention: A real-world evaluation of influence of timing of administration on effectiveness and tolerability

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Objective: To assess whether the timing of atogepant administration influences its tolerability and effectiveness over 12 weeks in patients with episodic and chronic migraine in a real-world setting.
Methods: This is a post-hoc analysis of the first 12 weeks of the STAR study, a prospective, multicenter study in Italy evaluating atogepant 60 mg for migraine prevention. Data were collected at baseline (T0) and after 12 weeks (T3). Patients were grouped by administration timing (morning vs. evening). Changes in monthly headache days (MHDs), migraine days (MMDs), and patient-reported outcome measures (PROMs) were assessed. Tolerability was evaluated via adverse events (AEs). Linear mixed-effects models (LMMs) were used.
Results: 81 patients (86% females, mean age 50.8±13.7) were included. At T3, MMDs dropped from 16.6 to 9.7 ($p<0.001$) and MHDs from 19.2 to 10.7 ($p<0.001$); 60% achieved ≥50% reduction in MMDs. AEs occurred in 43% of patients. Atogepant was taken in the morning by 57% and evening by 43% of patients. No significant differences in MMDs, MHDs, or AEs emerged between groups. Evening users had higher baseline MIDAS scores (70.0 vs. 39.9), but showed a greater reduction ($F(1,63)=6.29$, $p=0.015$), with similar final scores at T3 (25.1 vs. 23.9).
Conclusion: Timing of atogepant administration (morning vs. evening) did not affect overall effectiveness or tolerability. However, a greater MIDAS score reduction in evening users was observed. Whether this reflects a pharmacodynamic advantage or a ceiling effect remains unclear. Long-term and dedicated studies are needed to evaluate and confirm these findings.

P116

Low sodium oxybate use for nocturnal cluster headache: Efficacy, tolerability and safety – A phase 2 randomized, double-blind, placebo-controlled, bi-center study

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Objective: Cluster headache (CH) is characterized by severe headache attacks that typically occur during sleep. This study aims to evaluate the efficacy, tolerability and safety of low sodium oxybate (LXB) for nocturnal attacks in patients with chronic cluster headache (CCH). Data from this trial will determine whether deepening sleep with LXB reduces the frequency and severity of nocturnal CH attacks and improves sleep quality.
Methods: In this randomized, double-blind, placebo-controlled, bi-center trial, patients (18–75 years) with CCH and ≥4 nocturnal attacks per week will be enrolled. To achieve a statistical power of 0.8, a sample size of 60 patients is required. Patients with a contra-indication for LXB will be excluded. The study starts with a 4-week baseline phase. After this phase, patients will be randomized to receive either LXB or placebo during the treatment phase as a twice nightly regimen. All subjects will undergo an 8 week treatment titration phase followed by a 4 week fixed-dose phase.
Results: The primary outcome is change from baseline in the average weekly frequency of nocturnal CH attacks (defined as occurring between 22:00 and 07:00) as recorded in a headache diary over the fixed-dose treatment phase. Secondary outcomes include the change in total weekly frequency of CH attacks in

a 24-hr period over the fixed-dose treatment phase. Other secondary endpoints include pain intensity, abortive medication use, quality of life and improvement of sleep quality, sleep onset, sleep maintenance and sleep efficiency. This will be monitored using a diary and, optionally, two skin sensors that measure tri-axial actigraphy, heart rate, and core body temperature.

Conclusion: This is the first randomized, placebo-controlled trial investigating LXB for nocturnal CH. Findings may inform new therapeutic strategies targeting sleep-related CH pathophysiology and improve quality of life in this severely affected patient group.

Fig. 1

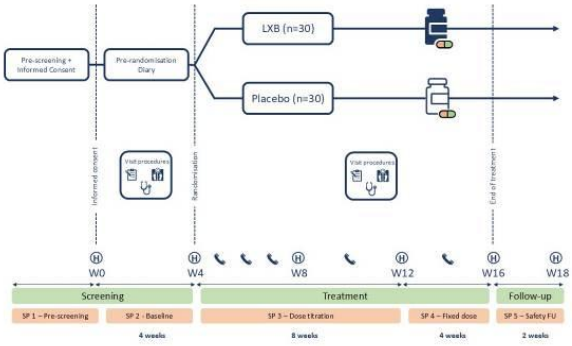
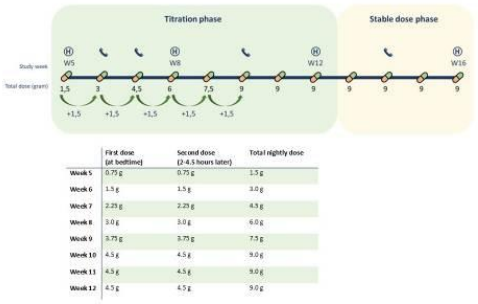


Fig. 2



	First dose (at bedtime)	Second dose (2-4.5 hours later)	Total nightly dose
Week 5	0.75 g	0.75 g	1.5 g
Week 6	1.5 g	1.5 g	3.0 g
Week 7	2.25 g	2.25 g	4.5 g
Week 8	3.0 g	3.0 g	6.0 g
Week 9	3.75 g	3.75 g	7.5 g
Week 10	4.5 g	4.5 g	9.0 g
Week 11	4.5 g	4.5 g	9.0 g
Week 12	4.5 g	4.5 g	9.0 g

P117

Pharmacogenetic profiles of migraine chronification and acute treatment efficacy: A pilot analysis of acute medication-related SNPs

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Objective: Migraine shows heterogeneity in progression and treatment response. While pharmacogenetics mainly targets prevention, genetic factors in acute medication efficacy and chronification (especially linked to medication overuse) are poorly understood. This pilot study explored associations between drug metabolism-related SNPs and: 1) migraine chronification risk (Chronic Migraine [CM] vs. High-Frequency Episodic Migraine [HFEM]), and 2) acute analgesic efficacy.

Methods: 46 propensity-score matched CM/HFEM patients (1:1, age/sex/duration balanced; ~82% NSAID users, rest triptans) underwent targeted genotyping of pharmacokinetically relevant SNPs. Quality-controlled data was analyzed using Fisher's Exact Test and logistic regression for: 1) CM vs. HFEM (chronification risk), 2) pooled efficacy (2-hour pain freedom).

Results: 1) **Chronification:** TRPM8 rs9468830 showed strong trend for CM risk (OR=6.9, 95% CI [1.91-25.4], p=0.06). 2) **Acute Efficacy:** rs11859453 significantly associated with treatment failure (reduced pain freedom OR=0.09, 95% CI [0.02-0.42], p=0.002). CYP2C9 rs10234636 trended towards positive response (OR=2.2, 95% CI [0.95-7.1], p=0.056).

Conclusion: Distinct SNPs may influence migraine chronification (TRPM8 rs9468830) and acute treatment response (CYP2C9 rs11859453/rs10234636). TRPM8's role in pain sensitization and CYP2C9's role in NSAID metabolism support biological plausibility. Despite limited sample size (wide CIs, reduced power), these candidate SNPs warrant validation in larger cohorts with functional analyses to advance personalized migraine management.

P118

Trigeminal neuralgia secondary to giant saccular aneurysm/endovascular procedure – Is lidocaine block an old treatment with a new indication?

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Objective: Trigeminal neuralgia is a chronic facial pain syndrome characterized by sudden, intense, and electric shock-like episodes, typically unilateral, affecting one or more branches of the trigeminal nerve. In most cases, it is idiopathic, but a subset is secondary to structural lesions such as brain tumors, demyelinating disease, or vascular compressions—particularly aneurysms—only detectable through neuroimaging. Carbamazepine is the standard first-line treatment, although alternatives such as

oxcarbazepine, lamotrigine, or pregabalin may be considered in cases of intolerance or poor response.
Methods: A 59-year-old woman presented with trigeminal neuralgia affecting the left V1–V2 territory. MRI revealed a giant saccular aneurysm of the left internal carotid artery"s communicating segment. She underwent endovascular treatment with simple coiling and was started on carbamazepine 400 mg twice daily. Two months later, she developed persistent pain and progressive bilateral visual impairment. MRI confirmed compression of both the trigeminal and optic nerves by the aneurysmal mass and coils. Due to poor control of pain (15 episodes/month) and intolerance to carbamazepine (ataxia, vertigo), eslicarbazepine was introduced. Trials with oxcarbazepine, lamotrigine, pregabalin, and levetiracetam were ineffective and poorly tolerated. After 12 months, imaging showed a reduction in aneurysmal size and partial visual recovery. However, neuralgic episodes persisted (4/month, each lasting up to 2 days).
Results: Given the refractoriness of symptoms, the patient was submitted to peripheral nerve block with 2% lidocaine at the auriculotemporal and supraorbital branches, resulting in marked improvement and a >50% reduction in frequency and severity of attacks.
Conclusion: Peripheral nerve block with lidocaine is a safe, accessible, and effective option for symptom relief and should be considered in cases of secondary trigeminal neuralgia refractory to pharmacological treatment.

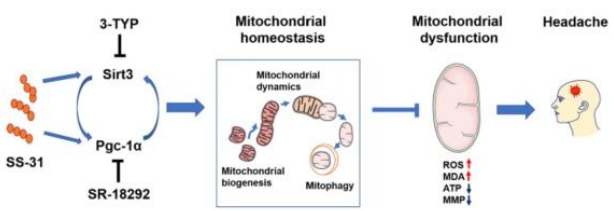
P120
Glymphatic dysfunction in migraine mice model
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Objective: The glymphatic system is essential for waste removal in the central nervous system, facilitated by aquaporin-4 (AQP4) at the end of astrocytes. While the glymphatic system plays a role in various neurological diseases, its involvement in migraine remains unclear. This study aims to investigate the relationship between glymphatic dysfunction and migraine, providing potential targets for migraine prevention and treatment.
Methods: The study used a nitroglycerin-induced migraine model in C57/BL6 mice. The glymphatic influx of cerebrospinal fluid (CSF) tracer was measured, and AQP4 expression and polarization were evaluated. The effect of glymphatic suppression via TGN-020 (an AQP4 blocker) on migraine pathology was also assessed.
Results: In the migraine model, glymphatic influx of CSF tracer was reduced, accompanied by decreased AQP4 expression and impaired polarization, indicating glymphatic dysfunction. Further suppression of glymphatic function by TGN-020 aggravated migraine-related pathological changes in mice.
Conclusion: Glymphatic dysfunction may worsen migraine pathology, with AQP4 being a potential therapeutic target for migraine.

P121
SS-31 alleviated nociceptive responses and restored mitochondrial function in a headache mouse model via Sirt3/Pgc-1α positive feedback loop
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Objective: To investigate whether the mitochondria-targeted antioxidant peptide SS-31 alleviates migraine by restoring mitochondrial function through the Sirt3/Pgc-1α positive feedback loop.
Methods: We used a mouse model to evaluate the effects of SS-31 on headache responses, mitochondrial function, and homeostasis induced by IS. The experiment includes headache model establishment, drug treatments (SS-31, Sirt3 inhibitor 3-TYP, Pgc-1α inhibitor SR-18292), and behavioral assessments (head scratching, mechanical threshold, and thermal pain response). Mice are divided into groups to investigate combination therapy mechanisms. PC12 cells are treated with H2O2, and molecular changes are analyzed by Western blot and immunofluorescence. Data are analyzed using one-way ANOVA.
Results: IS infusion leads to mitochondrial dysfunction, ultrastructural damage, and homeostatic imbalance in the trigeminal nerve ganglion (TNC). Behavioral and molecular analyses show activated pain responses and increased expression of c-fos and CGRP. Mitochondrial function is impaired, with decreased ATP levels, mitochondrial membrane potential, and increased oxidative stress. SS-31 treatment reverses these effects, restoring mitochondrial function and improving headache symptoms via activation of the Sirt3/Pgc-1α pathway.
Conclusion: SS-31 alleviates IS-induced nociceptive responses and mitochondrial dysfunction, partially blocked by inhibiting Sirt3 and Pgc-1α. SS-31 shows potential as a headache treatment, with the Sirt3/Pgc-1α loop as a target for intervention.

Fig. 1



P122

Inhibiting PAC1 receptor internalization and endosomal ERK pathway activation may ameliorate hyperalgesia in a chronic migraine rat model

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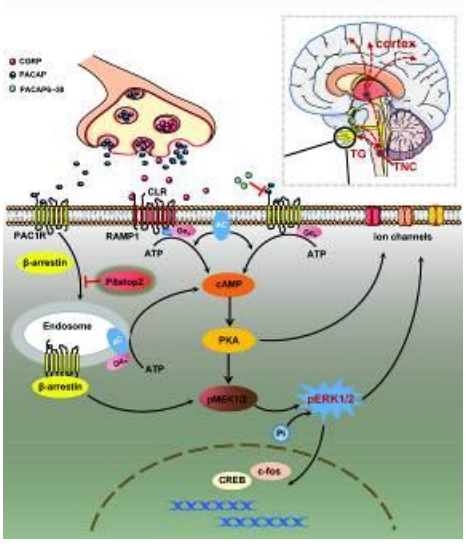
Objective: To explore the mechanisms of endogenous and exogenous PACAP in migraine attacks using a rat model.

Methods: The rat model of chronic migraine (CM) was established by repeated intraperitoneal injection of nitroglycerin (NTG). Von Frey filaments and hot plate tests were used to measure the mechanical and thermal thresholds. The expression levels of c-Fos, calcitonin gene-related peptide (CGRP), PACAP, PAC1, protein kinase A (PKA) and phosphorylated extracellular signal-regulated kinase (ERK) were assessed by western blotting or immunofluorescence staining. The internalization of PAC1 receptor was visualized by fluorescence microscope and laser scanning confocal microscope.

Results: The results showed that c-Fos and CGRP expression significantly increased after repeated administrations of NTG or PACAP. Pitstop2 notably improved hyperalgesia in CM rats, while PACAP6-38 offered no benefit. In addition, PACAP-induced PAC1 receptor internalization, PKA and ERK pathways activation were blocked by Pitstop2 instead of PACAP6-38.

Conclusion: Our results demonstrate that inhibition of PAC1 receptor internalization could effectively improve allodynia in CM rats by restraining ERK signaling pathway activation in a chronic migraine rat model. Modulation of receptor internalization may be a novel perspective to explore specific mechanisms of PACAP signaling activation in the trigeminal vascular system.

Fig. 1



P123

Arc-mediated synaptic plasticity regulates cognitive function in a migraine mouse model

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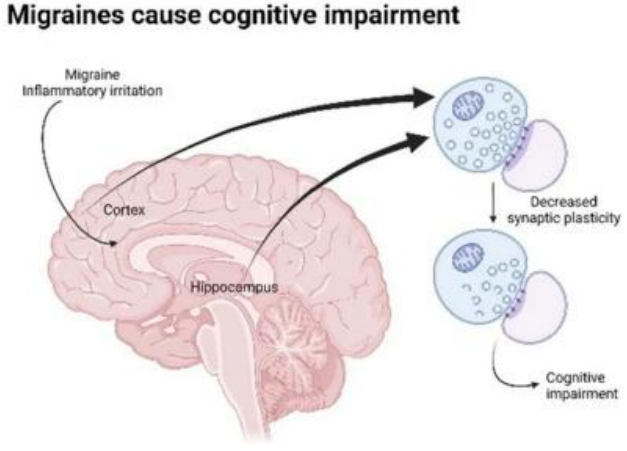
Objective: To investigate the impact of migraine on cognitive function and explore the role of Arc-mediated synaptic plasticity in this process using a murine model.

Methods: C57BL/6 mice were randomly divided into four groups: the IS group (migraine model induced by inflammatory soup, IS), IS+M group (IS model + memantine treatment), IS+S group (IS model + sumatriptan treatment), and a control group (PBS with no IS stimulation). Cognitive function was assessed through behavioral tests, including pain threshold for mechanical stimulation, learning and memory tasks, and attention assessment. Hippocampal neuron dendritic spine density and synaptic ultrastructure were evaluated using immunohistochemistry and electron microscopy. Arc protein expression in the hippocampus was analyzed as a marker of synaptic plasticity.

Results: Mice in the IS group exhibited a reduced pain threshold, impaired learning and memory, attention deficits, fewer dendritic spines in hippocampal neurons, and altered synaptic ultrastructure. The IS+M group showed significant recovery in cognitive function, with Arc protein expression returning to levels similar to those in the control group. In contrast, the IS and IS+S groups showed persistent cognitive deficits and lower Arc expression.

Conclusion: Cognitive dysfunction in the migraine model was associated with impaired synaptic plasticity, as indicated by reduced Arc expression. Memantine treatment alleviated cognitive deficits and restored synaptic function, suggesting that Arc-mediated synaptic plasticity may play a critical role in migraine-related cognitive impairment and could be a potential therapeutic target.

Fig. 1



P124

Piezo2 in trigeminal ganglion neurons contributes to mechanical hyperalgesia in chronic migraine

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Objective: This study aims to explore the role of the Piezo2 channel protein in trigeminal ganglion neurons during the chronic progression of migraine and its impact on the development of mechanical sensitization.

Methods: The animal model of chronic migraine was established by intermittent intraperitoneal injection of nitroglycerin (NTG), and adult male and female mice were selected as the research subjects. The mechanical sensitivity of rats was evaluated by measuring the periorbital mechanical threshold using Von Frey filaments. Western blot was employed to detect the expression level of Piezo2 in TG. Immunofluorescence staining was used to observe the co-localization of Piezo2 and nociceptive neurons. The role of Piezo2 was further verified by administering the Piezo2 inhibitor GsMTx4 (270ug/kg) and knocking down Piezo2 expression via adeno - associated virus (AAV). Additionally, the expression of calcitonin gene-related peptide (CGRP) in the trigeminal nucleus caudalis (TNC) was detected after Piezo2 knockdown.

Results: Repeated NTG administration induced acute and chronic mechanical hyperalgesia. Piezo2 was co-expressed with CGRP and isolectin B4 (IB4) in TG, and the expression of Piezo2 was significantly upregulated in both male and female mice after the establishment of the CM model. Administration of the Piezo2 inhibitor GsMTx4 alleviated the NTG - induced periorbital mechanical hyperalgesia in both genders. AAV - mediated knockdown of Piezo2 expression in TG inhibited the NTG - induced hypersensitivity, and the expression of CGRP in TNC decreased after Piezo2 knockdown.

Conclusion: This study demonstrates that Piezo2 plays a pivotal role in the mechanical sensitization of chronic migraine in both male and female rats. Targeting Piezo2 may represent a novel therapeutic strategy for CM - associated mechanical hyperalgesia.

P125

Neural signature of chronic migraine mice model and related photophobia in the primary visual cortex

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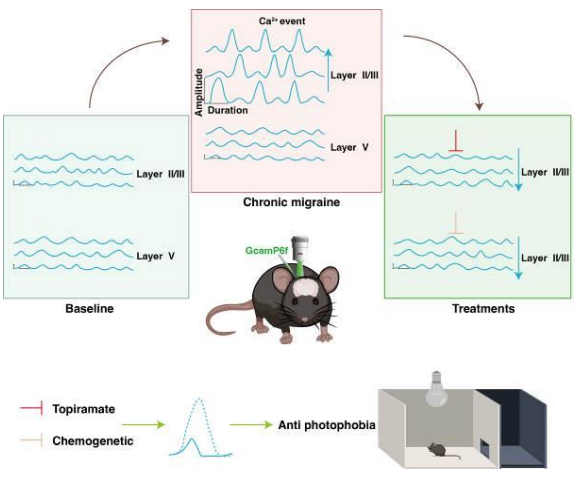
Objective: Migraine episodes are known to induce heightened photosensitivity. Neuroimaging investigations have revealed that the primary visual cortex exhibits abnormal activation patterns both during and between migraine attacks. Growing evidence suggests that altered cortical activity patterns may underlie the pathophysiology of neurological disorders. This study explored whether and how chronic migraine affects cortical activity patterns at single-cell resolution in the primary visual cortex during its progression.

Methods: *In vivo* two-photon calcium imaging was longitudinally performed in the primary visual cortex of a chronic migraine mouse model across multiple time points. Cortical circuit activity patterns and behavioral correlates were systematically assessed through combined chemogenetic manipulation and pharmacological interventions, with a particular focus on primary visual cortex functional modulation.

Results: Following chronic migraine induction, spontaneous hyperactivation emerges in cortical activity patterns within the primary visual cortex, with layer II/III neurons being identified as the principal contributors to this neural dysregulation, rather than their layer V counterparts. Notably, topiramate prophylactic treatment produced reduced both allodynia and photophobic behaviors while rescuing pathological cortical hyperactivity. However, chemogenetic inhibition of primary visual cortex layer II/III neurons ameliorated light aversion without attenuating pain sensitization, while normalizing aberrant spontaneous cortical hyperactivity of primary visual cortex.

Conclusion: These findings demonstrate dynamic alterations in spontaneous cortical neural signature within the primary visual cortex throughout chronic migraine progression, with modulation of these neural adaptations showing the potential to alleviate associated photophobic symptoms. This mechanistic insight advances our understanding of light sensitivity pathophysiology in chromic migraine.

Fig. 1



P126

nAChR modulation as a potential target in post-COVID headache and fatigue syndrome: Preliminary observational findings

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Objective: A significant number of patients experience persistent symptoms following SARS-CoV-2 infection. Common complaints include long-lasting headaches—often stabbing and stress-sensitive—and fatigue with both somatic and cognitive elements, such as brain fog. When these symptoms co-occur with musculoskeletal pain, dyspnea, weakness, or cognitive deficits, the condition is referred to as Post-COVID Fatigue Syndrome (PCFS). The pathophysiology remains unclear but is likely related to altered neuronal signaling. Evidence suggests a dysregulation of excitatory and inhibitory intracortical networks [Versace 2021]. Excitatory transmission is mainly mediated by cation-permeable ion channels, particularly glutamatergic receptors (AMPA, NMDA, kainate) and nicotinic acetylcholine receptors (nAChRs). Acetylcholine plays a key role in central synaptic activity, autonomic regulation, and neuromuscular function. Central cholinergic systems modulate arousal, reward, cognition, and motor control [Gil 2018]. Nicotine has been discussed as a protective factor in SARS-CoV-2 infection [Changeux 2020]. It has been hypothesized that COVID-19 and PCFS may involve impaired nAChR signaling, potentially modifiable by nicotine agonists.

Methods: We reviewed Post-COVID patient data from January 2020 to May 2025 at RC Bad Düben (n=302) with documented PCFS (n=228) and headaches (n=11), analyzing self-reported nicotine use.

Results: Only 11% of PCFS patients reported nicotine use. Notably, none of the patients with combined PCFS and headache were smokers (0%). This rate is markedly lower than the smoking prevalence in the general German population (22%).

Conclusion: These observations suggest a potential modulatory role of nicotine in post-COVID symptom expression. Preliminary experiences with nicotine patches have shown possible benefit. Controlled studies are needed to explore nAChRs as therapeutic targets in PCFS.

P127

The cognitive burden of cervicogenic headache: Unexplored neurophysiological links

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Objective: It is well-established that chronic pain adversely affects cognitive functions such as attention, memory, and executive functions, particularly in conditions like migraine and tension-type headache. However, the cognitive profile associated with cervicogenic headache (CGH) remains poorly understood. Therefore, the aim of this review is to elucidate the cognitive impairment in individuals with CGH and to synthesize the underlying neurophysiological basis of this relationship based on the current literature.

Methods: A literature search was conducted for the period 2015-2025 in the PubMed, Scopus, Web of Science, and Cochrane Library databases. The search utilized the following keywords: "cervicogenic headache", "cervicogenic chronic headache", "cognitive impairment", "cognitive dysfunction", "cognitive disability", "cognitive decline", "attention", "executive function", and "mental deterioration".

Results: In cervicogenic headache, the neuroanatomical substrate involves interneurons within the trigeminocervical nucleus, which facilitate a sensory information exchange between the upper cervical spinal nerves and the trigeminal nerve. Specifically, afferent sensory signals travel within the dorsolateral tract and the substantia gelatinosa. This persistent nociceptive input is hypothesized to form the basis for central sensitization in chronic CGH, which in turn is thought to impact higher-order functions such as perception, executive functions, attention, and memory.

Conclusion: Chronic pain resulting from CGH can lead to both anatomical and functional changes, while also imposing a significant cognitive load that potentially impairs parameters such as cognition, executive functions, memory, attention, and perception. This review highlights the critical importance of investigating cognitive factors and incorporating them into the holistic assessment and treatment planning for individuals with cervicogenic headache.

P128

The transient receptor potential melastatin type 3 plays a critical role in light aversion

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Objective: Transient receptor potential melastatin 3 (TRPM3) is a cation channel that contributes to activating trigeminal nerve fibres in neuropathic pain, While activation of trigeminal ganglion is essential for triggering light aversion behavior in mice. This project aims to identify whether TRPM3 contributes to light

aversion behavior and explore its underlying mechanisms.

Methods: Adult male C57BL/6J mice were used, and behavior procedures were approved by the University Research Ethics Review Panel and conducted following national and provincial guidelines. Light aversion was induced by intranasal injection of the TRPA1 activator, umbellulone. Mouse behavior was assessed by the total time they stayed in dark and light areas. qPCR and RNA-seq were used to detect *Trpm3* gene expression and related microRNA levels in the TG. RNA interactions were identified by dual-luciferase reporter gene assay.

Results: Inhibition of TRPM3 by intraperitoneal injection of ISO markedly reduced the total time in light and transition times of photophobia mice induced by umbellulone, indicating a crucial role of TRPM3 in mediating light aversion. In line with this, rapid induction of *Trpm3* gene expression following light aversion was observed in the trigeminal ganglion, suggesting TRPM3 translational machinery activation. Such upregulation of *Trpm3 gene expression* following photophobia corresponds to a downregulated miR-196a-5p. Furthermore, dual-luciferase reporter gene assay identified sequence-based physical RNA interactions between miR-196a-5p and *Trpm3* in HEK293 cells*. These data revealed that the* sustained *Trpm3* transcript production is attributed to the repressed miR-196a-5p level following photophobia.

Conclusion: TRPM3 plays a pivotal role in light aversion. TRPM3 channels would be a novel therapeutic target in preventing migraine-associated light aversion.

P129

Impaired venous outflow in migraine with and without aura: An MRV study

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Objective: Idiopathic intracranial hypertension without papilledema (IIHWOP) and migraine are almost clinically indistinguishable. Accumulating evidence suggests that impaired regulation of intracranial pressure (ICP), even if insufficient to cause overt intracranial hypertension (IIH), may represent a pathophysiological mechanism underlying migraine. Since venous sinus stenosis is the most prominent radiological marker of elevated ICP, this study aimed to quantify the degree of venous stenosis present in migraine patients to investigate this association.

Methods: We enrolled 161 consecutive patients, classifying them into three clinical cohorts —IIH (n=36), migraine without aura (n=97), and migraine with aura (n=36) —and compared their results with those of 37 healthy volunteers. Venous outflow compromise was quantified for each transverse sinus and for the superior sagittal sinus as follows: luminal narrowing <33% scored 0, 33–66% scored 1, >66% scored 2, and complete flow interruption ("flow gap") scored 3. One additional point was assigned when the confluence of sinuses showed torcular non-confluence. The distribution of these scores across the clinical groups was compared with the Kruskal-Wallis test.

Results: Both migraine without aura (median=3, IQR=2–4; p<0.001) and migraine with aura (median=3, IQR=3–4; p<0.001) groups had significantly higher stenosis scores than controls (median=2, IQR=1–3). The difference between the two migraine subtypes did not reach statistical significance (p=0.774). As expected, patients with IIH demonstrated the highest stenosis scores (median=6, IQR=5–6), significantly exceeding all other groups (p<0.001).

Conclusion: Migraine patients, both with and without aura, demonstrated significantly greater venous sinus stenosis compared to healthy controls. This finding suggests that impaired venous outflow and the consequent elevation in ICP, though insufficient to cause overt signs of IIH, might contribute to the pathophysiological mechanisms underlying migraine.

P130

A case report on the association of migraine with focal cortical dysplasia

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Objective: Migraine is associated with morphological alterations in the brain, cerebellum, and brainstem manifested as nontraumatic brain lesions, including deep white matter hyperintensities, infratentorial hyperintensities, infarct-like lesions in the posterior circulation territory, volumetric changes in the cortex, alterations in cytoarchitecture, and changes in the neuronal network. Variations in cortical thickness in migraine patients have been reported and are similar to focal cortical dysplasia (FCD) according to the criteria of the International League Against Epilepsy. The aim of this work is to argue for a causal relationship between FCD and migraine and analyze an associated case.

Methods: A 29-year-old woman has been experiencing worsening headache attacks for nearly 20 years. She was diagnosed with high-frequency episodic migraine without aura and currently has 5 to

10 migraine headache days per month. An MRI was performed for examination.
Results: Cortical neurons are implicated in migraine pathogenesis. The brain cortex exhibits several functional changes associated with migraine, such as cortical spreading depression (CSD), enhanced excitability, altered connectivity, and abnormal energy metabolism, which are underpinned by mitochondrial dysfunction in both interictal and ictal phases, suggesting a structural source. Structural alterations in the cortex were directly observed in migraine patients. An MRI of the case revealed signal abnormalities in the left occipital lobe, suggesting focal cortical dysplasia. A 3-month follow-up confirmed the initial diagnosis without any signs of change.
Conclusion: Cortical changes in migraine patients align with the FCD criteria, but further research is needed to establish or exclude a causal relationship between them.

P131

Exploring the role of melatonin and its receptors in primary headache pathophysiology: Insights from the trigeminovascular system

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Objective: Primary headache disorders such as migraine and cluster headache show circadian patterns, potentially linked to melatonin, a hormone that regulates biological rhythms. Melatonin has shown promise as a treatment; however, its precise mechanisms particularly - its interactions with the trigeminovascular system (TVS) remain unclear. This study investigates the expression and localization of melatonin receptors MT1 and MT2 in key regions of the TVS.
Methods: The hypothalamus, cerebral arteries, dura mater, trigeminal ganglion (TG), dorsal root ganglion (DRG), and sphenopalatine ganglion (SPG) were dissected from adult male and female rats. Immunohistochemistry and RT-qPCR were used to assess melatonin receptors expression.
Results: MT1 and MT2 were differentially expressed in TG, DRG, and SPG. MT1 was widely distributed in the cytoplasm and nuclei of neurons and satellite glial cells (SGCs), while MT2 localized mainly in the cytoplasm of neurons, Aδ-fibers, and SGCs. MT1 co-localized with CGRP and RAMP1, whereas MT2 co-localized with RAMP1. In SPG, both receptors co-localized with the neuropeptides VIP and PACAP, indicating involvement in autonomic regulation. No significant sex differences were found, although MT1 levels were approximately twice higher than MT2 in TG. MT2 immunoreactivity in Aδ fibers were found throughout the dura mater. Only MT1 was present in cerebral vessels, localized mainly in the endothelial and smooth muscle cells. RT-qPCR confirmed higher MT1 expression in TG compared to MT2 and lower MT1 expression in the hypothalamus relative to TG.
Conclusion: MT1 and MT2 receptors show distinct expression patterns within sensory and autonomic regions implicated in headache. The wider distribution and vascular presence of MT1 suggest a more prominent role in modulating trigeminovascular activity. These findings highlight potential mechanisms through which melatonin influences headache pathophysiology and support its future therapeutic use.

P133

Estradiol and other sex-hormones dynamics in menstrual migraine: Pathway analysis of hormonal fluctuations in a controlled cohort study

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Objective: Menstrual migraine (MM) is linked to hormonal fluctuations, but the precise role of sex hormones remains unclear. This study hypothesizes that women with MM experience a steeper decline in estradiol before menstruation.
Methods: In this prospective cohort study, 28 women with MM and 18 healthy controls were followed over two menstrual cycles. Blood samples were collected on standardized cycle days based on the LH surge (day 0), specifically on days 1, 2, 3, 8, 10, 12, and 14 post-surge, covering mid- and late-luteal phases. The primary outcome was the peak estradiol level during the mid-luteal phase (day 8) and its subsequent decline from day 8 to day 14. Secondary outcomes included levels of other sex hormones such as steroids (progesterone, testosterone), gonadotropins, and androgens, as well as hormone pair ratios.
Results: Women with MM had a 49% higher peak estradiol level during the luteal phase (1·49, 95% CI: 1·03–1·87, p=0·04) and a 90% greater decline from mid- to late-luteal phase compared to controls (1·90, 95% CI: 1·16–3·12, p=0·03). Secondary pathway analysis showed no differences in other sex hormones, although progesterone showed high variability and a peak difference of similar magnitude to estradiol.
Conclusion: Women with MM have a higher peak estradiol and a more pronounced estradiol decline during the luteal phase compared to controls, indicating that interventions for women with MM

need to focus on stabilizing estradiol fluctuations during the luteal phase for migraine attack prevention.

P134

Migraine attack incidence in relation to ovulation: A prospective cohort study

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Objective: Previous studies suggest the perimenstrual phase increases migraine risk without aura, while the link to the ovulatory phase remains unclear.
Methods: We conducted a longitudinal cohort study among 554 women with migraine and a regular menstrual cycle. Participants completed a validated e-headache diary including also the menstrual cycle. Of these women, 31 (who participated in our Women Hormones Attacks and Treatment (WHAT)-hormone study) performed urine luteinizing hormone (LH) surge tests during two menstrual cycles to validate the estimation of the ovulation. The association between the ovulatory phase and migraine incidence was assessed using a mixed logistic model with patient as random effect, and the ovulatory and menstrual window as fixed effects. Secondary analyses included a case-crossover model and a self-controlled case series (SCCS) model to strengthen data robustness and control for time-invariant confounders.
Results: E-diary data from 2,522 menstrual cycles, including 58 from the WHAT-hormone subgroup, were analyzed. Across all three statistical models, the ovulatory window showed no higher incidence of migraine (with or without aura) than other menstrual cycle days (mixed logistic model: OR 0.95, 95% CI 0.88–1.02; WHAT-hormone subgroup: OR 0.68, 95% CI 0.38–1.16). The perimenstrual window had the highest migraine incidence (SCCS model with luteal phase as reference: OR 2.57, 95% CI 1.51–4.39), followed by the follicular phase (OR 1.69, 95% CI 1.02–2.80).
Conclusion: There is no increased incidence of migraine attacks (with or without aura) during the ovulatory window in women, but a higher incidence during the follicular phase compared to the luteal phase was confirmed, potentially linked to lingering effects of perimenstrual estrogen decline.

P135

Paracetamol (Acetaminophen) and caffeine combination in headache management

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Objective: The aim of this work is to provide an overview of data on the cumulative analgesic effects of this combination and to clarify the mechanisms underlying the potentiation by caffeine of the antinociceptive effect of paracetamol in migraine and TTH.
Methods: A search was conducted in PubMed, MEDLINE, ClinicalTrials.gov and Cochrane Database from inception to March 2024 with a focus on paracetamol 1000 mg in combination with caffeine 130 mg.
Results: In preclinical studies caffeine has been shown to increase the antinociceptive effects of paracetamol with various mechanisms: inhibition of microglial COX2 via antagonism of adenosine A2A receptors or activation of glycinergic transmission. Two pharmacokinetic studies in healthy subject have shown that caffeine increases paracetamol absorption rate and decreases paracetamol clearance. Two randomized double blind clinical studies have both demonstrated that in patients suffering from TTH, the combination offers a significant higher pain relief compared to paracetamol alone. Two other TTH clinical trials have shown that the efficacy and safety of combination was comparable to Naproxen 550 mg and Ibuprofen 400 mg. One randomized, cross-over trial has shown a comparable efficacy/safety profile of the combination *vs* sumatriptan 50 mg in treatment of migraine attack. No data are available on the risk of medication overuse with the combination compared to paracetamol alone.
Conclusion: Caffeine accelerates and prolongs the analgesic effect of paracetamol over time with a significant improvement of pain relief in patients with primary headaches without added safety issues.

P136

Right-sided predominance in primary stabbing headache: From a large consecutive case series in Korea

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Objective: Right-sided pain predominance has been well-documented in cluster headache, and several studies suggest a similar lateralization tendency in migraine. However, pain lateralization in primary stabbing headache (PSH) has not been systematically investigated. This study aimed to evaluate the laterality of pain in PSH through a large consecutive case series.
Methods: We consecutively enrolled new patients diagnosed with PSH at the Headache Clinic of Nowon Eulji Medical Center, Korea. The diagnosis of PSH was based on the criteria of the International Classification of Headache Disorders, 3rd edition (ICHD-3).

Demographic characteristics (age, sex), clinical features (pain location, frequency, duration, and associated symptoms), and detailed pain lateralization (right, left, bilateral, side-shifting) were recorded through structured interviews and headache diaries. Patients with bilateral or alternating side pain were excluded from the lateralization analysis.

Results: Among 815 patients diagnosed with PSH during the study period, 19 patients (2.3%) reported bilateral or side-shifting pain and were excluded. The final analysis included 796 patients with clearly lateralized pain. The cohort was predominantly female (557 women, 70.0%), with a mean age of 55.1 years (standard deviation 16.4; range 12–88 years). Right-sided pain was reported by 421 patients (52.9%), whereas 375 patients (47.1%) had left-sided pain. The difference in laterality was statistically significant (p = 0.042).

Conclusion: In this large consecutive case series of PSH, right-sided pain was found to be more frequent than left-sided pain. These results suggest that lateralization patterns in PSH may reflect underlying hemispheric differences in pain processing or susceptibility. Further studies exploring neuroimaging correlates or neurophysiological mechanisms of PSH lateralization are warranted.

P137

Hormonal factors and the course of migraine in postmenopausal women: An observational study

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Objective: Migraine is known to be modulated by hormonal fluctuations throughout a woman"s life. However, the influence of hormonal events on the clinical course of migraine after menopause remains unclear. This study aims to characterise the hormonal history and the clinical course of migraine in women aged 60 years or older.

Methods: Observational, cross-sectional study, conducted in a headache clinic between September 2024 and March 2025. Women diagnosed with migraine, with or without aura, and aged 60 years or older were included. The questionnaire was either applied in person or by telephone. Of a total of 33 eligible patients, 31 agreed to participate.

Results: The median age was 66 years. The average age of menarche was 13 years, and menopause occurred on average at 49 years. 22,6% used hormone replacement therapy. After menopause, 64,5% of the patients reported and improvement of frequency and/or intensity of migraine attacks, while 25,8% reported worsening. Postmenopausal worsening was associated with higher disability scores (average MIDAS: 41 vs 21, p=0,04) and higher anxiety scores (average HADS-A: 13 vs 9; p=0,03). No significant differences were found regarding hormone therapy use or age at menopause. The prevalence of anxiety and/or depression, as measured by the HADS score, was high (51,6%), regardless of the clinical course.

Conclusion: In this study, most women reported an improvement in migraine symptoms after menopause, consistent with literature data. However, a relevant subgroup of patients experienced worsening, which was associated with greater functional disability and higher anxiety burden. These results highlight the need for an individualised approach that considers not only hormonal factors but also the emotional and functional impact of the disease in postmenopausal women.

P138

Functional Near-Infrared Spectroscopy(fNIRS) applications in migraine: A brief review

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Objective: Functional Near-Infrared Spectroscopy (fNIRS) is non-invasive, practical and cheap neuroimaging tool which allows recording hemodynamic responses of brain at natural settings of subjects. Although fNIRS can be widely used at cognitive and clinical research for last three decades., it's diagnostic potential in migraine has remained underestimated. We aim to highlight fNIRS potential for migraine at different approaches.

Methods: We conducted a systematic review assessment of peer-reviewed research articles on migraine-fNIRS publications after 2000, 16 relevant fNIRS-migraine study was found. We grouped included research papers into four different categories which represent different approaches to migraine: Cerebrovascular reactivity (CVR) pathophysiology research, comparative and pre-post drug efficacy studies, Arterial Wall Distensibility studies and Machine Learning (ML)-based classification of migraine with fNIRS.

Results: Migraine pathophysiology research distinctly shows that fNIRS neuroimaging tool can reliably captures migraine-related CVR alterations, particularly changes in cortical oxygenation during cognitive, sensory tasks on healthy and clinical populations . As another application area; fNIRS successfully detected changes at cortical hemodynamic responses to various migraine and headache drugs which hemodynamic changes can be marker for drug mechanisms and clinical efficacy. Additionally, fNIRS research on arterial wall distensibility identified prolonged cerebral arterial pulse wave delays which highlights vascular distensibility can be a potential biomarker for migraine. Finally, ML classification studies on brain hemodynamic data can reveal fNIRS"s predictive

power as correctly identify migraine subtypes with high accuracy.
Conclusion: fNIRS method can identify robust CVR and arterial-wall biomarkers in migraine pathophysiology. It can also effectively tracks drug-induced hemodynamic changes, which helps personalized migraine care.

P139

Capsaicin induced cell death in primary cultured neurons

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Objective: To determine the effect of capsaicin to central nervous system, we prepared morphologic changes and biochemical assay were investigated in mouse primary cultured CNS neuron.
Methods: The susceptability of capsaicin differs for different brain area. Cerebral cortex and hippocampus were more sensitive, and striatum, thalamus and midbrain area were less sensitive to capsaicin susceptability. After capsaicin treatment, cortical and hippocampal neurons were died in dose-and time-dependent manner. By observation of nuclear fragmentation of capsaicin treated neuron, it is thought that the type of cell death is apoptosis rather than necrosis. The capsaicin receptor immunoreactive cells were observed in the cortex and hippocampus. It is consistent with area of damaged neuron. In case of capsaicin treated neurons, NOS activity stain was positive , the product of nitrite and anti-nitrotyrosine immunoreactivity were increased, and agmatine, which is a competitive nitric oxide synthases (NOSs) inhibitor significantly protect cortical and hippocampal neurons from capsaicin-induced apoptosis.
Results: These results indicated that capsaicin induced influx of cation ions. These results showed that capsaicin induced influx of Ca2+, followed by neuronal NOS is activated by Ca2+ and induced cell death. Also, the activity of caspase 3 was increased after capsacin treatment in the cortical and hippocampal neurons.
Conclusion: These results demonstrate that capsaicin induced the apoptosis through acting with capsaicin receptors. Calcium influx due to capsaicin recptor activation may induce apoptosis, which is triggered the formation of peroxynitrite by activating NOS activity or is mediated by activating caspase 3 pathway.

P140

An unexpected side effect of a cardiac catheterization

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Objective: INTRODUCTION
Visual aura-like phenomena, with or without headache, have been described in the context of endovascular procedures. Although rare, they have been reported following cerebral angiography, catheter ablation for atrial fibrillation and Wolff-Parkinson-White syndrome, patent foramen ovale closure, and varicose vein sclerotherapy.
Methods: .
Results: CLINICAL CASE
A 59-year-old man with hypertension, dyslipidaemia, and a history of ischemic heart disease underwent a diagnostic coronary catheterization. Minutes after the procedure, he experienced a disturbance in his right visual field resembling a "fortification spectrum," accompanied by scintillating scotomas with centrifugal progression. He denied any personal or family history of migraine, neurological disease, or any other symptom. The episode was self-limited, resolving within approximately 20 minutes. Neurological examination at the time was unremarkable. About an hour later, he experienced a second, similar episode, which also resolved spontaneously. Brain MRI and electroencephalogram revealed no abnormalities. One year later, the patient remains asymptomatic, with no episodes of headache or migraine. A diagnosis of visual aura-like phenomenon following cardiac catheterization was established.
Conclusion: Aura-like phenomena following endovascular procedures—particularly coronary catheterizations—are rare and clinically heterogeneous, making recognition and diagnosis challenging. It is essential to exclude other potential aetiologies, namely vascular or epileptic. The underlying pathophysiological mechanism remains unclear, but proposed explanations include microembolic events, the release of bubbles from the catheter, or the action of local inflammatory mediators or vasoactive substances. Despite their rarity, these phenomena appear to be benign, with recurrences seldom reported. Case reporting remains important to enhance understanding of their potential clinical implications.

P141

Right internal carotid artery aneurysm: An unusual etiology of trigeminal autonomic cephalalgia

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Objective: Trigeminal autonomic cephalalgias are characterized by short-lasting, unilateral, and intensely painful headache attacks associated with autonomic symptoms. Although they may be secondary to structural lesions, establishing a causal relationship is often challenging.
Methods: We report a case of secondary trigeminal autonomic cephalalgia due to a rare underlying cause.
Results: A 47-year-old woman with a history of mitral stenosis and a previous episode of carotid transient ischemic attack presented to the emergency department with a one-month history of persistent right-sided hemicranial headache, accompanied by ipsilateral ptosis and conjunctival injection. Neurological examination was unremarkable. A contrast-enhanced CT scan showed no clinically significant abnormalities. Further diagnostic workup with contrast-enhanced MRI and angiographic study revealed arterial dilations and stenoses in the M1 and M2 segments of the right middle cerebral artery. Subsequent cerebral angiography identified an aneurysmal dilation of the right internal carotid artery, which was successfully treated surgically. The patient remains asymptomatic five years after the surgical intervention.
Conclusion: While trigeminal autonomic cephalalgias can be secondary to structural causes, vascular etiologies are relatively rare. This case highlights the importance of careful evaluation in patients presenting with trigeminal autonomic headaches and reinforces the need to consider vascular causes in atypical presentations.

P142

Do different types of migraines also mean different responses to triggers?

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Objective: To examine association between different migraine types (migraine with and without aura (MA, MO); low or high frequency episodic migraine (LFEM, HFEM) and chronic migraine (CM), as well as migraine time of appearance) and various habits.
Methods: 104 patients with migraine were enrolled in this study. Participants were diagnosed according to The International Classification of Headache Disorders (ICHD-3). They were asked to complete the questionnaire that included information on demographic data, migraine characteristics, and few habits. The study was approved by the Ethical Commission at the Medical University of Lublin.
Results: The average age was 36.36±13.69 years. Majority of the surveyed group were women (87.50%) and patients with MO (52.88%). 75% of patients never smoked cigarettes and 35 participants were exposed to passive smoking in childhood. Patients with MO, as well as group of patients experiencing HFEM and/or CM were more likely to report cigarette smoke caused migraine worsen or occur ($p>0.05$). The intensity of pain on the Numeric Rating Scale was higher in non-smokers compared to smokers ($p=0.03$). Patients exposed to tobacco smoke in childhood currently experience higher pain intensity than those who were not exposed at that time ($p=0.008$). Significant relationship ($p=0.05$) was found between drinking coffee and the frequency of migraine episodes. Respondents who claimed that coffee drinking caused migraine attacks more often have frequent migraine episodes compared to respondents in whom coffee did not cause a migraine episode.
Conclusion: Passive smoking in childhood may increase the intensity of migraine attacks in adulthood. Also, secondhand tobacco smoke may aggravate or cause migraine episode in patients with MO or with very frequent episodes. Nevertheless, among tobacco smokers, smoking may reduce the average intensity of migraine attack. Also people who reported that coffee caused migraine attacks had greater migraine frequency.

P143

Novel morphological fractal dimension features as a biomarker for migraine classification: A support vector machine approach

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Objective: Diagnosing migraine is challenging because it relies on subjective, self-reported symptoms due to the lack of an objective neuroimaging biomarker. Advanced tools are needed to identify the subtle structural brain changes visible on **MRI** in migraine patients. This study investigated using Fractal Dimension (FD)—a sensitive metric quantifying brain complexity and morphology—combined with a Machine Learning (ML) model as a reliable, objective diagnostic biomarker.
Methods: We analyzed axial MRI scans from 100 migraine patients (50 episodic, 50 chronic) and 100 matched healthy controls. All patient gave their informed consent to publish their details in an open access journal. The brain's gray matter was parcellated into 68 regions of interest (ROIs) using the Desikan-Killiany atlas, and FD was calculated for each.

We first performed group comparisons to find morphological differences. Then, the 68 sub-regional FD values were used as features in a Support Vector Machine (SVM) model to classify migraine patients from healthy controls.
Results: FD measures successfully differentiated the groups. Migraine patients showed significantly decreased FD values in 17 ROIs compared to controls, primarily in the left hemisphere. The proposed FD-based SVM classifier achieved robust diagnostic performance over 100 permutations, yielding a test accuracy: 88.0%, sensitivity: 82%, specificity: 94%, and area under the curve (AUC): 0.924 ($p<0.05$)
Conclusion: This pilot study demonstrates that FD is a potent neuroimaging biomarker for migraine. The FD-based SVM classifier achieved high diagnostic accuracy and provided valuable insights into sub-regional morphological alterations in the migraine brain. These findings hold significant promise for supporting objective clinical diagnosis and enabling future automated screening for migraine.

P144

Characterization of mental health in cluster headache a.k.a suicide headache

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Objective: Cluster headache is characterized by excruciatingly painful recurrent headaches and is sometimes referred to as suicide headache. Previous research has shown that cluster headache has a negative impact on the patient's quality of life. High rates of depression and suicidal ideation have been reported in cluster headache cohorts and case-reports, and genome wide association studies show a correlation to risk taking behavior and attention deficit hyperactivity disorder. While mental health issues significantly contribute to the burden of cluster headache, they remain understudied. We therefore wanted to investigate mental health in cluster headache and in relation to sex and subtype.
Methods: An anonymized web-based questionnaire was sent to 500 Swedish patients with cluster headache.
Results: Preliminary analysis showed that depression, anxiety and social withdrawal were commonly reported by individuals with cluster headache. Over 50% of the study participants reported suicidal ideation which can be compared to ~9% in the general population. In addition, more than 50% reported self-harm behavior during cluster headache attacks, revealing a strong inclination for individuals with cluster headache to resort to self-harm, possibly as an attempt to cope with the pain of a cluster headache attack.
Conclusion: Our results show a strong inclination of individuals with cluster headache to resort to self-harm. Further analysis will show if there is an impact on mental health also between bouts, which should be considered in the treatment and care of cluster headache and we will investigate potential differences in relation to sex and subtype.

P145

Orbital pain beyond the acute phase: A long-term manifestation of carotid dissection

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Objective: Cervical artery dissection is a recognised cause of secondary headache and stroke, often presenting with orbital/cervical pain.While usually involving a single vessel, multivessel dissections are rare and may suggest underlying vascular vulnerability.Persistent pain beyond vascular healing remains poorly understood.
Methods: We present a 45-year-old woman with hypertension and smoking history, admitted with acute right orbital pain and right-sided Horner"s syndrome, without additional neurological deficits. MRA revealed an occlusive dissection of the right internal carotid artery with intracranial extension to the petrous segment, a chronic left vertebral artery dissection, and reversed flow in the right vertebral artery, suggestive of proximal occlusion due to a third dissection.No signs of fibromuscular dysplasia were found in the conventional angiography and genetic screening for connective tissue disorders was negative.
Results: She was managed with clopidogrel, atorvastatin and antihypertensive therapy.Cardiology follow-up revealed frequent symptomatic ventricular extrasystoles, treated with bisoprolol and flecainide. Follow-up MRI confirmed complete recanalisation of the cervical internal carotid artery, with persistent intracranial irregularity.The patient returned to work but experienced ongoing disabling right orbital pain, refractory to conventional analgesics. Low-dose amitriptyline was initiated, with partial symptomatic relief.
Conclusion: Despite vascular recanalization, symptoms persisted, suggesting possible perivascular sympathetic fibre injury or central sensitization. Multidisciplinary assessment was essential to exclude recurrence or structural complications. This case highlights the need for long-term follow-up and

individualised pain management beyond radiological resolution.

P146

No differences in subcortical volume between people with and without migraine: A REFORM study

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Objective: To determine whether the volume of specific subcortical structures differ between people with migraine and healthy controls, and whether these volumes vary across distinct migraine subtypes and phases.
Methods: In this cross-sectional study at the Danish Headache Center in Denmark, conducted between January 2020 and December 2023, adult participants with migraine and age- and sex-matched healthy controls underwent a single magnetic resonance imaging session at 3 Tesla. T1-weigthed scans were acquired to measure the volumes of subcortical structures using automated segmentation techniques. The structures analyzed included the thalamus, putamen, caudate nucleus, pallidum, nucleus accumbens, amygdala, and hippocampus.
Results: Imaging data from 295 participants and 154 healthy controls were included in the final analyses. No significant differences were observed between migraine participants and healthy controls in thalamic volume (migraine: 7243 ± 923 mm^3 vs healthy controls: 7350 ± 782 mm^3; p = 0.774) or hippocampal volume (migraine: 4204 ± 398 mm^3 vs healthy controls: 4307 ± 446 mm^3; p = 0.337). No differences were observed in any other subcortical structure. Likewise, different subgroup analyses revealed no volumetric differences in episodic vs chronic migraine, migraine with aura vs without aura, ictal vs headache free, or between each migraine subgroup and healthy controls (all p > 0.05 after multiple comparison correction).
Conclusion: In this large cross-sectional study, we found no evidence of subcortical volume differences between adults with migraine and healthy controls. Furthermore, no differences were found across migraine subtypes or phases. These findings indicate that subcortical volumetric measures are not suitable as imaging biomarkers of migraine. Future research should explore functional and metabolic alterations in subcortical structures to better understand the neurobiologic underpinnings of migraine.

P147

Investigation of the rimegepant effect on cerebral and extracerebral arteries – A longitudinal magnetic resonance angiography study

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Objective: To determine whether rimegepant induces vasoconstriction of cerebral or meningeal arteries during acute migraine attacks.
Methods: This was a prospective, longitudinal study conducted at a single academic imaging center between January 12, 2024, and June 10, 2025. Eighteen women aged 18 to 40 years with menstrually related migraine without aura were enrolled. Fifteen participants completed high-resolution 3-tesla magnetic resonance angiography during a spontaneous migraine attack at all required time points and were included in the final analysis.
Results: No significant vasoconstriction was observed in either artery following rimegepant administration. Middle cerebral artery circumference remained stable (baseline 8.13 ± 0.93 millimeters; 30 minutes 8.02 ± 0.84 millimeters [p=0.404]; 60 minutes 8.15 ± 0.90 millimeters [p=0.918]). Middle meningeal artery circumference showed no significant change (baseline 4.30 ± 0.83 millimeters; 30 minutes 4.47 ± 0.68 millimeters [p=0.084]; 60 minutes 4.35 ± 0.78 millimeters [p=0.688]).
Conclusion: Rimegepant did not induce measurable constriction of either cerebral or meningeal arteries during spontaneous migraine attacks. These findings support its vascular safety profile and suggest that the therapeutic effect of CGRP antagonists is independent of vasoconstriction. Rimegepant may offer a safer alternative to triptans for individuals with cerebrovascular risk.

P148

Investigating neuromodulatory effect of transauricular vagus nerve stimulation on resting-state electroencephalography

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Objective: This study aimed to investigate the neuromodulatory effects of transauricular vagus nerve stimulation and to identify the optimal stimulation duration using resting-state EEG. As EEG is a key tool for objective assessment of brain function, these findings may provide new biomarkers and tailored strategies for headache diagnosis and treatment.
Methods: Fifteen healthy adults participated, receiving taVNS to both ears for 40 minutes in 1-min ON/OFF cycles (30 Hz, 200 ms pulse, intensity below

pain threshold). Resting-state EEG was recorded before and during stimulation with 31 scalp electrodes. Data were analyzed for power spectral density (PSD) across five frequency bands (delta, theta, alpha, beta, gamma) and network indices (clustering coefficient, path length) in both whole-brain and regional analyses. Statistical tests assessed time- and duration-dependent changes.

Results: TaVNS significantly increased EEG power in all frequency bands, with strongest effects after 20–30 minutes. Network analyses showed improved efficiency, notably in theta and gamma bands, with earlier effects after 10 minutes. Simultaneously, network analysis revealed significant increases in clustering coefficients and decreases in path length, especially notable in the theta and gamma bands, indicating improved global brain network efficiency during taVNS. Changes were widespread, especially in frontal for delta, and throughout the brain for higher bands. These neuromodulatory effects stabilized by 30 minutes and were robust across participants and brain regions.

Conclusion: taVNS induces reliable EEG changes, including enhanced oscillatory power and network integration, especially when stimulation lasts 20–30 minutes. These findings suggest taVNS-EEG can be refined as an objective tool to optimize headache assessment and personalized neuromodulation, advancing clinical translation in pain and neurological care.

Fig. 1

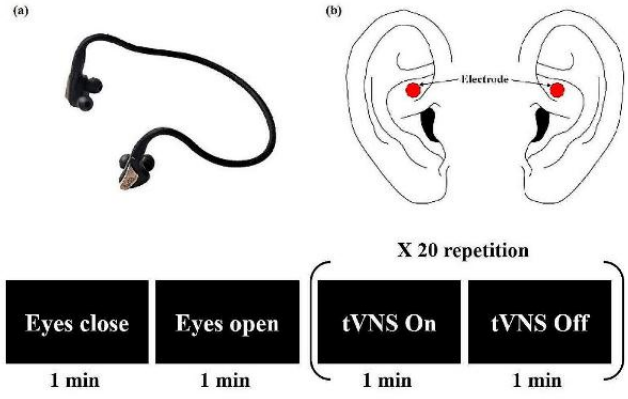


Fig. 2

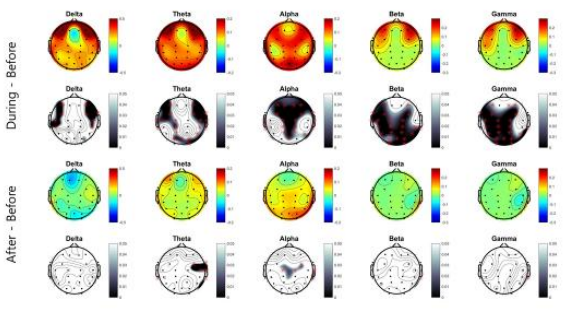
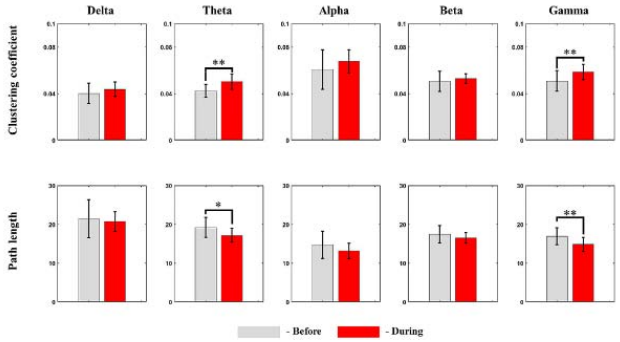


Fig. 3



P149

Evaluating agreement between physician and ChatGPT in migraine prophylaxis selection: A pilot comparative study

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Objective: To evaluate the level of agreement between human clinicians and an artificial intelligence (AI) model (ChatGPT) in recommending first-line prophylactic therapies for patients with migraine, and to assess the potential clinical value of AI-generated support.

Methods: In this observational pilot study, we analyzed 21 consecutive patients with a confirmed diagnosis of episodic migraine evaluated at a pain clinic.

For each patient, the treating clinician selected a first-line preventive treatment among four options: amitriptyline, propranolol, topiramate or flunarizine. Independently, ChatGPT was prompted with identical anonymous clinical data to generate therapeutic recommendation. Primary outcome was the agreement rate between physician and AI choices (molecule and dose). Statistical agreement was assessed via Cohen"s Kappa. Secondary endpoints included changes in pain intensity (NRS) at 3-month follow-up, adverse events, and treatment modifications.

Results: The observed agreement between the physician and AI treatment selection was 71.4% (15/21 patients, fig. 1). Cohen"s Kappa was 0.564 ($z = 3.75$; $p < 0.001$), indicating a statistically significant moderate agreement beyond chance. The average reduction in NRS at 3 months was −3.38 points (SD ± 0.78, fig. 2). Adverse events requiring treatment change occurred in 1 patient (4.8%). Most discrepancies occurred in the selection between topiramate and flunarizine.

Conclusion: This pilot study demonstrates that ChatGPT can produce clinically coherent prophylactic treatment proposals in the management of migraine, with a statistically significant moderate agreement with experienced pain physicians. Further validation on larger cohorts is warranted to explore its potential as a clinical decision support tool.

Fig. 1

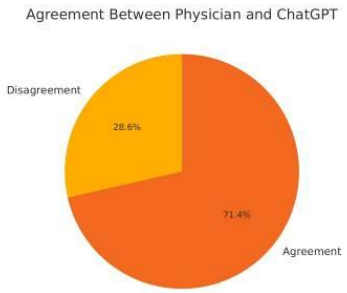
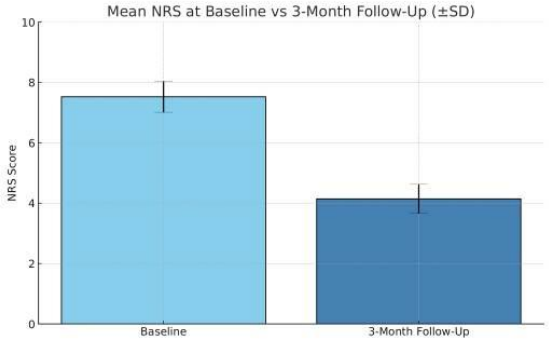


Fig. 2



P150

Clinical characterization of migraine using unsupervised learning on advanced diffusion MRI metrics

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Objective: Current migraine classification does not capture the disorder's clinical heterogeneity and no biomarkers exist for its diagnosis or progression. Neuroimaging, especially MRI, is a promising source of biomarkers, with diffusion tensor imaging (DTI) being the standard for studying white matter microstructure. However, DTI oversimplifies diffusion properties and advanced models, like AMURA and MISFIT, have emerged to overcome these limitations using acquisition protocols compatible with clinical routine. This study applies unsupervised learning to diffusion MRI data to explore migraine subtypes and assess whether AMURA and MISFIT provide complementary information to DTI.

Methods: A total of 107 migraine patients (56 chronic [CM], 51 episodic [EM]) were recruited. The clustering pipeline is summarized in Figure 1. Diffusion metrics from 48 white matter regions (JHU ICBM-DTI-81 Atlas) were extracted using DTI, AMURA, MISFIT and Moment-based MISFIT (Figure 2a). After dimensionality reduction and feature selection, three clustering techniques were applied to 12 datasets combining three clinical groups and four sets of descriptors.

Results: Two clusters consistently emerged, with subgroups based on distinct clinical features, as shown in Table 1, showing examples in Figure 2b. AMURA identified more clinically significant distinctions, particularly in migraine duration and migraine classification (CM/EM). MISFIT was more sensitive to medication overuse headache (MOH) and migraine frequency. DTI revealed fewer differences, mostly linked to sex, duration of migraine and headache frequency.

Conclusion: Unsupervised learning offers important insights into the migraine pathophysiology and can provide a basis for predicting long-term clinical outcomes. Combining AMURA and MISFIT with DTI improves white matter characterization and enables identification of migraine subgroups related to long-term progression and specific headache features.

Fig. 1

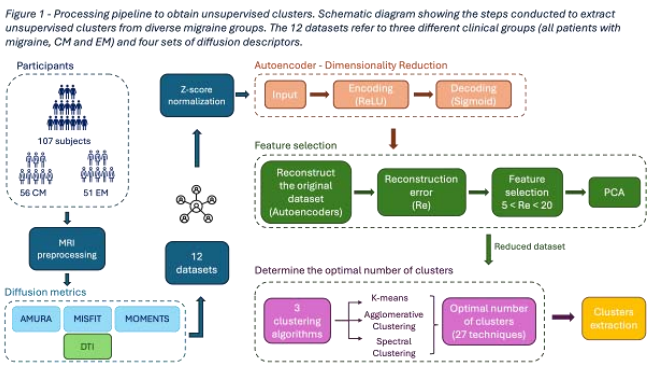


Fig. 2

Figure 2 – a) Diffusion metrics extracted for each diffusion model. b) Comparison of clinical characteristics between clusters. Violin plots comparing the number of months since the onset of CM between the clusters of the AMURA dataset, and barplots representing the distribution of the patients by sex in the clusters of the MISFIT dataset.

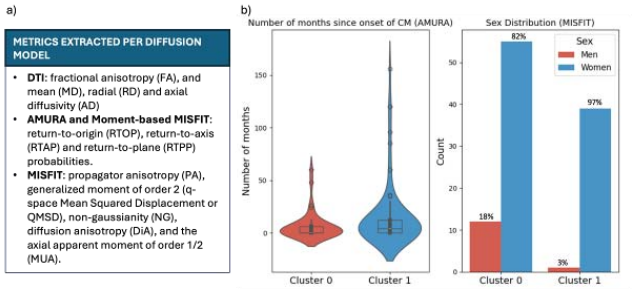


Fig. 3

Table 1 - Significant variables identified for patients with the whole sample across different clustering methods.

Clustering Method	Diffusion technique	Significant Variables
K-means	AMURA	Diagnosis of CM in the first MRI acquisition
		Age
		Number of years since onset of migraine
		Number of months since onset of CM
	MISFIT	MOH
		Diagnosis of CM in the first MRI acquisition
		Monthly migraine-like headache frequency
	MOMENTS	Sex
Agglomerative	DTI	Sex
		Number of years since onset of migraine
	AMURA	Number of months since onset of CM
		Number of years since onset of migraine
	MISFIT	MOH
		Diagnosis of CM in the first MRI acquisition
	MOMENTS	Sex
		Age
		Diagnosis of CM in the first MRI acquisition
Spectral	DTI	Monthly migraine-like headache frequency
	AMURA	Number of months since onset of CM
	MISFIT	MOH
		Diagnosis of CM in the first MRI acquisition
	MOMENTS	Sex
		Age
		Diagnosis of CM in the first MRI acquisition

P151

Precision medicine in migraine: Machine learning prediction of CGRP mAb treatment outcomes

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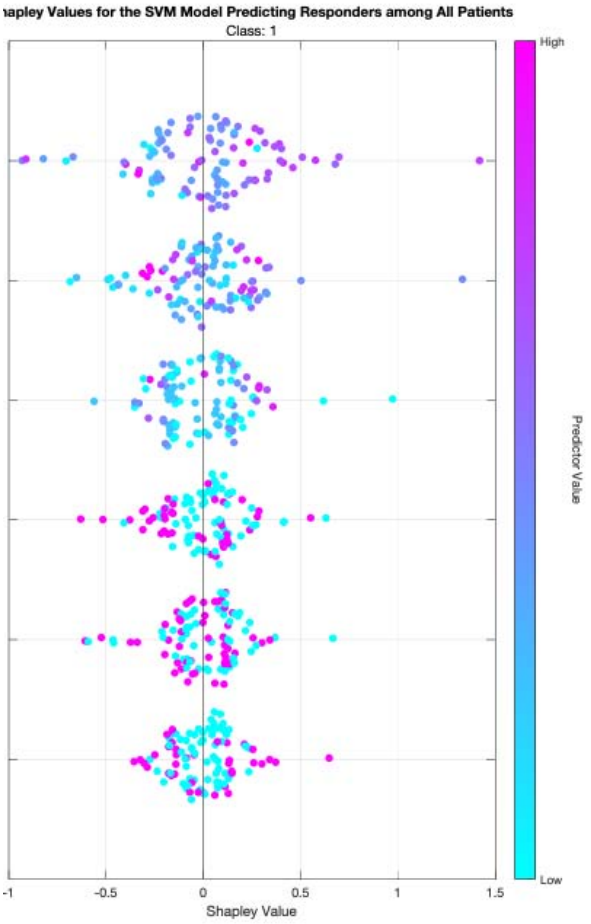
Objective: To evaluate the suitability and benefits of a dynamic treatment approach using CGRP monoclonal antibodies (mAbs) in chronic migraine (CM), and to assess the potential for machine learning (ML) models to predict individual treatment response based on patient-specific characteristics.

Methods: This observational, retrospective cohort study was conducted at SkåNeuro Neurology Clinic, Lund, Sweden, including CM patients receiving preventive treatment with anti-CGRP mAbs (erenumab, fremanezumab, galcanezumab). A dynamic treatment approach was applied at the clinic, involving individualized therapy adjustments based on clinical response and side effects. A ≥50% reduction in monthly headache days (MHDs) from baseline defined treatment response. Effectiveness was assessed over time, including after treatment switches or addition of complementary therapies. ML models were developed to predict individual treatment outcomes and side effect likelihood based on demographic and clinical features.

Results: The findings suggest that switching antibodies in cases of poor initial response often leads to improved outcomes in MHDs (p=0.005). Candesartan led to a significant reduction in MHDs at six months (p<0.001), whereas no additional benefit was observed with botulinum toxin. ML analyses identified key predictors of treatment success, which varied between different mAbs. Age, baseline MHDs, medication overuse headache (MOH), number of comorbidities, and menstrual migraine history were the most influential features (fig.1). Higher age was a strong positive predictor for erenumab response, while menstrual migraine history predicted poor response. In contrast, fremanezumab and galcanezumab responses were more strongly influenced by MOH and comorbidity burden.

Conclusion: Dynamic, personalized treatment enhances effectiveness of CGRP mAbs in CM. ML tools can support precision medicine by predicting likely responders and informing individualized care strategies.

Fig. 1



P152

Data driven phenotyping of migraine and its correlation with ICHD-3 criteria and polygenic risk scores

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[6]Norwegian University of Science and Technology, Public Health and Nursing, Trondheim, Norway
[7]University of Bergen, Clinical Medicine, Bergen, Norway
[8]Haukeland University Hospital, Department of Neurology, Bergen, Norway
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[10]St. Olavs University Hospital, Neuroclinic, Trondheim, Norway

Objective: Migraine is a criterially defined diagnosis, based on the presenting phenotype, without known definitive biomarkers. Unsupervised machine learning (UML) can identify complex data clusters and data-driven, naturally occurring phenotypes of headaches symptomatology. This study identified data-driven migraine phenotypes and compared these with known migraine risk loci and the ICHD-3 criteria.

Methods: This cross-sectional UML study used data from the 2nd Trøndelag Health Study, including demographics, self-reported headache traits and genotype. A series of UML models were evaluated to identify subgroups with similar patterns. Cluster quality was evaluated using the Silhouette score and Davies-Bouldin index. Top-performing models were optimized for the number of clusters. Two-dimensional embeddings from UMAP analysis were used to visualize the high-dimensional data. Migraine diagnosis, as defined by validated ICHD-3 criteria, and polygenic risk scores (PRS) were mapped onto the UMAP projection to explore their links to the identified clusters. Genome-wide association analysis (GWAS) was conducted on the migraine cases as defined by both ICHD-3 criteria and the data-driven phenotypes to assess genetic overlap.

Results: The analysis included 12,185 headache sufferers. Spectral clustering identified two clusters; one with 1,425 individuals, 94% of whom met ICHD-3 migraine criteria, and another including 10,760 individuals, 74% of whom with non-migraine headaches (Fig. 1). Although mean PRS was similar in both clusters (0.48±0.11 versus 0.47 ±0.11 respectively), high PRS samples are mainly grouped near the migraine cluster (Fig. 2). GWAS analysis of ICHD-3 labelling and data-driven phenotyping showed agreement in minimal allele frequency and BETA values (Fig. 3).

Conclusion: Data driven clustering of headache phenotype leads to the identification of a naturally occurring migraine cluster that seems to have a higher genetic susceptibility and near perfect agreement with the modified ICHD-3 criteria.

Fig. 1

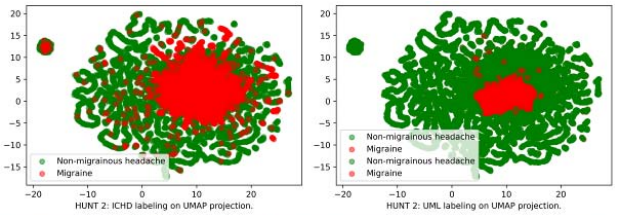


Figure 1: Labelling of migraine vs. non-migraine according to ICHD-3 criteria and unsupervised data-driven phenotyping, mapped onto two-dimensional embeddings from the UMAP analysis. Left: Red colored samples indicate that the corresponding patients fulfil ICHD-3 migraine criteria; Green colored samples indicate that the corresponding patients suffer from non-migrainous headache. Right: Samples with the same color indicate that the corresponding patients have similar characteristics underlying by their headache symptomatology data (red is used for patients with migraine characteristics and green for non-migrainous headache characteristics).

Fig. 2

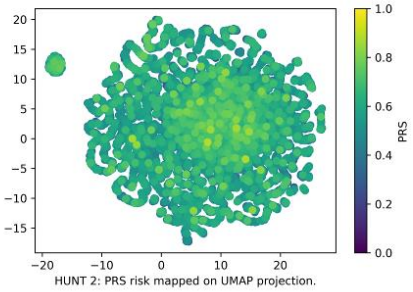


Figure 2: Distribution of normalized [0-1] polygenic risk score mapped onto a two-dimensional embedding from the UMAP analysis. Warmer colors correspond to higher PRS scores, while cooler colors to lower PRS scores.

Fig. 3

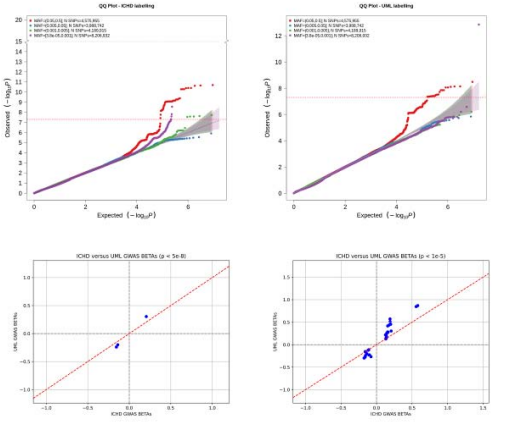


Figure 3: Results of the GWAS analysis of ICHD-3 defined migraine versus unsupervised data-driven phenotypes. The upper plots are QQ-plots of minimal allele frequencies of the ICHD-3 labelling (left) and the unsupervised data-driven labelling (right). The lower plots maps beta values for the most significant SNPs for the ICHD-3 labels versus the unsupervised data driven labels with different p-value thresholds (p<5e-8 for the left and p<1e-5 for the right plot). Both phenotyping approaches show remarkable agreement since the beta values of the most significant SNPs seem to follow the diagonal which represents the perfect agreement (line of identity).

P153

A nomogram for the prediction of response to anti-CGRP mAbs: The CGRP score

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Objective: The study aimed to develop and validate a nomogram for predicting response to anti-CGRP monoclonal antibodies (mAbs) in patients with migraine, to translate machine learning (ML) predictors of response into a clinically usable tool for personalized treatment planning.

Methods: This prospective cohort study included adults with migraine treated with anti-CGRP mAbs at two headache centers. Responders were defined as patients achieving ≥50% reduction in monthly headache days (MHDs) at 12 months. A logistic regression model was trained (80%) and tested (20%) using 11 baseline variables, including age, sex, migraine subtype, medication overuse, MHDs, and disability scores. Model performance was evaluated using accuracy, precision, recall, and F1-score. A nomogram was created for future research and clinical application. The model was then validated against an external test cohort treated with anti-CGRP mAbs.

Results: Among 430 patients, 311 completed 12 months of treatment, with 236 (55.1%) classified as responders. The external cohort included 109 patients. The ML model achieved an overall accuracy of 70%, with strong performance in identifying "responders" (precision: 0.66, recall: 0.84, F1-score: 0.74). The model yielded predictions with an overall accuracy of 74% when tested against an external test cohort. Chronic migraine status, older age, and lower baseline MHDs were associated with higher response likelihood. Medication overuse and frequent analgesic use were negatively associated with response. The nomogram provided a clinically interpretable tool to estimate response probability, providing a total score named "CGRP Score" (**C**GRP mAbs, **G**lobal **R**esponse **P**rediction).

Conclusion: This ML-based predictive score achieved strong performance in identifying responders to anti-CGRP mAbs. The nomogram has the potential to be a practical, user-friendly tool for supporting clinical decision-making after validation.

Fig. 1

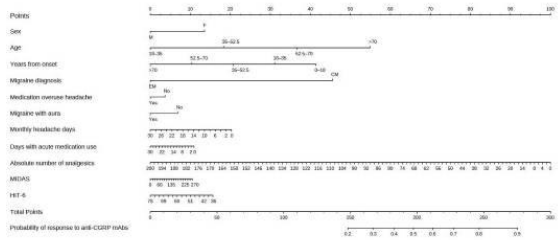
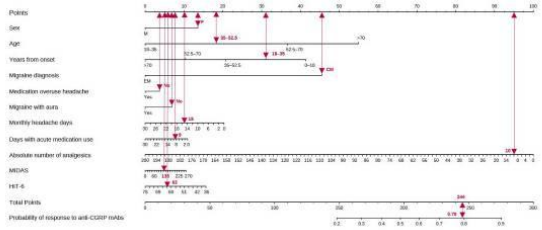


Fig. 2



P154

Can early imaging-based artificial intelligence (AI) replace lumbar puncture for idiopathic intracranial hypertension? A meta-analysis shows diagnostic comparability

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[2]National Chung Hsing University, Taichung City, Taiwan

Objective: Idiopathic intracranial hypertension (IIH) can cause irreversible vision loss, yet lumbar puncture (LP) is still the first diagnostic test. We asked whether imaging-based artificial-intelligence (AI) reads now rival experts and could underpin an "image-first, needle-second" workflow that trims LP use.

Methods: PRISMA-2020 and PROSPERO CRD420251073964 guided a PubMed search (2000-2025) for IIH AND imaging AND AI. Case reports and abstracts were excluded. Two reviewers applied QUADAS-2 and extracted 2 × 2 tables, keeping the best Youden marker. All studies used LP opening pressure > 25 cm H_2O as reference. Random-effects models pooled sensitivity (Se) and specificity (Sp); a covariate contrast between AI and expert groups. Publication bias was assessed with a Deeks funnel plot.

Results: Seventeen studies (1208 IIH; 1356 controls) met criteria. Pooled Se 0.77 (95 % CI 0.65–0.86), Sp 0.86 (0.79–0.92), AUC 0.84. AI (2 studies) showed Se 0.76, Sp 0.69; experts (15 studies) Se 0.77, Sp 0.89. ΔSe 0.01 (p = 0.92); ΔSp 0.20 (p ≈ 0.04). No relevant publication bias.

Conclusion: AI already offers expert-level sensitivity and can fast-track low-risk cases, lowering same-day LP demand. Because specificity is only ≈ 0.69, AI-positive scans still need LP (or expert review) for confirmation. Larger prospective, multimodal datasets are required before a fully image-first, needle-second pathway is safe.

Fig. 1

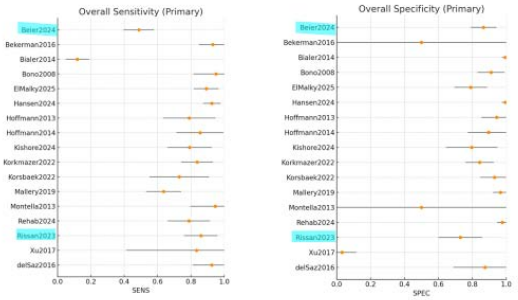
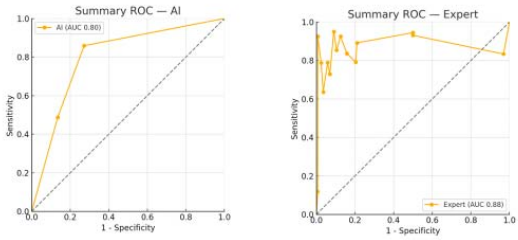


Fig. 2



P155

TARA diagnostic study: An interim report

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[1]University medical center Maribor, Neurology Division, Maribor, Slovenia

Objective: The TARA Diagnostic Study was designed to evaluate the clinical use of combining the e-headache diary and a wearable device in monitoring and managing patients with migraine. By prospectively collecting patient-reported migraine frequency, prodromes, triggers, and passively assessed real-time continuous data, a machine learning-based migraine prediction model can be developed.

Methods: Migraine patients documented attack frequency, prodromes, and triggers in real-time via the Opora App while continuous physiological data (heart rate, activity, SpO2, sleep) was captured by the FitBit Charge 6. We plan to include 80 patients with episodic and chronic migraine, with a follow-up of 10 months. An interim analysis of the collected data is reported.

Results: We report on preliminary analysis of 35 patients (28 female; mean age 43 years; range 21-70) followed for at least 1 month (median 3 months, range 1-6 months). Altogether, 637 episodes of migraine were detected, and 1927 prodromal events. The most frequent prodromes reported were "being sensitive to light, sound, or smell" (10.7%), "neck stiffness" (10.4%), and "fatigue" (10.4%). The most common self-reported triggers were "stress" (19,7%), "weather changes" (17.6%), and "sleep quality" (16.2%). The mean number of monthly migraine days in the sample was 6.2 (range 3-15), the initial mean HIT-6 score was 63, and the mean MIDAS score was 80. Eighty percent of migraines lasted 2-24 h. At inclusion, 59% of patients had preventive treatment with either anti-CGRP or gepants. The mean smartwatch wearing time was 22.1 hours per day (range 10.3-23.5) and was constant over the follow-up period.

Conclusion: Multimodal data integration from e-diary and wearable device demonstrates feasibility for migraine prediction, enabling proactive management. Good data quality and patient adherence are reported. A larger cohort and dataset could improve the accuracy of the prediction model for clinical deployment.

P156

CEFALEAPP: An app for the diagnosis and treatment of migraine in primary health care

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Objective: Among the factors of migraine chronification are the delay in the initiation of preventive drugs, with the consequent abuse of analgesics, and the trivialization of migraine in the population, mainly female, and this causes a delay in diagnosis. The end result is a significant number of years lived with disability. Our aim was to develop a digital application to support Primary Health Care (PHC) physicians in both the accurate diagnosis and early preventive treatment of migraine.

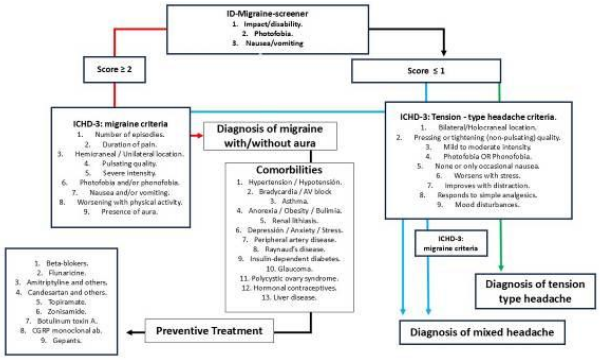
Methods: We designed a rules-based artificial intelligence system to analyze patient responses to the ID-Migraine screener—a 3-question probabilistic tool for identifying migraine in primary care. The

system determines whether a patient meets the International Headache Society diagnostic criteria for migraine (ICHD-3). If not, the app suggests an alternative diagnosis, such as tension-type headache. In addition, it includes an algorithm to guide the selection of preventive treatments based on the patient"s comorbidities. The application was developed in Java, with rules and associated data structured through XML files. [figure 1].

Results: CefaleApp enables the diagnosis of migraine, tension-type, or mixed headaches; estimates migraine-related disability using HIT-6 and MIDAS scores; and generates tailored recommendations for preventive treatment considering comorbidities. Initial validation in patients newly diagnosed with migraine in a Neurology clinic showed perfect concordance with clinical assessment (correlation = 1.0).

Conclusion: CefaleApp facilitates accurate clinical diagnosis of migraine in PHC settings and supports early, personalized preventive treatment. It is a digital tool for the clinical management of migraine. By leveraging artificial intelligence, it addresses the shortage of neurologists and empowers PHC providers in migraine management. CefaleApp enhances the quality of care by promoting preventive treatment in PHC, reducing migraine chronification, and improving patients' quality of life.

Fig. 1



P157

Tension-type headache vs. migraine: Role of ultrasound-guided dry needling in differentiation

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[2]New York Dynamic Neuromuscular Rehabilitation & Physical Therapy, New York, NY, United States

Objective: Headache disorders affect billions globally, with tension-type headache (TTH) and migraine being the most common subtypes. Despite overlapping clinical presentations, they have distinct pathophysiological mechanisms, necessitating precise differentiation for effective management. Ultrasound (US)-guided dry needling (DN) has demonstrated efficacy in pain conditions, including headache and migraine. This study explores the role of US-guided DN in distinguishing TTH from migraine by evaluating specific US markers and their dynamics during treatment.

Methods: Fifteen patients presenting with headache, vertigo, and central sensitization symptoms were enrolled. Based on diagnostic criteria, 5 were classified as definite migraine, 6 as clear TTH, and 4 as mixed/unknown cases. US-guided DN by R.Bubnov, aimed at restoring posture, targeted also trigger points in suboccipital muscles, focusing on structures attached to the dura mater. Real-time US imaging confirmed needle placement, M-mode visualization of dorsal and ventral root pulsations at C1-C2 was conducted. Ophthalmic artery Doppler assessments were performed pre- and post-treatment to analyze blood flow changes.

Results: DN successfully inactivated trigger points in suboccipital, shoulder, and temporomandibular muscles, improving muscle contractility. Migraine patients exhibited significant central sensitization, with altered spinal root pulsations and enhanced retinal, ciliary, and ophthalmic artery blood flow. TTH patients showed relapse correlated with trigger point reactivation but exhibited less pronounced central sensitization. Occipitalis muscle DN may be valuable for TTH, while suboccipital DN remains essential for dura mater-related sensitization.

Conclusion: US-guided DN aids in differentiating TTH from migraine by addressing trigger points and monitoring neuromuscular dynamics. M-mode ultrasound provides an objective tool for assessing spinal root oscillations, supporting targeted, personalized interventions.

P158

Ultrasound-guided dry needling approach for suboccipital muscles: A novel perspective on myodural modulation in headache disorders

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[2]New York Dynamic Neuromuscular Rehabilitation & Physical Therapy, New York, NY, United States

Objective: Headache disorders, including tension-type headache (TTH) and migraine, are widespread and significant health concerns. The myodural bridge, connecting suboccipital muscles (obliquus capitis inferior and superior) to the spinal dura mater, is implicated in modulating cerebrospinal fluid (CSF) dynamics and central sensitization. Ultrasound-guided dry needling (US-DN) targeting these muscles offers a potential approach for headache management.

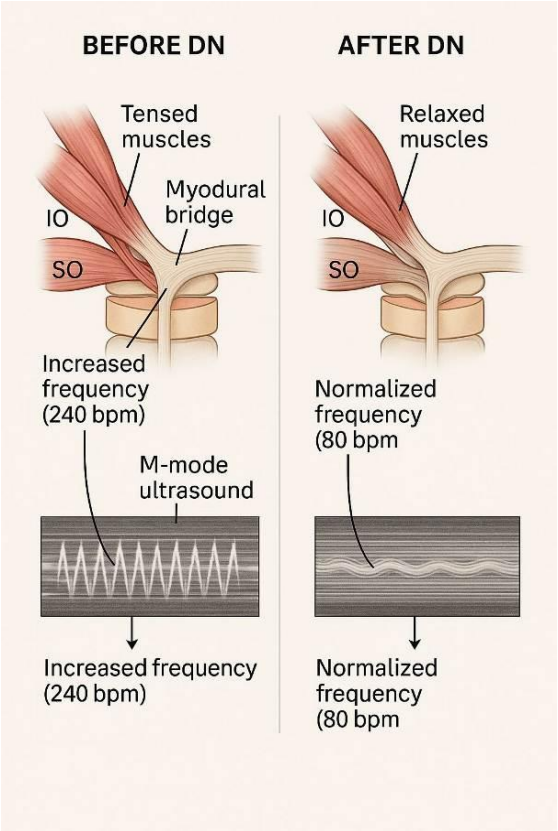
Objective: To assess the effects of US-DN on headache symptoms, spinal oscillatory patterns, and cerebrovascular dynamics.

Methods: Ten patients (4 migraine, 6 TTH) were treated with US-DN following real-time diagnostic assessment. M-mode ultrasound visualized spinal root oscillations at the C1–C2 level as in [https://doi.org/10.1177/03331024241280496#sec-206].

Results: Pathological dural oscillation frequencies—often 2–3× the cardiac frequency (e.g., 160–240 Hz vs. normal ~80 Hz)—were detected, particularly in migraine and centrally sensitized states. US-DN targeting the IO and SO muscles led to normalization of these frequencies post-intervention, supporting the hypothesis of a resonance mechanism wherein muscle-induced dural tension alters the frequency of mechanical pulsations (figure). Additional Doppler assessment of the ophthalmic artery confirmed improved hemodynamics post-DN, aligning with symptom relief.

Conclusion: These findings suggest that abnormal dural resonance, modulated by IO/SO tension, contributes to headache pathogenesis. Ultrasound-guided dry needling of the suboccipital muscles, particularly IO and SO, offers a promising personalized approach for treating headaches, especially those linked to central sensitization. Spinal duro-mechanical oscillation analysis via M-mode ultrasound may serve as a non-invasive biomarker for diagnosing and monitoring treatment efficacy.

Fig. 1



P159

A phase 4 randomized double-blind placebo-controlled study of rimegepant for acute treatment of migraine in adults unsuitable for triptan use

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[2]The New England Institute for Neurology and Headache, Stamford, CT, United States
[3]Pfizer, Inc., Princeton, NJ, United States
[4]Pfizer, Inc., Paris, France
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Objective: To assess rimegepant (Rim) for acute treatment of migraine in adults unsuitable for triptans (NCT05509400).

Methods: Participants (age 18–65 years with 4–14 migraine days per month) were unsuitable for triptans due to history of intolerance or lack of efficacy to ≥2 triptans, or contraindication. Participants were randomized to single dose Rim 75 mg orally disintegrating tablet or placebo (Pbo) to treat a migraine attack of moderate or severe pain intensity within 45 days. Primary endpoint was pain relief at 2h post dose. Key secondary endpoints were pain freedom at 2h; rescue medication use within 24h; normal function at 2h; sustained normal function from 2–24 and 2–48h; sustained pain relief from 2–24 and 2–48h; sustained pain freedom from 2–24 and 2–48h; and freedom from the most bothersome symptom (nausea, phonophobia, or photophobia) at 2h. A hierarchical gatekeeping approach controlled type 1 error. Adverse events (AEs) were also assessed.

Results: Participants receiving treatment (Rim=295, Pbo=290) were mostly female (89.1%), with a mean age of 42.9 years and 6.6 moderate to severe migraine days per month. Participants analyzed for efficacy (Rim=286, Pbo=284) had documented failure to ≥2 triptans with ≥1 reason due to prior intolerance (30.5%) or lack of efficacy (84.9%); 9.1% had a contraindication. Rim was superior to Pbo on the primary endpoint of pain relief at 2h post dose (55.9% vs 32.7%; difference [95% CI]: 23.2 [15.3, 31.1]; p<0.0001) and all key secondary endpoints (**Table**). AE frequency was similar in the Rim (12.5%) and Pbo (12.1%) groups; most were mild and none were serious.

Conclusion: Single dose Rim 75 mg demonstrated efficacy and a favorable safety profile for acute treatment of migraine in adults unsuitable for triptans. This is the first study to demonstrate efficacy of a gepant for acute treatment of migraine in this population.

A proprietary generative AI tool was used to develop the first draft; authors take responsibility for content.

Fig. 1

Table. Summary of primary and key secondary endpoints.[a]

Endpoint	Rimegepant 75 mg n/N (%)	Placebo n/N (%)	Difference (95%CI)	P value
Primary				
Pain relief at 2h	160/286 (55.9)	93/284 (32.7)	23.2 (15.3, 31.1)	<0.0001
Key Secondary				
Pain freedom at 2h	65/286 (22.7)	21/284 (7.4)	15.3 (9.6, 21.1)	<0.0001
Rescue medication within 24h	50/283 (17.7)	128/279 (45.9)	−28.2 (−35.6, −20.9)	<0.0001
Normal function at 2h[b]	67/232 (28.9)	30/237 (12.7)	16.2 (9.0, 23.4)	<0.0001
Sustained normal function 2–24h[b]	42/232 (18.1)	16/237 (6.8)	11.4 (5.5, 17.2)	0.0002
Sustained normal function 2–48h[b]	37/232 (15.9)	10/237 (4.2)	11.7 (6.4, 17.1)	<0.0001
Sustained pain relief 2–24h	111/286 (38.8)	41/284 (14.4)	24.4 (17.4, 31.3)	<0.0001
Sustained pain relief 2–48h	97/286 (33.9)	30/284 (10.6)	23.4 (16.8, 29.9)	<0.0001
Sustained pain freedom 2–24h	40/286 (14.0)	14/284 (4.9)	9.1 (4.3, 13.8)	0.0002
Sustained pain freedom 2–48h	35/286 (12.2)	8/284 (2.8)	9.4 (5.2, 13.7)	<0.0001
MBS freedom at 2h	89/286 (31.1)	53/284 (18.7)	12.5 (5.4, 19.5)	0.0005

[a]Testing utilized a hierarchical gate-keeping approach to control type 1 error. First, the significance of the primary endpoint was evaluated at the 0.05 level. Since the primary endpoint was significant at the 2-sided alpha level of 0.05, key secondary endpoints were tested hierarchically (each at a 2-sided alpha level of 0.05) in the prespecified order.
[b]Among participants with any level of functional disability at time of dosing.
MBS, most bothersome symptom among nausea, photophobia, or phonophobia; n, number of participants meeting the endpoint; N, number of evaluable participants.

P160

A clinical guide to assess and manage altered pain sensitivity and cervical musculoskeletal impairments migraine patients. Part 1: Assessment and profiling

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[1]Aalborg University, Department of Health Science and Technology, Rapallo, Denmark

Objective: Migraine is a complex neurological disorder characterized by different signs and symptoms, and patients are often presenting with an altered pain sensitivity and cervical musculoskeletalimpairments (1,2). Therefore, in the management of migraine patients the assessment and eventually a specific treatment of these aspects should be included. This abstract provides evidence-based guidance on assessment techniques and clinical reasoning strategies to help clinicians effectively evaluate and interpret these aspects in clinical practice

Methods: A review of the current literature has been performed and the results reported in this abstract are based on a recently published manuscript (1,2).
This abstract offers evidence-based guidance on how to perform and interpret assessment tests to effectively evaluate cervical musculoskeletal impairments and altered pain sensitivity in migraine patients.

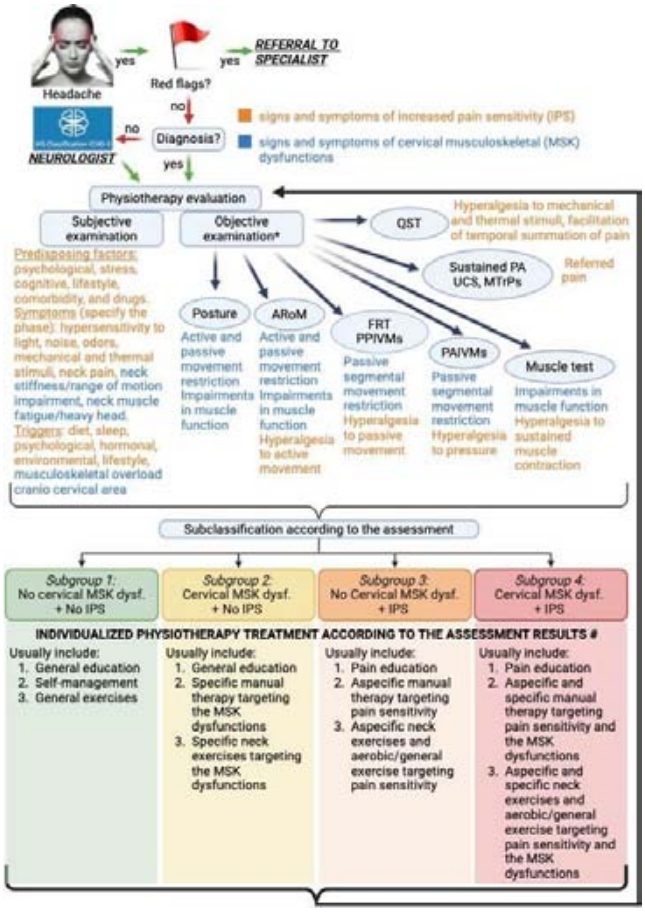
Results: This abstract provides a detailed explanation of how to perform a subjective examination (anamnesis) and an objective examination (physical examination): each test is described in detail, along with reference cut-off values that help identify the presence of these impairments. Based on the assessment results, each migraine patient is categorized into a specific subgroup according to the presence of cervical musculoskeletal impairments and/or altered pain sensitivity.

Conclusion: The ability to accurately assess increased pain sensitivity and cervical musculoskeletal impairments will enable clinicians to profile migraine patients based on these characteristics and implement a personalized treatment approach

Reference

1. Castaldo M, Arendt-Nielsen L, Di Antonio S. A clinical guide for physiotherapists to assess and manage cervical musculoskeletal impairment and pain sensitivity in migraine patients. J Man Manip Ther. 2025
2. Di Antonio S, Arendt-Nielsen L, Castaldo M. Cervical musculoskeletal impairments and pain sensitivity in migraine patients. Musculoskelet Sci Pract. 2023

Fig. 1



P161

A clinical guide to assess and manage altered pain sensitivity and cervical musculoskeletal impairments migraine patients. Part 2: individualised treatment

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Objective: Migraine is a complex neurological disorder characterized by different signs and symptoms, and patients are often presenting with an altered pain sensitivity and cervical musculoskeletal impairments (1). Therefore, in the management of migraine patients the assessment and eventually a specific treatment of these characteristics should be included. This abstract provides evidence-based guidance on the clinical reasoning and individualized treatment

approach, aiming to help clinicians in the management of these aspects in clinical practice.

Methods: A review of the current literature has been performed and the results reported in this abstract are based on a recently published manuscript (1)

This abstract is the second in a series; the first part focused on how to perform and interpret assessment techniques for evaluating cervical musculoskeletal impairments and altered pain sensitivity in migraine patients. This second part offers evidence-based guidance on how to manage migraine patients in an individualized manner, based on the findings of the assessment.

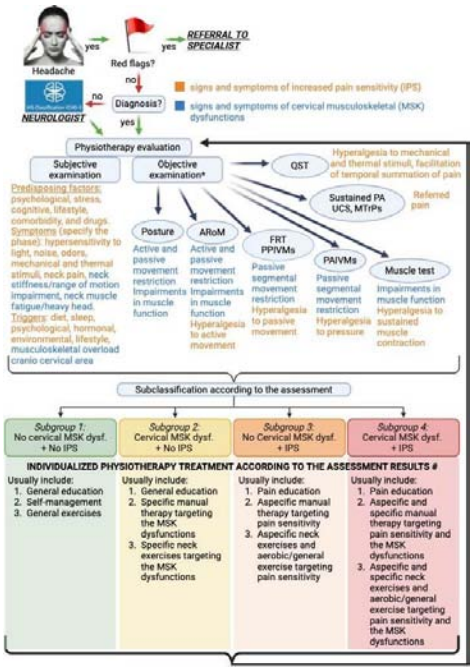
Results: This abstract provides a detailed explanation of how to manage the eventual presence of cervical musculoskeletal impairments and altered pain sensitivity in patients with migraine. The clinical reasoning behind the identification of distinct subgroup of migraine patients according to the presence of cervical musculoskeletal impairments and/or altered pain sensitivity is reported. Specific treatment techniques used for each migraine subgroup are explained in detail.

Conclusion: An individualized treatment approach aiming at addressing increased pain sensitivity and cervical musculoskeletal impairments, can improve the management of migraine patients. when present will improve migraine management.

Reference

1. Castaldo M, Arendt-Nielsen L, Di Antonio S. A clinical guide for physiotherapists to assess and manage cervical musculoskeletal impairment and pain sensitivity in migraine patients. J Man Manip Ther. 2025 May

Fig. 1



P163

Latent class analysis of headache disorders using population-based study: Searching for natural subgroups

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Objective: Headache disorders, despite their differing pathophysiologies, are currently diagnosed based on clinical criteria using ICHD-3. Migraine is typically characterized by unilateral, moderate to severe headache with nausea/vomiting and/or photophobia and phonophobia, whereas tension-type headache (TTH) is recognized as bilateral, non-pulsating, mild to moderate headache with few or no accompanying symptoms. However, ICHD-3–based diagnoses often present with overlapping symptoms or a wide variety of symptoms within a single diagnosis. This study aimed to identify natural subgroups of headache disorders and compare them with ICHD-3 diagnoses.

Methods: The CHASE study is a population-based survey investigating headache and sleep. Categorical variables based on ICHD-3 diagnostic criteria for migraine and TTH were analyzed using latent class analysis.

Results: Among 1,938 individuals with headache, five latent classes were identified, comprising 619 (32.0%), 365 (18.8%), 491 (25.3%), 61 (3.1%), and 402 (20.7%) individuals, respectively.

Class 1: Mild, short-duration headaches without nausea, resembling primary stabbing headache or other headache disorders.

Class 2: Moderate to severe headache with typical migraine features.

Class 3: Mild to moderate headache with migraine features and short duration, resembling probable migraine.

Class 4: Moderate, bilateral, non-pulsating headaches lasting more than 4 hours without nausea/vomiting, resembling TTH.

Class 5: Moderate headaches lasting less than 4 hours, without nausea or vomiting, suggesting mild TTH or other headache types.

Conclusion: Five natural subgroups of headache disorders were identified, reflecting migraine, TTH, and other headache types with varying severity and duration.

Fig. 1

Table 1. Characteristics of headache disorders according to the ICHD-3 diagnostic criteria, which were used as variables for LCA

Characteristic	Total	Class 1	Class 2	Class 3	Class 4	Class 5	p-value
N	1,938	619 (32.0%)	365 (18.8%)	491 (25.3%)	61 (3.1%)	402 (20.7%)	
Headache intensity							<0.001[a,b,c,d,g,h,i]
Mild	1,067 (55.1%)	609 (98.4%)	84 (23.0%)	309 (62.9%)	0 (0.0%)	65 (16.2%)	
Moderate	747 (38.5%)	10 (1.6%)	186 (51.0%)	179 (36.5%)	56 (91.8%)	316 (78.6%)	
Severe	124 (6.4%)	0 (0.0%)	95 (26.0%)	3 (0.6%)	5 (8.2%)	21 (5.2%)	
Unilateral location	994 (51.3%)	326 (52.7%)	190 (52.1%)	222 (45.2%)	0 (0.0%)	256 (63.7%)	<0.001[a,b,d,g,h]
Pulsating quality	873 (45.0%)	210 (33.9%)	201 (55.1%)	226 (46.0%)	1 (1.6%)	235 (58.5%)	<0.001[a,b,c,d,h,i]
Aggravation by routine physical activity	623 (32.1%)	110 (17.8%)	319 (87.4%)	35 (7.1%)	0 (0.0%)	159 (39.6%)	<0.001[a,b,c,d,g,i]
Nausea	749 (38.6%)	1 (0.2%)	284 (77.8%)	464 (94.5%)	0 (0.0%)	0 (0.0%)	<0.001[a,b,d,g,h,i]
Vomiting	358 (18.5%)	0 (0.0%)	169 (46.3%)	189 (38.5%)	0 (0.0%)	0 (0.0%)	<0.001[a,b,d,g,h,i]
Photophobia	495 (25.5%)	75 (12.1%)	259 (71.0%)	63 (12.8%)	7 (11.5%)	91 (22.6%)	<0.001[a,b,d,g,h,i]
Phonophobia	860 (44.4%)	292 (47.2%)	326 (89.3%)	5 (1.0%)	26 (42.6%)	211 (52.5%)	<0.001[a,b,d,g,h,i]
Headache frequency							<0.001[a,b,c,d,e,g,h,i]
<2	820 (42.3%)	376 (60.7%)	96 (26.3%)	203 (41.3%)	16 (26.2%)	129 (32.1%)	
2-7	947 (48.9%)	216 (34.9%)	207 (56.7%)	251 (51.1%)	35 (57.4%)	238 (59.2%)	
8-14	97 (5.0%)	14 (2.3%)	37 (10.1%)	14 (2.9%)	7 (11.5%)	25 (6.2%)	
≥15	74 (3.8%)	13 (2.1%)	25 (6.8%)	23 (4.7%)	3 (4.9%)	10 (2.5%)	
Headache duration							<0.001[a,b,c,d,g,h,i]
<30mins	1,240 (64.0%)	612 (98.9%)	175 (47.9%)	352 (71.7%)	0 (0.0%)	101 (25.1%)	
30mins-4hours	459 (23.7%)	0 (0.0%)	24 (6.6%)	134 (27.3%)	0 (0.0%)	301 (74.9%)	
4hours-72hours	200 (10.3%)	7 (1.1%)	145 (39.7%)	5 (1.0%)	43 (70.5%)	0 (0.0%)	
72hours-7days	26 (1.3%)	0 (0.0%)	15 (4.1%)	0 (0.0%)	11 (18.0%)	0 (0.0%)	
>7days	13 (0.7%)	0 (0.0%)	6 (1.6%)	0 (0.0%)	7 (11.5%)	0 (0.0%)	

Data are presented as n (%).

[a]: Significant difference between class 1 and class 2 in multiple comparisons

[b]: Significant difference between class 1 and class 3 in multiple comparisons

[c]: Significant difference between class 1 and class 4 in multiple comparisons

[d]: Significant difference between class 1 and class 5 in multiple comparisons

[e]: Significant difference between class 2 and class 3 in multiple comparisons

[f]: Significant difference between class 2 and class 4 in multiple comparisons

[g]: Significant difference between class 2 and class 5 in multiple comparisons

[h]: Significant difference between class 3 and class 4 in multiple comparisons

[i]: Significant difference between class 3 and class 5 in multiple comparisons

[j]: Significant difference between class 4 and class 5 in multiple comparisons

P164

A phase 4, open-label study evaluating the safety and tolerability of once daily rimegepant for episodic migraine prevention

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Objective: Rimegepant is well tolerated at approved doses; 75 mg as needed up to once per day for acute treatment of migraine and 75 mg every other day for prevention of episodic migraine (EM). This study evaluated long-term safety and tolerability of once daily (QD) rimegepant 75 mg for EM prevention.

Methods: Adults with 4-14 migraine attacks per month received open-label oral rimegepant 75 mg QD for up to 24 weeks. Standard-of-care medications for acute treatment of migraine were permitted as needed. Endpoints included adverse events (AEs) occurring in ≥5% of participants, serious AEs, AEs leading to rimegepant discontinuation, and Grade 3–4 laboratory test abnormalities.

Results: 250 participants received ≥1 dose of rimegepant (female=82.4%, White=86.4%, mean age=42.6 years) and 74.8% completed open-label treatment. Mean (SD) time on rimegepant was 19.3 (8.7) weeks. Overall, 53.6% of participants had ≥1 AE, none had a serious AE, 1.6% had a severe AE, and 2.8% had an AE leading to rimegepant discontinuation. AEs occurring in ≥5% of participants included nasopharyngitis (9.2%), COVID-19 (6.4%), and nausea (6.0%). Grade 3–4 laboratory test abnormalities included low lymphocytes (0.4%), high creatine kinase (3.8%), low glucose (0.4%), high LDL cholesterol (LDL-C; 9.8%), high fasting LDL-C (9.3%) high non fasting LDL-C (10.2%), high potassium (1.3%), high triglycerides (0.9%), high fasting triglycerides (1.3%), and urine glucose (0.5%). No elevations in liver transaminases (alanine aminotransferase [ALT] or aspartate aminotransferase [AST]) >5x the upper limit of normal (ULN) or potential Hy's law cases (ALT or AST >3x the ULN concurrent with total bilirubin levels >2.0x the ULN) were observed.

Conclusion: Rimegepant 75 mg QD for up to 24 weeks had a favorable safety profile for preventive treatment of EM. A proprietary generative AI tool was used with author review to develop the first draft; authors take full responsibility for content.

P165

Photophobia and visual triggers in vestibular migraine

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Objective: In this study, we aimed to meticulously examine interictal photosensitivity and the frequency of dizziness induced by visual triggers in patients with VM, with a specific emphasis on the role of photophobia. Our hypothesis posited that patients with VM and photophobia would exhibit heightened interictal photosensitivity and greater susceptibility to visual triggers compared with those in patients with VM devoid of photophobia and control participants.

Methods: We enrolled patients diagnosed with VM, with or without photophobia, across seven specialized vertigo and headache clinics in China. Healthy individuals were also included as a control group. Using a cross-sectional survey design, we collected data related to light intensity and dizziness frequency triggered by flicker, glare, and eyestrain using the Headache Triggers Sensitivity and Avoidance Questionnaire.

Results: A total of 366 patients were recruited. The photosensitivity and frequency of dizziness induced by flicker, glare, and eyestrain observed in patients with VM and photophobia were significantly elevated compared with those in patients without photophobia and control participants ($P < 0.001$). A significant positive correlation was observed between photosensitivity levels and dizziness frequency

triggered by flicker, glare, and eyestrain in patients with VM and photophobia ($P < 0.001$).

Conclusion: This study unequivocally established a positive association of ictal photophobia with interictal photosensitivity and visually triggering dizziness, strongly advocating the need for further research on exposure-based therapies for managing VM.

Fig. 1

Table 1. Photophobia questionnaire for patients with VM

1	During dizziness or vertigo, do you feel a greater sense of glare or dazzle in your eyes than usual by bright lights?	Yes	No
2	During dizziness or vertigo, do flickering lights, glare, specific colors, or high-contrast striped patterns bother you or your eyes?	Yes	No
3	During dizziness or vertigo, do you turn off the lights or draw a curtain to avoid bright conditions?	Yes	No
4	During dizziness or vertigo, do you have to wear sunglasses even in normal daylight?	Yes	No
5	During dizziness or vertigo, do bright lights hurt your eyes?	Yes	No
6	Is your dizziness or vertigo worsened by bright lights?	Yes	No
7	Is your dizziness or vertigo triggered by bright lights	Yes	No

VM, vestibular migraine

Fig. 2

Table 2. Baseline demographic and clinical characteristics of participants

	VM with photophobia (n = 183)	VM without photophobia (n = 183)	*P*-value
Sex (women, %)	124 (67.76 %)	127 (69.40 %)	0.822
Age (mean ± SD)	38.65 ± 13.29	40.60 ± 14.54	0.601
Age of vestibular symptom onset	35.77 ± 13.55	38.97 ± 14.17	0.143
Vestibular symptom			
Spontaneous vertigo[a]	124 (67.76 %)	136 (75.41 %)	0.167
Triggered vertigo[b]	113 (61.75 %)	82 (44.81 %)	0.001
Dizziness	33 (18.03 %)	25 (13.66 %)	0.316
Duration of attacks			
< 5 min	13 (7.10 %)	14 (7.65 %)	0.788
5–60 min	118 (64.48 %)	111 (60.66 %)	0.184
1–24 h	37 (20.22 %)	45 (24.59 %)	0.889
> 24 h	15 (8.20 %)	13 (7.10 %)	0.961
Motion sickness (n, %)	110 (60.11 %)	61 (33.33 %)	<0.001
Aura (n, %)	35 (19.13 %)	31 (16.94 %)	0.583
Vertigo intensity (VAS)	6.5 (6, 8)	6 (4, 7)	0.829
Phonophobia (n, %)	159 (86.89 %)	97 (53.01 %)	<0.001
Cochlear symptoms during attacks	33 (18.03 %)	30 (16.39 %)	0.782

SD, standard deviation; VAS, visual analogue scale; VM, vestibular migraine

[a]Spontaneous vertigo is a false sensation of self-motion or a false sensation that the visual surrounding is spinning or flowing;

[b]Triggered vertigo is vertigo that occurs with an obvious trigger

Fig. 3

Table 3. Light sensitivity and frequency scores of visual trigger-induced dizziness in participant groups

	Control (n = 146)	VM without photophobia (n = 183)	VM with photophobia (n = 183)	*P*
Light Sensitivity	1.68 ± 0.67	1.72 ± 0.73	2.67 ± 0.93	<0.001
Flicker	1.81 ± 0.77	1.73 ± 1.07	2.62 ± 1.46	<0.001
Glare	2.08 ± 0.79	2.10 ± 1.15	2.92 ± 1.26	<0.001
Eyestrain	2.67 ± 1.09	2.67 ± 1.23	3.28 ± 1.32	<0.001

SD, standard deviation; VM, vestibular migraine

Data are reported as the mean ± SD

P166

Efficacy and safety of two rimegepant dosing regimens for the prevention of episodic migraine: A double-blind, placebo-controlled study

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[5]Pfizer, Moscow, Russian Federation

Objective: To evaluate efficacy and safety of 2 rimegepant (RIM) 75 mg dosing regimens (every other day [EOD] and once daily [QD]) relative to placebo (PBO) for prevention of episodic migraine.

Methods: In this multicenter, randomized, double-blind, PBO-controlled study, a 28-day observation phase was followed by randomization to PBO QD, RIM 75 mg EOD/alternating PBO, or RIM 75 mg QD for a 12-week double-blind treatment (DBT) phase followed by a 12-week open-label (OL; RIM 75 mg QD) phase. The primary endpoint was mean reduction from observation phase in number of monthly migraine days (MMD) over the entire 12-week DBT phase. Safety was assessed based on adverse events (AEs) and liver function tests.

Results: Participants were randomized (*n*=699 total, PBO *n*=233, RIM EOD *n*=234, and RIM QD *n*=232). The primary endpoint was met for both RIM regimens with significantly greater reductions from observation phase in MMDs compared with PBO (least squares mean difference [97.5% confidence interval]) for RIM EOD (-0.6 [-1.22, -0.01], *P*=0.0220) and RIM QD (-1.8 [-2.35, -1.19], *P*<0.0001). All 5 key secondary endpoints were significant vs PBO for RIM QD (*P*<0.0001) while for RIM EOD, none were. Most AEs on DBT were mild or moderate (**Table**). There was a serious AE of status

migrainosus considered related to study drug in the RIM EOD group. There were no signals of drug induced liver injury.

Conclusion: RIM 75 mg EOD and RIM 75 mg QD regimens were both superior to PBO for prevention of migraine. Although not statistically tested, the efficacy response for QD appears more robust than for EOD. Both regimens were well tolerated. Clinicaltrials.gov NCT05217927. Funded by Pfizer.

Fig. 1

Table Safety Summary

n (%)	PBO QD (*n*=231)	DBT phase RIM EOD (*n*=232)	RIM QD (*n*=229)	OL phase RIM QD (*n*=573)
Any AE	117 (50.6)	102 (44.0)	100 (43.7)	227 (39.6)
Mild/moderate/severe AE*	91/43/2	73/42/4	86/22/3	-
AE leading to study drug discontinuation	4 (1.7)	6 (2.6)	1 (0.4)	6 (1.0)
Serious AE	1 (0.4)	3 (1.3)	2 (0.9)	6 (1.0)

*n/n/n

P167

Eptinezumab improved patient-reported disease burden and quality of life in a predominantly Asian population with chronic migraine: Secondary results from the SUNRISE trial

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Objective: To evaluate the impact of eptinezumab versus placebo on patient-reported migraine burden and health-related quality of life (HRQoL) in the phase 3 SUNRISE trial.

Methods: In the SUNRISE trial (NCT04921384), adults (18–75 years) diagnosed with chronic migraine were randomized 1:1:1 (after a 28–30-day screening period) to IV eptinezumab 100mg, 300mg, or placebo for a 12-week double-blind placebo-controlled period. Patient-reported outcomes assessed at Week 4 and Week 12 included Patient Global Impression of Change (PGIC; overall disease status), patient-identified most bothersome symptom (PI-MBS; migraine symptoms), Headache Impact Test (HIT-6; headache-related life impact), Migraine-Specific Quality-of-life questionnaire (MSQ v2.1; migraine-specific HRQoL), and EQ-5D-5L visual analogue scale (VAS; overall HRQoL) scores.

Results: Of 983 participants randomized, 939 (95.5%) completed the 12-week placebo-controlled period. Of 978 participants treated, 63.5% were from Asia; the remaining 36.5% were from Europe. Starting from the first post-baseline assessment (Week 4), eptinezumab 100mg and 300mg were associated with greater improvements from baseline *vs* placebo across patient-reported outcome scores: PGIC, PI-MBS, HIT-6, MSQ v2.1 domains, and EQ-5D-5L VAS (*p*vs placebo were generally sustained at Week 12.

Conclusion: Eptinezumab treatment was associated with greater improvements than placebo in headache-related life impact, overall disease status, and HRQoL in a predominantly Asian population with chronic migraine, with improvements across patient-reported outcomes seen as early as Week 4 and generally sustained at Week 12.

P168

Rimegepant for the prevention of episodic migraine in adults with prior inadequate response to oral preventatives

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Objective: Rimegepant 75 mg orally disintegrating tablet (ODT) taken every other day (EOD) is an approved preventive treatment for episodic migraine (EM) in many countries. This phase 4 trial evaluated the efficacy and tolerability of rimegepant for the prevention of EM in participants with a history of inadequate response to oral preventive medications (OPMs).

Methods: Participants with 4-14 monthly migraine days (MMDs), <15 monthly headache days (<7 non-migraine), and a documented history of inadequate response to 2-4 OPM classes were enrolled. Participants were stratified by MMDs in the observation phase (OP) and number of failed OPM classes, then randomised to EOD rimegepant 75 mg ODT or placebo. The primary endpoint was mean change in MMDs from the 28-day untreated OP through the 12-week double-blind treatment (DBT) phase. Key secondary endpoints were tested hierarchically for Type I error control.

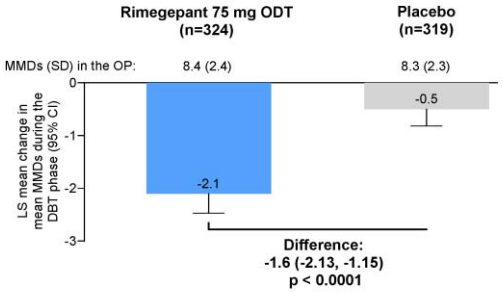
Results: 652 participants received treatment (328 rimegepant; 324 placebo); 35% had failed 3/4 OPM classes. MMDs (SD) in the OP were 8.4 (2.4) and 8.3

(2.3) in the rimegepant and placebo groups. Across the DBT phase, participants who received rimegepant had a significantly larger reduction in mean MMDs than those who received placebo (difference = -1.6 [95% CI: -2.13, -1.15]; p<0.0001; Figure). All key secondary endpoints were significant in favour of rimegepant (p<0.0007; Table). Rimegepant was well tolerated with no new safety findings.

Conclusion: Rimegepant 75 mg ODT EOD is efficacious and well tolerated for the prevention of EM in participants with a documented history of inadequate response to OPMs. NCT05518123

Fig. 1

Primary endpoint



Key secondary endpoints

	Rimegepant 75 mg ODT (n=324)	Placebo (n=319)	Difference
% participants with ≥50% reduction in mean MMDs with moderate or severe pain from the OP to the DBT phase, (95% CI)	34.0 (28.8, 39.1)	13.8 (10.1, 17.6)	20.1 (13.7, 26.5) p<0.0001
LS mean change in MMDs from the OP to the first month of the DBT phase, (95% CI)	-1.8 (-2.20, -1.38)	-0.1 (-0.45, 0.29)	-1.7 (-2.25, -1.17) p<0.0001
LS mean change in MMDs from the OP to the last month of the DBT phase, (95% CI)	-2.3 (2.72, -1.85)	-0.9 (-1.32, -0.39)	-1.4 (-2.05, -0.80) p<0.0001
LS mean change in MSQ restrictive role function score from baseline to the end of the DBT phase, (95% CI)	21.1 (18.95, 23.35)	14.6 (12.48, 16.68)	6.6 (3.60, 9.54) p<0.0001
LS mean change in MIBS score from baseline to the end of the DBT phase, (95% CI)	-1.9 (-2.24, -1.52) [n=322]	-1.0 (-1.36, -0.67) [n=319]	-0.9 (-1.36, -0.38) p=0.0006

Analyses of migraine frequency included all participants who were randomised once, took ≥1 dose of study medication, and had ≥14 days of electronic diary efficacy data (not necessarily consecutive) in the OP and ≥1 month in the DBT phase. Analyses of MSQ and MIBS scores include all participants who were randomised once, took ≥1 dose of study medication, and had non-missing scores at baseline and week 4, 8, or 12 of the DBT phase. CI = confidence interval; DBT = double-blind treatment; LS = least squares; MIBS = Migraine Interictal Burden Scale ; MMDs = monthly migraine days; MSQ = Migraine-Specific Quality of Life Questionnaire v2.1; ODT = orally disintegrating tablet; OP = observation phase; SD = standard deviation.

P169

Efficacy and safety of anti-CGRP monoclonal antibody therapy in hemiplegic migraine: A case series at a tertiary headache center

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Objective: To assess the efficacy and safety of anti-calcitonin gene-related peptide monoclonal antibodies (CGRP-mAbs) in patients with hemiplegic migraine (HM), a rare subtype of migraine characterized by motor aura.

Methods: We conducted a retrospective analysis of 17 HM patients who received CGRP-mAbs at the Tominaga Hospital Headache Center between May 2021 and May 2025. All patients were diagnosed according to the International Classification of Headache Disorders, 3rd edition (ICHD-3). Data on clinical characteristics, concurrent preventive medications, treatment duration, efficacy, and adverse events were analyzed.

Results: The patients (64.7% female) ranged in age from 17 to 58 years (mean, 33 years). Sporadic HM was observed in 70.6% of patients. Other aura symptoms included sensory (94.1%), brainstem (94.1%), speech (82.4%), and visual (70.6%) disturbances. Five patients (29.4%) had medication overuse headaches. Preventive medications at baseline included antiepileptic drugs (76.5%), calcium channel blockers (94.1%), antidepressants (17.6%) and ARBs (5.9%). The duration of anti-CGRP therapy ranged from 2 to 49 months (mean: 17.5 months). The mean monthly headache days decreased from 20.8 to 18.5, and the mean number of days with exertional motor aura decreased from 7.6 to 2.3. Adverse events included transient muscle weakness (two patients), rash (1), and ptosis (1). No treatment discontinuation occurred.

Conclusion: This study demonstrated that CGRP-mAbs may serve as a safe and effective preventive option for the treatment of hemiplegic migraine by reducing the frequency of both headache and motor aura symptoms.

P170

Do we still need non-specific oral prophylaxis for migraine treatment in CGRP-era? Real-life results from an Italian tertiary headache center

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Objective: In recent years new drugs targeting the calcitonin gene-related peptide (CGRP) have completely changed the therapeutic approach to migraine prevention. Consequently, the current need of non-specific oral preventive in real-life should be clarified, especially in Headache Centers setting.

Methods: This is a retrospective study focused on migraine prophylaxis prescription in migraine patients attending the Headache Centre of IRCCS-ISNB between 1st Jan 2024 and 31st May 2025.

Results: In a seventeen-month period data collection, we screened 632 patients with a history of migraine attending our Headache Center. Among them, 163 (25.8%; 134 F, 29M) received an oral conventional prophylaxis. Of the remaining, 354 (56%) received anti-CGRP agents and/or onabotulinumtoxinA injectios; 16 (2.5%) preferred a non-Pharmacological Treatment, and 99 (15.7%) did not need preventive prescription. Among those receiving oral prevention, the drug offered was: tricyclic antidepressants in 52

(31.9%) patients, Beta-blockers in 36 (22.1%), anticonvulsants in 19 (11.7%), Calcium Channel Blockers (flunarizine) in 26 (15.9%), SNRIs in 14 (8.6%), ACEIs/ARBs (candesartan) in 10 (3.7%) and combination of two drugs in 6 (3.7%).

Conclusion: A quarter of migraine patients attending our headache center received non-specific oral preventive. The most frequently prescribed treatments were antidepressants and Beta-blockers. In light of these observations, even in CGRP era, we suggest still an important role of oral conventional prophylaxis in the Headache Center setting.

P171

Efficacy and adverse effects of anti-calcitonin gene-realted peptide monoclonal antibodies: A retrospective analysis

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Objective: Prophylactic treatment (PT) is a core principle in the management of migraine and its use is a measure of high-quality care. PT is indicated in ~40% of patients with migraine.

Methods: The study included 148 patients who were treated with fremanezumab or erenumab at LSMUH Kaunas Clinics in 2024. Data collected: migraine type (with or without aura), episodic or chronic migraine (EM, CM), duration of migraine, non-specific PT, monthly migraine days (MMD) before anti-calcitonin gene-related peptide monoclonal antibody (CGRP mAbs) treatment and after 3-6 months, treatment efficacy and adverse events (AEs) were assessed. Bioethics approval was obtained: No.2024-BEC2-1369. Statistical analysis was performed using IBM SPSS version 30.0.

Results: The mean age (±SD) of patients was 41±11.7yrs; 89% of them were female. A greater proportion of patients had migraine without aura (76.9%) and not received previous PT (73.5%), migraine headache onset was more present in adulthood (56.6%), slightly higher proportion of patients had CM (51.7%). Fremanezumab was more commonly prescribed (85%, n=125) than erenumab (15%, n=23). The median MMD before specific PT was 15 (IQR: 8-17), and after the treatment with anti-CGRP mAbs, the MMD decreased to 4 (IQR: 2-6) ($p<0.001$). Erenumab reduced MMD by >75% in 31.8%, and Fremanezumab reduced MMD by >75% in 56% of patients ($p=0.026$). AEs occurred in 7.5% of patients. Fremanezumab induced AEs: hair loss (n=1), tachycardia (n=1), numbness of the extremities (n=1), choking sensation (n=1), allergic reactions (n=1), while constipation was reported in only one patient with erenumab. The occurrence of AEs was positively correlated with the duration of drug administration ($\rho=0.51$; $p=0.001$).

Conclusion: Both anti-CGRP mAbs are proven to be effective and safe drugs for the prophylaxis of migraine. Fremenezumab showed better results than erenumab, however, more equal distribution of patients is needed to make our findings more accurate.

P172

Patient-reported outcomes of atogepant versus topiramate in participants requiring preventive treatment for migraine: Results from the head-to-head TEMPLE trial

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Objective: We compared the functional outcomes between atogepant (ato), an oral calcitonin gene-related peptide receptor antagonist, and topiramate (topi) in participants requiring preventive treatment of migraine.

Methods: TEMPLE was a 24-week, randomized, double-blind (DB), double-dummy, active controlled trial to evaluate tolerability, safety, and efficacy of atogepant 60mg once daily (QD) compared to the highest tolerated dose of topiramate (50, 75, or 100 mg/day) for preventive treatment of migraine in participants with episodic or chronic migraine. In the modified intent-to-treat population (ato n=270; topi=257), we compared secondary endpoints including change from baseline (CFB) in Headache Impact Test-6 (HIT-6) total score, CFB in Migraine-Specific Quality of Life Questionnaire Version 2.1 (MSQ v2.1) Role Function-Restrictive (RFR) domain score, proportion of participants reporting "much better" or "very much better" as assessed by the Patient Global Impression of Change (PGIC) at Week 24, and CFB in Patient Reported Outcomes Measurement Information System Cognitive Function (PROMIS-CF) Abilities Subset Short Form 6a version 2.0 at Week 6.

Results: Atogepant demonstrated superior improvements in functional outcomes compared with topiramate as assessed by significantly greater reduction in HIT-6 total score (ato -11.7; topi -7.4; treatment difference (Δ): -4.3 [95% CI: -5.79,-2.72],

P<.0001) and significantly greater improvement in MSQ v2.1 RFR domain score (ato 33.5; topi 23.1; Δ: 10.4[6.59,14.18], *P*<.0001).A significantly greater percentage of participants receiving atogepant reported "much better" or "very much better" as assessed by PGIC compared with topiramate (ato 68.9%; topi 37.4%, RR: 1.85[1.55,2.22], *P*<.0001), and significantly greater improvement in PROMIS-CF Abilities score (ato 5.2; topi 0.2; Δ: 5.0[3.35, 6.69], *P*<.0001).

Conclusion: Atogepant 60 mg QD demonstrated clinically meaningful and statistically superior improvements in all secondary functional outcomes compared with topiramate.

P173

Achievement of 100% migraine response following eptinezumab treatment in adults with migraine: Post hoc analyses across 3 clinical trials

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Objective: To assess the impact of eptinezumab (EPTI) on achieving migraine freedom in adults with chronic migraine (CM) and those with migraine for whom 2–4 prior preventive treatments failed.

Methods: Data are from 3 EPTI trials (IV every 12 weeks [wks]) for migraine prevention: *PROMISE-2* (NCT02974153; adults with CM; 24-wk double-blind treatment with EPTI 100mg or 300mg *vs* placebo [PBO]); *DELIVER* (NCT04418765; adults with migraine for whom 2–4 prior preventive treatments failed; 24-wk double-blind treatment with EPTI 100mg or 300mg *vs* PBO followed by 48-wk dose-blind treatment with EPTI 100mg or 300mg); and *PREVAIL* (NCT02985398; adults with CM; 104-wk open-label treatment with EPTI 300mg). PROMISE-2 and DELIVER captured monthly migraine days (MMDs) via a daily eDiary. Migraine freedom over 12-wk intervals was defined as 100% MMD reduction from baseline for each respective 4-wk interval. PREVAIL captured headache days via the patient-reported Migraine Disability Assessment. Migraine freedom was defined as 0 headache days in the preceding 3 months. No *p*-values were generated.

Results: In PROMISE-2, migraine freedom was observed in 3% (100mg), 5% (300mg), and 2% (PBO) of participants after Dose 1, increasing to 7%, 10%, and 3%, respectively, after Dose 2. A similar trend was observed in DELIVER; 0.7% (100mg), 2.4% (300mg), and 0% (PBO) of participants had migraine freedom after Dose 1, increasing through the end of the trial. The proportion of participants with migraine freedom in PREVAIL increased from 9% (Dose 1) to 23% (Dose 8).

During the PBO-controlled periods, the proportion of participants with ≥1 migraine-free month was 35% (100mg), 40% (300mg), and 22% (PBO) in PROMISE-2; DELIVER: 22%, 27%, and 8%.

Conclusion: In people with CM and those for whom 2–4 prior preventive treatments failed, migraine freedom was observed in greater proportions of participants treated with EPTI than PBO. These proportions increased over long-term EPTI treatment, highlighting the build-up effect of continuous treatment.

P174

No additional benefit with detoxification strategies: A real world experience in 200 patients with chronic migraine and either simple or complex MOH treated with CGRP monoclonal antibodies

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Objective: Although withdrawal from analgesics with or without detoxification strategy represented a mainstay in medication overuse headache (MOH) management, recent evidence supports that it is no longer beneficial when CGRP-targeting monoclonal antibodies (CGRP-mAbs) are employed. MOH could be stratified into simple and complex phenotypes according to different clinical parameters (i.e., amounts and class of analgesics, psychiatric comorbidities, history of relapse after withdrawal, symptoms of central sensitization and maladaptive anticipatory response to pain experience). We explored the effectiveness of CGRP-mAbs plus detoxification strategy compared to CGRP- mAbs preventive treatment alone in patients with either simple or complex MOH phenotypes.

Methods: This is a six-month observational study including chronic migraine patients with MOH treated with subcutaneous CGRP-mAbs. Patients were stratified based on both MOH complexity and detoxification strategy to evaluate differences in the changes of monthly headache days, pain intensity and duration, and monthly days with acute medication intake during treatment period.

Results: Two hundred patients with migraine and MOH were recruited. Significant reduction of headache attacks frequency, intensity, duration and monthly days with acute medication intake has been observed both complex MOH (58.5%) and simple MOH (41.5%) after the first, third and sixth month of preventive treatment with CGRP-mAbs ($p < 0.001$). Furthermore, stratifying patients based on the MOH complexity and detoxification strategy, no differences were found in the reduction of monthly headache days as well as in other parameters of disease severity ($p > 0.05$).

Conclusion: Our findings might suggest a change in the mind-set of clinicians, still considering the withdrawal with or without detoxification strategy as a "conditio sine qua non" in patients with MOH, towards a novel approach where the reduction of analgesics intake represents the natural consequence of CGRP-mAbs effectiveness.

P175

Improved workplace productivity following preventive migraine treatment with eptinezumab: Results from a phase 3 trial in a predominantly Asian population with chronic migraine

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[5]Aversi Clinic LTD, Tbilisi, Georgia
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Objective: To evaluate the impact of eptinezumab versus placebo on migraine-related impairment in workplace productivity and overall activity in the phase 3 SUNRISE trial.

Methods: The SUNRISE trial (NCT04921384) confirmed the migraine-preventive efficacy and safety of eptinezumab in participants with chronic migraine, predominantly from Asian countries. Adults (18–75y) diagnosed with chronic migraine were randomized 1:1:1 to 12-week double-blind treatment with IV eptinezumab 100mg, 300mg, or placebo. The patient-reported Migraine-specific Work Productivity and Activity Impairment questionnaire (WPAI:M) was captured at baseline and at Weeks 4, 8, and 12. It quantifies the impact of migraine on productivity at work and daily activities (7-day recall). Changes from baseline in WPAI:M sub-scores included: absenteeism (% work time missed), presenteeism (% impairment while working), work productivity loss (% overall work impairment), and activity impairment (% activity impairment). As secondary endpoints, *p*-values for WPAI:M analyses are descriptive.

Results: Of 983 participants randomized, 939 (96%) completed the 12-week placebo-controlled period. Of 978 participants treated, 63% were from Asia (37% from Europe); mean baseline monthly migraine days was 17.4. The SUNRISE trial met the primary and all key secondary endpoints. Mean WPAI:M baseline sub-scores: absenteeism 7–10%; presenteeism 53–57%; work productivity loss 55–60%; activity impairment 58–60%. For the latter three, both eptinezumab doses were associated with greater improvements from baseline *vs* placebo at all time points ($p<0.05$). For absenteeism, low baseline scores may be due to participants working despite migraine symptom burden; both eptinezumab doses separated from placebo at Week 12 ($p<0.05$).

Conclusion: In a predominantly Asian population with chronic migraine, eptinezumab resulted in greater improvements than placebo in workplace productivity and activity levels, with improvements observed as early as Week 4 and sustained through Week 12.

P176

Could lamotrigine represent an effective treatment strategy in patients with migraine with aura? An observational study

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Objective: Although several drugs have demonstrated efficacy in the preventive treatment of migraine without aura, no pharmacological intervention has been specifically evaluated for patients experiencing only migraine with aura. Preclinical data suggest that glutamatergic hyperactivity underlies cortical hyperexcitability observed in these patients, especially in the visual cortex. The present observational study aimed to assess the effectiveness of lamotrigine in patients exclusively affected by migraine with aura.

Methods: Thirty-seven patients with migraine with aura (ICHD-III), experiencing ≥1 attack/month, were treated with lamotrigine 50–100 mg/day.Clinical data were collected prospectively before and after treatment. The primary outcome was the proportion of patients achieving a ≥50% reduction in monthly migraine with aura attacks. Secondary outcomes included changes in the mean frequency of attacks and aura duration.

Results: Of the 37 patients (28 females, 9 males; mean age 43 years), 25 (65.79%) and 36 (97.3%) experienced a ≥50% reduction in the frequency of migraine with aura attacks respectively at both 3 and 6 months of treatment. Mean attack frequency decreased significantly from 4 ± 4 to 1 ± 0.5 per month and mean aura duration decreased from 23.57 ± 14.04 to 19.38 ± 21.07 minutes. No adverse events were reported.

Conclusion: These findings support the efficacy and tolerability of lamotrigine as a preventive treatment for migraine with aura. We hypothesize that lamotrigine may mitigate aura symptoms by reducing glutamate release and thus decreasing cortical hyperexcitability in the visual cortex. This effect likely involves the inhibition of presynaptic voltage-gate Na^+, K^+, and Ca^{2+} channels, reducing cortical spreading depression susceptibility. These preliminary results suggest lamotrigine as a promising preventive option for patients with migraine with aura.

P177

Atogepant in treatment-refractory chronic migraine: Is a revision of current criteria for refractory migraine appropriate?

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Objective: Despite the emergence of novel targeted therapies, refractory migraine remains a major clinical challenge. According to the 2020 European Headache Federation (EHF) Consensus, patients experiencing ≥8 debilitating headache days per month are classified as "resistant" if they have failed at least three classes of preventive treatments, and "refractory" if they have failed all available classes. Treatments targeting the calcitonin gene-related peptide (CGRP) pathway—monoclonal antibodies and small-molecule antagonists—are currently grouped together. However, recent real-world evidence suggests that atogepant, a small-molecule CGRP receptor antagonist, may be effective in resistant migraine, including in those who failed anti-CGRP monoclonal antibodies.

Methods: This observational, prospective, non-randomized, open-label study, conducted over 24 weeks, enrolled 20 patients with treatment-refractory chronic migraine who received atogepant 60 mg once daily. Co-primary endpoints were: (i) change in monthly migraine days (MMDs) from baseline to Weeks 12 and 24; and (ii) proportion of responders, defined as those achieving a ≥50% MMD reduction at each time point.

Results: MMDs decreased by a mean of 3.7 days at Week 12 (SD 5.8; p=0.049) and 4.1 days at Week 24 (SD 6.0; p=0.047). The proportion of responders was 30% at Week 12 and 35% at Week 24.

Conclusion: These findings support the effectiveness of atogepant 60 mg daily as a preventive treatment in refractory migraine. The benefit in individuals who had failed all available preventive drug classes challenges current EHF criteria, suggesting that atogepant and CGRP-targeting monoclonal antibodies should be considered distinct therapeutic options. Several molecular mechanisms may underlie this enhanced CGRP pathway inhibition. Unlike monoclonals, atogepant is co-internalized with the CGRP receptor, inhibiting signalling in endosomes. Additionally, it binds receptors for amylin and adrenomedullin, neuropeptides involved in migraine pathophysiology.

P178

The role of hypertension in the relationship between leisure screen time, physical activity and migraine: A 2-sample Mendelian randomization study

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Objective: This study aims to investigate the causal relationship between lifestyle factors and migraine risk, and to identify the modifiable metabolic traits that mediate this relationship.

Methods: Independent genetic variants strongly associated with 20 lifestyle factors were selected as instrumental variables from corresponding genome-wide association studies. Summary-level data for migraine were obtained from the FinnGen consortium (18,477 cases and 287,837 controls) as a discovery set and the GWAS meta-analysis data (26,052 cases and 487,214 controls) as a replication set. Estimates derived from the two datasets were combined using fixed-effects meta-analysis. Two-step univariable MR and multivariable Mendelian randomization (MVMR) analyses were conducted to evaluate 19 potential mediators of association and determine the proportions of these mediators.

Results: The combined effect of inverse variance weighted revealed that a one standard deviation (SD) increase in genetically predicted Leisure screen time (LST) was associated with a 27.7% increase (95% CI: 1.14-1.44) in migraine risk, while Moderate or/and vigorous physical activity (MVPA) was associated with a 26.9% decrease (95% CI: 0.61-0.87) in migraine risk. The results of the mediation analysis indicated that out of the 19 modifiable metabolic risk factors examined, hypertension explains 24.81% of the

relationship between LST and the risk of experiencing migraine. Furthermore, hypertension and diastolic blood pressure (DBP) partially weaken the association between MVPA and migraines, mediating 4.86% and 4.66% respectively.

Conclusion: Our research findings indicated that both LST and MVPA in lifestyle have independent causal effects on migraine. Additionally, we have identified that hypertension and DBP play a mediating role in the causal pathway between these two factors and migraine.

Fig. 1

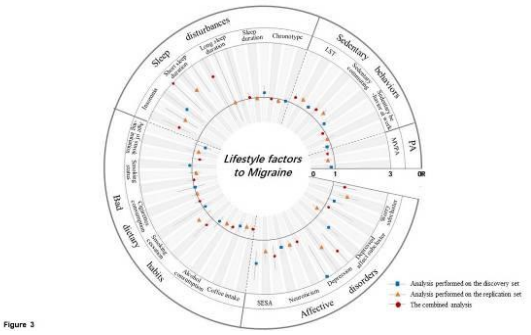


Figure 3

Fig. 2

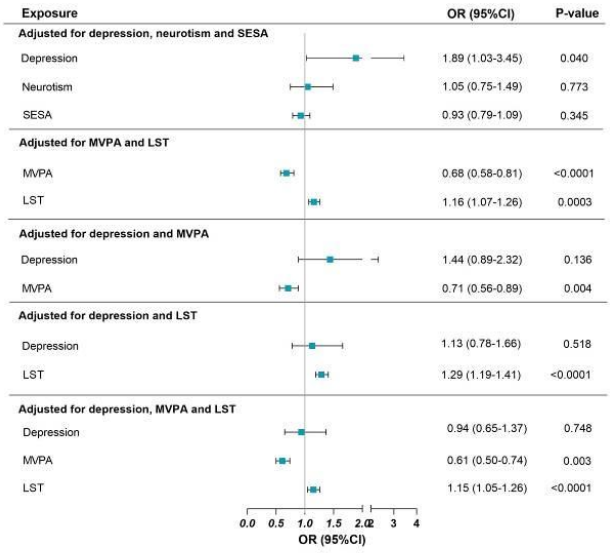


Figure 4

Fig. 3

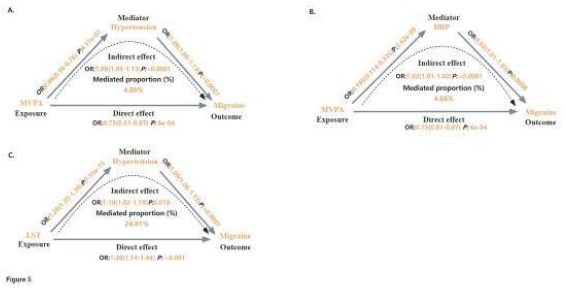


Figure 5

P179

Headaches and academic performance in nursing students in Albania

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Objective: To describe the epidemiology of headaches in Albanian University nursing students.

Methods: This study included third-year nursing students at the Albanian University. A headache questionnaire standardized by the International Headache Society was used. The questionnaire contains 15 questions and identifies personal headache history, pain intensity, trigger factors, psychological factors, pain intensity, consequences and impact on quality of life and daily work.

Results: This study included 191 students, 145 females (75.9%) and 46 males (24.08%). The mean age of females was 22 years and that of males was 21.6 years. The minimum age of the sample was 19 years and the maximum age was 42 years. Only 12 students (6.28%), 7 males and 5 females, reported that they had never had a headache in any period of their lives so far. 111 students (62% of the sample) presented with tension headaches with bitemporal localization, more frequent in females. 17 females (12.1% of females) presented with migraine-type pain with unilateral localization on the right in 11 of them, on the left in 3 and fluctuating in 3 students.

Conclusion: We recommend expanding it to a larger number of students, including other branches of study, with the aim of identifying functional consequences and preventing them.

P180

Clinical features and treatment outcomes of medication overuse headache in elderly patients: Insights from a nationwide prospective registry

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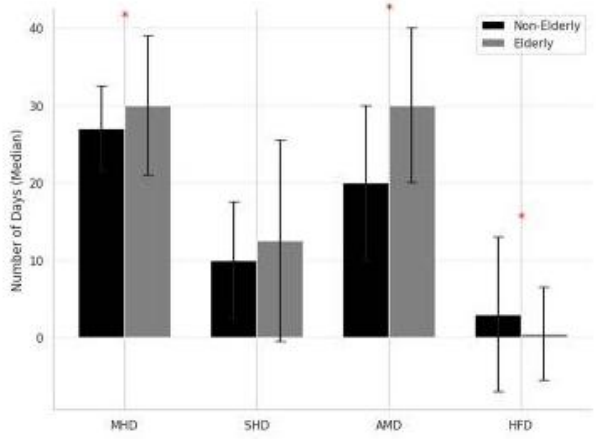
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Objective: Medication overuse headache (MOH) presents unique clinical challenges in the elderly due to age-related changes and comorbidities. However, data on MOH characteristics and treatment responses in this population remain limited. This study

investigated the clinical features, treatment patterns, and short-term outcomes of MOH in elderly patients.
Methods: We analyzed data from the RELEASE registry, a nationwide, multicenter prospective cohort of MOH patients in South Korea. Participants were stratified into elderly (≥65 years) and non-elderly (<65 years) groups. We compared clinical features, treatment patterns, and 3-month outcomes, and identified factors associated with treatment response in the elderly group.
Results: Among 791 patients, 72 (9.1%) were elderly. Compared to non-elderly patients, elderly patients reported more monthly headache days (30.0 vs. 27.0, p=0.012), more days using acute medication (30.0 vs. 20.0, $p < 0.001$), and fewer headache-free days (0.0 vs. 3.0, $p = 0.012$). They also experienced more severe headache days (12.5 vs. 10.0, $p = 0.056$). Despite this, elderly patients showed lower disability, with significantly lower Migraine Disability Assessment scores (30.0 vs. 46.0, $p < 0.001$) and a trend toward lower the Headache Impact Test-6 scores (64.5 vs. 66.0, $p = 0.065$). In multivariable analysis, poor adherence to preventive treatment (≤24%) was significantly associated with non-response (OR 0.13, 95% CI: 0.02–0.96, $p = 0.045$) at 3 months.
Conclusion: Elderly patients with MOH showed distinct clinical features, including higher headache frequency and severity but relatively lower disability. Improving adherence to preventive treatment may enhance treatment response. Age-specific management strategies are needed.

Fig. 1



P182
The effectiveness of anti-CGRP monoclonal antibodies in managing medication overuse headache in elderly patients
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Objective: Despite the relatively low prevalence of headaches among the elderly, clinicians frequently encounter elderly patients suffering from headaches in clinical practice. A significant proportion of these patients have been exposed to medication overuse. Recently, anti-CGRP monoclonal antibody therapy has been recommended as an effective treatment for medication overuse headache. The objective of this paper is to present cases that demonstrate the efficacy of this treatment approach in elderly patients.
Methods: A prospective review of patient records highlighted two cases of elderly patients with medication overuse headache.
Results: A 69-year-old woman with a history of migraine since her 20s visited the outpatient clinic. She had been taking a combination of analgesics for more than 15 days per month for over a year, and she had been taking analgesics daily for six months prior to this visit. She has a history of hypertension and hyperlipidemia, and her current headache is more like a chronic tension-type headache. In order to discontinue medication overuse, she was administered fremanezumab and prescribed oral steroids for a period of two weeks. The patient successfully discontinued the overused medication, and her headaches recurred only 1-2 times per month thereafter.
The second patient is a 77-year-old woman who has had migraines since her 30s. To cease medication overuse, she received fremanezumab injections along with two weeks of oral steroids. One month after treatment, the patient"s headaches significantly improved, and she was able to quit analgesic use. Currently, she continues maintenance therapy with fremanezumab alone.
Conclusion: These cases illustrate that anti-CGRP monoclonal antibody therapy can be an effective treatment option for elderly patients with medication overuse headache. Further studies in older patients are encouraging.

P183
Thirteen-year trajectories of depressive and anxiety symptoms in individuals with and without migraine: The Netherlands Study of Depression and Anxiety (NESDA)
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Objective: This study investigated 13-year trajectories of affective symptoms in individuals with and without migraine, both in those with and without an affective disorder at baseline.

Methods: The NESDA cohort included 2,981 participants followed over 13-years across six data waves. Anxiety and depressive symptoms were assessed using the Beck Anxiety Inventory (BAI) and Inventory of Depressive Symptomatology (IDS). Participants were divided into two subgroups: those with and those without a current affective disorder at baseline, as diagnosed using the Composite International Diagnostic Interview (CIDI). Linear mixed models analyzed symptom trajectories of the BAI and IDS by migraine status. Cox regression models estimated hazard ratios (HR) for onset and recovery from affective disorders (CIDI).

Results: Among 2,578 participants (1,448 with and 1,130 without an affective disorder at baseline), 453 had migraine, 1,274 non-migraine headache, and 551 non-headache. At baseline, migraine was associated with over twice the odds of having an affective disorder (OR for anxiety: 2.34; 95% CI [1.87, 2.93]; OR for depression: 2.85; 95% CI [2.27, 3.58]). Over time, individuals with migraine exhibited persistently higher BAI and IDS scores, regardless of baseline affective disorder status. Migraine was associated with an increased risk of new-onset affective disorder (HR:1.83; 95%CI [1.32,2.53]) and reduced likelihood of recovery (HR:0.82; 95%CI [0.70,0.98]). Notably, more than 40% of migraineurs without an affective disorder at baseline developed anxiety of depression during follow-up.

Conclusion: Migraine is linked to twice the baseline odds of anxiety or depression, greater long-term affective risk, and slower recovery from affective disorders. These findings underscore the importance of early identification and integrated treatment strategies for individuals with migraine.

Fig. 1

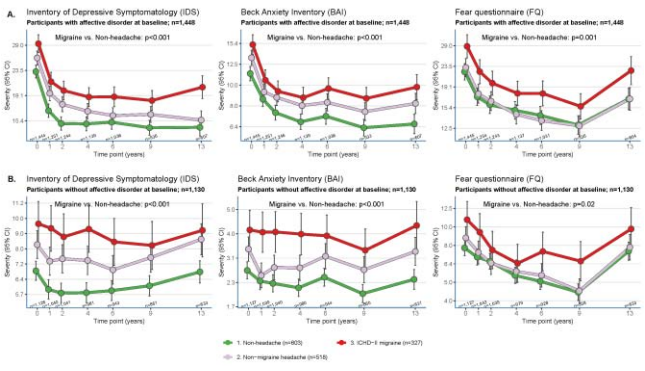
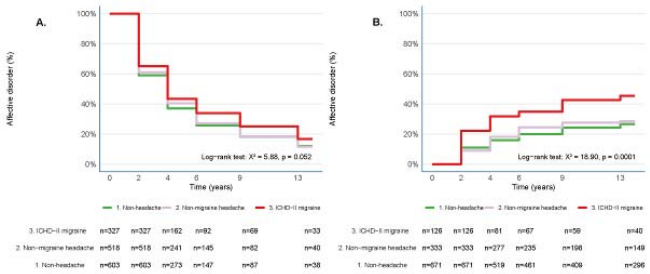


Fig. 2



P184

Does age impact headache diagnosis and migraine management in England? A retrospective cohort study of primary care medical records

D. P. Watson[1], R. Pawinski[2], M. Czachorowski[2], M. Araghi[2], C. Ellsbury[2], A. M. Williams[2], L. Camidge[3], E. Rottier[3], H. Gowman[3], S. Law[3], ***G. O'Neil***[2]

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[2]Pfizer, Ltd., Medical Affairs, Tadworth, United Kingdom

[3]Adelphi Real World, Bolington, United Kingdom

Objective: To examine diagnosis among people with headache in England by age and treatment patterns, including possible risk of medication overuse and titration of preventive medication, among people diagnosed with migraine by age.

Methods: A retrospective descriptive cohort study using the Clinical Practice Research Datalink Aurum was conducted. Adults aged ≥18-years were included in the study and indexed on the first observed migraine or other headache diagnosis between 19 September 2012 to 1 May 2023. Prescriptions 12-months post-index were analysed. Possible risk of medication overuse was defined as >10 days' (opiates/triptans) or >15 days' (analgesics/antipyretics/NSAIDs) supply in 3 consecutive months.

Results: Adults with migraine (N=476,191) or other headache (N=1,058,616) were included, the mean age was 42.1 years and 47.1 years respectively.

Primary headache disorders (including migraine) were diagnosed in 44.6% (N=353,029) of younger adults (aged ≥18-44 years), and 29.6% (N=99,146) of older adults' (aged ≥55 years] [Figure 1A]. Migraine was diagnosed in ≥70% of primary headache disorder group in all age cohorts [Figure 1B].

Minor differences in the percentage of the migraine cohort prescribed any acute medication were observed, however almost double the percentage of younger adults were prescribed a triptan compared to older adults (40.8% v 21.0%) [Figure 2A]. In contrast, the percentage prescribed any preventive medication increased with age [Figure 3A].

Possible risk of medication overuse increased with age for all medication classes, except triptans [Figure 2B]. Differences in titration of preventive medication to target dose [Figure 3B] between age cohorts were numerically small.

Conclusion: In older adults, 2 out of 3 patients with headache were not given a diagnosis. Older adults were also less likely to receive a triptan when diagnosed with migraine. These findings suggest a need to optimise migraine care in general practice for older adults.

Fig. 1

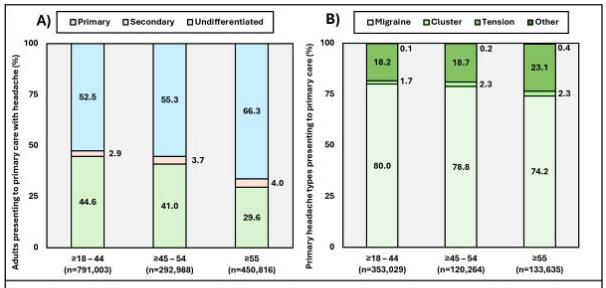


Figure 1: **A)** Percentage of adults with headache (aged ≥18 years) presenting to primary care with headache coded as primary headache, secondary headache, or unclassified/undifferentiated by age. **B)** Percentage of adults (aged ≥18 years) presenting to primary care with primary headache with each primary headache diagnosis by age.

Fig. 2

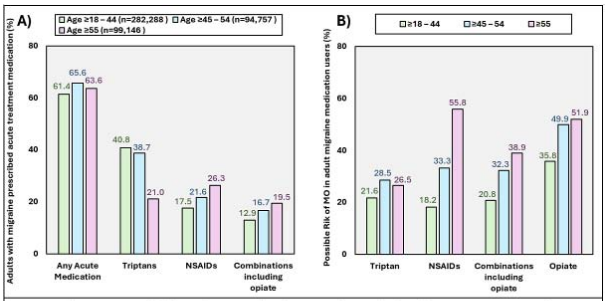


Figure 2: **A)** Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for acute treatment of migraine in the first 12 months after index by age. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed acute medication for migraine in the first 12 months after index with prescribing patterns suggestive of possible medication overuse by age.

MO: medication overuse. Possible Risk of MO was defined as >10 days' (opiates/triptans) or >15days'(analgesics/antipyretics/NSAIDs) supply in 3 consecutive months.

Fig. 3

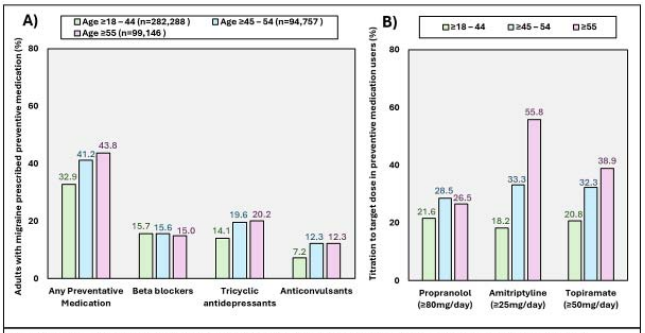


Figure 3: **A)** Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for preventive treatment of migraine in the first 12 months after index by age. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed preventive medication for migraine 12 months after index who are titrated to the NICE CKS/SIGN 155 recommended target dose.

P185

Does ethnicity impact headache diagnosis and migraine management in England? A retrospective cohort study of primary care medical records

D. P. Watson[1], R. Pawinski[2], M. Czachorowski[2], M. Araghi[2], C. Ellsbury[2], A. M. Williams[2], L. Camidge[3], E. Rottier[3], H. Gowman[3], S. Law[3], ***G. O'Neil***[2]

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Objective: To examine diagnosis among people with headache in England by ethnicity and treatment patterns, including possible risk of medication overuse and titration of preventive medication, among people diagnosed with migraine by ethnicity.

Methods: A retrospective descriptive cohort study using the Clinical Practice Research Datalink Aurum was conducted. Adults aged ≥18-years were included in the study and indexed on the first observed migraine or other headache diagnosis between 19 September 2012 to 1 May 2023. Possible risk of medication overuse was defined as >10 days' (opiates/triptans) or >15 days' (analgesics/antipyretics/NSAIDs) supply in 3 consecutive months. Ethnicity observations were taken using with the most frequently reported category in medical records. Where a patient had two mode categories OR where no observations were found, unknown was taken. This analysis focussed on those with a known ethnicity.

Results: Adults with migraine (N=476,191) or other headache (N=1,058,616) were included, ethnicity was unknown in 30.0% (N=143,077) and 28.6% (N=302,454) of whom respectively. The majority of patients were of White ethnicity in the migraine and other headache cohort: 55.1% (N=262,229) and 52.8% (N=558,700).

Primary headache disorders (including migraine) comprised the lowest percentage of headache diagnosis in the Black ethnicity population: 33.1% (N=14,700) [Figure 1A]. Migraine accounted for 80.0% (N=262,229) of primary headache diagnoses in the White population and 66.6% (N=9,797) of the Black population [Figure 1B].

Ethnicity did not appear to have a major influence on migraine management (Figures 2 and 3).

Conclusion: Primary headache disorders, including migraine, were diagnosed less often in Black and Asian populations. When diagnosed with migraine, management was equitable across all ethnicities. These findings suggest there are challenges making a diagnosis of migraine in diverse populations but care is equitable once a diagnosis is made.

Fig. 1

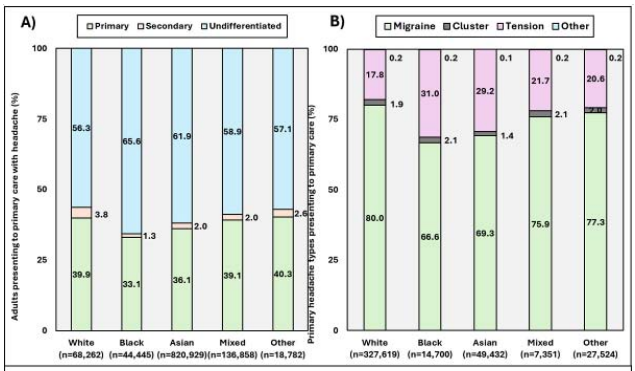


Figure 1: A) Percentage of adults (aged ≥18 years) presenting to primary care with headache coded as primary headache, secondary headache, or unclassified/undifferentiated by ethnicity. **B)** Percentage of adults (aged ≥18 years) presenting to primary care with primary headache with each primary headache diagnosis by ethnicity.

Fig. 2

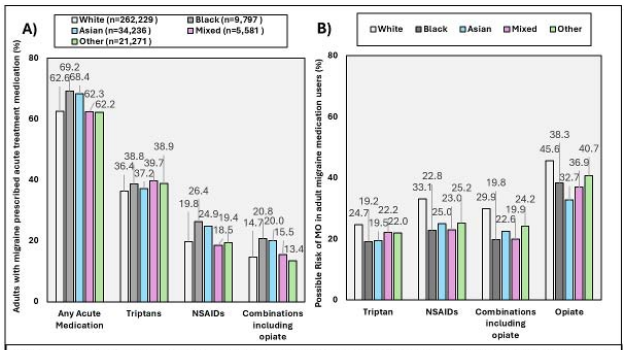


Figure 2: A) Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for acute treatment of migraine in the first 12 months after index by ethnicity. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed acute medication for migraine in the first 12 months after index with prescribing patterns suggestive of possible medication overuse by ethnicity.

MO: medication overuse. Possible MO was defined as >10 days' (opiates/triptans) or >15days'(analgesics/antipyretics/NSAIDs) supply in 3 consecutive months.

Fig. 3

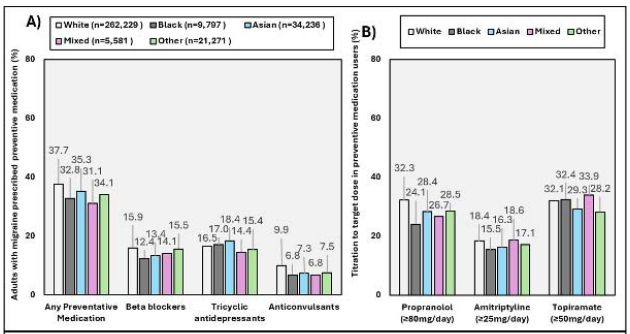


Figure 3: A) Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for preventive treatment of migraine in the first 12 months after index by ethnicity. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed preventive medication for migraine in the first 12 months after index who are titrated to the NICE CKS/SIGN 155 recommended target dose.

P186

Does deprivation impact headache diagnosis and migraine management in England? A retrospective cohort study of primary care medical records

D. P. Watson[1], R. Pawinski[2], M. Czachorowski[2], M. Araghi[2], C. Ellsbury[2], A. M. Williams[2], L. Camidge[3], E. Rottier[3], H. Gowman[3], S. Law[3], ***G. O'Neil***[2]

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[2]Pfizer, Ltd., Medical Affairs, Tadworth, United Kingdom

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Objective: To examine diagnosis among people with headache in England by deprivation and treatment patterns, including possible risk of medication overuse and titration of preventive medication, among people with migraine by deprivation.

Methods: A retrospective descriptive cohort study using the Clinical Practice Research Datalink Aurum was conducted. Adults aged ≥18-years were included in the study and indexed on the first observed migraine or other headache diagnosis between 19 September 2012 to 1 May 2023. Possible risk of medication overuse was defined as >10 days' (opiates/triptans) or >15 days' (analgesics/antipyretics/NSAIDs) supply in 3 consecutive months. Deprivation was captured via the index of multiple deprivation (IMD) value based on person-level postcode.

Results: Adults with migraine (N=476,191) or other headache (N=1,058,616) were included, the number of those with migraine was consistent across IMD categories, but the number of those with undifferentiated headache increased with deprivation. Primary headache disorder and migraine diagnoses rates were similar across IMD quintiles with a trend towards decreasing with increasing deprivation [Figure 1].

Deprivation had an increasing trend with the percentage of the migraine cohort prescribed medication: any acute medication (56.5%-70.2%) [Figure 2A]; any preventive medication (31.8%-42.7%) [Figure 3A].

Possible risk of medication overuse with opiates trended upwards with deprivation (36.8%-44.7% of users), in contrast triptans did not change with deprivation [Figure 2B]. Titration of preventive medications to target dose was poor across all quintiles [Figure 3B].

Conclusion: Migraine diagnoses rates were similar across IMD quintiles. Prescribing of any medication for migraine increased with increasing deprivation. These trends may be reflective of the NHS free-medication scheme.

Fig. 1

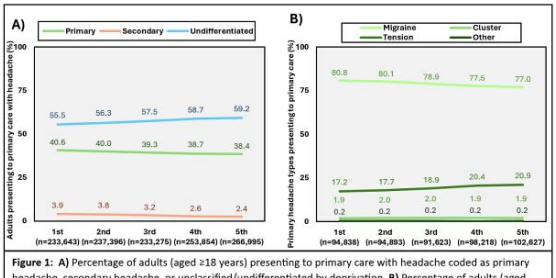


Figure 1: A) Percentage of adults (aged ≥18 years) presenting to primary care with headache coded as primary headache, secondary headache, or unclassified/undifferentiated by deprivation. **B)** Percentage of adults (aged ≥18 years) presenting to primary care with primary headache with each primary headache diagnosis by deprivation.

Fig. 2

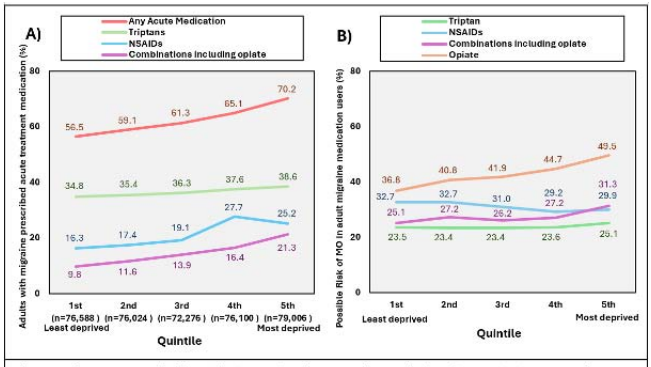


Figure 2: A) Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for acute treatment of migraine in the first 12 months after index by deprivation. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed acute medication for migraine in the first 12 months after index with prescribing patterns suggestive of possible medication overuse by deprivation.

MO: medication overuse. Possible Risk of MO was defined as >10 days' (opiates/triptans) or >15days'(analgesics/antipyretics/NSAIDs) supply in 3 consecutive months.

Fig. 3

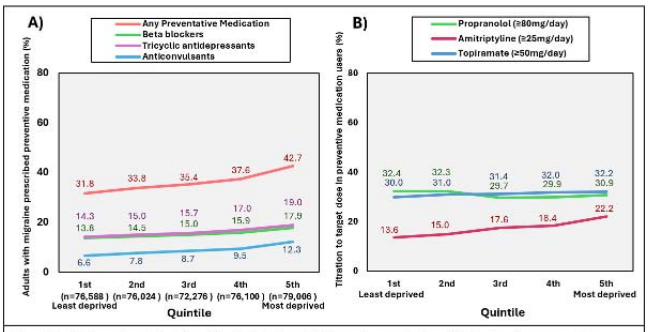


Figure 3: A) Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for preventive treatment of migraine in the first 12 months after index by deprivation. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed preventive medication for migraine in the first 12 months after index who are titrated to the NICE CKS/SIGN 155 recommended target dose.

P187

Undergraduate headache education: Coverage of Medication Overuse Headache (MOH) in neurology modules at the faculty of medicine, Universitas Indonesia

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Objective: Medication-overuse headache (MOH) is globally recognized to be managed in primary care. However, only migraine and tension-type headache are listed in the national standards to be fully managed by GPs, and not MOH. This study aims to analyze headache coverage, focused on MOH, in the undergraduate program of Faculty of Medicine, Universitas Indonesia.

Methods: We analyzed lesson plans of neuropsychiatry (preclinical) and neurology (clinical) modules regarding the proportion of headache. The domains are based on the lesson plan format, which consists of learning objectives, headache aspects (i.e. history taking, physical examination, diagnostic approach, and management), and learning methods (activity format, integration in online self-learning modules, and evaluation format). We also analyzed the student logbook from the neurology clinical module.

Results: Primary and secondary headaches were covered in undergraduate modules. History taking, physical examination, diagnosis, management, and referral in headache, were outlined in both lesson plans. However, MOH was not identified as a specific learning objective. In the preclinical module, headache accounts for 1 out of 25 hours of offline neurology-related lectures. In the clinical module, headache topics are allocated 4 of 30.5 hours (13.11%) of case-based discussions and presentations. Headache contributes to roughly 7% of all bedside teaching and clinical work cases, with no MOH reported.

Conclusion: Headache content in undergraduate modules has covered diagnostic classifications, red flags, and common headache in primary care. MOH was not outlined in the lesson plan and therefore exposure to students may vary. We suggest putting MOH in national competence standards, so that undergraduate modules that follow the national standards can include MOH on secondary headache learning objectives to ensure sufficient exposure. Our study also highlights the need of a continuing medical education program about MOH for general practitioners.

P188

Morphometric similarity networks in paediatric migraine without aura: Unravelling the role of gender

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Objective: Migraine causes structural and functional alterations on brain cortex and connectome, yet the underlying mechanism is still unclear. To our knowledge, morphometric similarity mapping (MSM) for studying cerebral connectivity and cortical pattern has never been applied to the study of pediatric migraine without aura. Our study aims to: a) identify differences in morphometric similarity networks (MSNs) in pediatric patients affected by migraine without aura compared to healthy controls and in subgroups of patients; and b) correlate these differences in MSNs with patients demographic and clinical characteristics.
Methods: Eighty-three patients affected by migraine without aura aged between 6 and 18 years, and 81 age- and sex-matched controls were retrospectively recruited from the archive of our Institution. 3D T1 MPRAGE and DWI/ADC were pre-processed to obtain eleven cortical parameters for the MSN analysis. Subsequently, both the global mean morphometric similarity (MS) and the regional mean MS were calculated. The statistical analysis was performed between patients and controls and within subgroups of patients divided by demographic and clinical characteristics.
Results: MSM identified significant differences in MSNs in pediatric patients affected by migraine without aura in relation to demographic and clinical parameters. In particular, gender appeared to be the most significant parameter affecting MSNs. The cerebral pathways that showed the most significant alterations encompassed the executive function pathway, the nociceptive pathway and the default mode network.
Conclusion: Differences in MSNs between controls and patients and within subgroups of patients suggest that migraine shapes cerebral connectome and favours neuronal plasticity. Gender is confirmed as a paramount parameter in migraine, supporting the hypothesis of a sex specific phenotype.

P189

Lost in transition: Factors associated with effective transition from pediatric to adult headache care

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[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy
[2]Insubria University, Varese, Italy
[3]Bambino Gesù Children's Hospital, Rome, Italy
[4]University of Rome Tor Vergata, Rome, Italy

Objective: Since 2020, Campus Bio-Medico University Hospital and Bambino Gesù Children Hospital have created a joint outpatient clinic to favor a proper transition from pediatric to adult headache care. The present study aims to assess factors associated with ineffective transition.
Methods: This is a prospective cohort study. At the joint headache visit, we collected headache frequency, bothersome associated symptoms, aura, migraine onset age, comorbidities, number of previous preventive therapies, and family history in patients aged 17-22 who were still under pediatric care. All patients were instructed to perform a control visit at Campus Bio-Medico University Headache Center within one year.
Results: Ninety-one patients were considered (69.2% females, aged 17.9 ys; SD 2.7); of these, 52.8% of subjects also suffered from comorbidities, 54.9% presented migraine family history, and 17.6% had aura. Phonophobia was the most common associated symptom (90.2%). The mean onset age was 11.5 (SD 0.6). Subjects had experienced a median of 1 preventive therapy (IQR 2). Monthly migraine days (MMDs) were 2.7 (SD 0.5) at the joint visit. Only 29 patients (31.9%) performed a visit in the adult settings. Higher MMDs (4.8 SD 1.4 vs 1.5 SD 0.1 SD) was the only variable associated with an effective transition among the considered variables
Conclusion: Most patients are lost in the transition from pediatric to adult care. Headache frequency is the main determinant of continuous takeover.

P190

My experience with the use of children's drawings in the differential diagnosis of primary headaches

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Objective: To examine whether children's drawings can support the differential diagnosis of primary headaches—especially migraine—in pediatric patients, and to evaluate their usefulness in identifying comorbid psychological traits.
Methods: A series of spontaneous drawings were collected from children suffering from primary headaches. Each drawing was qualitatively analyzed with a focus on specific visual motifs, color use, symbolism, and composition. The analysis was conducted in parallel with clinical assessments, allowing comparison between headache type and drawing characteristics.
Results: Drawings by children with migraine frequently contained elements that mirror typical migraine symptoms: high-intensity pain, photophobia, phonophobia, unilateral localization, and visual aura. In contrast, drawings from children with tension-type

headaches often featured dark colors and depicted emotional states—sadness, crying, or isolation—rather than physical pain. These findings suggest that drawings may reflect both the sensory and emotional experience of headache, depending on the type.
Conclusion: Children"s drawings offer a non-invasive, expressive tool that can enrich the diagnostic process in pediatric headache care. They can help distinguish between migraine and tension-type headache and may provide insights into coexisting emotional or behavioral problems. Integrating drawing analysis into clinical practice can support a more nuanced, child-centered approach to headache diagnosis.

P191

Pediatric migraine: A dual burden on cognition and emotion

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[2]University of Rome Tor Vergata, Systems Medicine Department, Rome, Italy

Objective: Pediatric migraine is often associated with cognitive difficulties and internalizing symptoms, potentially impacting academic and social functioning. This study aimed to examine the associations between migraine frequency, age of onset, and prophylactic treatment use with cognitive and emotional functioning in children and adolescents.
Methods: Fifty-two patients (mean age = 12.5 ± 2.6 years; 30 females, 22 males) with migraine were assessed using a comprehensive battery, including verbal memory (Digit Span Forward/Backward, BVN 5-18), verbal fluency (BVN 5-18), attention and executive functions (NEPSY-II: Visual Attention, Inhibition), processing speed (SDMT), intelligence (Raven"s Colored Progressive Matrices), and internalizing symptoms (SAFA-A, SAFA-D). Migraine duration (in months/years) was recorded. Frequency was categorized as high (weekly/daily) or low (≤3/month), and patients were grouped based on prophylactic treatment use within the past year.
Results: Among patients completing the NEPSY-II Inhibition task, 47.7% scored below average at time 1, 43.2% at time 2, and 40.9% at time 3. No significant differences emerged in visual attention or overall inhibition scores between groups ($p > 0.05$). Patients with high-frequency migraine and those who received prophylactic treatment in the past year showed significantly lower backward digit span scores ($p = 0.00$ and $p = 0.01$, respectively). No significant differences were found in processing speed, verbal fluency, or Raven"s scores ($p > 0.05$). Higher levels of generalized anxiety, school-related anxiety, and guilt were observed in the high-frequency group ($p = 0.04$, $p = 0.03$, and $p = 0.04$, respectively).
Conclusion: High migraine frequency and prophylactic treatment use are associated with reduced working memory. Increased anxiety may further impact cognitive performances. These findings highlight the importance of addressing both cognitive and emotional domains in pediatric migraine.

P192

A multicenter, retrospective case series of trigeminal autonomic cephalalgias in pediatric age

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[3]Sapienza University of Rome, Pediatrics Unit, Neuroscience, Mental Health and Sense Organs (NESMOS) Department, Faculty of Medicine and Psychology, Rome, Italy
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[5]A.O.U. Città della Salute e della Scienza di Torino, Department of Pediatric Emergency, Regina Margherita Children's Hospital, Turin, Italy
[6]University of L'Aquila, Department of Clinical Medicine, Public Health, Life and Environmental Sciences, L'Aquila, Italy
[7]University of L'Aquila, Department of Biotechnological and Applied Clinical Sciences, L'Aquila, Italy
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[9]Aalborg University, Center for Sensory-Motor Interaction, Aalborg, Denmark

Objective: Trigeminal autonomic cephalalgias (TACs), encompassing cluster headache (CH), paroxysmal hemicrania (PH), hemicrania continua (HC), and short-lasting unilateral neuralgiform headache attacks (SUNCT/SUNA), are rare primary headache disorders in the pediatric population. Their diagnosis is challenging due to their rarity, limited awareness, and possibly to showing atypical characteristics in the paediatric age.
Methods: We conducted a retrospective review using hospital electronic medical records and personal clinical encounters to identify patients diagnosed with TACs before the age of 18. Our study population was composed of patients evaluated in six italian paediatric headache centres. Inclusion required fulfillment before the age of 18 of criteria for TACs or for probable TACs as per the International

Classification of Headache Disorders, 3rd edition (ICHD-3). Clinical features, treatment responses and treatment outcomes were analyzed.
Results: The study included 33 paediatric patients with TACs: 19 with CH, 4 with PH, 3 with HC and 7 with SUNA.
Conclusion: Pediatric TACs present diagnostic and therapeutic challenges due to their rarity and, possibly, to their atypical clinical characteristics. Differences in the clinical characteristics between TACs in paediatric age and in adult age seem to exist. PH and SUNA showed a lower frequency of headache attacks than described in ICHD-3 criteria. Response to indomethacin was observed also in patients with CH and SUNA. Centralization of cases and greater collaboration between headache centres can contribute to deepening our understanding of these features.

P195

Reducing headache impact and drug use in tension-type headache: The role of auricular acupuncture

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Objective: To evaluate the efficacy and safety of auricular acupuncture in reducing the impact of tension-type headaches (TTH) and the reliance on symptomatic medication in women aged 30–50.
Methods: Twenty female patients (aged 30–50) with a clinical diagnosis of TTH and ongoing symptomatic use of NSAIDs and muscle relaxants were enrolled. Auricular acupuncture was performed with sterile disposable 0.2×40 mm needles bilaterally inserted at the master cerebral, thalamus, cervical paravertebral musculature, occiput, and muscle relaxant points. Each session lasted 20 minutes and was followed by the application of ear seeds with intradermal needles (0.15×0.6 mm) left in place for five days. The treatment consisted of weekly sessions for one month, then biweekly sessions for another month. Headache-related disability was assessed using the HALT questionnaire: HALT-90 at baseline, HALT-30 after one and two months.
Results: At baseline (HALT-90), 15 patients had moderate headache-related impact (Grade 3), and 5 had mild impact (Grade 2). After one month (HALT-30), 15 patients reported mild impact (Grade 1), and 5 had moderate impact (Grade 2). After two months, 5 patients had minimal impact (Grade 1), and 15 had mild impact (Grade 2). All participants reported a decrease in the use of symptomatic medication. No adverse effects or contraindications were observed.
Conclusion: Auricular acupuncture is a safe, well-tolerated, and potentially effective complementary therapy for managing tension-type headaches. It significantly reduces headache-related disability and reliance on symptomatic drugs. Further controlled studies are needed to confirm these promising results.

P198

Home-based biofeedback treatment for people with post-traumatic headache: A usability and feasibility study

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Objective: Despite the high prevalence of the disabling condition post-traumatic headache (PTH), we lack evidence-based treatments. Home-based biofeedback using a mobile app and wearable sensors has shown promising results as a prophylactic treatment for episodic migraine. Migraine is the most common phenotype of PTH, therefore, we aimed to investigate the adaptability of home-based biofeedback in people with PTH.
Methods: This was an iterative mixed-method usability and feasibility study, with one iteration including a 28-day home testing. The outcomes were mHealth App Usability Questionnaire (MAUQ) and Mobile App Rating Scale (MARS) scores, adherence during the home-testing period, and descriptions of adverse events.
Results: Twenty-three adults with PTH (median age 52 years, 80% female) were included in the user group, and six clinicians (median age 53 years, 50% female) with a mean of 13 years of PTH experience were included in the clinician group. The usability of the biofeedback app was rated 5.2 (SD 1.0) out of 7 on the MAUQ by the user group. The clinician group rated the app quality at 4.1 (IQR 4.5-4.1) out of 5 on the MARS. The adherence rate among the user group during the 28-day home testing was 84.3% (IQR 28-19). Two adverse events occurred in one participant, who experienced dizziness and headache during and after biofeedback sessions on several occasions. Symptoms resolved spontaneously within two hours.

Conclusion: The home-based biofeedback solution is usable, feasible, and safe to use in people with PTH. In this study, we have gathered valuable insights on the necessary adaptations to improve and tailor the solution to people with PTH.

P199

Thiamine could improve migraine characteristics: A randomized double-blind controlled trial

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Objective: Migraine represents a prevalent neurological disorder that impacts around 14% of people worldwide and is considered the sixth leading cause of disability globally. Vitamin B1 can potentially help prevent migraine due to its cofactor role in energy metabolism enzymes. Therefore, this research aimed to investigate the effects of high-dose thiamine on women experiencing episodic migraines (EM).

Methods: This double-blind, placebo-controlled, randomized clinical trial was carried out with 40 women suffering from EM. The participants were allocated into two groups: the B1 group (n = 20) and the placebo group (n = 20). Individuals in the B1 group were administered 990 milligrams of thiamine three times daily, while the placebo group received an equivalent dosage of 990 milligrams of maltodextrin. Headache frequency, duration, and severity were documented using the Headache Diary Questionnaire. The Migraine Disability Assessment Questionnaire (MIDAS) was employed to assess migraine disability. Serum levels of CGRP were evaluated both before and after the intervention.

Results: Following a 12-week duration of study, thiamine supplementation yielded a statistically significant reduction in MIDAS scores ($P = 0.002$), migraine frequency ($P < 0.001$), and duration ($P = 0.001$) in comparison to the placebo group. Both groups showed a significant decrease in headache intensity by the study's conclusion, with the intervention group demonstrating a considerably greater reduction in severity. Serum CGRP levels declined in both groups, although no significant differences were observed either within or between the groups.

Conclusion: The findings of this study suggest that high-dose thiamine supplementation may be a beneficial adjunctive treatment for episodic migraines. Additional research with longer intervention durations is needed to confirm these results.

P201

Acupuncture in migraine prevention: High-quality evidence from double-dummy randomized controlled trials and its implications in clinical practice

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Objective: Migraine is a disabling primary headache disorder where preventive drugs are often limited by poor tolerability and adherence. Acupuncture is widely used in migraine treatment, but physician acceptance remains limited due to high sham response rates and persistent concerns regarding methodological heterogeneity, bias, and blinding. Double-dummy randomized controlled trials (RCTs) address this issue and greatly minimize expectation bias and substantially enhance physician confidence in acupuncture for migraine treatment. Objective: To systematically review double-dummy RCTs comparing acupuncture with pharmacological preventives for migraine, focusing on efficacy, safety, and patient-reported outcomes.

Methods: Comprehensive keyword searches were conducted in PubMed, Embase, and the Cochrane Library (2000–2024). Eligible studies included adults with episodic or chronic migraine, comparing acupuncture plus placebo versus sham acupuncture plus active medication. Outcomes included migraine frequency, responder rates, disability, safety, and acceptability.

Results: Two double-dummy RCTs met inclusion criteria. Wang et al. (2011, n=140) compared acupuncture with flunarizine and found higher ≥50% responder rates (56% vs. 37% at 16 weeks), and greater reductions in migraine days (−4.1 vs. −2.0 at week 16). Liu et al. (2024, n=60) compared acupuncture with topiramate, reporting larger reductions in monthly migraine days (−5.6 vs. -2.8 at 12 weeks), higher ≥50% responder rates (33.3% vs. 6.7%), and fewer adverse events (10% vs. 26.7%).

Conclusion: Limited high-quality double-dummy RCTs indicate that acupuncture is an effective and well-tolerated preventive therapy, demonstrating efficacy comparable to or superior to pharmacological treatments with fewer adverse effects. Large-scale, multicentre double-dummy trials remain essential to generate robust evidence to strengthen physicians' confidence in adopting acupuncture as a viable option for migraine management.

P202

Efficacy of strength training in tension-type headache: A single-arm meta-analysis

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Objective: Tension-type headache (TTH) is the most common type of headache worldwide. Although pharmacological therapies are the mainstay of treatment, non-pharmacological therapies like strength training may represent a safe and cost-effective approach in reducing the frequency, intensity and duration of headache. This study aims to systematically evaluate the efficacy of strength training on these clinical outcomes.

Methods: We systemically searched PubMed, Embase, and Scopus for trials that had within-group information on strength or resistance training interventions in patients with TTH. A total of 55 studies were found, of which three studies met our inclusion criteria. The primary outcome was headache frequency; secondary outcomes were duration and intensity of headache. Pooled effect sizes (mean differences, MD) were calculated using a random-effects model.

Results: Three studies (n = 63) were included. Strength training resulted in a significant reduction in headache frequency by 2.57 days/month (95% CI: 1.94–3.20; I^2 = 0%). For headache duration, a mean difference of 2.57 hours/day (95% CI: -6.81 – 11.96) was found with high heterogeneity (I^2 = 79.9%). Intensity decreased non-significantly by 0.93 NRS points (95% CI: -0.91 – 2.76; I^2 = 73.2%).

Conclusion: Strength training overall significantly improved headache frequency, although the effects on duration and intensity were uncertain due to heterogeneity. However, further studies are required to substantiate the evidence, given the limited quality of the current data.

Fig. 1

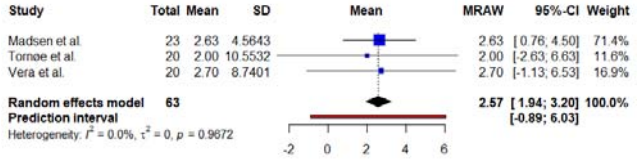


Fig. 2

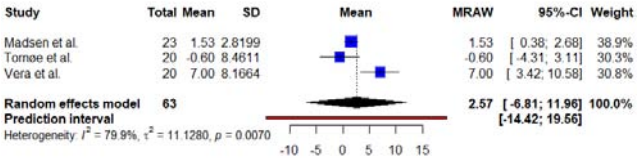
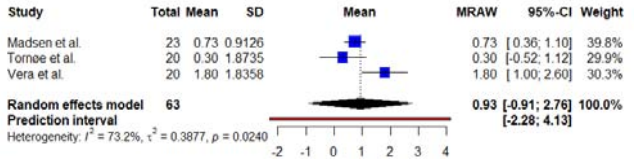


Fig. 3



P203

Post-spontaneous intracranial hypotension headache

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Objective: While spontaneous intracranial hypotension (SIH) is primarily characterized by orthostatic headache, some patients experience headaches after CSF leak has resolved. This study aimed to investigate the characteristics of post-SIH headache.

Methods: This prospective study included patients with imaging evidence of SIH at baseline who achieved radiological remission between March 2022 and January 2025. We collected patients' demographics, disease characteristics, migraine history, lifestyle factors, comorbidities, Pain Catastrophizing Scale scores, and the date of complete remission. Remission was defined as complete resolution of imaging abnormalities. Headache status, phenotype, monthly headache days, and chronicity (defined as ≥15 headache days/month) were evaluated at 1, 3, 6 and 12 months after remission. Logistic regression analyses were performed to identify risk factors for post-SIH headache.

Results: A total of 32 patients (mean age 40.7 ± 9.72 years; 71.9% female) were included. The duration from remission to last follow-up was 251.6 days (range, 23.0–735.0 days). Post-SIH headache was reported by 21 patients (65.6%), 14 patients (51.9%), 12 patients (44.4%), and 10 patients (37.0%) at 1, 3, 6, and 12 months after remission, with the following phenotypes: tension-type-like in 18 patients (69.2%), migraine-like in 5 patients (19.2%), neuralgic in 3 patients (11.5%). Chronic headache was present in 81.0%, 58.9%, 50.0%, and 26.3% of post-SIH patients at 1, 3, 6 and 12 months. No independent association was observed between baseline characteristics and post-SIH headache at 1 month.

Conclusion: Post-SIH headache is common after complete resolution of CSF leak. Recognizing this entity would improve patient care and help avoid

unnecessary invasive procedures in remitted SIH patients.

P204

Effects of fremanezumab discontinuation on migraine frequency and structural brain alterations: A prospective observational study

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Objective: Monoclonal antibodies targeting the calcitonin gene-related peptide (CGRP) pathway are effective preventive treatments for migraine. However, their potential for disease modification and the proportion of patients with sustained benefit after discontinuation remain unclear. This study examined changes in migraine frequency and brain microstructure following the cessation of fremanezumab after 9–12 months of use.

Methods: In this prospective study (2022–2025, Headache Center Charité), patients with episodic or chronic migraine discontinued fremanezumab after 9–12 months. MRI (DTI, VBM) and clinical assessments were performed at baseline (T1) and 16 weeks after discontinuation (T2). Age- and sex-matched healthy controls (HC) were scanned once. TBSS analyzed fractional anisotropy (FA), axial (AD), and radial diffusivity (RD) using FSL's randomise (5,000 permutations, TFCE correction). Main outcomes included changes in monthly migraine days (MMD) and DTI parameters.

Results: Fifteen patients (47.4 ± 12.2 yrs) and 15 HC (46.0 ± 6.9 yrs) were included. Sustained response (MMD increase <30%) occurred in 46.7%. MMD rose from 5 ± 3 to 8 ± 6 ($p = 0.014$). No significant FA changes occurred from T1 to T2. RD increased significantly post-discontinuation (20 clusters, max 50 voxels, TFCE $p < .05$), notably in longitudinal fasciculi and cingulum. AD showed bidirectional changes: increases (e.g., splenium, IFOF) and decreases (e.g., brainstem, SLF) (TFCE $p < .05$). Compared to HC, patients at T1 showed higher FA and lower RD in the forceps minor (TFCE $p < .05$).

Conclusion: Following fremanezumab discontinuation, nearly half the patients maintained clinical benefit. While FA remained stable, RD and AD changes suggest dynamic white matter adaptation. Baseline forceps minor differences may reflect disease-related remodeling. Final VBM and correlation analyses will be presented at the congress.

P205

Eptinezumab for difficult-to-treat migraine: Who responds and who needs more

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Objective: Eptinezumab, a monoclonal antibody (mAb) targeting the calcitonin gene-related peptide (CGRP), was recently approved for migraine prevention. This study evaluated the rates of responders and super-responders to eptinezumab and assessed clinical predictors of treatment response and dose escalation over 9 months.

Methods: Fifty-eight migraine patients were enrolled. Clinical data, including monthly headache (MHD) and migraine days (MMD), acute medication use (pills (AMP) and days (AMD)), intensity (NRS), disability (MIDAS), impact (HIT-6), and allodynia (ASC-12) scores, were collected at baseline and after 3 (M3), 6 (M6), and 9 (M9) months. Adverse events were recorded at all time-points. Responders and super-responders were defined as patients with a ≥50% or ≥75% MMD reduction, respectively. All patients started on 100 mg eptinezumab; dose was increased to 300 mg at M3 or M6 if response was suboptimal.

Results: The median baseline clinical values were: MHD: 20, MMD: 16, AMP: 20, AMD: 11, MIDAS: 69, HIT-6: 66, NRS: 8, ASC-12: 7. Patients had failed a median of five prior preventive treatments (IQR 3–6), and 47% had previously received an anti-CGRP mAb. At M3, 40% were responders (21% super-responders); at M6, 23% (5% super-responders); at M9, 46% (17% super-responders). A significant predictor of non-response to treatment after M3 was prior therapy with mAb ($p = 0.0137$). Dose escalation occurred in 72% patients at M3 and 87% at M6. Factors associated with dose escalation were higher baseline MHD and MMD ($p<0.05$) and previous anti-CGRP failure ($p<0.04$). Only two patients reported mild adverse events.

Conclusion: Eptinezumab is effective and well tolerated in difficult-to-treat migraine patients, with sustained benefits up to nine months. Patients with higher baseline migraine frequency and prior exposure to anti-CGRP mAbs are more likely to require dose escalation. Our study suggests that the initial dosage should be tailored to the patient in order to optimize response.

P206

Real-world effectiveness of fremanezumab in migraine prevention: Final outcomes of the pan-european PEARL study

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Objective: PEARL (EUPAS35111) was a 24-month observational, prospective, Phase 4 study evaluating the real-world effectiveness and safety of fremanezumab for episodic and chronic migraine (EM, CM) prevention. Here we report effectiveness, and treatment adherence and persistence outcomes after 24 months of follow-up.

Methods: Eligible participants were adults with EM or CM receiving fremanezumab for migraine prevention, who maintained a daily headache diary prior to and throughout the study. Primary endpoint: proportion of participants with ≥50% reduction in monthly migraine days (MMD) during the 6-months after fremanezumab initiation. Secondary endpoints at Months 1–24: mean change from baseline in MMD; treatment adherence (participants who took their prescribed dose within ±5 days of the scheduled monthly/quarterly dosing regimen, per injection) and persistence.

Results: Of 1140 participants enrolled, 1129 were included in the effectiveness analysis (EM, 33.1%; CM, 66.9%; 87.2% female). In participants with available data, 56.5% (637/1128) achieved ≥50% MMD reduction from baseline during the 6-months after fremanezumab initiation (**Fig. 1**). Proportions of participants with ≥50% reduction in MMD were sustained across Months 1–24 (**Fig. 2**), as were reductions in mean MMD (**Fig. 3**). Injection adherence rates remained high throughout the study (~90%) and 75.6% (854/1129) of participants completed the study.

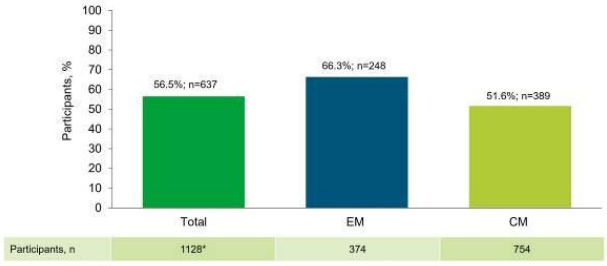
Fig. 1 Proportion of participants reaching ≥50% reduction in MMD from baseline during the 6-month period after fremanezumab initiation (primary endpoint), by migraine type

Fig. 2 Proportion of participants reaching ≥50% reduction in MMD from baseline at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24, by migraine type

Fig. 3 Mean change from baseline in the monthly average number of migraine days at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24, by migraine type

Conclusion: These findings underscore the sustained effectiveness and robust injection adherence of long-term fremanezumab treatment in migraine prevention.

Fig. 1



CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days

*Of the 1140 enrolled participants, 11 were excluded from the effectiveness analysis set for one or more of the following reasons: baseline visit was unsigned, <4 migraine days in the baseline period were documented, <10 diary entries were documented after the first dose of fremanezumab. One participant from the effectiveness analysis set did not have data available for the primary endpoint.

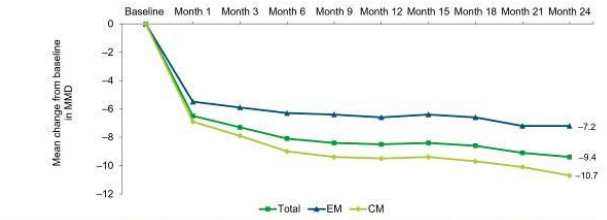
Fig. 2



CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.

The drop in data at post-baseline timepoints is due to participants who prematurely discontinued the study. Missing data are excluded.

Fig. 3



Total participants, N	1129	1125	1105	1062	1017	987	928	888	860	712
EM participants, n	374	374	364	351	341	336	321	310	302	255
CM participants, n	755	751	741	711	676	651	607	578	558	457

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.

The drop in data at post-baseline timepoints is due to participants who prematurely discontinued the study. Missing data are excluded.

P207

Real-world safety and tolerability of fremanezumab in migraine prevention: Final outcomes of the PEARL study

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Objective: PEARL (EUPAS35111) is a 24-month observational, prospective, Phase 4 study evaluating the real-world effectiveness and safety of fremanezumab for episodic and chronic migraine (EM, CM) prevention. Here we present safety and tolerability outcomes from the PEARL study after 24 months of follow-up.

Methods: Eligible participants were adults with EM or CM receiving fremanezumab for migraine prevention, who maintained a daily headache diary prior to and throughout the study period. Primary endpoint: the proportion of participants with ≥50% reduction in monthly migraine days (MMD) during the 6-month period after fremanezumab initiation. Safety and tolerability were assessed by adverse event (AE) reporting.

Results: In total, 637/1128 (56.5%) participants with available data achieved the primary endpoint. All enrolled participants (N=1140) were included in the safety analysis. Overall, 642/1140 (56.3%) participants reported ≥1 AE (**Table 1**). Drug-related AEs were reported by 376 (33.0%) participants; the most common being general disorders and administration site conditions (n=253, 22.2%) and gastrointestinal disorders (n=79, 6.9%; **Table 1**). Drug-related serious AEs were infrequent, occurring in four (0.4%) participants; the most common was drug hypersensitivity (n=2, 0.2%). AEs leading to treatment discontinuation were reported by 61 (5.4%) participants; the most frequent reasons were drug ineffectiveness (n=36, 3.2%), injection site erythema (n=5, 0.4%), and injection site pruritus (n=4, 0.4%).

Table 1 Safety analysis

Conclusion: The favorable long-term safety and tolerability of fremanezumab demonstrated in this analysis are consistent with the known safety profile of fremanezumab from previous PEARL interim analyses and randomized controlled trials, supporting its continued clinical use for migraine prevention.

Fig. 1

	SAS (N=1140)
Participants with ≥1 AE, n (%)	642 (56.3)
Common AEs, n (%)*	
General disorders and administration site conditions	280 (24.6)
Infections and infestations	268 (23.5)
Nervous system disorders	134 (11.8)
Gastrointestinal disorders	127 (11.1)
Participants with ≥1 drug-related AE, n (%)†	376 (33.0)
Participants with drug-related serious AEs, n (%)†	4 (0.4)
Participants with AEs leading to discontinuation, n (%)	61 (5.4)
Common drug-related AEs, n (%)†‡	
General disorders and administration site conditions	253 (22.2)
Injection site erythema	98 (8.6)
Drug ineffective	75 (6.6)
Injection site pruritus	61 (5.4)
Injection site swelling	47 (4.1)
Injection site pain	30 (2.6)
Fatigue	21 (1.8)
Injection site rash	17 (1.5)
Injection site warmth	15 (1.3)
Gastrointestinal disorders	79 (6.9)
Constipation	58 (5.1)
Nervous system disorders	38 (3.3)
Migraine	14 (1.2)
Skin and subcutaneous tissue disorders	24 (2.1)
Psychiatric disorders	21 (1.8)
Infections and infestations	18 (1.6)
Musculoskeletal and connective tissue disorders	14 (1.2)

*Includes MedDRA system organ class reported in ≥5.0% of the study population.
†Drug-related AEs that have been classified by the investigator to be related to fremanezumab treatment.
‡Includes MedDRA system organ class and associated preferred terms reported in ≥1.0% of the study population.
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; SAS, safety analysis set.

P208

Long term persistence of onabotulinumtoxinA versus calcitonin gene-related peptide monoclonal antibodies in new initiators with chronic migraine

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Objective: Traditional oral generic migraine preventive medications show low persistence, impacting clinical and economic outcomes. Initial studies suggest onabotulinumtoxinA(onabotA) for chronic migraine(CM) leads to better persistence than calcitonin gene-related peptide(CGRP) monoclonal antibodies(mAbs) in new initiators, but did not compare persistence long-term (>12 months). This analysis compares real-world long-term persistence in CM patients newly initiating onabotA relative vs branded CGRP mAbs.

Methods: Using Merative Marketscan Commercial and Medicare database, this retrospective observational study included adult patients with CM initiating onabotA or a CGRP mAb (erenumab, fremanezumab, galacanezumab, eptinezumab) who stayed on index treatment 12-24 months. Exclusions included preventive gepant, onabotA, or CGRP mAb use during ≥6-month pre-index period, diagnosis of onabotA non-migraine indications during the study, or patients initiating >1 CGRP mAb or onabotA on index date. Persistence was measured as proportion of patients without treatment gaps (>60 days for fills/administration). Adjusted persistence was calculated via logistic regression adjusting for age, gender, baseline health plan, region, Charlson Comorbidity Index, baseline acute and preventive medication classes, index year, migraine-related comorbidities, and index treatment provider.

Results: Of the eligible patients, 5,079 (mean age 43 yrs, 84% female) initiated CGRP mAbs, and 2,223 (mean age 43 yrs, 87% female) initiated onabotA. Adjusted analysis showed significantly higher persistence with onabotA at 12 months (50.3%), vs CGRP mAb (40.4%; OR: 0.67[95% CI:0.61-0.74];*P*<0.001). A significantly higher persistence with onabotA continued at 18 months (38.1% vs 29.8%; OR: 0.69[95% CI:0.61-0.78]; *P*<0.001), and 24 months (32.1% vs 23.0%; OR: 0.63[95% CI:0.54-0.74];*P*<0.001).

Conclusion: Patients with CM initiating onabotA showed greater persistence at all long-term time points for up to 24 months compared to those initiating CGRP mAb.

P209

Long term persistence of patients with chronic migraine switching to onabotulinumtoxinA or a different calcitonin gene-related peptide monoclonal antibody (CGRP mAb) after initial CGRP mAb treatment

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Objective: Chronic migraine(CM) is associated with high healthcare resources utilization and costs, worsened by medication discontinuations and switches. OnabotulinumtoxinA(onabotA) has showed greater persistence over CGRP mAbs in among patients naïve to branded preventive CM treatments. No study has assessed persistence to onabotA among patients initially treated with CGRP mAb. This analysis compares real-world long-term persistence in patients with CM who switched CGRP mAb brands vs those who switched to onabotA after initial CGRP mAb treatment.

Methods: Using Merative Marketscan Commercial and Medicare database, this retrospective observational study included adult patients with CM with ≥1 CGRP mAb claim, then initiated another CGRP mAb (erenumab, fremanezumab, galacanezumab, eptinezumab) or onabotA for 12-24 months. Exclusions were gepant or onabotA treatment during the ≥6-month pre-index, diagnosis of onabotA non-migraine indications during the study, or combination use of onabotA and CGRP mAb or >1 CGRP mAbs on the index date. Persistence was measured as patients without treatment gaps (>60 days). Adjusted persistence used logistic regression adjusting for age, gender, baseline health plan, region, Charlson Comorbidity Index, baseline acute and preventive medication classes, index year, migraine-related comorbidities, and index treatment provider.

Results: Patients were treated with CGRP mAbs (N=1,734, mean age 45 yrs, 86% female) or onabotA (N=805, mean age 43 yrs, 88% female) for ≥12 months. A significantly higher proportion of onabotA-treated patients were persistent at 12 months (55.5%), vs CGRP mAb-treated patients (32.9%; OR: 0.39[95% CI:0.33, 0.47];*P*<0.001). This continued to 18 months (46.2% vs 25.9%; OR: 0.41[95% CI:0.33, 0.51]; *P*<0.001), and 24 months (35.1% vs 17.8%; OR: 0.40[95% CI:0.30, 0.54];*P*<0.001).

Conclusion: Patients with CM who switched to onabotA treatment after an initial CGRP mAb were

more likely to remain persistent for 12-24 months vs those who switched to another CGRP mAb.

P210

Experience in switching between antibodies against CGRP in a headache unit

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Objective: The therapeutic strategy of anti-CGRP monoclonal antibody switching provides positive results in a variable number of patients. Our aim is to contribute to the elucidation of the potential benefit of switching this treatment and to determine the patient profile that would most benefit from this switch.

Methods: We conducted a single-centre, retrospective study in a Headache Unit. Subjects undergoing immediate antiCGRP switch (a gap of less than a month) were included. A descriptive and comparative analysis of demographic variables, comorbidities, headache and migraine days per month (MHD and MMD), monthly analgesic consumption (SM), and medication overuse (MO) in the previous month before the switch and months 3 and 6 after the switch was conducted.

Results: Eighty-five patients with a mean age of 52.18 years (87.1% female) were included. 95.3% met chronic migraine criteria, with a mean of 12.83 years of chronification. There was a significant reduction in MHD at month 3 (-5.8, p=0.000) and 6 (-5.7, p=0.000); MMD at month 3 (-5.84, p=0.000) and 6 (-7.17, p=0.000) as well as in monthly consumption of symptomatic medication (-5.55 and -6.34; p=0.000) and in subjects with MO (57.5% at baseline vs 36.4% p=0.001 at month 3 and 28.6% p=0.000 at month 6). 29.4% had a ≥50% response at month 3 and 32.3% at month 6. 41.2% in month 3 and 46.2% in month 6 responded at least 25%. The improvement was significant and independent of the change in the mechanism of action of the second anti-CGRP. Either patients who had no response to the first antibody or those who had a loss of efficacy, experienced a significant reduction in MMD, MHD and SM at both 3 and 6 months after switching.

Conclusion: Monoclonal antibody switching is effective in up to one-third of migraine patients who have failed to a first one. These results are maintained over time and are independent of the switch mechanism and previous experience with other anti-CGRP therapy.

P211

Three-month atogepant treatment modulates dopaminergic-related functional connectivity in episodic migraine

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Objective: Episodic Migraine (EM) is a highly prevalent neurological disorder. Recent therapeutic advances have targeted the calcitonin gene-related peptide (CGRP), a neuropeptide implicated in migraine pathophysiology. Promising results have been obtained with a new class of drugs consisting of small-molecule CGRP receptor antagonists, known as gepants, potentially capable of crossing the blood-brain barrier. Atogepant, an oral anti-CGRP, is effective in EM prevention, yet its effects on central brain activity and neurotransmitter circuits remain largely unclear. This study investigates brain functional connectivity changes related with key neurotransmitter systems, following three months of treatment with Atogepant in a group of EM patients.

Methods: 15 adult EM patients underwent clinical assessments and resting-state functional MRI before treatment and after 3 months of daily Atogepant 60mg administration. Functional connectivity analyses were performed within the novel neurotransmitter-related functional connectivity framework (REACT) to investigate longitudinal connectivity changes associated with the distribution of serotonin, noradrenaline, mesocorticolimbic and nigrostriatal dopamine.

Results: Following 3 months of Atogepant treatment, headache frequency reduction was observed in all patients. Moreover, patients exhibited increased functional connectivity at follow-up within the mesocorticolimbic dopaminergic system (D1 receptor and DAT transporter), in the medial orbitofrontal cortex.

Conclusion: Atogepant treatment is associated with neurotransmitter-related functional connectivity changes within the dopaminergic system and reduced

headache frequency in EM patients. Such findings highlight the potential involvement of central neurotransmitter systems in EM pathophysiological processes influenced by preventive migraine treatments. A deeper understanding of these central changes could provide valuable insights into EM and its therapeutic targets.

P212

Refractory primary cough headache: More than just a nuisance

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Objective: Primary cough headache arises moments after intense exercise or Valsalva maneuvers. All patients must perform brain MRI - Arnold-Chiari malformation type 1 is the most common finding.

Methods: Case report and literature review.

Results: 54-year-old male with a medical history of transient vertical diplopia with mesencephalic captant lesion on brain MRI by the age of 40 years old. He was initially followed for seven years with no other symptoms. When he was 53 years old, he returned to the neurology consult, now reporting severe, pulsating headaches (which lasted for one/two minutes) exclusively triggered by coughing, defecatory effort and Valsalva maneuvers of any kind. Several medications were tried without significant control (indomethacin, acetazolamide, propranolol, amitriptyline, topiramate and valproic acid). The patient also underwent lumbar puncture with removal of 30 mL of CSF with no benefit. The patient remained symptomatic which led to the suspension of all medications. He remains with a lack of headache control.

Conclusion: Although other primary headaches are usually regarded as benign because of their specific triggers, this case highlights the major impact they can have on a patient's quality of life.

P213

Medication overuse headache: Findings from the China Headache Disorders Registry Study (CHAIRS)

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Objective: Medication overuse headache (MOH), considered a condition where pain and emotion are intertwined, is prevalent worldwide. However, comprehensive recognition of its clinical profile and related burden remains limited. This study aimed to present new data on the Chinese population and explore headache characteristics and psychological conditions between MOH subgroups classified using machine learning.

Methods: This cross-sectional study included 1,155 patients from CHAIRS (552 with migraine, 202 with other primary headaches, and 401 with MOH). Sociodemographic and neuropsychological profiles were compared between MOH and non-MOH groups. K-means clustering was used to identify psychological subtypes. Patterns of acute medication and specific overused drug components in the MOH group were also analyzed.

Results: Patients with MOH were more likely to be female ($p < 0.001$), have lower education ($p = 0.002$), and report sleep disorders (84.6% vs 69.8%, $p<0.001$). They also exhibited greater disability ($p<0.001$), lower life satisfaction ($p = 0.002$), higher levels of depression ($p = 0.009$), and poorer sleep quality ($p<0.001$). Psychological subgrouping identified two clusters (n=105 and n=169), with Cluster One showing worse cognitive function, sleep quality, and higher depression and anxiety (Figure 1). VAS scores were significantly higher in this cluster. Most patients still relied on combination analgesics(Figure 2), with caffeine as the most frequently overused ingredient(Figure 3).

Conclusion: This study updates MOH data in China and machine learning-based classification supports the need for neuropsychological evaluation to enhance individualized care. Our findings also highlight the urgent necessity to raise awareness about the overuse of combination analgesics.

Fig. 1

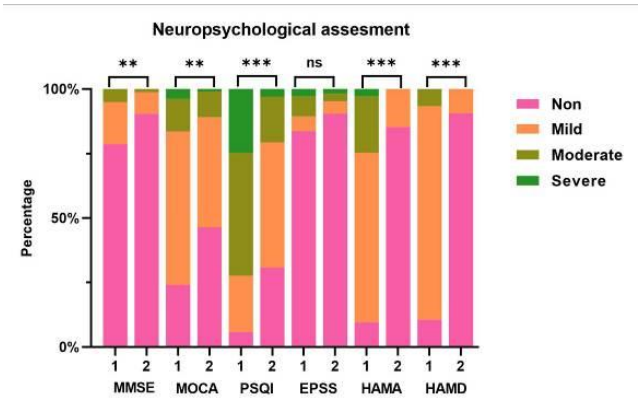


Fig. 2

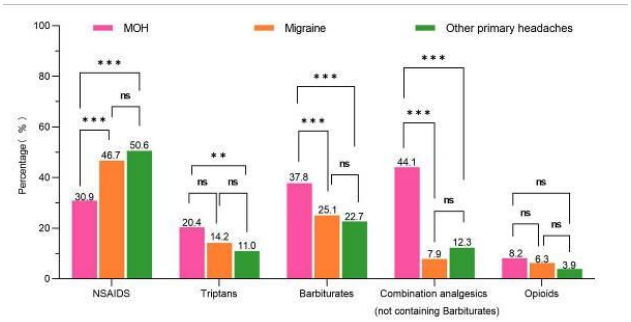
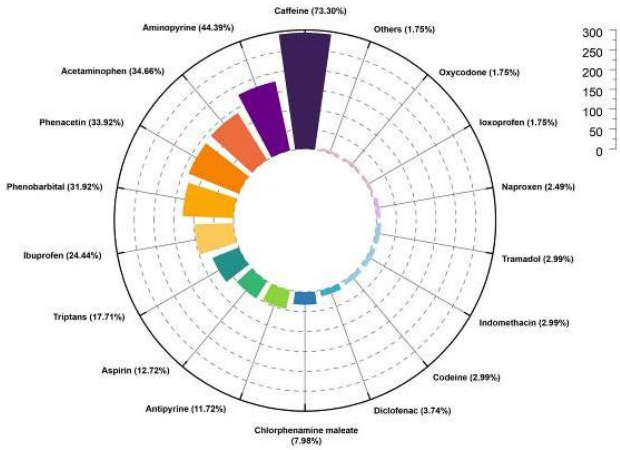


Fig. 3



P214

Atogepant in episodic cluster headache: A case report on efficacy and tolerability

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Objective: To describe the clinical response and tolerability of atogepant in a patient with episodic cluster headache (ECH), in whom standard preventive treatments were ineffective or poorly tolerated.

Methods: We report the case of a 37-year-old male with a 5-year history of episodic cluster headache, fulfilling ICHD-3 diagnostic criteria. Previous preventive therapies with high-dose verapamil (240 mg twice daily) and topiramate (50 mg/day) offered limited benefit, with 1-2 bouts of the disease each year. Off-label initiation of atogepant, a selective oral calcitonin gene-related peptide (CGRP) receptor antagonist, was undertaken at a dosage of 60 mg/day during an active cluster period.

Results: Treatment with atogepant led to complete suppression of cluster attacks, with therapeutic onset observed within the first 36 hours. Attack frequency declined from three severe episodes per week to none, and no acute medication (e.g., triptans) was required during therapy. However, after 5 days, the patient developed marked gastrointestinal adverse effects, namely epigastric pain, nausea, and anorexia,—necessitating discontinuation. Remarkably, the patient remained attack-free, despite cessation of treatment.

Conclusion: This case suggests that atogepant may represent a promising preventive approach for selected patients with episodic cluster headache, particularly when conventional treatments fail. Although adverse effects limited its use in this case, the rapid and complete response warrant further investigation. Controlled studies are warranted to assess its efficacy, safety and potential role in the management of cluster headache.

P215

Cluster headache impairs quality of life and daily functioning of Portuguese patients

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Objective: Cluster headache is a rare primary headache disorder known to significantly impair quality of life and daily functioning. To date, no data are available regarding its impact on the Portuguese population. This study aimed at evaluating the quality of life of Portuguese patients diagnosed with cluster headache.

Methods: Cross-sectional, multicenter study including participants from 17 specialized headache centers across Portugal. Eligible individuals were aged ≥18 years, with cluster headache diagnosis (ICHD-3 criteria) and with, at least, one cluster episode in the past three years. Socio-demographic and clinical data were collected, and the Portuguese version of the Cluster Headache Quality of Life Questionnaire (CHQ-P) was administered. Statistical analysis was conducted using SPSS®.

Results: A total of 127 participants were included, 81.1% of whom were male, with a median age of 49 years (IQR 18). Chronic cluster headache was diagnosed in 29.9% of patients. Acute-phase treatment with two or more therapies was reported by 47.6% of participants, most commonly zolmitriptan and high-flow oxygen. Preventive treatment was used by 72.4% of patients, with 29.9% receiving two or more preventive medications. The median number of clusters per year was 2 (IQR 2), each lasting a median of 15 days (IQR 30). Patients reported a median of 2 attacks per day (IQR 3) during clusters, each lasting a median of 60 minutes (IQR 90). More than half of the patients reported frequent or constant limitations in daily activities (59%), anxiety (77%), and low vitality (58%). Mood disturbances and interpersonal difficulties were reported by 25% of patients. Younger

age and chronic cluster headache were identified as predictors of greater impact on mood and interpersonal relationships.
Conclusion: Cluster headache is associated with significant impairment in quality of life and daily functioning among Portuguese patients. These findings highlight the need for strategies to prevent or mitigate this burden.

P216

Comparative effects of anti-CGRP monoclonal antibodies and atogepant on migraine disability, sleep quality, and attack frequency: A 12-month observational study

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Objective: Migraine is frequently associated with sleep disturbances, which significantly contribute to the overall disease burden. CGRP-targeted therapies have shown strong efficacy in reducing migraine frequency and disability. However, limited data are available regarding their impact on sleep quality. This study explores the relationship between monthly migraine days, MIDAS, and sleep quality (PSQI) in patients with treatment-refractory chronic migraine treated with anti-CGRP monoclonal antibodies or atogepant.
Methods: This retrospective observational study included patients with chronic migraine refractory to first-line preventives, treated with erenumab, galcanezumab, fremanezumab, or atogepant. Clinical data were collected at baseline and at 1, 3, 6, 9, and 12 months. Variables included MIDAS, PSQI total score, and monthly migraine days. Descriptive statistics and Pearson correlation analyses were performed ($p < 0.05$).
Results: Forty-eight patients were included: 18 treated with galcanezumab, 11 with erenumab, 8 with fremanezumab, and 8 with atogepant. All mAb-treated groups showed a reduction in migraine frequency and MIDAS scores, with galcanezumab showing the most consistent long-term improvement. A significant correlation between MIDAS and PSQI was observed in the erenumab group at 9 months. In the atogepant group, 4 of 7 patients with complete data showed PSQI improvement at 3 months. Estimated MIDAS-equivalent changes ranged from −16 to +10 points, suggesting heterogeneous but potentially meaningful individual benefit.
Conclusion: Anti-CGRP therapies reduced migraine burden in patients with refractory chronic migraine. Notably, erenumab was associated with a strong correlation between disability and sleep quality. Atogepant showed promising early improvements in sleep in selected patients. These findings support multidimensional monitoring—including disability and sleep quality—in migraine care.

P217

Clean days index – A new patient based questionnaire for a future new scoring system

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Objective: The paradigm in migraine treatment has significantly evolved in recent years. Nowadays, with more effective preventive treatments available, the aim is a pain free state, including the absence of non-headache symptoms that frequently accompany a migraine episode and/or can be present without the further development of the headache phase of migraine.
Methods: However, the most widely used clinical outcome measures in migraine clinical practice tend to focus mainly on headache-related symptoms and its impact. To address this gap, we developed a patient-reported outcome measure questionnaire Clean Days Index (CDI) – aimed at capturing the non-headache symptoms namely its frequency and impact in daily life.
This new questionnaire is based on the 28 items identified in Quintela"s report. In the future we aim to identify which variables are more frequently reported and have more relative impact in daily living, to develop a reliable and clinically useful scoring system.
Results: Based on this exploratory study, in due course, we hope to create a tool for measuring the burden of non-headache symptoms in migraine, how these symptoms are affected by preventive treatments and its contribution to patients" perception of treatment effectiveness.
Conclusion: The overarching objective is to improve migraine patients' care highlighting their participation in the management of the disease.

P219

Exploratory study evaluating nightly daridorexant in patients with chronic migraine and comorbid insomnia (DORMI Study)

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Objective: Anecdotal evidence suggests that insomnia not only increases the risk of developing migraines but

may also contribute to their chronicity. However, data on the potential impact of Daridorexant—a dual orexin receptor antagonist—on migraine frequency with comorbid insomnia remains limited.

Methods: The DORMI study is a prospective, open-label pilot trial enrolling 30 adults recruited from an outpatient clinic with high-frequency episodic migraine (>8 monthly migraine days) and chronic migraine (≥15 monthly migraine days) and comorbid insomnia, defined as sleep-onset or maintenance difficulties occurring ≥3 times per week. Participants will receive 50 mg of daridorexant nightly for three months. Regular monitoring and documentation of adverse effects will be performed throughout the treatment period. Polysomnography will be conducted to exclude other primary sleep disorders; individuals with psychiatric comorbidities or alternative headache diagnoses will be excluded. Data will be collected using a formal interview. Primary analysis will include changes in monthly migraine days. In contrast, secondary outcomes include shifts in insomnia severity and migraine-related disability, measured via the Insomnia Severity Index (ISI) and the Migraine Disability Assessment (MIDAS), HIT-6, and global impression of change (PGIC), respectively. Descriptive statistics, together with paired t-tests and measures of variance, will be used for analysis

Results: We anticipate improvement in migraine-free days and lower scores for ISI and migraine disability scores with this intervention.

Conclusion: Should this pilot reveal clinically meaningful improvements in sleep and headache frequency, it would warrant further investigation through a larger, randomized controlled trial.

P220

Refractory morning headaches in a young adult: Clinical relevance of borderline obstructive sleep apnea

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Objective: Chronic morning headaches in young adults often present a diagnostic challenge, particularly when neuroimaging and standard therapeutic approaches are inconclusive.

Methods: We report the case of a 28 year old male who began experiencing daily periorbital headaches at age 16. The pain alternated between eyes, was pulsatile or pressure-like, and predominantly occurred upon awakening, lasting 2–3 hours or occasionally the entire day. There was no photophobia, phonophobia, or movement sensitivity, and symptoms improved with physical exercise. He had no known medical history, including hypertension, and was normotensive on examination. He had a history of snoring that resolved after ENT surgery, but without improvement in headache. Brain MRI revealed a non-specific T2 hyperintense lesion in the left cingulate gyrus. In the past, a diagnosis of hypnic headache was considered and empirical treatment with lithium, melatonin, and caffeine was attempted without benefit. Although he denied daytime sleepiness, he reported persistent fatigue.

Results: Given the strong circadian pattern and lack of response to treatment, a sleep disorder was suspected. Polysomnography revealed an AHI of 5,9/h and ODI of 6.2/h, consistent with mild obstructive sleep apnea. Though the AHI was only slightly above the normal threshold, and would often be dismissed as clinically insignificant, the alignment between symptoms and sleep-related headache features was striking. CPAP therapy was initiated and resulted in near-complete resolution of symptoms, with only one headache in the following three months.

Conclusion: This case highlights the importance of considering even borderline sleep study findings when the clinical picture is suggestive. In young patients with refractory morning headaches and compatible features, low AHI values should not be undervalued, as they may conceal a modifiable cause with significant therapeutic implications.

P221

Age-related differences in migraine clinical characteristics in Armenian population

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Objective: Sex differences in migraine are well known, but age-related clinical characteristics remain insufficiently explored. In addition, migraine research is lacking in Armenia. We aimed to investigate the age-related clinical features of migraine in Armenian population.

Methods: Data was collected from medical records of a single neurology center with a high admission rate of headache patients. We studied the frequency and duration of attacks, association with the menstrual cycle in women, frequency of non-pain symptoms, nature of pain, family history, experience and effectiveness of using triptans and NSAIDs and potential triggers (including alcohol, soda, odors, sleep deprivation, spicy food, nuts, hunger, screen exposure, cold, light and stress). Migraine diagnosis was based on the ICHD-3 criteria.

Results: The study included 94 migraine patients with an average age of 34.6 years (16-66), females - 69.1% (n=65). All subjects were divided into two groups: a younger group (YG) (age <35) and an elder group (EG) (age ≥35). Statistically significant differences were observed between two groups regarding sex distribution, some migraine triggers, family history, triptan trials, and frequency of menstrual-associated migraine (Table). No statistically significant differences were found between the two groups for other variables.

Conclusion: According to our data, odors were the only trigger which was more frequently reported by elders. Female sex prevalence became more pronounced after 35. Migraine family history is more common among younger individuals. Interestingly, elders were more likely to try triptans, although efficacy was similar. In premenopausal women, the association between migraine attacks and the menstrual cycle appears to decrease with increasing age. There was no significant difference in attack frequency and duration, pain characteristics or non-pain symptoms. We did not investigate pain intensity or quality of life - important indicators for migraine.

Fig. 1

Clinical Feature	YG (%)	EG (%)	p-value
Female sex	59.6	78.7	<0.05
Odors as migraine trigger	4.3	19.2	<0.05
Positive family history of migraine	64.9	40.5	<0.05
Previous triptan trials	23.4	44.7	<0.05
Menstrual-associated migraine*	45.5	10.7	<0.05
* In premenopausal women (n = 61, mean age 34.1, range: 16–49)			

P222

Participant perspectives on clinical trial experience: Insights from exit interviews from the anti-PACAP antibody Phase 2 HOPE trial for migraine prevention

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Objective: To explore perspectives and experiences of clinical trial participation among people living with migraine who participated in the Phase 2 HOPE trial (NCT05133323) investigating the efficacy and safety of Lu AG09222, an anti-pituitary adenylate cyclase-activating polypeptide (anti-PACAP) monoclonal antibody in development for migraine prevention.

Methods: Qualitative interviews were embedded in the trial design and conducted within 14 days after the week 12 safety follow-up visit. Participation was voluntary and offered to all participants. Interview questions explored motivations for trial participation, as well as experiences and challenges of the trial, including use of the eDiary. Treatment efficacy and safety were not evaluated. To enable a mixed-methods approach, interview results were coded using Atlas.ti software and organised by content using thematic analysis.

Results: In total, 50 participants were interviewed; 49 (98.0%) provided ≥1 key motivator, including migraine management and symptom alleviation (n=39; 79.6%), supporting development of new therapies (n=9; 18.4%), potential improvements in quality of life (n=6; 12.2%) and altruism towards contributing to research (n=5; 10.2%). Positive interactions with site staff were reported by 38 of 50 participants (76.0%). Challenges were described by 23 of 50 participants (46.0%), of which 8 (34.8%) each mentioned operations and logistics of participation, as well as issues with eDiary functionality. Feedback on the eDiary was provided by 28 participants (56.0%); 25 (89.3%) felt the content was important and relevant, and five (17.0%) made suggestions for future eDiary topics, including migraine pain location, acute medication use and migraine triggers**.**

Conclusion: Incorporating qualitative exit interviews into the trial design enabled people living with migraine to provide their perspective on clinical trial participation. Insights from these interviews can inform a participant-centric approach to future trial designs.

P223

Invisible pain at work: Perceptions, accommodations, and stigma surrounding migraine in the workplace

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Objective: To explore how migraine is perceived and accommodated in the workplace, and to assess the impact of stigma, organizational empathy, and policy on workers living with migraine.
Methods: A cross-sectional study was conducted with 30 adult employees formally diagnosed with migraine. Participants completed a structured questionnaire covering five domains: demographic/professional profile, migraine characteristics, workplace attitudes, organizational policies, and professional/emotional impact. The adapted Stigma Scale for Chronic Illness (SSCI-8) was used to assess both enacted and internalized stigma.
Results: Participants (mean age: 41.6) reported 9.3 migraine days/month. Work productivity during attacks was low (mean = 2.0/5). Although 90% felt free to take medication, 63% had felt pressured to keep working, and 60% had hidden their condition. Migraine legitimacy was rated moderately (mean = 3.1/5). While 63% had remote work options, only 30% had additional breaks, and 10% had access to quiet/dark spaces. Just 17% reported training on invisible illnesses. Career impact was significant: 67% felt limited in progression, and 63% had considered changing jobs due to lack of support. Only 23% felt emotionally supported. SSCI-8 scores showed low overt stigma (means 1.2–1.8), but internalized stigma was common: 43% felt ashamed of limitations, and 30% felt responsible for their condition.
Conclusion: Migraine significantly affects employees" productivity and career development. Despite some accommodations, internalized stigma and lack of emotional support remain widespread. These findings underscore the need for greater awareness, inclusive workplace practices, and targeted training to foster empathy and support.

P224

PGIC vs MIDAS: PROMs in anti-CGRP migraine mAb therapy

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Objective: To evaluate the utility of patient-reported outcome measures (PROMs) in assessing response to anti-CGRP monoclonal antibody (mAb) therapy in migraine.
Methods: This retrospective, observational study included migraine patients treated with anti-CGRP mAbs at a single centre. Monthly headache days (MHD) and Migraine Disability Assessment (MIDAS) scores were collected at baseline and quarterly thereafter. The Patient Global Impression of Change (PGIC), a 7-point scale reflecting patient-perceived improvement, was recorded quarterly from month 3 to 12. Changes in MHD and MIDAS were expressed as percentages. PGIC was treated as an ordinal variable (1 = very much improved to 7 = very much worsened). Correlations were assessed using Spearman"s coefficient; Fisher"s exact test was used for categorical comparisons.
Results: Data was available from 63 patients, totalling 104 MIDAS and 98 PGIC forms. Sixteen patients (25%) filled out MIDAS forms incorrectly at least once, compared to 1 (2%) who incorrectly filled the PGIC form once. Education level was not significantly associated with form errors (p=0.13). All patients who reported a >50% reduction in MHD rated their PGIC as "very much improved" or "improved" (PGIC = 1 or 2). Non-responders (<30% reduction in MHD) rated their status from PGIC 1 to 5, with PGIC 1 or 2 responses increasing from 3 of 7 (43%) to 5 of 7 (71%) by month 9. MIDAS moderately correlated with MHD (rs=0.61, p<0.05), while PGIC showed a weak positive correlation (rs=0.39, p<0.05).
Conclusion: MIDAS moderately reflects changes in headache frequency, limiting its added value as a PROM. PGIC correlated poorly with headache frequency, reflecting perceived improvements in severity, duration, or impact of migraine attacks that may better capture the full therapeutic benefit of anti-CGRP mAbs. Findings align with prior data and, given PGIC's ease of completion, support its inclusion in routine migraine monitoring to enhance individualized care.

P225

Quality of life in migraine: The burden of psychiatric comorbidities

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Objective: Migraines are disabling neurological disorders frequently associated with psychiatric comorbidities. These comorbidities may worsen symptoms, hinder treatment response, and negatively impact quality of life (QoL). This study aimed to assess QoL in migraine patients and evaluate how psychiatric comorbidities influence it.
Methods: A one-year case-control study (January–December 2022) was conducted at the Military Hospital of Instruction of Tunis. It included 100 migraine patients and 200 age- and sex-matched healthy controls. QoL was measured using the SF-36 questionnaire, which assesses eight domains and provides physical and mental component scores with higher scores indicating better QoL. Psychiatric

comorbidities were diagnosed using standardized clinical criteria. Comparisons were made between groups with and without comorbidities.

Results: Migraine patients had significantly lower SF-36 scores than controls: physical component (48.7% vs. 82.6%), mental component (42.2% vs. 74.6%), and global score (47.9% vs. 80.3%). Psychiatric comorbidities further worsened outcomes. Migraineurs with depression had a global score of 39% vs 48% in those without. Those with anxiety disorders scored 42% vs. 49%. Generalized anxiety and panic disorder were associated with the greatest reductions in mental component scores. Migraine patients with psychiatric comorbidities consistently reported lower QoL than both controls and migraineurs without such conditions.

Conclusion: Psychiatric comorbidities significantly impair quality of life in migraine sufferers. Early identification and integrated management of these conditions are essential for improving overall outcomes and reducing the burden of migraine.

P226

Measurement properties of Patient-Reported Outcome Measures (PROMs) for assessing physical functioning and quality of life in adults with migraine: A systematic review

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Objective: To systematically evaluate the measurement properties validity, reliability, and responsiveness of Patient-Reported Outcome Measures (PROMs) used to assess the impact of migraine on patients' physical functioning and Quality of Life (QOL).

Methods: A systematic literature search was conducted in PubMed and Web of Science for studies published in English between 2004 and July 2025. Eligible studies assessed the measurement properties of PROMs evaluating physical functioning and/or QoL in adults with migraine. Independent reviewers performed the studies selection, data extraction, assessed methodological quality, rated measurement properties and synthesized the results according to COSMIN (Consensus-based-Standards for selection of health Measurement Instruments) guidelines.

Results: Out of 3,554 articles, 32 met the inclusion criteria, covering 16 distinct PROMs, in which the Migraine Specific Quality of Life Questionnaire Version 2.1 (MSQv2.1), the Headache Impact Test (HIT-6TM), and the Migraine Impact and Disability Assessment Scale (MIDAS) were the most extensively studied instruments. Considering the evaluation of the psychometric properties, most studies focused on aspects of validity (construct, convergent validity) and reliability (test-retest and internal consistency). These PROMS also demonstrated responsiveness, including the establishment of thresholds for clinically significant change. MSQ v2.1 and HIT-6 had a moderate to high level of evidence.

Conclusion: The MSQ v2.1, HIT-6TM and MIDAS are the most thoroughly investigated PROMS for assessing physical functioning and QoL in individuals with migraine. Among these, the MSQ v2.1 has the best-established measurement properties with moderate to high level of evidence. Future research should clarify domains coverage and assess the value of combining instruments to provide a comprehensive picture of migraine"s impact.

P227

The effects of allodynia on the pain perception during botulinum toxin treatment for migraine: A cross-sectional study

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Objective: Migraine patients may develop cutaneous allodynia (CA), characterized by increased pain sensitivity. We hypothesize that CA leads to higher pain perception during onabotulinumtoxinA administration compared to patients without CA, potentially affecting treatment adherence. Recent data show that same-day administration of peripheral nerve blocks and onabotulinumtoxinA has a safety and tolerability profile similar to either treatment alone, suggesting nerve blocks could help reduce injection pain.

Methods: In this ongoing study, we included patients diagnosed with chronic migraine treated with botulinum toxin according to the PREEMPT protocol at the Headache Clinic of Hospital de Santa Maria, Lisbon. CA was assessed using the ASC-12 scale, and pain perception was evaluated with Likert and VAS scales, controlling for confounding factors. We excluded patients who had a great occipital nerve block within the past 3 months, were on corticosteroids, or had significant neurological or systemic disease.

Results: A preliminary analysis of 68 patients (median age 49.75 years, 67 females) revealed a significant correlation ($p<0.001$) between the two pain scales. Among them, 29 patients (42.6%) reported moderate to severe allodynia, and 46 (70.6%) experienced acceptable or slight pain during injections. No

significant difference in pain perception was found between patients with or without allodynia, nor with respect to days since last attack or headache presence at the time of injection. A multivariate analysis will be performed.

Conclusion: This study aims to determine if allodynia is associated with increased pain perception during onabotulinumtoxinA administration, to potentially justify combining toxin treatment with nerve blocks in these patients. Based on current data, we did not observe a significant association between allodynia and pain perception. We intend to repeat this analysis in a larger cohort, incorporating all confounding variables

P228

Outcomes after discontinuation of preventive treatment blocking calcitonin gene-related peptide in migraine: A real-world study

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Objective: Use of monoclonal antibodies that targets the calcitonin gene-related peptide (CGRP) pathway is considered a third line preventative treatment for episodic and chronic migraine, often serving as last available option for preventative treatment. We aimed to investigate why patients discontinue anti-CGRP treatment and which subsequent treatment options are recommended when anti-CGRP treatment is no longer viable due to inefficacy or adverse events.

Methods: We conducted a retrospective real-world study including migraine patients that discontinued treatment with anti-CGRP at the Danish Headache Center. We reviewed electronic medical records of migraine patients after they terminated treatment with anti-CGRP at the Danish Headache Center.

Results: In total, 160 patients were included (98% with chronic migraine). Hereof, 135 patients (84%) discontinued anti-CGRP treatment due to lack of efficacy, while 25 patients (16%) discontinued anti-CGRP treatment due to adverse events. Forty-one patients (26%) had tried more than one anti-CGRP treatment. Subsequent treatment recommendations were Botox (n=74, 46%), optimization of acute treatment (n=6, 4%), other preventive therapy (n=31, 19%), and no recommendations (n=49, 31%). In total, 110 patients had previously tried Botox therapy, whereas 35 of the 74 patients that received Botox were de novo patients.

Conclusion: In conclusion, our study shows that Botox may be an effective treatment option to consider for patients with chronic migraine, when anti-CGRP treatment is not an option.

P229

Insomnia and migraine: Insights from therapeutic response

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Objective: Insomnia frequently coexists with migraine. We aimed to assess whether migraine therapies - monoclonal antibodies (mAbs) targeting CGRP or onabotulinumtoxinA (Botox) - lead to insomnia improvement.

Methods: We included 67 migraine patients treated with mAbs or Botox. All were assessed before and after treatment using the Insomnia Severity Index (ISI) and Hospital Anxiety and Depression Scale (HADS). Treatment response was defined as ≥50% reduction in headache frequency. ISI change was compared across treatment types and response status. Linear regressions assessed whether baseline ISI, depressive symptoms, or response status predicted insomnia improvement. A subanalysis focused on patients with clinically significant insomnia (ISI > 7), and an additional analysis was performed based on patients receiving sedative medications as migraine preventives (ex: ADT) or other pathologies.

Results: Overall, ISI scores changed minimally after treatment with mAbs ($p = 0.298$). No significant differences in ISI change were found between responders and non-responders ($p = 0.385$), nor between treatment types ($p=0.148$). In multivariable regression, only baseline ISI predicted sleep improvement ($B = –0.336$, $p = 0.004$); response status, depression scores (HADS) and sedative medications were not significant. The subgroup with ISI > 7 showed similar results, with no significant treatment effect. Finally, in patients not receiving sedatives, no significant differences in ISI change were observed between treatment types or response status.

Conclusion: Insomnia symptoms improved only modestly after migraine treatment and were unrelated to headache response, treatment type or depressive symptoms. These findings suggest that migraine and insomnia may not share a direct mechanistic link, and support the need for separate, targeted management of sleep disturbances in migraine patients.

P230

IMprovIng Distress pErception and mutuAlity in caRegivers (MI-DEAR study) of migraine patients – An observational prospective real-life study to evaluate the effectiveness of fremanezumab for reducing the caregivers" burden and increasing reciprocity within the dyads

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Objective: Migraine negatively impact patients" and family members daily lives. We investigated whether clinical improvement in patients with depressive symptoms receiving fremanezumab can favorably modify stress and enhance mutuality in the dyad.
Methods: This is a multicenter, observational, prospective study involving adult patients with migraine receiving fremanezumab with symptoms of depression (PHQ-9 ≥5) and their caregivers. At baseline and after 6 months (T6), monthly migraine days (MMDs), pain intensity (NRS), migraine-related disability (MIDAS; HIT6), and depressive symptoms (PHQ-9), were evaluated in migraine patients. At baseline and T6, perceived stress in caregivers (Relatives Stress Scale -RSS) and reciprocity in the dyad (Mutuality Scale MS) were assessed.
Results: 116 dyads were enrolled (caregivers: 34.5% females, 48.7 ys, SD 1.1). Caregivers were the patients' partners in 80.5% of cases. At baseline, patients reported moderate symptoms of depression (PHQ-9 11 SD 5 SD5.1). Caregivers presented moderate distress (RSS 20.37, SD 11.3). Mutuality scales scores were high in patients (3.0, SD 0.6) and caregivers. (3.2 SD 0.5). At baseline, MMDs were related to PHQ scores ($p = 0.009$) but not to MS in patients and caregivers, or to RRS (p consistently > 0.1). Conversely, RRS scores were associated with PHQ-9 scores ($p=0.004$), MIDAS ($p=0.021$), and inversely related to MS in patients ($p=0.009$) and caregivers ($p< 0.001$). At T6, MMDs, PHQ-9, MIDAS, and HIT-6 scores decreased ($p < 0.001$ consistently), while MS and RSS scores did not differ statistically from baseline. The reduction in PHQ-9 was associated with a decrease in RRS ($p=0.003$).
Conclusion: Caregivers of patients with disabling migraine present a moderate burden of perceived stress, which is associated with patients' depressive symptoms and negatively affects mutuality in the couple. The treatment with fremanezumab alleviated patients" depressive symptoms, which in turn reduced caregiver perceived stress.

P231

Bone health in migraine patients treated with anti-CGRP monoclonal antibodies: A prospective observational pilot study

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Objective: Calcitonin gene-related peptide (CGRP) is implicated in migraine pathophysiology and plays a regulatory role in bone metabolism. Concerns have emerged regarding possible osteocatabolic effects of anti-CGRP monoclonal antibodies (mAbs) used as preventives in migraine patients. We report the 6-month results from an ongoing 24-month prospective study assessing the impact of anti-CGRP mAbs on bone mineral density (BMD), trabecular bone score (TBS), and bone turnover markers in migraine patients.
Methods: Migraine patients initiating anti-CGRP mAbs (erenumab, galcanezumab, or fremanezumab) and with no comorbidities or medications affecting bone metabolism, were compared to age- and sex-matched migraine patients with no preventive migraine therapies. BMD was measured at lumbar spine (L1-L4), TBS was calculated using the TBS iNsight® software from lumbar images. Bone metabolism turnover markers included β-CTX and P1NP. Changes from baseline to month 6 were analyzed using non-parametric tests and linear mixed-effects models including time × group interaction.
Results: Thirty-eight patients (25 treated, 13 controls; mean age 36.3 ± 9.2 years; 84% female) completed 6-month evaluations. At baseline, BMD, TBS, and bone markers were within normal ranges and comparable. At 6 months, lumbar spine BMD remained stable in both groups (treated +0.02 g/cm², $p=0.65$; controls –0.01 g/cm², $p=0.32$). TBS was unchanged in treated

patients (–0.001; p=1.000) but increased in controls (+0.052; p=0.026), with a significant time × group interaction (p=0.022). β-CTX and P1NP showed no significant changes or interaction. Treated patients reported a reduction in monthly migraine days (–9.13; p<0.001).

Conclusion: Anti-CGRP mAbs treatment was not associated with significant changes in BMD, TBS or bone turnover markers over 6 months in migraine patients

P232

Circulating CGRP as a diagnostic biomarker in female migraineurs: A single-center case-control study

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Objective: Migraine constitutes the predominant cause of disability-adjusted life years, yet remains diagnostically challenging due to the absence of clinically validated biomarkers. Calcitonin gene-related peptide, recognized as the pathophysiological cornerstone of migraine, mediates cephalic vasodilation and neurogenic inflammation through its release from activated trigeminal ganglion neurons. Despite the therapeutic breakthrough of anti-CGRP therapies, reliable bedside quantification of CGRP levels remains elusive, hindering personalized treatment strategies.

Methods: This study enrolled 184 female migraineurs and 85 age-matched controls. Serum CGRP was measured by magnetic bead-based chemiluminescent immunoassay. High-/low-expression subgroups were stratified by predefined CGRP cutoff. Patients receiving CGRP antagonist rimegepant acutely were analyzed.

Results: Circulating CGRP was higher in female migraineurs vs. controls. ROC analysis determined 40.00 pg/mL as cutoff for stratification. Patients classified: high-CGRP (n=112) and low-CGRP (n=72). High-CGRP group had higher monthly attack frequency (P=0.013) and more tender points (P=0.026). With rimegepant, 45.0% achieved pain-free at 2h. Shorter attack duration independently predicted response (P=0.027). Baseline CGRP moderately elevated in responders vs. non-responders, but non-significant.

Conclusion: Elevated blood CGRP distinguishes female migraineurs from healthy controls. Baseline CGRP showed no direct association with rimegepant response, but pretreatment levels positively correlated with migraine attack frequency—a feature predicting reduced therapeutic efficacy.

P233

Survey on adherence and tolerability of atogepant used as migraine preventive treatment

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Objective: atogepant is a novel anti-calcitonin gene related peptide treatment (CGRP) used in migraine prevention. Our primary aim was to assess its therapeutic adherence, tolerability of the drug, as well as perceived effectiveness when used during a migraine attack

Methods: we conducted a survey involving 51 migraine individuals undergoing atogepant treatment at the Headache Centers of Carlo Besta Neurological Institute in Milan and Mondino Foundation in Pavia. The survey was made on "Microsoft Form" institutional doodle. We investigated therapeutic adherence, treatment tolerability, individuals" satisfaction, as well as atogepant efficacy despite some missed pills missed, and acute effictiveness during pain

Results: Participants had a mean age of 42y (±8.4), they received treatment for a median of 24 weeks of them 42 out of 51 take atogepant in the morning. Of the total sample, 59% of individuals missed few pills during the follow-up period. Among them, approximately 70% noticed no change in the drug"s effectiveness, suggesting a degree of resilience to occasional non-adherence. Almost all respondents (72.5%) reported a high level of satisfaction with the treatment, describing a "significant improvement" in managing migraine attacks. Twenty-one participants took atogepant during an acute attack, determining pain freedom within 2hours from intake in 16/21. Adverse effects were reported by 48% of participants, mainly nausea and mild average weight loss (of approximately 2kg). Only two individuals dropped out due to adverse event (e.g. nausea) after 6 months of treatment

Conclusion: Overall, atogepant proved to be a well-tolerated treatment, with high adherence in clinical practice. Clinical efficacy was maintained despite some missed pills. Mild adverse events were declared by half of participants, mainly nausea and slight weight loss

P234

Prevalence and mechanisms of headache disorders in relation to sarcopenia among older adults in China: A chinese cross-sectional analysis

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Objective: Despite the rising global burden of sarcopenia and headache disorders, the potential bidirectional link between neurologically-driven pain syndromes and musculoskeletal deterioration remains poorly understood. This study examines the associations between headache disorders and sarcopenia characteristics in a population-based cross-sectional study.
Methods: This cross-sectional study utilized data from wave 3 (2015) of the China Health and Retirement Longitudinal Study (CHARLS). Headache disorders were evaluated by self-reported head pain and the ID Migraine questionnaire. Sarcopenia was diagnosed according to the latest criteria (2019) outlined by the Asian Working Group for Sarcopenia (AWGS). Multivariate logistic regression models were constructed to assess the associations of headache and migraine with sarcopenia.
Results: A total of 14215 participants were included in the cross-sectional analysis. Individuals with headache or migraine had higher odds of possible sarcopenia (OR = 1.32, 1.45, respectively), sarcopenia (OR = 1.53, 1.49, respectively), low muscle mass (OR = 1.47, 1.50, respectively), low muscle strength (OR = 1.33, 1.53, respectively), and reduced physical performance (OR = 1.27, 1.27, respectively) than healthy controls did. Additionally, migraine was independently associated with an increased likelihood of severe sarcopenia (OR=1.57, 95% CI: 1.13–2.16).
Conclusion: This first nationwide study demonstrates robust links between headache disorders and sarcopenia in Chinese middle-aged/older adults. Migraine showed particularly strong associations with severe sarcopenia.

Fig. 1



P235
Real-world use of atogepant: Experience from a secondary-level hospital

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Objective: Atogepant is a calcitonin gene-related peptide (CGRP) receptor antagonist approved for the preventive treatment of both episodic and chronic migraine. Although randomized clinical trials have demonstrated its efficacy and safety, their external validity may be limited by controlled study conditions. This study aimed to assess the real-world effectiveness and tolerability of atogepant in patients with high-frequency episodic or chronic migraine managed at a secondary-level healthcare facility.

Methods: This prospective, longitudinal study included 93 patients who initiated atogepant treatment between 2024 and 2025. Demographic and clinical variables were collected, including age, sex, migraine subtype, disease duration, prior preventive therapies, comorbidities, and adverse events. The primary outcome was the change in monthly migraine days from baseline to one and three months after treatment initiation. Secondary outcomes included changes in HIT-6 scores and response rates (≥50%, ≥75%, and 100%).

Results: Thirty-nine patients completed the three-month follow-up. The mean number of monthly migraine days decreased from 17 to 10, showing a sustained response over time. A reduction of 50% or more was achieved in 41% of patients, and 68% of those with chronic migraine converted to episodic migraine. HIT-6 scores decreased from 66 to 58. Patients with psychiatric comorbidities exhibited less clinical improvement. The most common adverse event was constipation (28%). The mean number of prior preventive treatments was 4.62

Conclusion: Atogepant demonstrated sustained efficacy and favorable tolerability in real-world clinical practice and may represent a promising therapeutic option for patients with refractory migraine. The primary limitation of the study was the relatively small sample size.

Fig. 1

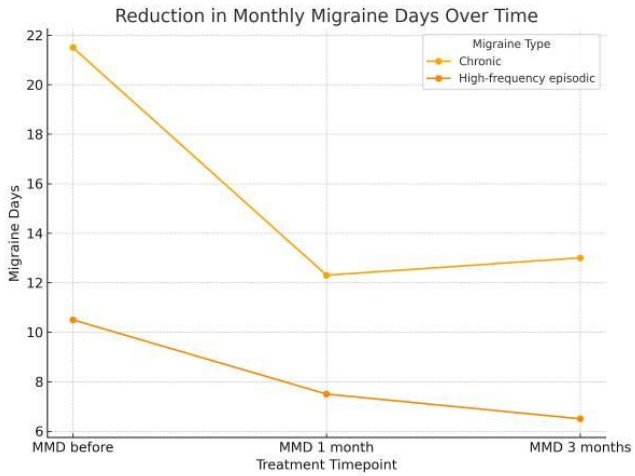
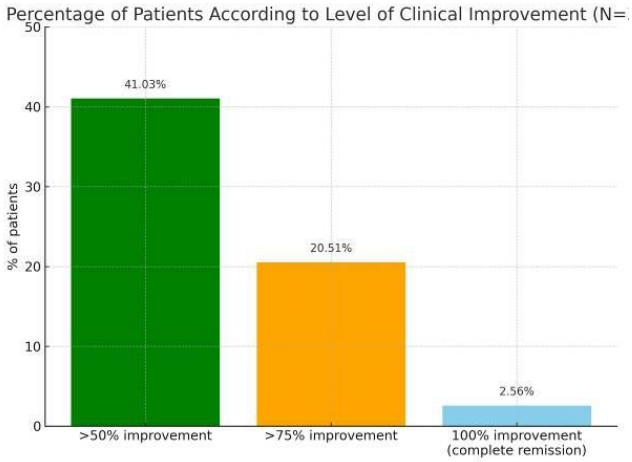


Fig. 2



P236

Effectiveness of eptinezumab in patients with migraine and previous preventive anti-CGRP treatment failures: A real clinical practice study in the Valencian community

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Objective: To provide further relevant information about the effectiveness of eptinezumab as a preventive treatment in routine clinical practice in patients with migraine and to assess its best prescription regimen.

Methods: Observational, retrospective, multicenter, chart review study conducted in a real-world setting between March 2023 (eptinezumab approval in Spain) and April 2025, in patients diagnosed with migraine and treated for the first time with eptinezumab (100mg/12 weeks) for 6 months.

Results: 182 (100%) patients were included (83.0% women), with a mean age of 48.1 years. 72.5% of patients were diagnosed with chronic migraine, 69.2% presented with psychiatric and/or neurological history, and 55.8% had comorbidities. 89.6% of patients presented with ≥1 anti-CGRP previous treatment failure. A significant change from baseline (5.3 [8.5], p<0.0001) in the mean of Monthly Migraine Days (MMD) [SD] was observed at 6 months of treatment with eptinezumab (17.3 [7.3] and 12.2 [8.4], respectively). At 6 months, 50.0% of patients achieved a ≥30% reduction in MMD, 30.7% a ≥50% reduction, and 9.1% a ≥75% reduction. Visual Analogic Scale (VAS) - Pain Intensity (mean [SD]), significantly

decreased (change: 1.0 [1.5], p<0.0001) at 6 months (6.6 [2.3]) from baseline (7.8 [1.8]). Patients reported an improvement in their Headache Impact Test (HIT-6) from baseline to 6 months (mean [SD]: 66.4 [9.3] and 61.5 [11.1], respectively). According to previous anti-CGRPs treatment failures groups, 54.5% of naïve patients (no previous anti-CGRP) showed a ≥30% reduction in Monthly Headache Days (MHD), higher than those observed in patients with ≥1 anti-CGRP previous treatment failure (46.2% and 44.7%, respectively). Triptan use decreased from baseline to 6 months (72.0% and 19.5% of patients, respectively).
Conclusion: This study shows the effectiveness of eptinezumab as a preventive treatment of migraine in a real-world setting in Spain.

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Erenumab vs. topiramate for reducing triptan use in migraine: A target trial emulation study

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Objective: This study aimed to compare the effectiveness of Erenumab versus Topiramate in reducing triptan utilization in patients with migraine.
Methods: Using Norwegian health registry data, we emulated a target trial comparing Erenumab and Topiramate. To adjust for baseline confounding, overlap weights were applied. It yeilded an an effective sample size (ESS) of 6,325. Three outcomes were evaluated over 12 months: triptan daily defined doses (DDDs), percentage change in triptan use from baseline, and achievement of ≥50% reduction in triptan use. Weighted linear mixed-effects models were used for continuous outcomes, and a weighted generalized linear mixed-effects model with a logistic link was used for the binary outcome. Data were obtained from national prescription and patient registries.
Results: Baseline characteristics were well balanced after weighting. In the intention-to-treat analysis, Erenumab was associated with a significant reduction in triptan DDDs compared to Topiramate in the 0–3 month period (Coefficient = –2.58, 95% CI: [–4.78, –0.39], p = 0.022), and in percentage change (see Figure 1) (Coefficient = –8.74, 95% CI: [–13.63, –3.86], p = 0.001). % change for Erenumab and Topiramate can be seen in figure 2. Erenumab also increased the odds of achieving a ≥50% reduction in triptan use (OR = 1.21, 95% CI: [1.04, 1.40], p = 0.012). No significant group differences were observed beyond 3 months. In the per-protocol analysis, Erenumab showed significantly greater reduction in triptan DDDs at 0–3 months (Coefficient = –3.12, CI: [–5.84, –0.40] p = 0.025) and 3–6 months (Coefficient = –4.19, CI: [–7.47, –0.91] p = 0.012), and a significant reduction in percentage use at 0–3 months (Coefficient = –10.18, CI: [–16.06, –4.31] p = 0.001).
Conclusion: This study suggests that Erenumab provides an early advantage over Topiramate in reducing triptan utilization among migraine patients, particularly during the first 3 months of treatment.

Fig. 1

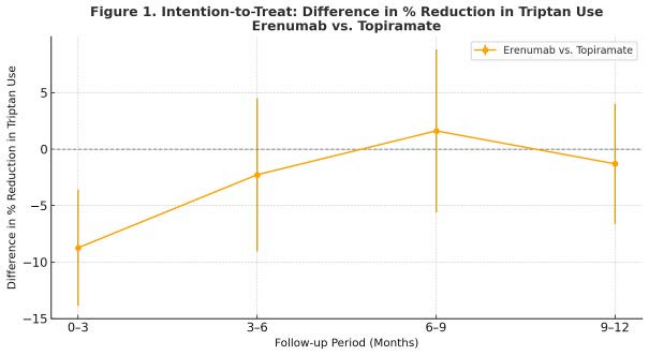
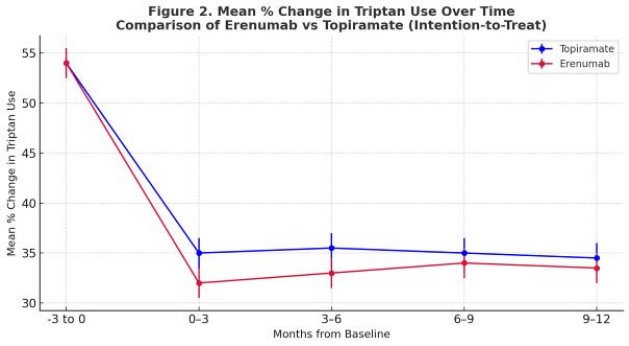


Fig. 2



P238

Real-world evidence of safety and effectiveness of atogepant: A prospective study from a Portuguese tertiary centre

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Objective: Atogepant is an antagonist of calcitonin gene-related peptide (CGRP) receptor, whose clinical trials have shown promising results in the preventive treatment of migraine. However, more real-world data is needed to assess these results. The aim of this study was to evaluate the effectiveness, safety, and tolerability of atogepant in patients with episodic or chronic migraine in a Portuguese tertiary centre.
Methods: Ongoing prospective study of a consecutive cohort of migraine patients treated with atogepant. Sociodemographic and clinical data, adverse effects, monthly headache days (MHD), monthly migraine days (MMD), disability (Headache Impact Test–6: HIT-6) and treatment satisfaction (Patient Global Improvement Change Scale: PGIC) were collected through medical records and voluntary questionnaire.
Results: Patient inclusion began in January 2025 and a total of 56 patients were enrolled: 89% female (n=50), with a median age of 41.5 years. Most patients (89%) had previously been treated with multiple prophylactic therapies (including antidepressants, antiepileptics, antihypertensives, OnabotulinumtoxinA, and anaesthetic blocks), and 16 patients with anti-CGRP monoclonal antibodies, with a median of 4 previous treatments, while 6 patients were naïve. The median pre-treatment HIT-6 was 59 and after 3 months was 52. The median PGIC score was very much improved. The median reduction in MHD was 9 days and the median reduction in MMD was 5 days. Patients reported 26 median "crystal clear days". Side effects were reported in some patients, namely nausea, loss of appetite, fatigue, constipation, and insomnia. Treatment was discontinued in 4 patients (due to adverse effects).
Conclusion: Preliminary findings indicate that atogepant shows substantial promise in reducing both headache and migraine days in a real-world setting, with a favourable tolerability profile. However, the study is still in the patient inclusion phase, therefore we hope to obtain more results to attest to its efficacy and safety.

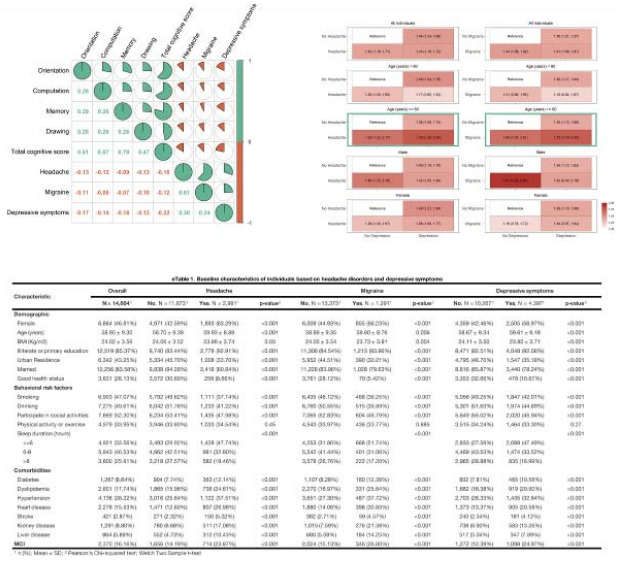
P239

Joint impact of headache disorders and depressive symptoms on mild cognitive impairment in older adults: Evidence from a longitudinal cohort in China

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Objective: This study elucidates the intricate interplay between headache disorders, depressive symptoms, and the incidence of mild cognitive impairment (MCI) in middle-aged and elderly populations. While prior research has independently examined these factors, their synergistic and mediating effects on cognitive decline remain poorly understood.
Methods: This longitudinal study analyzed 2015-2020 CHARLS data from 8,137 middle-aged/elderly participants. Headache was assessed by self-report and ID-Migraine™, depression by CESD-10, and cognition via orientation/memory/calculation/drawing tests. MCI was defined as AACD. Cox models examined: (1) depression/headache-MCI associations; (2) their mediation/joint effects.
Results: Baseline analysis showed that individuals reporting headache, migraine, or depressive symptoms had significantly lower cognitive performance. In adjusted models, patients with headache (HR = 1.288, 95% CI: 1.120, 1.481), migraine (HR = 1.274, 95% CI: 1.049, 1.547), and depressive symptoms (HR = 1.357, 95% CI: 1.199, 1.535) demonstrated a substantially higher incidence of MCI. Furthermore, the study indicated that depressive symptoms partially mediated the association between headache and MCI incidence but fully mediated the link between migraine and incident MCI. The joint effects of headache disorders and depressive symptoms were significant among individuals aged ≥60 years.
Conclusion: These findings underscore the complex interplay between headache disorders, depression, and cognitive decline, underscoring the need for integrated neurological and psychological healthcare to prevent MCI.

Fig. 1



P240

Study on the prevalence of migraine in pregnant women in Riyadh, Saudi Arabia and health seeking behavior

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Objective: To determine the prevalence of migraines in pregnant women. To identify demographic, obstetric, and lifestyle factors associated with an increased risk of migraines during pregnancy. To assess the impact of migraines on maternal health and quality of life. To explore the types of migraine (episodic, chronic) prevalent during pregnancy. To examine the relationship between migraine and pregnancy-related complications, such as hypertension and preeclampsia.

Methods: A survery questionnaire of pregnant women attending antenatal clinics at King Abdullah Bin Abdulaziz University Hospital, Princess Norah Bint Abdulraman University, Riyadh, Saudi Arabia. Participants were also recruited from various hospitals and healthcare centers in Riyadh in appropriate neurology clinics at both private and governmental hospitals in Riyadh, Saudi Arabia

Inclusion Criteria: Pregnant women, aged 18-45 years, in any trimester of pregnancy, attending antenatal clinics with established diagnosis of migraine. Data was collected through a validated migraine screening tool such as the *Migraine Disability Assessment (MIDAS)* or *Headache Impact Test (HIT-6)*

Results: This study included 298 woman with diagnosis of migraine in pre pregnancy perior, it was found that more than half of woman reported headache attacks at least once a week, of which those who were diagnosed with migraine reported either recurrence of their infrequenct attacks or those with frequent attacks reported increased frequency. Mean age of participating pregnant woman was 32 year, (18-45 years) Their mean gestation age was 28.31 ± 8.64 (min: 14; max: 41) weeks. Diabetes mellitus and hypothyroidism were the most common comorbidites.

Conclusion: Pregnant woman in this study experienced more migraine attacks during pregnancy that pre pregnancy time. It is recommended to include migraine risk assessment by health professionals to pregnant woman to best needed info regarding condition and management lines.

P241

Clinical characterisation and treatment patterns in tension-type headache: A retrospective study from a public hospital cohort

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Objective: To describe the clinical and demographic characteristics of patients diagnosed with tension-type headache (TTH) between January and June 2025 in a Portuguese headache consultation, and to identify subgroups based on headache frequency, psychiatric and chronic pain comorbidities, and treatment patterns.

Methods: Adult patients diagnosed with TTH according to ICHD-3 criteria were retrospectively reviewed. Data collected included demographics, headache features, psychiatric and pain comorbidities, acute and preventive treatments, adherence, and perceived efficacy.

Results: Of 278 records reviewed, 26 patients (9.4%) met diagnostic criteria for TTH—14 chronic and 12 episodic. Most were female (69%) and of working age, with a mean age of 56.8 years (SD=14.3). Psychiatric comorbidities were present in 73%, mainly anxiety and depression. A minority also fulfilled diagnostic criteria for other chronic pain disorders, including migraine (11.5%) and fibromyalgia (7.7%). Preventive treatment was prescribed in 84.6%, primarily due to attack frequency and impact. Four eligible patients declined it due to reluctance to take daily medication. The most prescribed preventives were amitriptyline, duloxetine, and venlafaxine. Of those prescribed, 22.7% did not initiate treatment, and 60% of these missed follow-up. Among adherent patients, 54.5% reported clinical improvement. Only one discontinued due to side effects. Treatment response was difficult to assess due to clinical heterogeneity and variable adherence.

Conclusion: TTH shows a heterogeneous clinical profile and frequent overlap with psychiatric and chronic pain comorbidities. Identifying these patterns may help optimise individualised and multidisciplinary treatment approaches. The small and selected cohort, limited to a tertiary care setting, restricts generalisability and further correlation.

P242

Perceived ease-of-usability and local tolerability using CGRP monoclonal antibodies autoinjectors versus syringe: An online questionnaire-based study in patients with migraine

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Objective: The aim of the present cross-sectional study was to assess the experience of patients with migraine using either monoclonal antibodies acting on

the CGRP pathway (CGRP-mAbs) prefilled syringes or autoinjectors, regarding local tolerability and perceived ease-of-usability.

Methods: A self-administered electronic questionnaire was created using "Google questionnaires" to collect in patients with migraine treated with CGR-mAbs: demographic and clinical parameters; data related to ongoing preventive CGRP-mAbs treatments and their local tolerability; data on perceived ease-of-usability; data on putative previous Onabotulinumtoxin-A treatment.

Results: The questionnaire was sent to 405 migraine patients and, after 10 days, 69.87% of patients filled-in the electronic form. No significant differences were found among groups in data related to ease-of-usability and local tolerability of CGRP-mAbs regarding simplicity and modality of administration, injection site pain (ISP) and other reactions at the sites of administration. Nevertheless, we could identify young women with chronic migraine as the phenotype more prone to experience ISP during the CGRP-mAbs treatment. Among 96 patients who previously received at least 3 OnabotulinumtoxinA administrations, injections site pain was significantly higher with Onabotulinumtoxin-A compared to CGRP-mAbs (6 ± 4 vs 4 ± 5; p<0.001).

Conclusion: No differences in perceived ease-of-usability and local tolerability can be observed. These findings may also arise economic and ecological implications, considering the lower impact on costs and environmental pollution of prefilled syringes compared to more expensive and polluting plastic autoinjectors.

P243

Head-to-head observational cohort study on the effectiveness and tolerability of subcutaneous monoclonal antibodies acting on CGRP pathway in patients with high frequency episodic migraine and chronic migraine

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Objective: We aimed to compare the effectiveness and safety of galcanezumab, fremanezumab and erenumab for the treatment of chronic and episodic migraine, through real-world data.

Methods: During the run-in period and after the first, the third and the sixth month of treatment, 186 migraine patients treated with erenumab (29.9%), galcanezumab (36.2%) or fremanezumab (33.9%), underwent an extensive interview to assess clinical parameters of disease severity (headache days per month, monthly symptomatic medication intake, average headache pain intensity and headache attack duration) and putative tolerability issues.

Results: After the sixth administration, a statistically significant reduction in monthly headache days compared to baseline was observed for erenumab (12.77 ± 7.9, p<0.001), galcanezumab (11.67 ± 8.61, p<0.001) and fremanezumab (12.76 ± 6.64, p<0.001). Similarly, a statistically significant reduction compared with baseline was observed in monthly symptomatic medication intake, average headache pain intensity and headache attack duration. We found no significant differences between monoclonal antibodies (mAbs) in the reduction of mean monthly headache days after 6-months in the three groups under examination (p=0.119). Contrariwise, a significant higher percentage of patients reported constipation among erenumab group (14% vs 7% vs 4% p=0.02).

Conclusion: No evidence suggests that one antibody may be superior to the others in terms of effectiveness, both in chronic and episodic patients, although galcanezumab and fremanezumab have a lower incidence of constipation due to their ability of inhibiting the effects of CGRP at both the CGRP and AMY1 receptors.

P244

Is atogepant an effective option for migraine patients with treatment failure to Anti-CGRP monoclonal antibodies and OnabotulinumtoxinA? Real-world evidence from 535 patients from the ATO-only consortium

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[9]Hospital Universitario Donostia, Neurología, San Sebastian, Spain
[10]Hospital Universitario de Álava- Txagorritxu, Neurología, Alaba, Spain
[11]Hospital de Tudela, Neurología, Tudela, Navarra, Spain
[12]Hospital Universitario, Neurología, Albacete, Spain
[13]Hospital Universitario Reina Sofia, Department of Neurology, Córdoba, Spain
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Objective: To assess the effectiveness and tolerability of atogepant 60 mg daily over 12 weeks in patients with chronic migraine (CM) who have failed treatment with onabotulinumtoxinA and anti-CGRP monoclonal antibodies (mAbs).
Methods: This ongoing, multicenter, prospective cohort study is being conducted at 16 specialized Headache Units. We focus on patients with CM who failed onabotulinumtoxinA (Botox group) or both onabotulinumtoxinA and anti-CGRP mAbs (Botox+ mAbs group). All participants initiated atogepant and were followed for 12 weeks. Demographics, monthly migraine days (MMD) and Headache Impact Test (HIT-6) were recorded. A good response was defined as a 50% reduction in MMD and a "much or very much improvement" on Patient Global Impression (PGI-C) at 12 weeks of treatment. Retention rate and Treatment Emergent Adverse Events (TEAEs) were monitored.
Results: A total of 535 patients have been registered, of whom 457(85.4%) with CM were classified into the Botox failure group (n=194) and Botox+mAbs failure group (n=215).
Baseline characteristics were similar between groups: mean age 47.3 vs 50.6 years; female 86.1% vs 84.2%; baseline MMD 14 vs 15; HIT-6 median 68 in both.
At 3 months, the atogepant retention rate was higher in the Botox group (74.5% vs 52%; p=0.01), with lower discontinuation due to inefficacy (8.5% vs 25.2%; p=0.01). A ≥50% reduction in MMD was achieved by 51.5% in the Botox group vs 30.8% in the Botox+mAbs group (p=0.001). "Much or very much improved" on PGI-C was also higher in the Botox group (51.9% vs 27.6%; p=0.001).
Conclusion: Atogepant appears to be effective and well-tolerated in chronic migraine patients refractory to onabotulinumtoxinA or mAbs. Moreover, about half of patients "naive" to anti-CGRP therapy appear to have a good response.

Fig. 1

Variables	Chronic Migraine refractory to Botox (n=194)	Chronic Migraine refractory to Botox and MAB (n=215)	p-value
Age, mean (SD)	47.3 (13.2)	50.6 (13.4)	n.s.
Female n (%)	86.1%	84.2%	n.s.
Previous oral preventive n [IQR]	4 [3-5]	4 [3-6]	n.s.

At baseline	Chronic Migraine refractory to Botox (n=194)	Chronic Migraine refractory to Botox and MAB (n=215)	p-value
MMD	14 [10-18]	15 [10-25]	n.s.
HIT6 median [IQR]	68 [65-72]	68 [65-74]	n.s.
3 Month Follow up	n=106	n=123	n.s.
Atogepant retention rate	74.5%	52.o%	0.01
STOP Ineffectivity	8.5%	25.2%	0.01
STOP Tolerability	17.0%	22.8%	n.s.
MMD 3M	8 [3-15]	15 [7-25]	0.002.
50% reduction MMD at 3M	51.5%	30.8%	0.001
"Much or very improved" in PGI-C at 3M	51.9%	27.6%	0.001

P245

Effects of pausing and re-initiating fremanezumab after continuous 24-months treatment for preventing difficult-to-treat migraine: Prospective, multicenter, real-world data from the GRASP study group

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Objective: Current evidence shows that migraine can relapse in previous responders in terms of both increasing frequency and severity following treatment cessation with antiCGRPS. This study, designed by the Greek Research Alliance for Studying headache and Pain (GRASP), aimed to i) prospectively evaluate the effects of treatment cessation in fremanezumab-responsive patients after two years exposure and ii) assess variations in response rates after migraine worsening and treatment re-initiation.
Methods: After obtaining informed consent, we analyzed 149 patients with high-frequency episodic (HFEM) or chronic migraine (CM), who completed 24 months of fremanezumab; mandatory paused fremanezumab and re-initiated it after their migraine worsened. To assess longitudinal variations mostly in monthly migraine/headache days (MMD/MHD) and other efficacy variables, patients were interviewed at baseline (T0); at month-3 (T1); month-24 (T2);

treatment pause period (T3) and at month-3 after fremanezumab re-initiation (T4). The primary objective was to assess the ≥50% response rate at T4, compared to T3 and T2.
Results: Migraine relapsed in all previous responders at T3 with an average duration to re-initiation of 3 months (range: 3 - 5). Fremanezumab re-initiation was not equally effective, as evidenced by lower response rates, mostly in CM patients. At T4, 6 HFEM and 27 CM failed to obtain ≥50% MMD/MHD reduction, compared to T3. The rate of super-responders also dropped at T4, compared to T2.
Conclusion: Discontinuation of fremanezumab after month-24 leads to a rise in MMD/MHDs. After fremanezumab re-initiation, a relatively reduced effectiveness in the first three months might occur, compared with the pre-fremanezumab cessation. Our findings doubt the rationale behind mandated treatment pauses.

P246

Cognitive functions comparison between osmophobic and non-osmophobic migraine sufferers

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Objective: Osmophobia (Osm) is a particular type of odour aversion often associated to migraine. Instead, olfaction deficit has been associated to cognitive impairment. Thus, we inquired whether Osm migraine patients could exhibit a different cognitive profile compared to those without this symptom (NOsm).
Methods: We conducted a cross-sectional prospective study involving Osm and NOsm migraine subjects. After excluding conditions potentially affecting olfaction or cognitive functioning, migraine characteristics were collected. Then, cognitive performance was assessed using the Montreal Cognitive Assessment (MoCA), the Rey Auditory Verbal Learning (RAVL), the Rey-Osterrieth Complex Figure (ROCF), the Multiple Features Target Cancellation (MFTC) and the Stroop Colour and Word (SCW) tests. Statistical significance was set at $p < 0.05$.
Results: We enrolled 50 migraine patients with median age of 38.0 (29.0-45.0) years, 27 of whom with Osm. Osm patients reported a median of 5 worsening and 2 causative odours, with cigarette smoke being the most frequently mentioned in both cases (85.2% and 37% of Osm patients, respectively). Osm patients resulted to have a longer migraine history, more frequent pain exacerbation with physical activity and complaint of nausea/vomiting. Cognitive performance did not differ significantly between Osm and NOsm groups in none of the tests. The only significant difference was a slower Stroop Reading Time Score in NOsm patients. Both groups performed below average on cognitive tests compared to the general population, showing that migraine patients, regardless of Osm presence, present with slight cognitive impairment.
Conclusion: To our knowledge, this is the first study to compare neuropsychological functions of Osm and NOsm migraine patients. Despite greater clinical severity in Osm patients, no cognitive differences were found. Overall, migraine patients performed slightly below the general population"s expected levels.

P247

Rimegepant for acute treatment of atypical headache syndromes: A case series

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Objective: Rimegepant, an oral CGRP receptor antagonist approved for migraine treatment, has shown excellent efficacy in typical migraine, but its role in atypical headache syndromes remains poorly defined. Given the suspected involvement of CGRP in several rare headache disorders, we report our experience using rimegepant for acute treatment in three patients with migralepsy, familial hemiplegic migraine (FHM), and airplane headache, all resistant to standard therapies.
Methods: Three young adults (aged 20–50) were treated: a male with migralepsy, a female with FHM, and a female with airplane headache. The migralepsy patient became resistant to NSAIDs; the FHM patient had limited, inconsistent response to prochlorperazine and ketorolac, and no benefit from NSAIDs, dexamethasone, acetazolamide, or IV magnesium sulfate. The airplane headache patient was unresponsive to any treatment. Rimegepant 75 mg was taken at attack onset. Two patients were on preventive therapy; the airplane headache patient was not. None had neurological comorbidities.
Results: All patients had complete symptom resolution within 5–90 minutes, without rescue medication. Response remained stable over one year. Attack frequency was ~3/month (migralepsy), 4–5/year (FHM), and ~2/month (flight-triggered). No adverse events occurred. The airplane headache patient regained confidence in flying for work, improving quality of life. Others also reported improved functional stability and reduced attack-related anxiety.

Conclusion: These cases support the potential of rimegepant as a safe and effective acute treatment in select atypical headache syndromes with suspected CGRP involvement. Further studies are needed to confirm these findings.
Patients gave their consent to publish their details in an open access journal.

Fig. 1

N° Case	Diagnosis	Age/sex	Prior Treatments	Reasons of suspension	Attack Frequency	Prophylaxis
Case 1	Migralepsy	24/M	NSAISs, cetaminophen, Betamethasone	Poor efficacy	3/months	Lamotrigine
Case 2	Familial Hemiplegic migraine	45/F	NSAIDs, ketorolac, dexamethasone, acetazolamide, $MgSO_4$	Ineffective	4-5/years	Topiramate
Case 3	Airplaine headache	28/F	NSAIDs, triptans	Ineffective, adverse reaction	2/months	No

Fig. 2

N° Case	NRS	Therapy	Pain free	Adverse event	Pain recurrence after 2 hours	Rescue medication in the 24 hours
Case 1	10	Rimegepant 75 mg	70-90 min	No	No	No
Case 2	8	Rimegepant 75 mg	30 min	No	No	No
Case 3	0	Rimegepant 75 mg	5 min	No	No	No

P248

Real-world treatment patterns in migraine in six European countries: A systematic review

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Objective: Migraine affects 14%-26% of adults in Europe, with a higher prevalence in women than in men. In the absence of a simple diagnostic test for migraine, many people remain undiagnosed and without adequate care despite the availability of a range of effective treatments. This systematic review aims to identify and summarize real-world evidence on treatment patterns for migraine in Europe.
Methods: We searched MEDLINE, Embase, and grey literature sources for observational studies published from 2018-2024. Eligibility criteria were studies conducted in France, Germany, Spain, Italy, or the United Kingdom (EU5) or Belgium reporting migraine treatment patterns data.
Results: From 4,481 records identified by the literature searches, 102 observational studies were included, mostly from Italy (40%) and Spain (30%). Evidence from Italy, Spain, Germany and the UK indicates that more than 20% of patients do not receive any migraine-specific treatment despite meeting migraine diagnostic criteria. In line with clinical guidelines, triptans are the most frequently used acute treatment; however, some evidence from Spain indicates divergence from guideline advice against the use of opioids and ergots as acute treatments. Approximately 25%-40% of patients in the EU5 receive some form of preventive medication, but estimates vary widely and data on specific drug classes are lacking. Adherence to preventive therapy is low; about 75% of patients discontinue treatment within a year, mostly due to adverse events. Despite the higher prevalence of migraine in women, evidence relating to female-specific migraine (eg menstrual migraine, migraine during pregnancy/breastfeeding) are sparse.
Conclusion: Our findings reveal some disparities between clinical guidelines and clinical practice in diagnosing and managing migraine appropriately. The paucity of data on preventive therapies and female-specific migraine highlights important evidence gaps that should be addressed to improve treatment strategies and patient outcomes.

P249

Mediating effect of depressive symptoms on the relationship between chronic headache, migraine and cardiovascular disease among Chinese population: Evidence from CHARLS

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Objective: This study aims to explore the relationship between chronic headache, migraine and the risk of cardiovascular disease in middle-aged and older Chinese adults, particularly assessing the mediating effect of depressive symptoms.
Methods: Utilizing data from the China Health and Retirement Longitudinal Study (CHARLS), the analysis included 10,172 participants aged 45 and older who were free of cardiovascular disease at baseline in 2011. Longitudinal data were collected over a nine-year period using validated questionnaires to assess the presence of chronic headache, migraine, and depressive symptoms were measured using the CES-D-10 scale. New cases of cardiovascular disease were identified based on reported stroke or cardiac events. Multivariable logistic regression models were employed to evaluate the associations and mediation effects.
Results: The findings demonstrated a significant increase in cardiovascular disease risk among individuals with chronic headache (OR=1.34, 95% CI: 1.15-1.55) and migraine (OR=1.42, 95% CI: 1.15-1.76). Depressive symptoms mediated approximately 32.8% and 30.1% of the relationship between chronic headache/migraine and cardiovascular diseases risk, respectively. Subgroup analyses indicated that age

significantly influenced the association between migraine and cardiovascular disease.

Conclusion: Chronic headache and migraine are associated with the risk of cardiovascular disease in middle-aged and older Chinese adults. Depressive symptoms mediate the association between chronic headache, migraine, and cardiovascular disease risk.

Fig. 1

Variables	Model1		Model2		Model3		Model4	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Headache								
No	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Yes	1.58 (1.39 ~ 1.81)	<.001	1.57 (1.37 ~ 1.80)	<.001	1.56 (1.36 ~ 1.80)	<.001	1.34 (1.15 ~ 1.55)	<.001
Migraine								
No	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Yes	1.70 (1.39 ~ 2.06)	<.001	1.69 (1.38 ~ 2.06)	<.001	1.67 (1.35 ~ 2.05)	<.001	1.42 (1.15 ~ 1.76)	0.001

OR: Odds Ratio, CI: Confidence Interval
Model1: Crude
Model2: Adjust: sex, age, marry, education, location
Model3: Adjust: sex, age, marry, education, location, gxy, tnb, sleep, bmi, drinke, smokee
Model4: Adjust: YY, sex, age, marry, education, location, gxy, tnb, sleep, bmi, gan, shen, drinke, smokee

Fig. 2

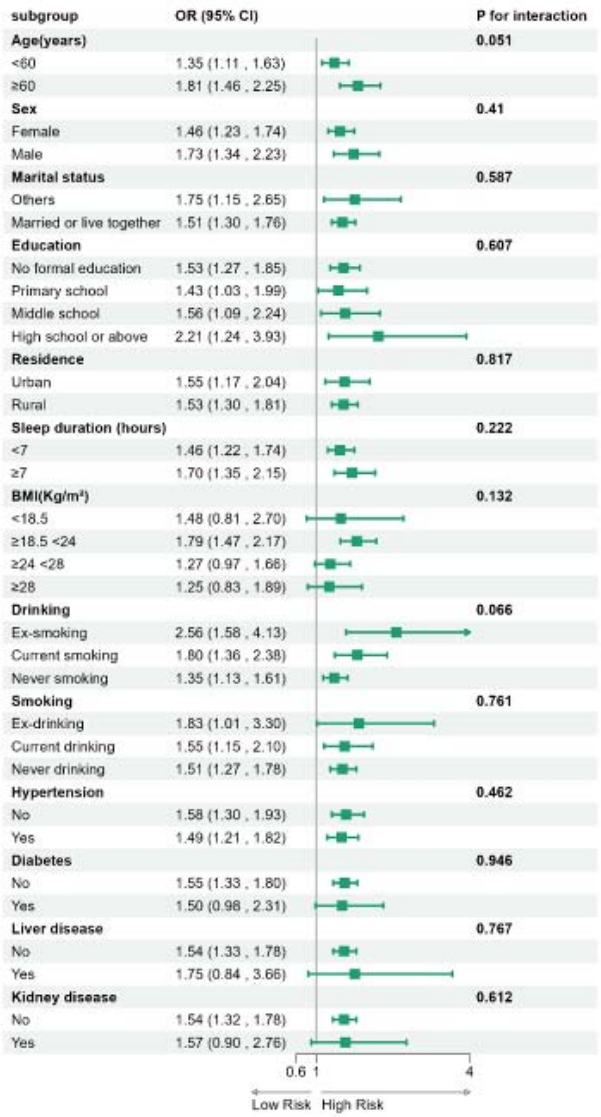
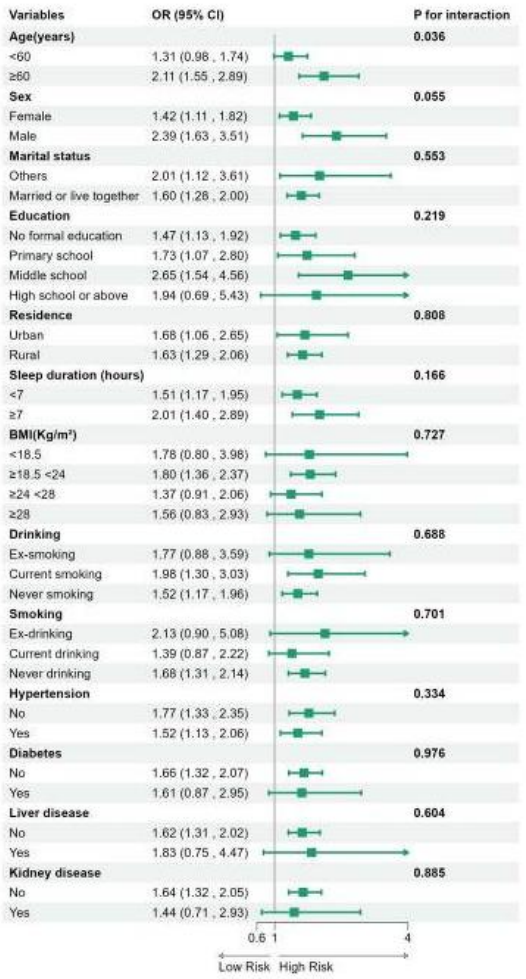


Fig. 3



P250

Prospective, real-world data from the Greek Research Alliance for the Study of headache and Pain (GRASP), on the efficacy and safety of eptinezumab in migraine prophylaxis

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Objective: The aim of this real-world prospective study, designed by GRASP, was to determine the efficacy and safety of prophylactic treatment with eptinezumab in patients with high-frequency episodic migraine (HFEM) or chronic migraine (CM) who had previously failed at least 3 prophylactic treatments.

Methods: After obtaining their informed consent, 100 patients (45 HFEM / 55 CM) who received at least 1 cycle of eptinezumab 100mg, were studied. Clinical response (at least 50% MHD reduction) was calculated by recording the change in MHD after eptinezumab treatment compared to baseline. The changes in moderate/severe MHD and monthly days with acute medication intake (MAI) after eptinezumab treatment, compared to baseline, were also calculated. The effect of treatment on the patients" disability and quality of life was assessed using the MIDAS, HIT-6 Test and EQ-5D scales.

Results: An at least 50% MHD reduction compared to baseline was observed in the majority of treated patients (68/100; 68%). A reduction in moderate/severe headache days/month (−72%) and in MAI (−77%) was also observed after eptinezumab treatment, compared to baseline. Patients' disability scores decreased in MIDAS (−60%) and HIT6 (−20%), while their quality of life improved significantly (+150%). The potential rapid efficacy of eptinezumab during the 1st month after treatment onset, compared to baseline, was assessed in a subgroup of 21 CM patients having >22 MHD. After the 1st week of treatment, a significant reduction in headache days was observed in the majority of these patients (13/21; 61.9%), compared to baseline and remained stable throughout the 1st month post-eptinezumab. Eptinezumab was generally safe and well tolerated.

Conclusion: Our prospective results in a real-world setting further support the view that eptinezumab is an effective and safe prophylactic treatment in difficult-to-manage patients with HFEM or CM. The onset of its response is generally rapid.

P251

Effectiveness and tolerability of Atogepant: Real world evidence in a large cohort of 313 migraine patients with 3 month- follow-up. AtoOnly consortium

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Objective: Atogepant has shown efficacy and safety in treatment of episodic and chronic migraine (CM). However, the population represented in randomized clinical trials (RCTs) differs from the population observed in real-world setting. The aim of this study is to describe the effectiveness and tolerability of Atogepant 60mg daily in clinical practice in a large series of patients with migraine, some of them excluded from RCTs.

Methods: Multicenter prospective cohort study of consecutive patients with chronic and high-frequency episodic migraine (HFEM) assessed in 17 Headache Units with prior failure to three or more migraine preventive drugs including Anti-CGRP monoclonal antibodies (mAbs) or OnabotulinumtoxinA according to the national guideline for public reimbursement of Atogepant.

Headache neurologists routinely collected demographic variables, monthly migraine days (MMD) and Headache Impact Test (HIT-6) at baseline and further follow-up.

A good response was defined as a 50% reduction in MMD and a Good Impression "much or very much improvement" on Patient Global Impression (PGI-I) at 12 weeks of treatment. Retention rate and Treatment Emergent Adverse Events (TEAEs) were monitored.

Results: We enrolled 574 patients and we present data of the 313 patients already achieving 3 months follow-up. Age 46.6 yo (SD 13.0), females 84.7%, chronic migraine 256 (81.2%). HFEM with failure to at least 3 oral preventive drugs (n=46), HFEM with also failure to mAbs (n=11), CM with OnabotulinumtoxinA resistance (n=110) and CM refractory to both OnabotulinumtoxinA and mAbs (n= 142). The retention rate was 69.0%. The main reasons for treatment discontinuation were inadequate tolerability (16.6%) and lack of effectiveness (14.4%).

The 50% responder rate and Good impression PGI-I were 36.4% and 42.5%, respectively.
Conclusion: Atogepant is a new treatment option for migraine patients considered resistants or refractory, although in 31% of cases, treatment needs to be withdrawn before 3 months.

P252

Blood pressure trends and adverse effects in migraine patients receiving anti-CGRP monoclonal antibodies

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Objective: To evaluate the safety and side effect profile of anti-CGRP monoclonal antibodies (mAbs) in a real-world cohort of migraine patients, with particular attention to vascular-related events and blood pressure changes.
Methods: This observational, retrospective study included 59 patients treated with anti-CGRP mAbs at a single centre. Data on adverse effects were collected from clinical records. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded at treatment initiation and quarterly thereafter per protocol. Data was analysed using paired t-test, linear mixed-effects model or pairwise comparison to baseline. Adjustments to antihypertensive medications were also documented.
Results: Most patients were on anti-CGRP ligand mAbs (n=55, 93%). Side effects were infrequent and mild. Raynaud's phenomenon was reported in 3 patients (5%), one of whom required permanent treatment discontinuation. Constipation led to mAb switch in 2 patients (3%). There were no significant changes in mean SBP or DBP from baseline to T3 (SBP p=0.77, DBP p=0.98), or during extended treatment (SBP p=0.64, DBP p>0.05 in all pairwise comparisons). Antihypertensive therapy adjustments were needed in 6 patients (10%). Of these, 2 had a prior diagnosis of hypertension; 1 patient continued to experience hypertension after interruption of mAb therapy, while another required only transient dose changes that were quickly reversed. No serious cardiovascular events were reported during the observation period.
Conclusion: In this real-world cohort, anti-CGRP mAbs were generally well tolerated. While vascular-related side effects such as Raynaud's phenomenon and blood pressure fluctuations were observed in a minority of patients, they were often incidental and rarely led to permanent discontinuation. These findings underscore the need for individualized monitoring, especially in patients with pre-existing vascular conditions, but support the overall safety of anti-CGRP mAbs in clinical practice.

P253

Use of GLP-1 receptor agonists is linked to increased migraine risk and enhanced migraine-specific medication utilization in patients with T2DM

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Objective: Type 2 diabetes mellitus (T2DM) and migraine are both prevalent conditions. Preclinical evidence suggests that reduced glucagon-like peptide-1 (GLP-1) receptor activity may contribute to chronic migraine pathophysiology. This study examined whether GLP-1 receptor agonists (GLP-1 RAs), as well as dipeptidyl peptidase-4 inhibitors (DPP-4Is) and sodium-glucose cotransporter 2 inhibitors (SGLT2Is), are associated with an increased risk of migraine in T2DM patients.
Methods: Using the TriNetX database, we retrospectively analyzed data from T2DM patients on Metformin (aged ≥18 years) between 2015 and 2024. Participants with a pre-existing migraine diagnosis or fewer than two clinical visits were excluded. The outcomes assessed were triptan and CGRP antagonist use, along with new migraine diagnoses. Kaplan–Meier survival analysis and propensity score matching ensured balanced comparisons over a minimum follow-up of six months.
Results: In matched cohorts, GLP-1 RA users (n = 52,593 per group) exhibited significantly higher rates of triptan use, CGRP antagonist use, and migraine diagnoses compared with those on sulfonylureas (SUs). Similarly, DPP-4I treatment (n = 51,046 per group) was linked to an increased migraine diagnosis rate, and SGLT2I users (n = 58,685 per group) showed higher CGRP antagonist use versus SUs.
Conclusion: Among T2DM patients on Metformin, GLP-1 RAs appear to be associated with a higher prevalence of migraine and migraine-specific medication use compared to SUs, DPP-4Is, and SGLT2Is. Further investigations are warranted to validate these findings and explore their underlying mechanisms.

Fig. 1

Table 1 Comparison of hazard ratios and survival probability for triptan use, CGRP antagonist use, and migraine diagnosis between GLP-1RAs and SUs

N=52593				
Triptans				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + GLP-1 RAs	338	97.059%	1.801	(1.494, 2.171)
Metformin + SUs	163	99.004%		
CGRP antagonists				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + GLP-1 RAs	130	98.564%	2.356	(1.692, 3.280)
Metformin + SUs	48	99.506%		
Migraine				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + GLP-1 RAs	512	95.372%	1.740	(1.498, 2.022)
Metformin + SUs	256	97.664%		

Fig. 2

Table 2 Comparison of hazard ratios and survival probability for triptan use, CGRP antagonist use, and migraine diagnosis between DPP-4Is and SUs

N=51046				
Triptans				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + DPP-4Is	119	99.074%	1.206	(0.921, 1.579)
Metformin + SUs	95	99.444%		
CGRP antagonists				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + DPP-4Is	37	99.701%	1.280	(0.783, 2.091)
Metformin + SUs	28	99.785%		
Migraine				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + DPP-4Is	198	97.914%	1.244	(1.008, 1.535)
Metformin + SUs	154	98.342%		

Fig. 3

Table 3 Comparison of hazard ratios and survival probability for triptan use, CGRP antagonist use, and migraine diagnosis between SGLT2Is and SUs

N=58685				
Triptans				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + SGLT2Is	149	98.003%	1.229	(0.963, 1.568)
Metformin + SUs	114	99.472%		
CGRP antagonists				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + SGLT2Is	67	97.570%	1.885	(1.247, 2.849)
Metformin + SUs	34	99.800%		
Migraine				
	Patient with Outcome	Survival Probability	HR	95% CI
Metformin + SGLT2Is	233	96.574%	1.153	(0.952, 1.396)
Metformin + SUs	191	97.728%		

P254

The CONFIDENCE study: Impact of timing, headache severity and functional impairment at intake of rimegepant on pain relief, return to function and treatment satisfaction

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Objective: Investigate the effect of timing, headache intensity and functional impairment when taking rimegepant (RIM) on meaningful pain relief (MPR), meaningful functional improvement (MFI) and treatment satisfaction (SAT).

Methods: This study was conducted amongst US adults with migraine, recruited in the Migraine Buddy app, completing a 28-day daily diary for acute RIM treatment, assessing time to MPR and MFI, and SAT. Disability and pain intensity at medication intake were measured, as was time in relation to the start of the attack. Achieving "the endpoints", MPR and MFI at 2h and overall SAT is reported as % attacks [%MPR; %MFI; %SAT].

Results: For every RIM-treated attack (n=2104), medication intake was recorded (% attacks):

- Before any sign of the migraine attack, but in anticipation of one starting (2.0)
- At the first sign of the migraine attack, before the pain started (18.2)
- At the first sign of headache pain (29.5)
- After the pain has started (40.9)
- After another drug had not provided enough relief (8.2)
- Other (1.2)

The % of attacks achieving the endpoints was assessed at 6 post-treatment timeframes (Fig1a):

- 16-30 min [68;59;68]
- 31-45 min [65;61;72]
- 46-60 min [65;63;76]
- >1h -2h [62;57;70]
- >2h [52;50;62]

The % of attacks achieving the endpoints was assessed based on headache pain intensity at RIM intake (Fig1b):

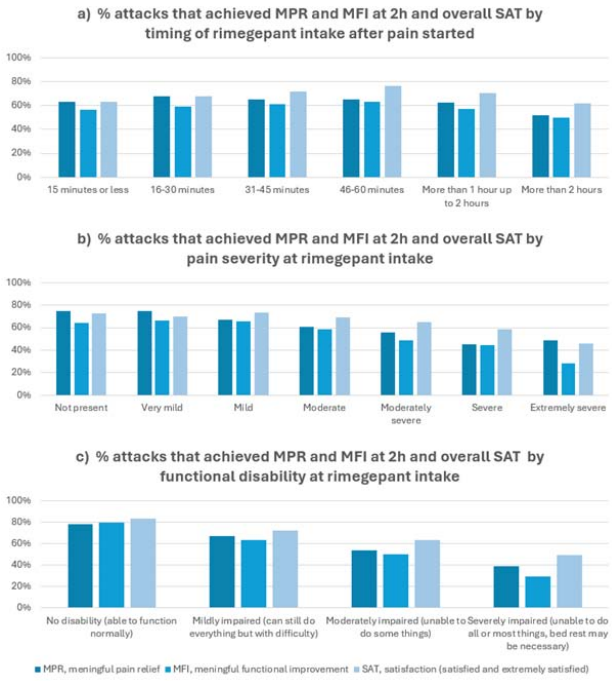
- not present [75;64;73]
- very mild [75;66;70]
- mild [67;65;74]
- moderate [61;59;69]
- moderately severe [56;49;65]
- severe [45;45;59]
- extremely severe [49;29;46]

The % of attacks achieving the endpoints was assessed based on ability to perform daily activities at RIM intake (Fig1c):

- No disability [78;79;83]
- Mildly impaired [67;64;72]
- Moderately impaired [54;50;63]
- Severely impaired [39;29;49]

Conclusion: This study suggests that RIM outcomes improve if headaches are treated soon after onset, at lower levels of pain intensity and at lower levels of disability using measures of MPR and MFI at 2h and overall SAT.

Fig. 1



P255

Clinical predictors of sustained response in patients with resistant migraine afterdiscontinuation of anti-CGRP monoclonal antibodies

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Objective: Monoclonal antibodies targeting CGRP (CGRP-Mabs) have shown efficacy as preventive treatment in migraine. The optimal duration of treatment has not been clearly established. We aim to evaluate clinical predictors of response after discontinuation of therapy.

Methods: Ambispective, unicentric, observational cohort study conducted at a tertiary hospital. Patients diagnosed with Chronic or High Frecuency Episodic Migraine (CM, HFEM) who showed a positive response to anti-CGRP monoclonal antibodies were included. Treatment duration was determined by the Regional Health Authority and standardized to 12 months. At least one year of follow-up after discontinuation was done. Patients were classified according to their response at the end of treatment in Excellent (absence of headache), Optimal (fewer than 4 headache days/month), Modest (4–6 days/month) and Insufficient (more than 6 days/month). Kaplan–Meier survival curves estimated time from treatment cessation to relapse, defined as initiation of new preventive therapy or return to baseline headache frequency.

Results: A total of 143 patients were included, with median age of 46.6 years [IQR: 39.3–52.7]. 87.3% were female. 115 patients (80.4%) had CM and 28 (19.6%) HFEM. At treatment completion, 6 patients had an excellent response, 51 optimal, 89 modest and 51 insufficient. Median time to relapse was 46.4 months [IQR: 39.6–52.8]. A significant difference was observed in relapse timing based on the number of headache days per month (p=0.04).

Conclusion: Patients with a better response to CGRP-Mabs may experience a more sustained response when therapy is discontinuated.

Fig. 1

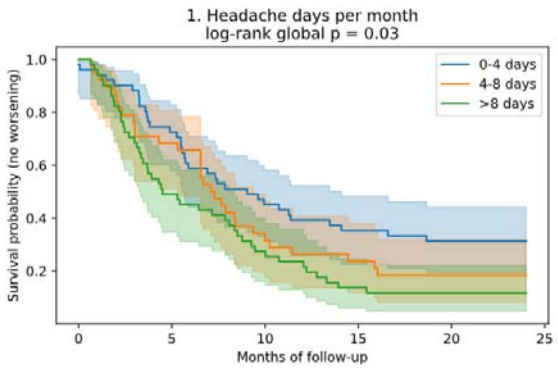
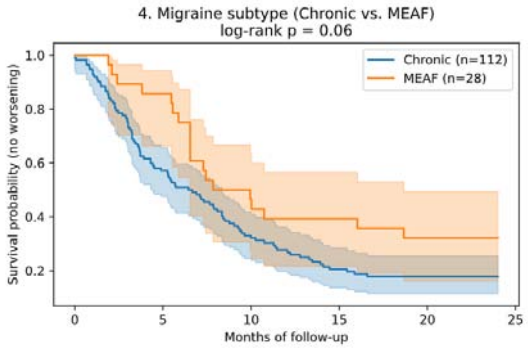


Fig. 2



P256

Understanding diagnosis and misdiagnosis in resistant and refractory migraine: Findings from the REFINE study

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Objective: A subset of migraine patients do not respond well to preventive treatments, leading to resistant or refractory migraine, which significantly affects their lives. These patients may be at risk of being misdiagnosed or subjected to unnecessary testing. We evaluated the history of misdiagnosis and use of neuroimaging in patients with resistant (ResM) and refractory migraine (RefM) compared to those without resistance or refractoriness (NRNRM).

Methods: Participants from the multicenter, prospective REFINE study were classified as RefM, ResM, and NRNRM, according to the proposed European Headache Federation criteria. We assessed the baseline data about diagnosis, including misdiagnosis, clinical and instrumental access in the medical history of those patients.

Results: In a cohort of 689 migraine patients (82.7% female, median age 46 [IQR 37.0-54.0]), 51.5% were classified as NRNRM, 37.9% as ResM, and 10.9% as RefM. Patients with ResM and RefM were older, had longer disease duration, more chronic migraine, more treatment failures and higher disability and psychological distress scores (HIT-6, HADS) compared to NRNRM (all $p<0.001$). Misdiagnosis occurred in 28.1% of cases, most commonly involving cervical spine disorders, sinusitis, hormonal headache, and temporomandibular disorders. Misdiagnoses were less frequent in RefM patients (15.0%) than in ResM (31.1%) and NRNRM (28.4%) groups ($p=0.025$). ResM and RefM patients underwent neuroimaging (MRI/CT) more often than NRNRM and had more additional diagnostic evaluations. No significant associations were found between misdiagnosis and factors such as age, disease duration, or clinical scale scores.

Conclusion: ResM and RefM migraine patients experience greater disease burden and undergo more diagnostic testing. Misdiagnosis is common across all groups, but less frequent in RefM, often resulting in unnecessary, time-consuming, and costly diagnostic procedures. These challenges further amplify the psychological, social and economic burden of migraine.

P257

Eptinezumab in patients with prior failure to other anti-CGRP monoclonal antibodies compared to naive patients: A real-world study in two Portuguese hospitals

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Objective: Eptinezumab, the latest antiCGRP monoclonal approved in Europe for migraine prevention, is being used mostly in patients that did not respond to other monoclonals, a condition not evaluated in any clinical trial rendering RWE so important in this context. The objective of this study was to evaluate efficacy of eptinezumab in a population that previously failed antiCGRP monoclonal antibodies comparing to its effectiveness in a naïve population.

Methods: Retrospective study in two Portuguese centres of all patients treated with Eptinezumab, for the last 18 months, comparing patients that have

never used antiCGRP treatments (naïve) to those patients that previously failed one or two of them

Results: 77 patients included, 80% women, median age 46 Y. Median number of headache/month was 17.3 days; 24.4% had daily headache. 69% previously failed one (36 patients) or two (17 patients) antiCGRP monoclonal antibodies. In anti-CGRP naïve migraineurs Eptinezumab reduced headache days by half in 3 months and to a quarter in 6 months, whereas is patients that switched from another monoclonal the reduction was less than 35% at month 3 and 20% at month 6. Half of naïve patients had at least a 75% reduction of mean headache days/month and only 7% of the other group achieved similar reduction. Half of the monoclonal failure"s patients did not respond to Eptinezumab (less than a 30% reduction in headache frequency) compared with 22% in naïve patients. All naïve patients scored 6 or 7 in the Global Impression of Change scale.

Conclusion: Eptinezumab achieved excellent results in CGRP treatment naïve patients (75-100% response in half of our patients) with improvements in QoL in all of them compared to a modest but still significant response in patients with previous CGRP treatment failure. Treating earlier will produce much better outcomes and permit aiming for migraine freedom.

P259

Clinical treatment of cluster headache with the serotonergic indoleamine psychedelics psilocybin and LSD and with ketamine: A case series

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Objective: Cluster headache is an excruciating condition for which standard treatments are usually insufficient. Evidence has accumulated that serotonergic psychedelic indoleamines including psilocybin and LSD can be effective in preventing attacks.

Methods: In this case series, nine patients with episodic and chronic cluster headache that didn"t respond to conventional treatments were treated at a clinic with psilocybin or LSD, under compassionate use provisions, and in most cases separately with ketamine.

Results: All patients responded positively to at least one of the treatments, and eight of nine responded positively to the treatment with the psychedelic indoleamines, in several cases with extended periods free of attacks.

Conclusion: These clinical data, though of an exploratory nature, add to the existing pool of evidence for the usefulness of these substances for treating cluster headache, and further support the lowering of legal and regulatory barriers to medical access to the psychedelic indoleamines.

Fig. 1

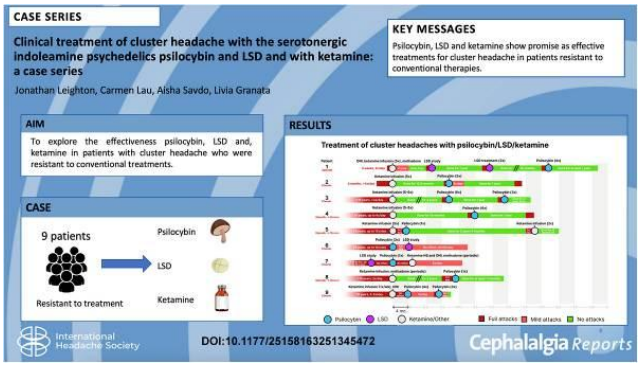
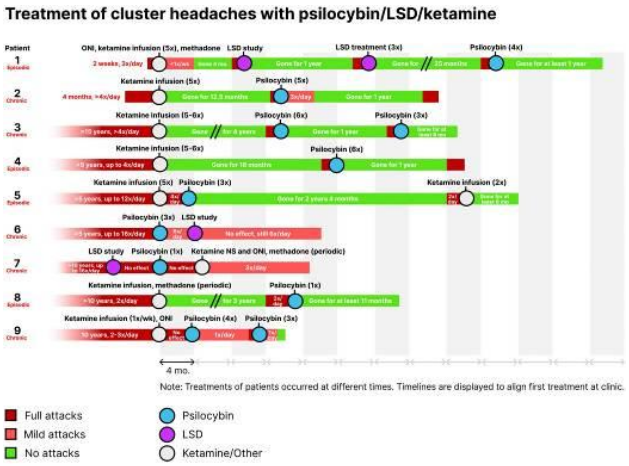


Fig. 2



P260

Migraine and visual snow syndrome: Exploring shared pathways through hallucinogen-induced perceptual disturbances

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Objective: Visual Snow Syndrome (VSS) is a condition marked by persistent visual phenomena resembling television static, often accompanied by afterimages, entoptic effects, and nyctalopia. Migraine is the most frequent comorbidity, though the basis for this association remains unclear. VSS pathophysiology points to dysfunction in the salience network and thalamo-cortical visual processing—both similarly affected by certain hallucinogens.

Methods: This work is based on two clinical case reports.

Results: The first case refers to a 29-year-old male factory worker with episodic migraine without aura developed persistent bright dots, photic flashes, and

entoptic phenomena after a single LSD use, lasting six months and more evident in bright environments. Neurological and ophthalmological exams were normal, brain MRI revealed a pineal cyst, with normal EEG and OCT. Treatment with amotrigine 25 mg improved headache but visual symptoms persisted. The second case concerns a 24-year-old female engineering PhD student with chronic migraine with visual aura, hypothyroidism, polycystic ovary syndrome, and ADHD. After a single exposure to MDMA, she reported continuous "visual noise" and afterimages lasting eight months, worsened by screen exposure. Neurological and ophthalmological evaluations were normal. Brain MRI revealed a pineal cyst. She showed no improvement with lamotrigine or gabapentin but responded to valproate 250 mg and cognitive behavioral therapy.

Conclusion: Hallucinogens modulate thalamic activity, particularly its inhibitory role in sensory processing, contributing to perceptual disturbances. In migraine, a lowered thalamic threshold may promote visual symptoms, further exacerbated by hallucinogens. These cases suggest overlapping pathophysiological mechanisms between VSS and hallucinogenic effects, highlighting the thalamus as a key structure involved in both conditions.

P261

Global trends in headache disorder burden across socio-demographic index regions: A comprehensive analysis using global burden of disease data (1990-2021)

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Objective: To analyze global trends in headache disorder burden from 1990 to 2021 across different sociodemographic regions and sex groups.

Methods: We utilized data from the Global Burden of Disease Study 2021 to examine headache disorder trends across six regions stratified by Socio-demographic Index (SDI): High, High-middle, Middle, Low-middle, Low SDI, and Global estimates. Estimated Annual Percentage Change (EAPC) with 95% confidence intervals was calculated for DALYs, incidence, and prevalence from 1990-2021, stratified by sex. We used linear regression to calculate EAPCs. Statistical significance was assessed based on non-overlapping confidence intervals with zero.

Results: DALYs: Global burden increased (EAPC: 0.24%, CI: 0.22–0.26), with males showing greater rises (0.30%, CI: 0.29–0.32) than females (0.20%, CI: 0.17–0.22). Middle SDI countries had the sharpest rise (0.46%, CI: 0.42–0.51); High SDI showed stability (−0.001%, CI: −0.015–0.013). **Incidence:** Global increase was modest (0.06%, CI: 0.04–0.07). Middle SDI rose (0.23%, CI: 0.19–0.26); High SDI declined (−0.10%, CI: −0.11 to −0.09). Males had greater increases across most regions. **Prevalence:** Global prevalence rose (0.19%, CI: 0.17–0.21), with the greatest rise in Middle SDI (0.41%, CI: 0.37–0.46). High SDI remained stable.

Conclusion: Headache disorders are an escalating global burden with marked disparities. Middle SDI countries showed the steepest increases, while High SDI remained stable or declined. Males exhibited consistently higher burden growth, especially in DALYs and incidence. These findings underscore the need for targeted, SDI-sensitive and sex-specific strategies to reduce the headache burden.Headache disorders are an escalating global burden with marked disparities.

Fig. 1

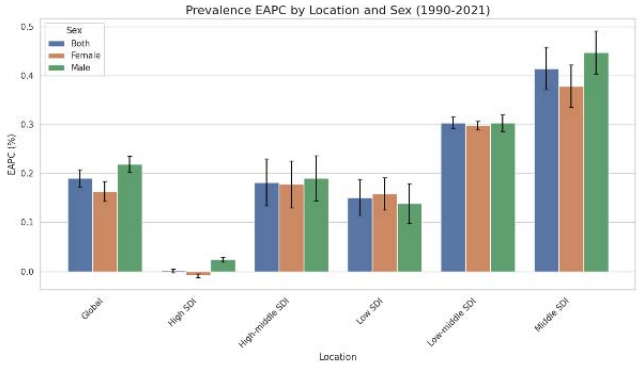


Fig. 2

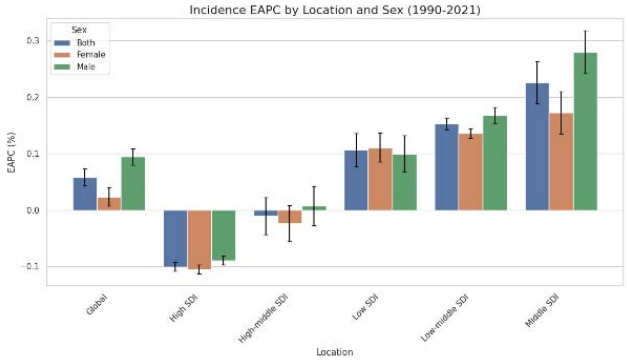
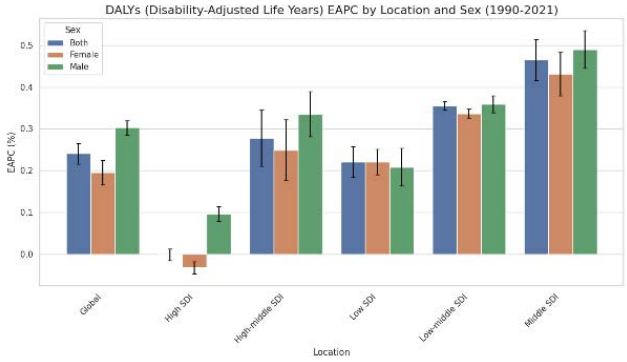


Fig. 3



P262

Migraine patients with cranial autonomic symptoms and their response to monoclonal antibodies against CGRP(R) – A real world study

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Objective: The Austrian Migraine Register (AMR) collects data from patients receiving CGRP-targeted migraine preventive treatment. Cranial autonomic symptoms (CAS), associated with better triptan response, may also predict CGRP monoclonal antibody (mAb) efficacy. CAS severity is assessed using the Cranial Autonomic Parasympathetic Symptoms (CAPS) scale. Objectives:

• To evaluate differences in monthly headache day (MHD) reduction between CAS-positive and CAS-negative subjects.

• To assess whether MHD reduction differs across CAPS severity groups.

• To examine sex-based differences in MHD reduction and CAPS severity.

Methods: This real-world study aims to enroll 100 participants. AMR patients who reported CAS and agreed to contact were interviewed by phone. A standardized interview confirmed CAS-related migraine, and the CAPS scale (0–10) was collected. Follow-up interviews are scheduled ≥3 months later. CAPS scores were grouped as mild (1–2), moderate (3–4), severe (5–6), and very severe (≥7).

Results: So far, 56 CAS-positive patients are eligible (50 female, 6 male; mean age 40.6). No significant difference in MHD reduction was found across CAPS groups ($p = 0.335$). A weak but significant correlation was found between CAPS and MHD reduction ($r = 0.295$, $p = 0.029$). No significant sex-based difference was observed.

Conclusion: liminary data suggest that greater CAPS reduction correlates with greater MHD reduction, indicating stronger treatment response in patients with prominent CAS. Recruitment is ongoing to complete the planned sample and allow full analysis.

P263

Vestibular migraine response to gepant dual therapy – A case report

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Objective: Atogepant and rimegepant are new drugs blocking the CGRP receptor for migraine prevention (atogepant and rimegepant) or migraine acute therapy (rimegepant). Their role in vestibular migraine is not yet defined: some evidence suggest efficacy of monoclonal antibody antiCGRP therapies in vestibular migraine (1), CGRP receptors are abundant in vestibular nuclei (2) and in animal models CGRP intervenes in vestibular symptomatology (3). Simultaneous off-label use of more than one gepant is being more frequently reported in real world: patients taking one gepant daily for migraine prevention take another gepant for acute treatment. The safety and efficacy of this combination is not known.

Methods: We report a case of vestibular migraine, using both gepants, with a good response to atogepant preventively and to rimegepant acutely. Informed consent was given.

Results: Case Report: a 36-year-old female with a 10 year long vestibular migraine and fibromyalgia, previously failed 4 oral preventive treatments. She started rimegepant for migraine prevention with excellent response. Later treatment was switched to atogepant for migraine prevention but maintained rimegepant for acute treatment. With gepants migraine days were reduced from 10 to 15 days/ month to 1-2 per month. She did not experience any side effects. Vertigo disappeared completely after starting atogepant and fibromialgic symptoms were also greatly reduced. She is on atogepant now for 6 months and uses rimegepant as acute treatment whenever she gets a migraine: rimegepant works very fast (less than one hour) and is very effective (pain free in less than 2 hours).

Conclusion: In this vestibular migraine patient, gepants proved to be very effective in treating both headache and vertigo. The fact that rimegepant continues to be effective as acute medication in a patient already taking 60 mg of atogepant daily for prevention, suggests that there is room for additional CGRP blockade, without, in this case, inducing side-effects.

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P264

Greater occipital nerve blocks in episodic cluster headache – Real-world clinical experience

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Objective: Real-world experience with greater occipital nerve blocks (GONBs) for the preventive treatment of episodic cluster headache (EHC) is lacking. We aim to describe the clinical experience with GONBs for the preventive treatment of EHC in a Headache Unit of a Spanish hospital.

Methods: Retrospective observational study. Adult patients with ECH, according to the ICHD-3, treated with GONBs as a preventive treatment were included. Patients with other concomitant headache types were excluded.

Treatment protocol includes a first GONB as soon as bout begins. If no response after 1 week, a second GONB is performed. If bout persists, oral preventive treatment is advocated. Data was retrieved from clinical records from 2015 to 2025. Patients were asked to evaluate their individual perceived benefit after GONBs according to the Patient"s Global Impression of Change (PGIC) score. Descriptive analysis and linear regression models adjusted to cofounders were performed.

Results: A total of 51 patients were included [median years of disease of 9.0 (IQR 4.5-17.5)]. Median PGIC score after GONBs was 2.0 (IQR 1-3) with 86.2% of patients scoring ≤3. No patients reported worsening. Median bouts per patient treated with GONBs was 3 (IQR 1-4.5) with a mean total of GONBs per bout of 1.5±0.7. Median days elapsed until the first GONB since bout beginning, per patient, was 9.0 (IQR 4-15). Patients treated with GONB experienced a 59% shorter duration compared to untreated patients, after adjusting for cofounders ($p < 0.001$). For each day of delay in first GONB, duration of bout increased by 0.7% ($p < 0.001$). Longer delays (>14 days) after bout begining was associated with higher PGIC scores ($p = 0.0205$).

Conclusion: GONBs are effective as preventive treatment in ECH patients as shown by objective measures and patient related outcomes. Given these results, we advocate that GONBs should be considered mandatory in ECH patients as a preventive or even as a type of abortive treatment.

P265

Efficacy and tolerability of atogepant during the perimenstrual phase of female cycle

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Objective: This study aims to evaluate the efficacy and tolerability of atogepant—an oral, small-molecule CGRP receptor antagonist—during the perimenstrual phase.

Methods: An ambispective study is currently underway, enrolling consecutive female patients initiating atogepant treatment(60mg/daily), with preserved menstrual cycles (i.e., not using hormonal suppression), and meeting the ICHD-3 diagnostic criteria for menstrually related migraine or pure menstrual migraine. The perimenstrual phase was defined as days −2 to +3 of menstruation. Outcomes assessed include mean number of migraine days, mean migraine intensity, and responder rate (≥50% reduction in migraine frequency) during the perimenstrual phase, evaluated up to three months post-treatment initiation.

Results: A total of 24 women of reproductive age (median age 41 years, IQR 36–45), from a single tertiary centre, were included. None met the criteria for pure menstrual migraine. Prior to atogepant initiation, the mean number of perimenstrual migraine days was 4.38 ± 0.21. At follow-up, this had significantly decreased to 1.69 ± 0.50 days ($p < 0.001$). A ≥50% reduction in perimenstrual migraine days was observed in 58% of patients ($n = 14$). Approximately 30% of patients no longer required acute treatment during the perimenstrual phase. According to the Patient Global Impression of Change (PGIC) scale, 15 patients reported significant improvement specifically during the perimenstrual window. The most frequently reported adverse events were constipation, nausea, and somnolence, however, none of the patients discontinued the medication due to side effects.

Conclusion: Preliminary data suggest that atogepant may reduce the burden of menstrually related

migraine. The treatment was well tolerated in this cohort. Ongoing data collection will further clarify the impact of hormonal fluctuations on treatment response throughout the menstrual cycle.

P266

Mid-term effectiveness and tolerability of atogepant in the prevention of migraine: A real life, prospective, multicentric study (the STAR study)

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Objective: To assess the impact of atogepant in preventing migraine after 24-week of treatment.
Methods: Adult patients treated with atogepant 60 mg daily were included. At baseline (T0), after 12 (T3) and 24 weeks (T6) since atogepant first administration, monthly migraine days (MMDs), HIT-6, MIDAS, mTOQ-6, MSQ, ASC-12 and MIBS-4 scores were assessed. The co-primary endpoints were the changes in MMDs and percentage 50%RR responders (i.e. reduction of MMDs≥50%) from T0 to T6.
Results: 128 patients (56 [43.8%] with chronic migraine [CM], 115 female [89.9%], age 48.3±13.3) completed the 24-week observation. In the whole group, MMDs reduced from 16.5±8.5 at baseline to 8.0±8.4 at T3 and 8.6±9.2 at T6. Overall, 64.8% of patients were 50%MMDs responders at T3 and 61.7% at T6 (68.1% and 66.7% in the episodic migraine group and 60.7% and 55.4% in the CM group at T3 and at T6, respectively). To note, 81.9% of responders at T3 maintained MMDs 50%RR also at T6, while 24.4% of patients among non-responders at T3 became 50%RR at T6. The 50%RR at T6 was higher in patients who had not previous ineffective anti-CGRP mAbs treatment (63.3% vs. 36.7%, p=0.027) and in those who were not on medication overuse at baseline (55.7% vs. 44.3%, p=0.046). Previous anti-CGRP mAbs failure was the only characteristic associated with the responder status in the multiple regression analysis (p=0.031). From T0 to T6 analgesic use, HIT-6, MIDAS, ASC-12, MIBS-4 and mTOQ-6 scores reduced (p<0.001), and MSQ role-function restriction increased (p<0.01). Changes mainly occurred from T0 to T3, except for MIBS-4 which also decreased from T3 to T6 (p<0.001). Since T3, only 10 subjects (7.8%) dropped out: 6 for lack of effectiveness, of these one also for poor tolerability, and 4 for patients" decision. Weight reduced of 0.8±3.1 kg (p<0.001) from T0 to T3, while from T3 to T6 remained stable.
Conclusion: The multicentric STAR study confirms atogepant effectiveness and tolerability at 24-week follow-up.

P267

OnaBotulinumtoxin-A in chronic migraine patients with short or long disease history and psychiatric comorbidities: Preliminary data from the Italian observational prospective multicentric study BACH study

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Objective: To investigate whether the duration of Chronic Migraine (CM) for over or less than 10 years can predict Onabotulinumtoxin-A (OBT-A) effectiveness and to evaluate if patients" psychopathological profile may influence their outcome.
Methods: Consecutive CM patients undergoing OBT-A treatment have been enrolled since January 2024. Evaluation times were at baseline and after 3, 6, 9 and 12 months. We collected Monthly Headache Days (MHDs), number of Monthly Acute Medications (MAMs), HIT-6 and MIDAS scores. Pain intensity was evaluated by NRS. The psychopathological profile was evaluated by BDI-II, BIS-11, STAI-Y, DERS, TAS-20 questionnaires.
Results: We have currently enrolled 185 patients (mean age 46.9 yrs, SD 15.7; 160 female, 85.5%), undergoing OBT-A for the first time; 115 patients (62.7%) had a CM history longer than 10 years. At latest data reconnaissance, 163 participants (88%) have been followed for ≥3 months, 140 (76%) for ≥6 months, 111 (60%) for ≥9 months, 83 (45%) for 12 months. To capitalize on all available follow-up measurements and taking into account drop-outs, a mixed-linear model was applied. MHD, MAMs, MIDAS, HIT-6 and NRS showed a significant decrease ($p<.001$) across the follow-up. In almost all cases, the trend was neither influenced by disease duration, psychiatric comorbidities, nor by their combination ($p>0.05$). Only for MIDAS a clear dependence on psychiatric symptoms was found ($p=0.002$). This interaction is due to the higher scores in the group with psychiatric comorbidities (PSY+) at baseline and at three months, while afterwards the PSY+ and PSY- groups reached approximately the same levels of migraine-related disability. In addition, a slight significance ($p=0.064$) was found for the triple interaction duration x psychiatric comorbidities x time.
Conclusion: In this preliminary report OBT-A effectiveness was not affected by disease history or psychiatric comorbidities, except for the latter influencing MIDAS in the short term.

P268

Adverse effects and predictors of their occurrence in a series of patients with resistant migraine treated with atogepant

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Objective: Although it is generally well-tolerated, adverse effects are commonly reported with atogepant treatment. We evaluated their occurrence in a series of patients and assessed possible predictors of their occurrence.
Methods: We analyzed a series of patients diagnosed with resistant migraine treated with atogepant. We evaluated clinical and demographic variables, including those related to migraine and concomitant treatments. We considered effectiveness and adverse effects after 3 months of therapy.
Results: We included 41 patients (40 women) aged 44.2 ± 9.5 years (26-58). 37 (90.2%) of them had chronic migraine and 4 had high-frequency episodic migraine. 22 patients (53.7%) had been previously treated with a monoclonal antibody against CGRP.
Only 6 patients (14.6%) did not report any adverse effects related to the use of atogepant. Most frequently described adverse effects were constipation (19, 46.3%), nausea (15, 36.6%), asthenia (11, 26.8%), hyporexia (9, 22%), weight loss (4, 9.8%), sleep disturbance (4, 9.8%), dizziness (3, 7.3%), cognitive complaints (3, 7.3%), and pruritus (2, 4.8%).
In 8 patients (19.5%), it was necessary to either discontinue or reduce the dose of atogepant, mainly due to gastrointestinal symptoms. Among patients with no adverse effect weight (59±7.6 vs 70.4±16.6 kilograms, p: 0.017) and body mass index (BMI) (21.5±3.2 Kg/m2 vs 26.3±5.2, p: 0.012) were lower.
Conclusion: In our cohort, higher body weight was associated with a greater incidence of adverse effects related to Atogepant. Further studies are needed to confirm these data and determine whether this association is related to the absorption, transport, or metabolism of this drug.

P269

Response to Eptinezumab in a real-world setting – A 24 month experience in a Portuguese hospital

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Objective: Eptinezumab, being the only antiCGRP monoclonal antibody for migraine prevention administered intravenously thus, with a more favourable pharmacodynamic profile, has been used, in real world, in particularly challenging patients such as those with chronic migraine, medication overuse headache and previously monoclonal failure. We present the results of the first 24 months of treatment with eptinezumab in our headache centre

Methods: Unicentric retrospective study of all patients treated with Eptinezumab for migraine prevention in our hospital. All patients received 100 mg of Eptinezumab every 12 weeks.
Results: 52 patients were included, 6 men and 46 women with a median age of 46 years. Most patients had a long migraine history (median 26.7 years); half had chronic migraine (21% daily headache) and 33% high frequency migraine (8-15 /days per month). 33% of patients were overusing acute medication. 60.6% had already failed previous anti-CGRP monoclonal antibodies. In all patients HIT-6 scores were above 50.
Eptinezumab treatment resulted in a reduction of median headache days from 14 at baseline to 8 at 1 month($p<0.001$), 8 at 3 months ($p<0.001$), 5 at 6 months ($p<0.05$) and 4 at 12 months (p=n.s.). After 12 months, a slowly progressive decrease continued. As soon as 1 month 45% of patients had a more than 50% response, that increased to 60% of patients at month 6. At month 6 there was a higher than 75% reduction in moderate to severe headache in half the patients. All patients stopped overusing acute medication after 1- 3 months. Eptinezumab was extremely well tolerated and 50% of patients classified improvement as grade 5 or higher in the Patient Global Impression of Change (PGIC) scale.
Conclusion: Eptinezumab efficacy and tolerability was confirmed in this real-world setting. It improved even very difficult migraine patients and reversed analgesic overuse in all patients. After 12 months of therapy improvement continued to be seen, stressing the importance to maintain therapy on the long run.

P270

Use of gepants in the acute treatment and bout modulation of cluster headache: A retrospective case series

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Objective: Cluster headache (CH) is a rare but highly disabling primary headache with limited options for acute relief and bout control. Gepants, oral CGRP receptor antagonists approved for migraine, are not indicated for CH. This study evaluated their use in acute and bout-phase management of CH. Notably, no traditional preventive therapies (e.g., verapamil, corticosteroids) were used during the reported bout
Methods: Retrospective case series of six CH patients who used gepants during a recent cluster bout. Data were collected via structured telephone interviews. Outcomes included attack characteristics and Patient Global Impression of Change (PGIC). Follow-up extended beyond the bout to assess sustained benefit (mean: 5 months)
Results: Six patients (3 men, 3 women; mean age 54.2; mean disease duration 14 years) were included. Five had episodic CH, one chronic CH. Rimegepant 70 mg (every other day, 16–28 days) was used by four patients; two used atogepant 60 mg/day (28 days). Five patients (episodic CH) reported clinical benefit; the chronic CH case did not. Mean time to benefit: 7.2 days. Responders had >50% reduction in daily attack frequency; pain intensity dropped by 5.4/10. Three required no additional acute therapy; two used oxygen (one also a triptan). Three patients reported shorter bout duration. No other preventives were introduced during or after. Benefit persisted through follow-up. Adverse effects (mild nausea, constipation) occurred in two. PGIC was rated "very much improved" by four, "much improved" by one, and "no benefit" by one
Conclusion: Gepants may represent a promising and well-tolerated therapeutic option for both acute treatment and bout modulation in episodic CH, even in the absence of traditional preventive therapies. Their efficacy in chronic CH remains uncertain. These preliminary findings warrant confirmation in prospective, controlled studies

P271

Gender differences in clinical features and psychiatric comorbidities among migraine patients: A case-control Tunisian study

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Objective: Migraine is a chronic neurological disorder that can be associated with psychosocial burden.Gender differences in migraine have been reported but insufficiently explored in North African populations.Our study aimed to compare clinical characteristics and psychiatric comorbidities between male and female migraine patients.
Methods: We conducted a case-control study including migraine patients diagnosed according to the International Headache Society (IHS) 2018 criteria,and healthy controls.Psychiatric comorbidities were assessed using the MINI DSM-5 structured interview.We used chi-square,Fisher"s exact,and Student"s t-tests for statistical analysis with significance defined as $p<0.05$.
Results: We enrolled 200 healthy controls and 100 migraine patients with mean age of 37 years and a F/M ratio =2.23. Intense migraine attacks were reported by 49% patients. Frequent attacks(≥5/month) were reported by 10,1% of women vs. 9,7% of men (p=0.646), and intense pain in 50.7% of women vs. 45.2% of men(p=0.985). Stress was the

most commonly reported trigger (69%), followed by weather changes (34%) and sleep deprivation (14%).Psychiatric comorbidities were more frequent in women although not significant:depressive disorders in 30.4% vs. 25.8% (p = 0.635), generalized anxiety disorder in 31.9% vs. 22.6% (p = 0.343) and panic disorder in 11.6% vs. 6.5% (p=0,658).One female patient presented mild suicidal ideation. Notably,no cases of substance use disorders, delusions, or anorexia nervosa were reported in this group,while all were observed among controls.

Conclusion: Our study revealed a non-significant trend toward a higher prevalence of psychiatric comorbidities among Tunisian women with migraine,highlighting the importance of considering gender in clinical evaluation and follow-up.These findings support the importance of psychiatric screening in migraine management and emphasize the need for larger studies to confirm these associations.

P272

The cognitive dimension of migraine: Adressing a treatable burden

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Objective: Cognitive complaints, such as memory and concentration difficulties, are increasingly recognized as part of the clinical spectrum of migraine, rather than merely consequences of comorbid conditions such as depression. We aimed to evaluate whether memory complaints improve with effective preventive treatment for migraine.

Methods: We conducted a prospective observational study including 68 patients with migraine initiating preventive treatment with monoclonal antibodies or OnabotulinumtoxinA. Responders were defined as those who achieved ≥50% reduction in monthly headache days. Cognitive complaints were assessed using the Memory Complaint Scale (MCS), and depressive symptoms with the Hospital Anxiety and Depression Scale (HADS), both at baseline and at 3 months follow-up.

Results: A preliminary analysis of 68 cases treated with monoclonal antibodies (N=37, 54%) or OnabotulinumtoxinA (31, 46%), 34 responders and 34 non-responders, showed that responders had a greater reduction in subjective memory complaints compared to non-responders (mean variation -0.82 ± 2.32 vs +0.68 ± 2.33; $t(66) = -2.662$; $p = 0.010$), independently of changes in depressive symptoms (p = 0.048). The type of preventive treatment used did not significantly influence cognitive outcomes ($p = 0.890$).

Conclusion: Memory complaints are a frequent and burdensome symptom of migraine, reflecting its broader clinical impact beyond pain. Effective preventive treatment is associated with significant improvement in these cognitive symptoms, reinforcing their role as part of the migraine spectrum.

P273

Four-year real-world efficacy and tolerability of anti-CGRP therapies in a tertiary headache centre in England

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Objective: Anti-CGRP therapies show good efficacy and few side effects in clinical trials. We report four years of real-world data from a single tertiary headache centre in England.

Methods: Retrospective analysis of adults (≥18 years) treated with anti-CGRPs from April 2021 to July 2025. Changes in monthly migraine days at 12 weeks were calculated from headache diaries, in line with NICE guidelines for the management of migraine. The top 3 discontinuation reasons were identified. Treatment success was defined as meeting NICE criteria and not stopping treatment due to adverse effects or loss of efficacy.

Results: A total of 548 treatments were initiated in 415 patients (rimegepant: n=57; atogepant: n=60; erenumab: n=283; fremanezumab: n=136; galcanezumab: n=12). Overall, 52% of treatments were successful. Success rates were: fremanezumab 57.4%, rimegepant 54.4%, atogepant 51.7%, and erenumab 47.7% (**Figure 1**). Discontinuation occurred in 48% of cases, mostly due to insufficient response at 12 weeks (27.4%), adverse effects (9.1%), and loss of efficacy (7.1%) (**Figure 2**). Insufficient response rates at 12 weeks were highest for rimegepant (38.6%), with similar rates for erenumab (26.5%), fremanezumab (28.7%), and atogepant (21.7%) (**Figure 3**). Discontinuation due to adverse effects was highest with atogepant (23.3%), followed by erenumab (10.6%); rates were <4% for rimegepant and fremanezumab.

Conclusion: Real-world efficacy broadly aligns with clinical trial data, though our galcanezumab findings are limited by small sample size. While direct comparisons outside of randomised trials are limited,

agents differed in both effectiveness and tolerability. Rimegepant was well tolerated but was associated with the lowest effectiveness at 12 weeks. Atogepant was associated with the most adverse effects, with constipation, dizziness, and "brain fog" reported. Fremanezumab was associated with a higher treatment success rate than erenumab, rimegepant, and atogepant in our cohort.

Fig. 1

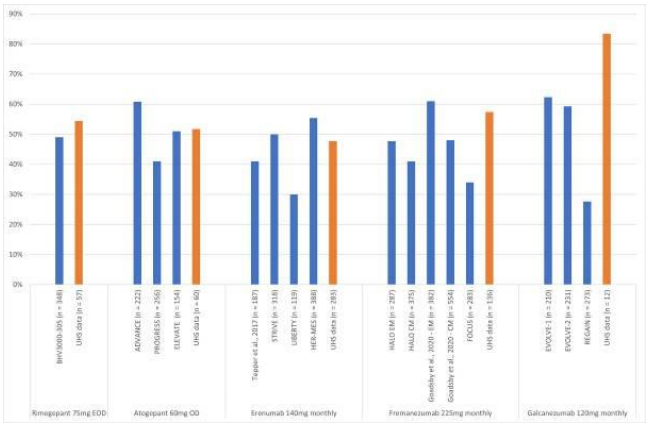


Fig. 2

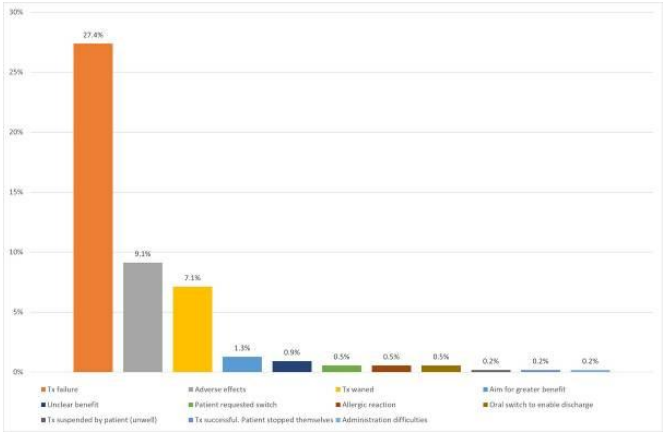
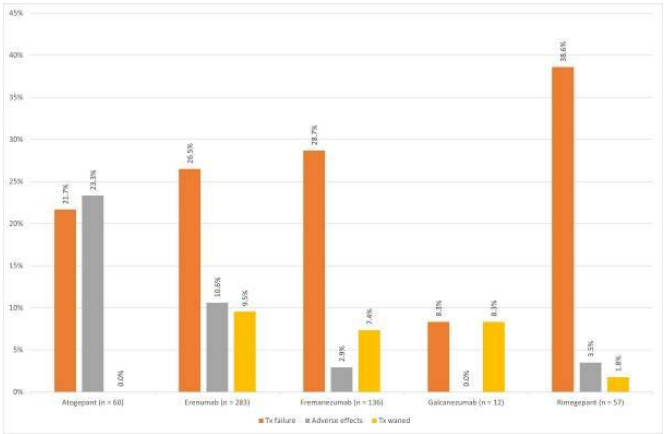


Fig. 3



P274

Recurrent severe headache with a background of functional vomiting and normal brain MRI, in paediatric reversible cerebral vasoconstriction syndrome (RCVS)

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Objective: We discuss the learning points in this case of reversible cerebral vasoconstriction syndrome (RCVS) in a 10 year old boy initially diagnosed as migraine.

Methods: A 10 year old with several years history of vomiting episodes presented to hospital with vomiting followed by confusion, thunderclap headache and full recovery within 4 hours twice a day. These events were stereotypical, starting with nausea, vomiting, confusion followed by severe occipital headaches peaking within 2 mins and lasting 1-4hours before fully resolving. He was diagnosed as migraine by the general paediatric team and treated with NSAIDs and paracetamol. Sumatriptan had made his headaches worse.

Physical examination was normal.

Initial CT and MRI of the brain were normal. Two days later, magnetic resonance angiography (MRA) revealed characteristic multifocal segmental arterial constriction consistent with RCVS. Subsequent MRA 2months later revealed normalization of his vessels.

Results: After the diagnosis of RCVS, he was started on oral Nimodipine and his headaches events reduce in frequency and severity to once a day. At the 3rd day of treatment he stop Nimodipine. His events returned dramatically and Nimodipine was restarted the following day reducing his events and severity of headaches, before finally resolving at day 10.

We include images of the abnormal and normlised MRA

Conclusion: RCVS is a rare condition normally seen in middle age. The pathogenesis is unknown and recurrence is uncommon. Severe cases can lead to stroke due to vasoconstriction. RCVS is easily mistaken for status migranosus. Triptan treatment could potentially worsen this condition due to vasoconstriction as part of its mode of action.

P275

Evaluation of treatment persistence and individual subgroups in German migraine care: A retrospective cohort approach

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Objective: This study aims to assess treatment persistence among individuals receiving either acute or prophylactic pharmacological migraine therapies in Germany.

Methods: This retrospective study utilized anonymized pharmacy dispensing data (German IQVIA™ LRx). Adults (≥18 years) with at least one migraine-specific therapy prescription between 05/2022-04/2023 were included. Analyses focused on individuals initiated on acute (Triptans, Ditans) and advanced prophylactic migraine therapies (monoclonal antibodies or Gepants). Treatment frequency for acute therapy was calculated by average number of prescriptions within defined time periods after therapy initiation. Treatment persistence for prophylaxis was assessed using Kaplan-Meier analysis. All therapies were evaluated over 12 and 24 months.

Results: A total of 292,091 individuals were initiated on acute therapy, while 14,822 were initiated on advanced prophylactic therapy during the study period. Out of individuals initiated on acute migraine therapies 31% still received acute therapy medication in months 12-24. About 40% of individuals on acute therapies had ≥2 prescriptions in months 1-12; amongst those still treated in months 12-24, 51.8% received ≥2 prescriptions. At 12 months after initiation, on average 48.2% of individuals with advanced prophylactic therapy were persistent, with 32.2% at 24 months. Of patients discontinuing advanced prophylactic therapy across 24 months of treatment on average 31.5% switched to a different advanced prophylaxis, 17.4% had an excessive therapy gap (>120 days) and 51.1% stopped.

Conclusion: Longer-term acute therapy was associated with higher frequency of prescriptions. About 50% of individuals discontinued advanced prophylactic therapies within 12 months. These findings highlight the importance of optimizing both acute and preventive strategies to adequately manage migraine patients, considering current recommendations.

P276

Migraine-related stigma at Erasmus Medical Center: Preliminary findings from a Dutch survey

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Objective: Migraine-related stigma is an important yet underrecognized challenge that adversely affects patients" quality of life, and is linked to job-related disability. As part of the Migraine Friendly Workplace Project, endorsed by the European Migraine and Headache Alliance, we aimed to gain insights into migraine-related stigma in the workplace at Erasmus MC, a university medical center and medical faculty in The Netherlands.

Methods: Cross-sectional study using two descriptive and quantitative surveys, launched in May 2025. The surveys were distributed to all employees at Erasmus MC via advertisement on the intranet page. Survey 1 was designed for individuals with migraine, while Survey 2 targeted those without.

Results: As of July 2025, Survey 1 received 218 responses. The majority (93%) reported moderate to severe attacks with significant daily impact; 30% must stop working during an attack, while 50% stated this depends on the severity. 37% perceived stigma in the workplace, while 30% were unsure. Half reported a lack of understanding from colleagues around sick leave and disagreed that supervisors understand migraine. 23% reported negative experiences after disclosing their migraine to supervisors; 5% preferred not to respond. Most (89%) emphasized the need for migraine education, inclusive language, and storytelling at Erasmus MC.

Survey 2 received 229 responses. The majority (82%) knew someone with migraine. Workplace stigma was acknowledged by 49%, while 38% were unsure. 64% considered migraine as serious. Half perceived societal ignorance; the rest believed migraine is seen as harmless.

Conclusion: Migraine has substantial impact on daily functioning and work participation, also in a university medical center setting. Stigma increases the burden of migraine in patients' work life, especially in the context of insufficient supervisor awareness, inadequate support or knowledge and negative experiences after disclosing migraine. These findings highlight the urgent need for interventions.

P277

Inside the night, outside the pain: Assessing the impact of shift work on migraine among healthcare professionals

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Objective: Background: Disruption of sleep and circadian rhythms is a recognized trigger for migraine. Shift work—particularly night or irregular shifts—can worsen these disruptions, potentially increasing migraine frequency and severity. A "shift worker migraine subtype" has recently been proposed to describe this specific vulnerability. However, the relationship between shift work and migraine remains insufficiently studied within Portuguese healthcare settings.

To assess the prevalence, frequency, and severity of migraine among healthcare professionals working

shifts compared to those with regular daytime schedules. Secondary objectives include evaluating the association between night shift frequency, sleep disturbances, migraine characteristics, medication use, and functional impact

Methods: A cross-sectional observational study is being conducted at São João University Hospital, enrolling staff from all departments and professional categories. Data are being collected using both online and paper-based questionnaires, covering demographics, work schedule, sleep quality, migraine diagnosis (with or without aura), attack frequency, medication use, and validated tools (HIT-6, MIBS-4, PGIC).

Results: Data collection is ongoing. We hypothesize that shift workers, particularly those with frequent night shifts, report higher frequency and greater severity of migraine attacks compared to daytime-only workers. We also expect to observe an association between circadian misalignment, sleep disturbances, and increased migraine-related disability and medication use.

Conclusion: This study aims to clarify the association between shift work and migraine burden. Findings may inform targeted preventive strategies and contribute to the ongoing discussion about recognizing "shift work-associated migraine" as a distinct clinical entity.

P278

Preventive migraine care before headache clinical referral: Are we doing it right?

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Objective: Early use of preventive migraine therapy in primary care is recommended by current guidelines. However, the adequacy of referrals to tertiary headache clinics remains variable. This study analyzes how the profile and prior management of patients referred from primary care changed over six years in a Portuguese hospital.

Methods: Retrospective study of adult migraine patients referred from primary care to a tertiary headache clinic in 2017 and 2023, excluding those with previous neurology follow-up. Variables analyzed included pre-referral preventives, treatments initiated in the clinic, and follow-up duration.

Results: A total of 54 eligible patients were included (32 in 2017; 22 in 2023). Both groups showed a female predominance, though patients in 2023 were significantly older (mean age 41.6 vs. 33.9 years; p=0.018).

Preventive treatment criteria were met by 90.9% in 2023 versus 75.0% in 2017. Pre-referral management improved markedly: in 2023, 77.3% of patients had tried at least one preventive treatment (vs. 28.1% in 2017; p<0.001), with a higher mean number of preventives attempted (2.0 vs. 0.34; p<0.001).

Commonly prescribed agents in primary care shifted from propranolol and amitriptyline in 2017 to topiramate and amitriptyline in 2023. In the headache clinic, more advanced therapies, particularly CGRP-targeted monoclonal antibodies were introduced in 2023, often in patients with more complex or refractory profiles. Follow-up duration was also significantly longer (452 vs. 289 days; p=0.004).

Conclusion: Our findings suggest a clear evolution toward more appropriate and guideline-informed referral practices. Primary care providers are increasingly initiating preventive therapy before seeking specialist input.

P279

Switch or maintain: Real-world use of BoNT-A and Anti-CGRP mAbs

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Objective: BoNT-A and anti-CGRP mAbs are both recognized as effective disease-specific preventive treatments for chronic migraine. However, real-world data on treatment sequencing between these two approaches remains limited.

To evaluate treatment patterns in chronic migraine patients with a prior history or undergoing BoNT-A treatment after initiating mAb therapy.

Methods: We conducted a retrospective cohort study including chronic migraine patients treated with mAbs at a tertiary hospital center. Patients were followed for 12 months to assess treatment adjustments, including switching from prior BoNT-A to mAb monotherapy *versus* dual therapy. Clinical and demographic data were analyzed to identify factors influencing treatment strategies.

Results: Among the 65 patients included (mean age 46 years; 85% female), 47.7% transitioned from BoNT-A to mAb, while 9.2% received combined treatment. From the latest, three patients maintained dual therapy throughout follow-up. Within the mAb monotherapy group, 4.6% initiated BoNT-A during follow-up, with one patient later switching to BoNT-A. The main reason for adding or switching to BoNT-A

was due to the insufficient efficacy of the mAb treatment. Notably, patients undergoing dual therapy did not experience significant adverse effects. The proportion of patients with ≤15 headache days per month rose from 19.3% at baseline to 82.2% at the 12-month mark (*p-value* < 0.001). Similar outcomes were seen in the subgroup analysis of patients who switched from BoNT-A to anti-CGRP mAbs.

Conclusion: In our cohort, a substantial proportion of patients successfully transitioned from BoNT-A to anti-CGRP mAbs with a notable increase in the number of headache-free days. While dual therapy was less commonly used, it should be considered in selected cases. These findings offer real-world insight into current treatment approaches and support the development of personalized strategies.

P280

From monotherapy to combination: Use of OnabotulinumtoxinA and anti-CGRP monoclonal antibodies in a tertiary Portuguese hospital

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Objective: OnabotulinumtoxinA and anti-CGRP monoclonal antibodies (mAbs) are key therapeutic options for migraine prevention.

Methods: Retrospective study of patients treated with onabotulinumtoxinA in a headache clinic between January 2023-May 2025. All patients fulfilled diagnostic criteria for chronic migraine. Patients were classified into four therapeutic groups: (1) botulinum toxin monotherapy, (2) transition from toxin to mAb, (3) transition from mAb to toxin, and (4) combined therapy. For each group and year, data were collected on number of patients, mean age and sex distribution.

Results: A total of 70 patients received onabotulinumtoxinA: n=18 in 2023, n=29 in 2024, and n=23 in 2025 (until May).

The proportion of patients receiving toxin monotherapy decreased over time: n=14, 77.8% in 2023; n=18, 62.1% in 2024; and n=12, 52.2% in 2025. Conversely, combination therapy increased from n=1, 5.6% in 2023 to n=3, 10.3% in 2024 and n=8, 34.8% in 2025.

Patients on monotherapy became progressively older (mean age 43.9 in 2023 to 51.5 in 2025), while those on combination therapy showed stable age trends (43.0 in 2023, 50.3 in 2024, 47.3 in 2025).

Switches from toxin to mAb were observed in n=2, 11.1% in 2023 and n=6, 20.7% in 2024, all female, mean ages 45.0 and 43.5 years. Switches from mAb to toxin occurred in n=1, 5.6% in 2023, n=2, 6.9% in 2024, and n=3, 13.0% in 2025, with rising mean ages of 22.0, 30.5, and 41.7 years, respectively.

Conclusion: In this tertiary hospital, onabotulinumtoxinA is used exclusively for chronic migraine. These results suggest a shift toward increased use of combined therapy with mAbs. Further studies are needed to evaluate the impact of this approach.

P281

Impact of sleep disorders on anti-CGRP monoclonal antibodies treatment response in migraine: A cross-sectional study

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Objective: Aim of our study is to assess sleep quality and screen for sleep disorders (SDs) in patients undergoing treatment with anti-CGRP mAbs. Particularly, the study aims to investigate the potential predictive role of these parameters in treatment response.

Methods: We included patients with a diagnosis of migraineundergoing anti-CGRP mAbs treatment with adequate compliance. Patients were grouped as follows after data collection: responders (>50% reduction in mean headache days (MHDs) compared to baseline) and non-responders (<50% MHDs compared to baseline). Additionally, we subdivided patients in super-responders, when observing a >75% reduction in MHDs. atients completed a structured interview assessing sleep quality, chronotype, and screening for major sleep disorders using the following questionnaires: Pittsburgh Sleep Quality Index (PSQI), Epworth Sleep Scale (ESS), Fatigue Assessement Scale (FAS), Morning-Eveningness Questionnaire (MEQ), STOP-Bang, Restless Leg Syndrome assessment test. Numeric variables were compared by means of one-way analysis of variance Kruskal-Wallis test or Mann-Whitney U-test. Categorial variables were analyzed by means of table of contingency Pearson"s chi-squared.

Results: We included 50 patients: five (10%) were classified as non-responders, fourteen (28%) as responders and thirty-one (62%) as super-responders. Pearson"s chi-square test revealed a statistically significant association between optimal therapeutic response and the absence of concomitant sleep disturbances (p < 0.001) across the three groups.

Notably, when the analysis was restricted to responders and super-responders, the absence of sleep disorders remained significantly associated with an excellent response to mAbs ($p < 0.001$). A higher PSQI score, as a continuous variable, was significantly associated with responders in comparison to super-responders ($p=0.004$).

Conclusion: Our results show that a good sleep quality and the absence of SDs correlates with an optimal response to anti-CGRP mAbs.

P282

Uncommon cause, common symptom: dAVF presenting as migraine-like headache (case report)

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Objective: Dural arteriovenous fistulas (dAVFs) are a type of brain high-flow vascular malformation, usually acquired, that can be asymptomatic but can cause serious problems ranging from pulsatile tinnitus, epileptic seizures and headaches to intracranial bleeding.

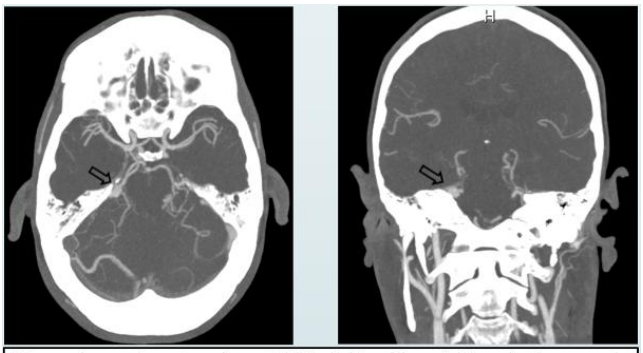
Methods: This case report highlights the need to exclude secondary headaches evem in patients with a primary headache history.

Results: A 32-year-old patient presented with an intense throbbing headache in the right occipital region, unresponsive to analgesics, accompanied by photophobia, nausea, vomiting and dizziness. The patient has a medical history of migraine without aura. Neurologic examination and basic blood test were normal. In the emergency department the patient deteriorated to GCS 7 (E1/V1/M5) with psychomotor agitation requiring intubation. Brain CT and CTAg showed a dAVF in the right posterior fossa without active haemorrhage. Cerebrospinal fluid analysis was normal. Post-extubation, the patient had no focal neurodeficit, a GCS of 15 and headache resolution. Diagnostic DSA (digital subtraction angiography) and MRA demonstrated a dAVF at the tip of the right pyramid, fed by branches of the a. meningea media dextra. Embolization of the dAVF was performed, a follow-up MRA showed that the fistula had been removed from the circulation. The patient had no migraine headaches in the 6-months follow-up.

Conclusion: This case meets the ICHD-3 diagnostic criteria for *Headache attributed to dAVF*. The pathogenesis of dAVF related headache is not fully understood. An increase in vascular pulsatility leading to increased irritation of perivascular sensitive nerve endings of the trigeminovascular system is discussed. Subsequent release of neuropeptides from these nerve endings may induce a neurogenic inflammatory response underlying migraine-like headache. Thus, by removing dAVF from the circulation, both headaches and other serious complications can be prevented.

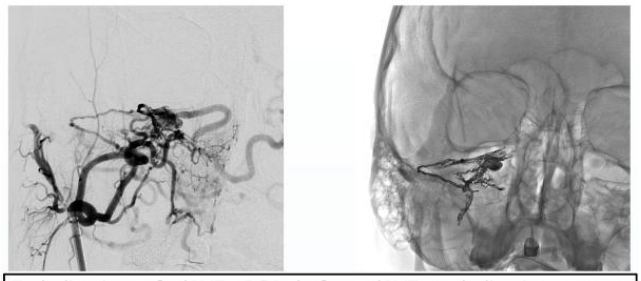
Patient gave his consent to publish his details in an open access journal.

Fig. 1



CT angiography showing dAVF at the tip of the right pyramid (arrow). Left axial plane, right coronal plane.

Fig. 2



Embolization of dAVF. DSA before dAVF embolization, access through the right a. carotis externa and a. meningea media (left). X-ray verifying the position of the glue used for embolization (right).

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Fulminant intracranial hipertension secondary to cerebral venous thrombosis: A case report

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Objective: Idiopathic intracranial hypertension is a common condition with predominance in women and obese individuals and characterized by headache and visual changes. This case report aims to discuss the case of a 22-year-old obese male patient with unusual headaches, diagnosed with fulminant intracranial hypertension (i.e. severe progression in less than 4 weeks). The late diagnosis of the primary cause led to severe involvement of the optic nerve, causing irreversible blindness. The patient had been initially treated at another service for optic neuritis due to findings on MRI. Subsequent ophthalmologic

evaluation showed bilateral papilledema and intense adherent retinal exudates.

Methods: The methodology was based on the consultation of medical records, previous and current examinations, as well as consultation in the medical literature.

Results: This case show us how important is to recognize signs and symptoms of this pathology and other diseases. In the current case, the presence of confounding factors demonstrated by neuroimaging examinations (initial suspicion of neuritis) was discussed, increasing the importance of discussing differential diagnoses in patients with unusual headache pattern associated with neurological deficits.

Conclusion: The unfavorable evolution in this case and literature allows us to emphasize the importance of early diagnosis and intervention due to the possibility of avoiding irreversible sequelae pertinent to this pathology.

Keywords: intracranial hypertension, headache, cerebral venous thrombosis

P284

Exploring the short-term impact of the environmental exposome on migraine: Weather and air pollution as potential attack triggers

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Objective: To analyse the relationship between weather and pollution changes on migraine attack onset, and to develop a prediction model to understand the impact of the environmental exposome in migraine.

Methods: This prospective observational study included individuals who used a mobile application to record daily migraine symptoms during one year or more. GLMM were applied using the *glmmTMB* and *glmmPQL* packages for both descriptive and predictive analyses. Environmental exposures were assessed at 96, 72, 48, and 24 hours prior to headache onset, for geolocalised weather data and air pollutants concentrations[https://mediambient.gencat.cat/ca/05_ambits_dactuacio/atmosfera/qualitat_de_laire/vols-saber-que-respires/descarrega-de-dades/]. All analyses were conducted in R.

Results: A total of 8,577 observation days were collected from 61 participants (80% women, mean age: 49.8 years). Models developed with *glmmTMB* showed a higher predictive performance than those using *glmmPQL*(AUC: 0.712 vs. 0.698; accuracies ~0.77, both), although the difference was not statistically significant. Significant associations were identified between attacks and environmental factors 48h prior: clinical diagnosis(OR [95% CI]: 2.493 [1.630 – 3.812], adj.p <0.001), accumulated precipitation(1.016 [1.004 – 1.027], adj.p = 0.042), and maximum concentration of SO_2(1.061 [1.016 – 1.108], adj.p = 0.042) (triggering effects), while solar radiation on the previous day(0.976 [0.958 – 0.994], adj.p = 0.046), and wind speed 96h before(0.904 [0.840 – 0.979], adj.p = 0.046) showed a protective effect.

Conclusion: GLMM demonstrated robust and comparable predictive performance. Exposome-related influences on migraine attack onset were best captured using lagged exposures, particularly 48h before.

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Post-migraine hemorrhagic manifestations: Evidence from two clinical cases

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Objective: Post-migraine ecchymosis is an underrecognized and seldom reported phenomenon characterized by localized skin bruising following acute migraine attacks. Although primarily neurological, migraine may also present with peripheral signs beyond the nervous system. Accounts of unexplained ecchymotic patches—typically around the periorbital region, temples or cervical area—emerging after migraine episodes have raised questions about the pathophysiological link between vascular instability, neurogenic inflammation and cutaneous manifestations.

Methods: Characterization of patients presenting with cutaneous/mucosal bleeding within 24 hours of a migraine attack, attending Headache consultation of Unidade Local de Saúde de Gaia e Espinho from 1/1 to 18/6 of 2025.

Results: Two cases were identified. The first is a 42-year-old woman with chronic migraine since age 36, on propranolol 40mg/day. Since February 2025, she noted localized hematomas consistently appearing the day after migraine attacks, most often during menstruation. After starting a continuous progesterone-only pill in May, both headaches and bruising completely resolved. The second is a 40-year-old woman with episodic migraine since age 30, on topiramate 100mg/day. Her migraine became chronic at 39, refractory to topiramate, with gingival bleeding during the first or second day of each attack. Greater occipital nerve blocks with lidocaine led to marked improvement in migraine frequency and intensity, and bleeding.

Conclusion: These cases highlight peripheral vascular signs—ecchymosis and mucosal bleeding—as possible migraine-associated phenomena. The link between attacks and bleeding, along with improvement following hormonal or neural interventions, suggests a possible interplay between neurovascular dysregulation, hormonal modulation and peripheral tissue response. Greater clinical awareness of these manifestations may enhance diagnostic and therapeutic approaches in migraine care.

P286

Case report: Atypical trigeminal herpes zoster in a migraineur: Diagnostic and therapeutic challenges

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Objective: Patients with migraine are known to exhibit alterations in immune function, characterized by elevated levels of pro-inflammatory cytokines and reduced counts of cytotoxic and regulatory T cells, which may increase their susceptibility to opportunistic infections, as illustrated in the present case. We report a 57-year-old female with a history of migraine, admitted due to a severe, pulsatile, right-sided hemicranial headache with migrainous features that had begun seven days earlier. Initially considered status migrainosus, the condition was atypical due to its severity and resistance to treatment. On the second day, erythematous plaques and vesicles appeared in the ophthalmic branch of the trigeminal nerve. A diagnosis of herpes zoster was established, and intravenous acyclovir was initiated. From that point, pain control improved with the use of advanced multimodal approaches.
Methods: Methodology included chart review, interdisciplinary assessments, and literature review on the topic.
Results: The initial delay in diagnosis was due to the uncommon pre-eruptive viral phase presentation and migraine as a confounding factor. Nevertheless, the favorable clinical evolution highlights the importance of early diagnosis and prompt antiviral therapy to reduce the risk of complications and long-term neurological sequelae.
Conclusion: Although a direct link between migraine and herpes zoster remains unproven, immune imbalance in migraine patients may predispose them to atypical infections. Therefore, herpes zoster should be included in the differential diagnosis when managing refractory or atypical headache presentations.
Keywords: migraine, herpes zoster

P287

Effect of low-dose esomeprazole on headache frequency in migraine patients with Gastritis symptoms: An observational study

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Objective: Migraine patients often report gastrointestinal symptoms such as nausea, vomiting, and heartburn. Unlike typical gastrointestinal patients, migraineurs exhibit increased pain sensitivity, which may exacerbate their discomfort. Proton pump inhibitors (PPIs) are frequently co-prescribed to mitigate gastric symptoms, but some reports suggest that PPIs may act as potential migraine triggers. This study aimed to explore whether the dosage of PPIs influences migraine frequency.
Methods: We conducted a prospective observational study involving migraine patients presenting with gastritis symptoms at a neurology outpatient clinic. At the initial visit, baseline frequencies of migraine attacks and gastritis episodes were recorded via structured history-taking. Patients were then prescribed low-dose esomeprazole magnesium (10 mg once daily) for one month. Follow-up interviews assessed changes in headache and gastritis frequency after treatment.
Results: Treatment with low-dose esomeprazole was associated with a significant reduction in the frequency of migraine attacks ($p < 0.05$) and a notable improvement in gastritis symptoms ($p < 0.01$).
Conclusion: Low-dose esomeprazole may alleviate both gastric and migraine symptoms in patients with comorbid conditions. These findings suggest that PPI dosage could be an important factor in modulating migraine frequency, and that lower doses may reduce the risk of PPI-associated migraine exacerbation.

P288

Dual pressure headache: A case of headache due to intracranial hypertension and hypotension

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Objective: Hypertension and hypotension represent opposite ends of the spectrum of headaches due to variations of cerebrospinal fluid (CSF) pressure. We present a case of idiopathic intracranial hypertension (IIH) with significant worsening after lumbar puncture (LP).
Methods: Clinical case description.
Results: A 22-year-old woman, with history of migraine and obesity (BMI 33 kg/m²), presented to

the emergency department with 1-month history of holocranial headache, worsened in supine position and refractory to analgesics. She also reported binocular horizontal diplopia in bilateral lateral gaze. Regular medication included combined oral contraceptive. Neurological examination showed decreased visual acuity and fundoscopy revealed bilateral papilledema. Brain-CT and CT-venography excluded venous sinus thrombosis and other structural abnormalities. The LP opening pressure was superior to 50 cmH_2O; cytochemical and microbiological analyses were normal. It was withdrawn approximately 15 ml of CSF (5ml for analysis and 10 ml drainage). The case was interpreted as IIH and acetazolamide was initiated.
One day after LP, she was readmitted due to increased headache intensity, worsened by orthostatism and improved in decubitus position; associated with neck pain, nausea and vomiting, photophobia and dizziness. Brain-MRI with contrast, performed on the 4th day post-LP, showed signs of IIH. Analgesia, fluid therapy and oral hydration were optimized, and bed rest was maintained. She showed favorable evolution over the following week.
Conclusion: We present a case of headache associated with IIH that, after LP, acquired typical features of CSF hypotension. We acknowledge the already described possibility of increased sensitivity to pressure variation in these patients, and this phenomenon alone should not prompt reconsideration of the diagnosis. We also aim to discuss the therapeutic role of lumbar punctures in the context of IIH.

P289

Development of the medication overuse headache assessment questionnaire

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Objective: Medication overuse headache (MOH) is an important yet often overlooked condition. This study aimed to develop and validate a self-administered questionnaire to screen for MOH, with the goal of enhancing early detection—an essential first step in MOH care.
Methods: A self-administered Thai-language questionnaire was developed to screen for MOH based on the International Classification of Headache Disorders, 3rd edition (ICHD-3), the Leeds Dependence Questionnaire, and the Severity of Dependence Scale **(Figure 1)**. The questionnaire underwent iterative refinement through expert consultation with four Thai headache specialists, patient feedback, and linguistic adjustments. The final questionnaire was launched and data were collected from headache patients attending Neurology or Headache Outpatient Clinics between 1 June 2024 and 31 December 2024. Items in the questionnaire were selected and optimized to maximize sensitivity and specificity, using the final diagnosis made by headache specialists according to ICHD-3 criteria as the gold standard. Performance analysis–including sensitivity, specificity, predictive values, and the area under the receiver operating characteristic curve (AUC-ROC)–was conducted for each item individually. Combination of items were selected based on their individual AUC-ROC values.
Results: Among 61 patients (93.4% female; median [IQR] age: 38.0 [30.0–46.0] years)), migraine was the most common diagnosis (90.2%, n = 55), followed by myofascial pain syndrome (4.9%, n = 3). MOH was diagnosed in 10 patients (16.4%). Diagnostic performance of individual and combined questions is shown in **Tables 1 and 2**. A combination of Q1 and Q2, both answered "Yes," showed the highest accuracy, with 100% sensitivity (95% CI: 72.3–100), 94.1% specificity (95% CI: 84.1–98.0).
Conclusion: The Medication Overuse Headache Assessment Questionnaire is self-administered and demonstrates high sensitivity and specificity in headache clinic settings, supporting its utility as an effective screening tool.

Fig. 1

Thai Version of the Medication Overuse Headache Assessment Questionnaire
(แบบสอบถามประเมินความเสี่ยงโรคปวดศีรษะจากการใช้ยาแก้ปวดมากเกินความจำเป็น ฉบับภาษาไทย)

You can indicate whether you agree or disagree with the following statements by checking the box next to each item.
ท่านสามารถเลือกคำตอบว่าท่านเห็นด้วยหรือไม่เห็นด้วยกับข้อความดังกล่าวโดยกากบาทในช่องข้างหลังคำถาม

	Question	Agree	Disagree
Q1	In the past month, have you experienced headaches on at least 15 days? (ใน 1 เดือน ท่านมีอาการปวดศีรษะอย่างน้อย 15 วัน)		
Q2	In the past month, have you taken headache painkillers on at least 10 days? (ใน 1 เดือน ท่านรับประทานยาแก้ปวดศีรษะอย่างน้อย 10 วัน)		
Q3	Have you been taking the same amount of headache painkillers continuously for 3 months? (ท่านรับประทานยาแก้ปวดศีรษะในปริมาณเท่าเดิม เป็นเวลาติดต่อกัน 3 เดือน)		
Q4	Do you feel that headache painkillers are necessary for your daily life? (ท่านคิดว่ายาแก้ปวดศีรษะจำเป็นสำหรับการดำเนินชีวิตประจำวัน)		
Q5	Have you ever planned to take another dose of painkillers once the effect of the first dose wears off? (ท่านเคยวางแผนที่จะรับประทานยาแก้ปวดหลังจากยาชุดแรกที่กินเริ่มหมดฤทธิ์)		
Q6	Do you usually need to take headache painkillers three times a day—morning, noon, and evening? (โดยส่วนใหญ่เมื่อท่านต้องกินยาแก้ปวดศีรษะ ท่านจำเป็นต้องรับประทานในทั้ง 3 เวลา เช้า กลางวัน และตอนเย็น)		
Q7	Do you think you are taking too much headache medication? (ท่านคิดว่าท่านรับประทานยาแก้ปวดในปริมาณมากเกินไป)		

Fig. 2

Item	Sensitivity	Specificity	PPV	NPV	AUC-ROC
Q1	100.0 (100.0–100.0)	80.4 (69.5–91.3)	50.0 (28.1–71.9)	100.0 (100.0–100.0)	0.90 (0.85–0.96)
Q2	100.0 (100.0–100.0)	78.4 (67.1–89.7)	47.6 (26.3–69.0)	100.0 (100.0–100.0)	0.89 (0.84–0.95)
Q3	80.0 (55.2–100.0)	45.1 (31.4–58.6)	22.2 (8.6–35.8)	92.0 (81.4–100.0)	0.63 (0.48–0.77)
Q4	100.0 (100.0–100.0)	29.41 (16.9–41.9)	21.7 (9.8–33.7)	100.0 (100.0–100.0)	0.65 (0.58–0.71)
Q5	70.0 (41.6–98.4)	56.7 (43.3–70.5)	24.1 (8.6–39.7)	90.6 (80.5–100.0)	0.63 (0.47–0.80)
Q6	50.0 (19.0–81.0)	84.3 (74.3–94.3)	38.5 (12.0–64.9)	89.6 (80.9–98.2)	0.67 (0.50–0.84)
Q7	50.0 (19.0–81.0)	72.6 (60.3–84.8)	26.3 (6.5–46.1)	88.1 (78.3–97.9)	0.61 (0.44–0.79)

Data are presented as point estimates (95% confidence interval) except for AUC-ROC
Abbreviations: AUC-ROC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value

Fig. 3

Item	Sensitivity	Specificity	PPV	NPV	AUC-ROC
Q1 and Q2 (Both–yes)	100.0 (72.3 – 100.0)	94.1 (84.1 – 98.0)	76.9 (49.7 - 91.8)	100.0 (92.6 – 100.0)	0.97 (0.94–1.00)
Q1 or Q2 (Either–yes)	100.0 (72.3 – 100.0)	64.7 (51.0 - 76.4)	35.7 (20.7 - 54.2)	100.0 (89.6 – 100.0)	0.82 (0.76–0.89)
Q1+Q2+Q6 (Score ≥ 2)	100.0 (72.3 – 100.0)	86.3 (74.3 – 93.2)	58.8 (36.0 – 78.4)	100.0 (92.0 – 100.0)	0.93 (0.88–0.98)
Q1–Q7 (Score ≥ 6)	70.0 (39.7 – 89.2)	98.0 (89.7 – 99.7)	87.5 (52.9 – 97.8)	94.3 (84.6 – 98.1)	0.84 (0.69–0.99)

Data are presented as point estimates (95% confidence interval) except for AUC-ROC
Abbreviations: AUC-ROC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value

P290

Retrospective analysis of MRI changes among patients with migraine

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Objective: Migraine is considered a benign disease, but recently there has been debate about the long-term effects of migraine. There is increasing evidence for migraine as a potential risk factor for structural changes in the brain.
Methods: An analysis of data from 170 patients who were treated at LSMUH Kaunas Clinics in 2023 – 2024 was performed. Data collected: age and gender of patients, type of migraine (with or without aura), monthly migraine days (MMD), episodic or chronic migraine (EM, CM), acute treatment, changes on MRI, comorbidities. Bioethics approval was obtained: No. 2024-BEC2-1369. Statistical analysis was performed using IBM SPSS version 30.0.
Results: The study included 157 (91.8%) women. The median age of the subjects was 38 years (IQR: 27-48). Migraine had occurred in a greater proportion of patients since childhood (51.5%), more patients had EM (60.2%) and slightly more proportion of patients had migraine without aura (60.9%). The median MMD was 8 (IQR: 3-15). The most commonly used acute treatment options were nonsteroidal anti-inflammatory drugs (NSAIDs) (40.9%), triptans (22.8%), and combinations of NSAIDs and triptans (19.3%) and these medications were effective in 34.9% of patients. Both nonspecific and specific prophylactic treatment were prescribed to a small proportion of patients, 25.1 and 29.8%, respectively. White matter changes (WMC) were found on MRI in 36.8%, and chronic microangiopathic changes (CMC) in 5.8% of patients. WMC changes were observed in 8.7% of patients with EM and in 1.5% of patients with CM (p=0.03). A statistically significant higher incidence of CMC on MRI was observed in older patients (58-77 years) (p<0.001). MRI changes correlated with female gender (r=0.199, p=0.009). No correlations were found with comorbidities.
Conclusion: The most common MRI findings are WMC. CMC on MRI findings were more common in older and in patients with episodic migraine.

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Multimodal assessment of neck musculature in children and adolescents with headache disorders: Palpation, algometry, infrared thermography, and ultrasound

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Objective: Headaches in childhood are frequently associated with complaints in the neck region, which is linked to central pain processing mechanisms by the trigemino-cervical complex. Currently, the muscular component is assessed by clinical examination that do not deliver quantifiable measures. Therefore, pressure pain threshold measurement (algometry), infrared thermography (IRT), and ultrasound are being evaluated as non-invasive, imaging-based, point-of-care tools for diagnosis and follow-up of muscular involvement.
Methods: This cross-sectional study involved symptom-oriented history, clinical examination of the neck muscles, algometry, IRT, and ultrasound in healthy children and children with primary headache disorders or post-traumatic headaches (following traumatic brain injury). A longitudinal follow-up was performed at 3 and 6 months for patients.
Results: Children with primary headache disorders had lower pressure pain thresholds, indicating higher muscular sensitivity (p=0.010-p=0.249). Greyscale analysis showed significant differences between groups with significantly higher mean grey level values in the headache group (p<0.001). Preliminary descriptive analysis showed higher temperatures in the trapezius muscle area in the headache group compared to controls. This may suggest an inflammatory process in the trapezius muscle.
Conclusion: The diagnostic methods of physiotherapy, algometry, IRT, and ultrasound are being evaluated for their utility in objectifying manually assessed muscular findings. In addition, the potential of IRT and ultrasound to differentiate between children with and without headache disorders is being explored.

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Headache disorders in youth: A school-based validation of the Italian HARDSHIP questionnaire

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Objective: This study aims to validate the Italian version of the Child and Adolescents Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire, a standardized tool for assessing headache prevalence and burden, developed by the Global Campaign Against Headache.
Methods: The study was conducted within the REPICEF registry (Registro Epidemiologico delle Cefalee in Età Evolutiva), approved by the Ethics Committee of the Abruzzo Region - Itlay (protocol 035018). Children and adolescents aged 6–17 years from selected schools in L"Aquila were enrolled between February and December 2024. The Italian version of the HARDSHIP questionnaire was developed via TRAPD methodology. Questionnaire-based diagnoses were compared against clinical assessments performed by headache specialists using ICHD-3 criteria. Diagnostic performance was evaluated through sensitivity, specificity, positive and negative predictive values (PPV-NPV), and Cohen's kappa.
Results: Of 1023 screened students, 858 were included in the cohort; the first 535 (62.4%) were selected for validation analyses. Based on the HARDSHIP questionnaire, the most common diagnoses were migraine in 68 (7.9%), Tension-Type Headache (TTH) in 86 (10.0%), probable Migraine (pMig) in 175 (20.7%), probable Tension-Type Headache (pTTH) in 144 (16.7%), and Undifferentiated Headache (UDH) in 105 (12.2%) children and adolescents. The agreement between questionnaire-based and clinical diagnoses was moderate for pMIG (κ = 0.432) and fair for pTTH (κ = 0.327). Specificity was high for both pMIG and pTTH, while sensitivity remained low.
Conclusion: The validated Italian version of the HARDSHIP questionnaire provides a useful instrument for epidemiological research and for the improvement in diagnosis of pediatric headache disorders.

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No strings attached: A case of sporadic hemangioblastoma in the spinal cord

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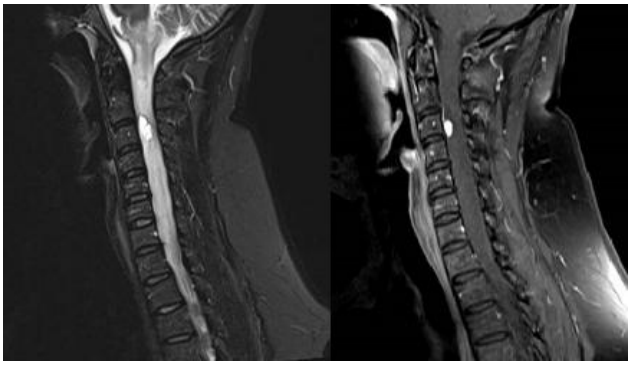
Objective: Hemangioblastomas are rare, benign, highly vascularized central nervous system tumors. They occur sporadically (75%), typically as solitary cerebellar lesions, or in association with Von Hippel–Lindau (VHL) disease. In VHL, 50% occur in the spinal cord, 40% in the cerebellum, and 10% in the brainstem. Solitary spinal cord hemangioblastomas are less common and require evaluation to exclude VHL.
Methods: Case report.
Results: A 39-year-old woman presented with a one-month history of left-sided hemicranial headache radiating to the occiput, worsened by cervical motion.

She described painful neck flexion/extension, hoarseness, hypophonia, and progressive numbness in the left upper limb. Neurological exam revealed weakness and hypoesthesia in the C5–C6 dermatome, brisk reflexes, an indifferent plantar response and positive Hoffman's sign on the left. No bulbar signs were found despite her complaints. Brain CT showed medullary and cervical cord hypodensity with cerebrospinal fluid space effacement. CT angiography identified a vascular saccular lesion at C3–C4. MRI showed an expansile lesion at C3, with edema extending from the medulla to the upper thoracic cord, suggestive of hemangioblastoma (Fig.1). VHL workup was negative (normal ophthalmologic exam, abdominal imaging, and plasma metanephrines). Angiography excluded arteriovenous malformation. The patient underwent uneventful surgical resection of an intradural lesion with intramedullary and extramedullary components at C3–C4. Findings were consistent with hemangioblastoma. Neurological status was stable at discharge. Histopathological confirmation is pending.

Conclusion: Clinical presentation of hemangioblastomas varies by location, driven by mass effect, edema, or hemorrhage. Notably, this disabling spinal cord-related headache pattern is not categorized in the International Classification of Headache Disorders, 3rd Edition.

Disclosure: Informed consent for publication of this case and related details was obtained from the patient.

Fig. 1



P294

Posterior circulation stroke or vestibular migraine? Registry-based analysis of predictors in patients presenting with acute dizziness and headache in the emergency department

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Objective: In cases of acute dizziness accompanied by headache (HA), distinguishing between posterior circulation vestibular stroke (VS) and vestibular migraine (VM) in the emergency department (ED) proves challenging.

Methods: This registry study included 814 patients, who presented to the ED with acute dizziness. Patients were screened for the presence and characteristics of accompanying HA. Demographic and cardiovascular risk factors were systematically collected. The etiology of the dizziness syndrome was classified based on clinical neurological, neuro-otological and imaging findings (cCT/CT-A, MRI) according to current diagnostic guidelines. Using multiple regression models and machine learning (ML, Random Forest), factors were analyzed that can reliably differentiate VS and VM.

Results: In the total cohort, 24.1% reported accompanying HA. In this subgroup, VM was the most common diagnosis (30%), followed by VS (25%). The most frequent etiology of VS was vertebral artery dissection (53%). VS lesions regularly involved the PICA territory (74%) and dorsolateral medulla (58%). Abnormalities on CT-A were found in 57% of VS and 0% of VM patients. In a multiple regression model, the following factors were indicative of VM: younger patient age (OR: 0.89), lower diastolic blood pressure (OR: 0.91) and a positive HA history (OR: 10.4). The ML-based calculation of diagnostic probability for VM vs. VS identified age, diastolic blood pressure, HA history, systolic blood pressure, and pulsating HA quality as distinguishing variables, which were integrated into a nomogram based on their diagnostic weight for graphical representation.

Conclusion: When acute dizziness and HA occur synchronously, reliable differentiation of benign (VM) and harmful etiologies (VS) is possible based on demographic criteria, HA characteristics, CT-A findings and cardiovascular risk. In VS with HA, dissections are most common, with lesions involving the dorsolateral medulla and PICA territory.

P296

The psychometric properties of an e-headache diary in migraine

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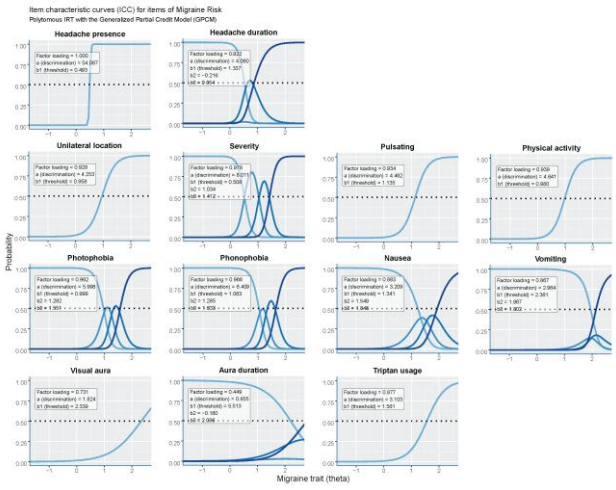
Objective: To evaluate the psychometric characteristics of a previously validated electronic headache diary with automated algorithm for the purpose of identifying migraine days.

Methods: The psychometric properties of 13 variables in this e-diary were analyzed using item response theory (IRT) in migraine patients from the Leiden Headache Center. The included items were headache presence, duration, unilaterality, severity, pulsating, aggravation by physical activity, visual aura, aura duration, nausea, vomiting, photophobia or phonophobia, and triptan usage. The added value to the end-diagnosis of an already validated migraine day of the individual items was assessed. A generalized partial credit model was used to evaluate the items. A discriminative value α ≥1.70 indicated an excellent discrimination.

Results: In total 1,418 migraine patients were analyzed with a mean age of 43 years, 89% were women, 38% reported aura symptomatology. All items demonstrated excellent discriminative value [α:1.82-54.1], except for aura duration [α:0.86] which was moderate. The Cronbach"s α was 0.91. The answers options of headache duration, photophobia, phonophobia, nausea, vomiting did not reach the probability threshold of 0.5.

Conclusion: The items in this e-headache diary demonstrated good overall psychometric performance, though certain items, particularly aura-related and multi-categorical items, may benefit from category merging or further refinement.

Fig. 1



P297

Myofascial headache: A new branch on the headache tree

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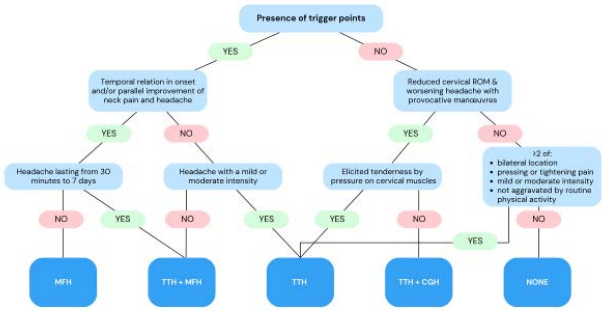
Objective: Recently, the International Headache Society postulated a new type of headache, myofascial headache (MFH). It is classified as a subtype of cervicogenic headache (CGH) and aims to resolve the existing overlap between CGH and tension type headache (TTH). In MFH, headache originates from the myofascial structures in the neck, a region that is often affected in TTH as well. This cross-sectional study aims to explore the relationship between the criteria established in the International Classification of Headache Disorders for CGH, TTH and the newly constructed MFH.

Methods: 91 participants with regular headache and neck pain completed the Headache Screening Questionnaire to score the criteria for TTH and to identify and exclude migraine. Further, an anamnesis and clinical investigation was performed by an experienced physiotherapist, wherein all criteria of CGH and MFH were investigated. To evaluate the correlation between the criteria, a trivariate Jaccard Similarity Index (JSI) was calculated. Next, a multilabel random forest analysis was performed and a decision tree was constructed.

Results: 33 participants were classified as probable or definite TTH, 2 participants as CGH, 6 as MFH, 42 as a combination of TTH and MFH and 5 as a combination of TTH and CGH. 3 participants could not be classified into any category. The duration of TTH episodes and the temporal relation of onset and parallel improvement/deterioration of headache and neck pain in CGH and MFH show high correlations (JSI: 0.69-0.79). The decision tree marks the presence of trigger points as the most defining criterium to discriminate between headaches. Not enough subjects were classified as CGH to include this as an outcome of the tree.

Conclusion: 56% of people with TTH also scored positive for MFH. This myofascial componeny is the most defining criterium in differentiating headaches, which justifies the development of the MFH criteria as a specific subtype of headache. More people with CGH are needed to expand the decision tree.

Fig. 1



P298

Development of the EMHA migraine scoring system

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Objective: The EMHA developed the Migraine Scoring System to enhance patient-clinician communication about migraine burden and reduce stigma, offering a practical tool for patients in clinical and advocacy contexts. Though not intended for diagnosis, it may help track meaningful changes in severity over time (e.g., transitions between episodic and chronic migraine).
Development followed key opinion leader workshops and pilot testing in a Spanish patient cohort (n ≈ 300). The final 4-item tool assesses: (1) monthly headache days, (2) effectiveness of acute medication (days with "good response"), (3) pain intensity, and (4) overall attack intensity (categorical scale). This is the first psychometric validation of the tool, as a step toward broader multilingual implementation, with English language validation already conducted with a UK patient cohort (n ≈ 50).
Methods: Psychometric evaluation in the Spanish cohort included confirmatory factor analysis (CFA) to assess dimensionality and internal consistency using reliability coefficients. Measurement invariance tested whether the scale functioned equivalently across Spanish and English languages. The same methodology is planned for multilingual validation in Danish, Dutch, German, Greek, and Portuguese.
Results: CFA supported a unidimensional model with excellent fit (CFI=1.000,TLI=1.001,RMSEA=0.000,SRMR=0.002), with the general factor explaining 74.4% of variance. Internal consistency was acceptable (Cronbach"s α=0.73) and higher when adjusting for item weightings (Omega Total=0.83). Measurement invariance confirmed full equivalence across language, supporting cross-group comparisons.
Conclusion: The EMHA Migraine Scoring System is unidimensional, interpretable, and standardized tool with adequate psychometric properties. Ongoing multilingual validation in five European languages will assess its broader applicability, additionally to the already tested Spanish and English languages.

P299

Aura images are not enough to diagnose migraine with aura

N. van Veelen[1], ***E. van Eijk***[1], *I. de Boer*[1], *G. M. Terwindt*[1]

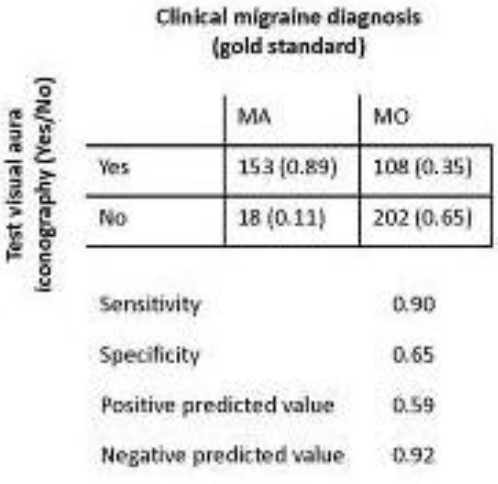
[1]Leiden University Medical Center, Neurology, Leiden, Netherlands

Objective: Accurate diagnosis of migraine with aura is crucial. Visual aura images may enhance diagnostic accuracy.
Methods: Patients with clinical migraine diagnoses were included. Upon enrolment, participants completed a survey followed by a questionnaire featuring an image depicting visual aura disturbance. The diagnostic accuracy of the iconography alone and the iconography in combination with a questionnaire were compared to clinical diagnoses.
Results: A total of 481 migraine patients were included. The visual aura image alone demonstrated a sensitivity of 90% and a specificity of 65%. When a validated extensive questionnaire was added, the sensitivity decreased to 53%, while the specificity increased to 90%.
Conclusion: The visual aura image alone may identify more migraine with aura (MA) cases compared to adding an extensive questionnaire. However, more false positive cases will be identified.

Fig. 1



Fig. 2



P300

Lasmiditan-overuse headache?: Time-series clustering analysis for treatment pattern of lasmiditan for two years from the initial prescription

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Objective: Migraine is a highly prevalent neurological disorder and a leading cause of disability worldwide. Although triptans and non-steroidal anti-inflammatory drugs (NSAIDs) are widely used, a substantial proportion of patients show inadequate responses. Lasmiditan, a selective 5-HT1F receptor agonist introduced in Japan in January 2022, represents a novel acute treatment option that lacks vasoconstrictive activity and can be prescribed even in patients with cardiovascular risk. However, little is known about the trend of its long-term real-world use. To characterize two-year lasmiditan prescription patterns using time-series clustering.

Methods: Data were extracted from the REZULT database for patients aged ≥15 years diagnosed with migraine (ICD-10 code G43) between January 2022 and December 2024. Prescription claims were analyzed in 90-day intervals for up to 24 months after the initial lasmiditan prescription. Time-series clustering was applied to identify subgroups with distinct trajectories of lasmiditan use.

Results: Lasmiditan was prescribed to 21,199 out of 167,461 (12.7%) migraine patients, with a mean age of 33.8 ± 10.3 years, and 76.6% being female. In the first three months, 86.2% were prescribed 50 mg tablets, 12.8% were prescribed 100 mg tablets, and 1.0% received both dosage. About half were also prescribed single analgesics, and 66.7% received triptans, while 33.9% were given prophylactic drugs. The dosages of lasmiditan were gradually tapered down over the two years. The main long-term prescription pattern was a combination of analgesics, triptans, and lasmiditan. Time-series clustering identified three patient groups: Cluster 1 used lasmiditan consistently over time, cluster 2 gradually decreased its usage, and cluster 3 reduced it immediately.

Conclusion: According to real-world data, there are three prescription patterns. There might be a possibility of lasmiditan overuse. The appropriate use of lasmiditan should continue to be investigated.

P301

Safety, tolerability and efficacy of atogepant added to onabotulinumtoxina for the preventive treatment of chronic migraine: A phase 3, multicenter, 24-week, open-label study

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[6]The Los Angeles Headache Center, Los Angeles, CA, United States

Objective: To evaluate the safety, tolerability, and efficacy of adding atogepant to onabotulinumtoxinA (onabotA) for the preventive treatment of chronic migraine (CM).

Methods: In this 24-week, Phase 3, open-label, multicenter study (NCT05216263), 75 participants on a stable dose of onabotA (155-200U) received add-on atogepant 60mg once daily. Primary safety endpoints included treatment-emergent adverse events (TEAEs), and efficacy assessments included changes in mean monthly migraine days (MMDs), and responder rates (RR) (≥50% and ≥75% MMDs) over weeks 1-12 and weeks 13-24.

Results: The mean age of study participants was 48 years; 89% were women, and 97% were white. Participants had an established CM diagnosis for 15

(13.27) years (mean (SD)) and had been treated with onabotA for 4 (3.45) years (mean (SD)). In the safety population (n = 75), the incidence of TEAEs was 65.3%. TEAEs occurring in ≥5% of patients were constipation (n=12, 16.0%), nausea (n=10, 13.3%), and urinary tract infection (n=6, 8.0%). Treatment-emergent serious AEs occurred in 2 participants, neither considered treatment-related by the investigators. In the modified intention-to-treat population (n = 72), the change from baseline of 14.34 MMDs was -6.45 MMDs [95% CI: -7.72, -5.19] across weeks 1-4, -6.89 MMDs [95% CI: −8.15, −5.62] across weeks 1-12 and −7.20 MMDs [95% CI: −8.49, -5.91] across weeks 13-24 (least square means). A ≥50% RR was achieved by 54.2% and 61.9% of participants, across weeks 1-12 and weeks 13-24 of combined treatment, respectively. A ≥75% RR was achieved by 30.6% and 38.1% participants, respectively.

Conclusion: Combination management with onabotA and atogepant for CM appears to be safe and generally well-tolerated. In this study the addition of atogepant to onabotA resulted in clinically meaningful reductions in migraine days and improvement in responder rates, reflecting the potential benefit of utilizing combination therapy with distinct but complementary mechanisms of action for CM management.

P302

Efficacy and safety of antimigraine therapy with or without fluoxetine for migraine: A systematic review and meta-analysis

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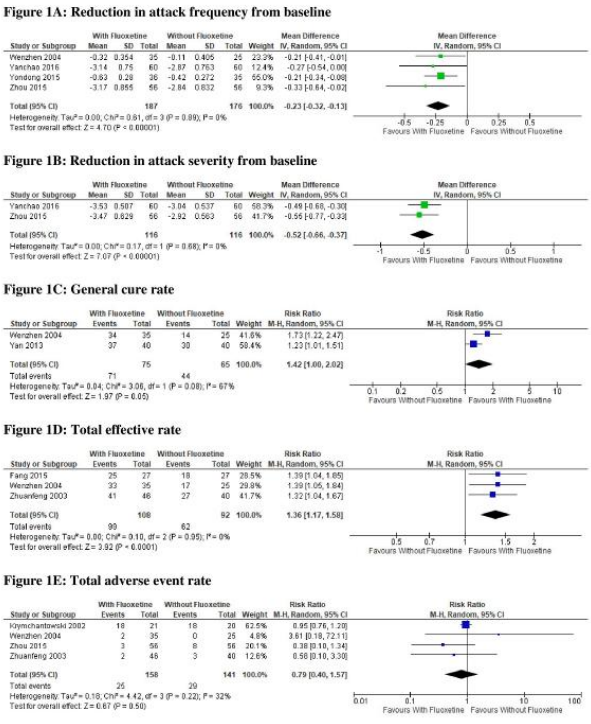
Objective: To systematically evaluate the effectiveness of fluoxetine addition to antimigraine regimens.

Methods: We searched PubMed, Embase, Scopus, Web of Science, ChongQing VIP Chinese Journals Platform, Cochrane and ClinicalTrials.gov from inception to September 2025 for randomized controlled trials comparing fluoxetine addition to antimigraine therapy versus no addition. RevMan v5.4.1 was used for statistical analyses, and dichotomous outcomes were pooled as risk ratios (RR) and continuous outcomes as mean differences (MD), with 95% confidence intervals (CI). A P-value <0.05 was considered statistically significant.

Results: Eight trials (N = 610) were included. Compared to control, fluoxetine addition was associated with a significant reduction in attack frequency (MD -0.23, 95% CI -0.32 to -0.13) and attack severity (MD -0.52, 95% CI -0.66 to -0.37). Pooled analysis suggested improved total effective rates (RR 1.36, 95% CI 1.17 to 1.58). No significant difference was observed for general cure rates or total adverse event rates between groups.

Conclusion: The addition of fluoxetine to standard antimigraine therapy appears to confer modest but clinically meaningful benefits in reducing attack frequency and severity, and in improving overall treatment effectiveness, without a corresponding increase in adverse events. However, evidence for cure rates remains inconclusive. Given the limited number and variable quality of included trials, further large-scale, rigorously designed randomized controlled trials are needed to confirm these findings and to better define the role of fluoxetine in antimigraine regimens.

Fig. 1



P303

MIGRA-MS: A case series on chronic migraine and multiple sclerosis

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Objective: To describe the clinical and therapeutic characteristics of patients with multiple sclerosis (MS) and chronic migraine, assessing their evolution under conventional and emerging therapeutic strategies.

Methods: A retrospective analysis of six adult patients with MS (2017 McDonald criteria), and chronic

migraine (ICHD-3 criteria) resistant to conventional therapies. Data collected included sociodemographic variables, headache characteristics, demyelinating disease features, and therapeutic approaches. All patients gave their consent to publish their details in an open access journal

Results: Six patients (five women, median age 50 years) with relapsing–remitting MS and psychiatric comorbidities, under adequate relapse control, were included. Prior treatments included interferons and glatiramer acetate; current therapies consisted of ocrelizumab, natalizumab, alemtuzumab, teriflunomide, or dimethyl fumarate. Chronic migraine developed after a mean of 15 years from MS diagnosis, with a median of 27.5 headache days per month (14 severe). All received a median of three classic preventives (amitriptyline in all cases) and onabotulinumtoxinA (PREEMPT, 155 IU) with only one responder; two patients received an extended dose (195 IU) without benefit and later CGRP monoclonal antibodies (galcanezumab, erenumab, eptinezumab) with no response, and atogepant with only transient or partial benefit. No adverse effects were observed. One patient improved after menopause.

Conclusion: Migraine is more prevalent in MS patients than in the general population, and their coexistence represents a therapeutic challenge. In this case series of relapsing–remitting MS with chronic resistant migraine, response to onabotulinumtoxinA and anti-CGRP therapies was limited, with no drug interactions or adverse effects observed. An individualized approach and further studies are needed to assess emerging treatments in this subgroup.

P304

Efficacy of greater occipital nerve block in refractory vertex pain

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Objective: Vertex pain syndromes may present as atypical variants of migraine, tension-type headache, or cervicogenic headache. Because the greater occipital nerve (GON) provides overlapping afferents to the trigeminocervical complex, targeted blockade can relieve pain extending to the vertex. The objective of this study was to evaluate the efficacy of greater occipital nerve block (GONB) in patients with refractory vertex pain.

Methods: Twelve adults (7 women, 5 men; mean age 38 ± 9 years) with chronic vertex pain unresponsive to conventional therapy underwent bilateral GONB using 2 mL of 1% lidocaine + 40 mg triamcinolone per side. Pain intensity (VAS 0–10) and headache frequency were recorded at baseline, 1 week, 4 weeks, and 8 weeks.

Results: Mean baseline VAS was 8.1 ± 0.9, which improved to 3.4 ± 1.6 at 1 week, 3.9 ± 1.8 at 4 weeks, and 4.8 ± 2.0 at 8 weeks ($p < 0.001$). Headache days/month decreased from 22 ± 5 to 10 ± 6 at 4 weeks ($p < 0.001$). Nine patients (75%) achieved ≥50% pain reduction, with better responses in those with migrainous features. No major adverse events occurred; transient local tenderness in 2 patients resolved spontaneously.

Conclusion: GONB provided rapid and sustained relief in most patients with vertex-predominant headache, supporting convergence of occipital and trigeminal pathways as a therapeutic target. It should be considered as an adjunct for refractory vertex pain and atypical migraine variants.

P305

Dorso lateral prefrontal cortex stimulation vis TMS in chronic migraine patients refractory to anti CGRP monoclonal antibodies: Effects on clinical, neuropsychological and neurophysiological variables

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Objective: The aim of the present study was to test the efficacy of an accelerated protocol of theta burst stimulation via the dorso lateral prefrontal cortex - DLPC- in a group of chronic migraine patients who did not respond to monoclonal antibodies against CGRP.

Methods: This was a controlled single-blind study in 12 chronic refractory migraine patients. An accelerated protocol of intermittent theta burst stimulation (iTBS) on DLPC was preceded by a sham session and followed by a 2-month follow-up. Cognitive and emotional Stroop testing was performed at basal, after sham and real stimulation, and at follow-up during high-density EEG recording to obtain event-related potentials Stroop data from an age- and sex-matched control group were compared with those of migraine patients.All patient gave their informed consent to publish their details in an open access journal.

Results: Migraine features, anxiety, depression, and cognitive performance, improved after real stimulation.. The Stroop test was impaired in the basal condition, as evidenced by an increase in reaction time and a decrease in N2 and LP in the cognitive task, which returned to normal after real iTBS and at follow-up.

Conclusion: The results support the efficacy of iTBS as a non-invasive neuromodulation approach for the treatment of chronic, refractory migraine and highlight the role of cognitive fog and psychopathological symptoms in refractoriness to

anti-CGRP medications. They propose this non-pharmacological approach as an additional promising therapeutic option for such problematic patients.

Fig. 1

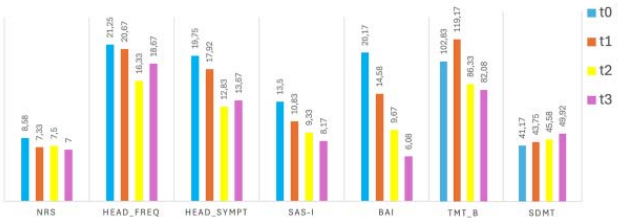


Fig. 2

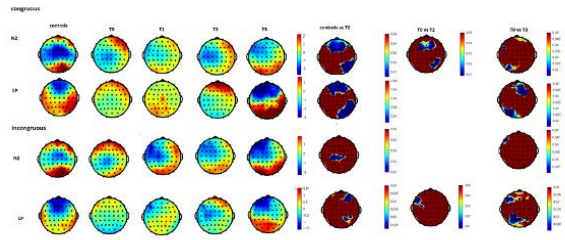
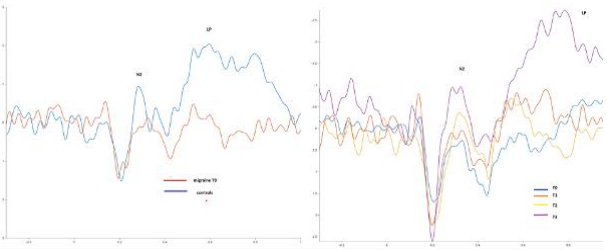


Fig. 3



P306

Investigating the neuromuscular mechanisms of repetitive Neuromuscular Magnetic Stimulation (rNMS): A randomized sham-controlled study in healthy adults

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[5]University Hospital Ulm, Department of Diagnostic and Interventional Radiology, Ulm, Germany

Objective: Repetitive neuromuscular magnetic stimulation (rNMS) targeting the upper trapezius muscles (UTM) has shown promising results as a non-invasive, non-pharmacological treatment approach for episodic migraine. Its therapeutic effects are presumed to involve modulation of the trigemino-cervical complex. However, the precise neuromuscular and central mechanisms of action remain insufficiently understood. This randomized, sham-controlled, multiparametric diagnostic study aimed to explore the physiological effects and underlying mechanisms of rNMS in healthy individuals.

Methods: 70 healthy adults (age 18-35 years) were randomly assigned to receive either active (verum) or sham rNMS. The intervention consisted of 6 sessions over a 2-week period, with bilateral stimulation of the UTM (20Hz, 7s on/10s off, 15min per side). The verum group received rNMS using a certified device (Zimmer MedizinSysteme GmbH, Neu-Ulm, Germany), while the sham group was treated with an identical-appearing device that did not emit electromagnetic fields. Assessments were conducted at baseline, post-intervention, and at 3-month follow-up, including physical examination, identification of myofascial trigger points, measurement of pressure pain thresholds (PPT) using algometry, infrared thermography (IRT), and B-mode ultrasound imaging.

Results: To determine the neuromuscular effects of rNMS, changes in PPT, thermal distribution (IRT), and sonographic features of the UTM are being analyzed and compared between the verum and sham groups at all timepoints. Data analysis is currently ongoing, and final results will be presented at the conference.

Conclusion: This study is expected to provide deeper insights into the physiological mechanisms of rNMS at the level of the UTM. The findings may support the optimization of rNMS treatment protocols and contribute to a better understanding of its application in clinical populations, such as patients with episodic migraine.

P307

Repetitive neuromuscular magnetic stimulation in pediatric headache: Insights from extensive clinical practice

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Objective: Primary headache disorders are often associated with significant limitations in participation and daily functioning. In addition, myofascial symptoms—particularly in the upper trapezius muscle—frequently occur. Repetitive neuromuscular magnetic stimulation (rNMS) has emerged as a safe and promising intervention targeting both headache symptoms and associated muscle dysfunction via bottom-up neuromodulation of the trigemino-cervical complex. This observational study presents clinical insights and outcomes from the application of rNMS in a large cohort of pediatric patients.
Methods: The rNMS treatment protocol consisted of six sessions over three weeks, with each session delivering 30 minutes of net stimulation time. Pediatric patients receiving care at our headache center underwent a comprehensive evaluation, including headache-specific questionnaires, clinical and physiotherapeutic assessments, pressure algometry of the UTM, and safety monitoring. Feedback from patients and their caregivers regarding treatment experience was also gathered.
Results: By the time of the conference, data from 100 completed treatment blocks will be available. Preliminary analysis of 78 blocks showed a significant reduction in headache frequency ($p=0.016$). Pressure pain thresholds in the UTM increased significantly post-treatment, with these improvements persisting at the three-month follow-up ($p<0.001$). The intervention was well tolerated, with approximately 80% of patients reporting no adverse events, and adherence was high, with over 85% of sessions completed as scheduled.
Conclusion: The high acceptance rate and sustained clinical benefits support rNMS as a promising, non-invasive treatment option for primary headache disorders in pediatric patients. While these initial findings are encouraging, further validation through controlled clinical trials is essential to confirm the efficacy and broaden the understanding of rNMS in this population.

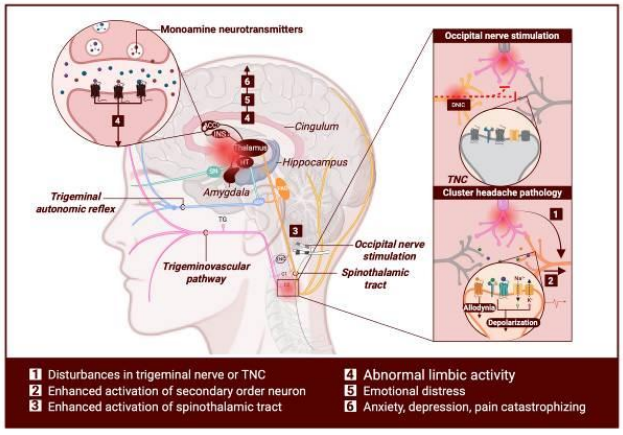
P308

Mind over cluster headache: Charting the dynamics of occipital nerve stimulation and emotional distress

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Objective: Cluster headache (CH) is associated with higher rates of depression and anxiety, highlighting the role of psychological factors in the condition. Nevertheless, studies often prioritize quantitative outcomes, such as improvements in attacks, while neglecting critical qualitative dimensions, including emotional distress and psychological well-being. As a result, awareness of the psychological impact remains limited, and the validity of current definitions of responders to treatments like occipital nerve stimulation (ONS) becomes questionable. This study evaluates the relationship between CH, ONS, and factors of emotional distress including anxiety, depression and pain catastrophizing.
Methods: Data on the Hospital Anxiety Depression Scale (HADS), Pain Catastrophizing Scale (PCS) and attack intensity/frequency/duration are collected at baseline, 3-, 6- and 12-months follow-up, in patients with intractable CH treated with ONS. A literature analysis is performed to propose a theory connecting CH pathology, ONS outcomes and emotional distress.
Results: Forty patients (42 ± 12.7yrs)(M=23) are included in this study. Overall, ONS improves attack frequency, intensity and duration with 81%. HADS and PCS scores were reduced by 78% and 72% respectively, including in those who would usually be classified as partial or non-responders to ONS (<30% reduction in attack intensity and/or frequency). Higher preoperative HADS/PCS scores are correlated to reduced improvements in postoperative pain scores ($r=0.8$)($p=0.04$). The theory suggests that trigeminal dysfunction in CH may trigger abnormal limbic activation, while ONS may restore balance via diffuse noxious inhibitory control (DNIC) into the trigeminal nucleus caudalis (TNC). Dysfunction in limbic structures and the trigeminal system may contribute to poor outcomes with ONS.
Conclusion: Emotional distress is a significant contributor to CH and ONS, and should therefore be assessed in prospective studies evaluating course of the disease and treatment outcomes.

Fig. 1



P309

Neuromodulation in trigeminal autonomic cephalalgias: 11-year experience of non-invasive vagus nerve stimulation

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Objective: To evaluate the effectiveness and tolerability of non-invasive vagus nerve stimulation (nVNS) as acute or preventive treatment, or both, in a cohort of Trigeminal Autonomic Cephalalgias (TACs) patients.

Methods: A service evaluation retrospectively included patients with TACs between January 2014 to February 2025 who had used, or currently use, nVNS. Data were collected from clinical letters. Data are presented as descriptive statistics analysis and nonparametric tests were performed.

Results: A total of 108 patients were included, 74 patients with cluster headache (CH), 10 with paroxysmal hemicrania, 15 with hemicrania continua, four with Short-lasting Unilateral Neuralgiform headache with Conjunctival injection and Tearing (SUNCT), three with Short-lasting Unilateral Neuralgiform with cranial Autonomic symptoms (SUNA) and two with undifferentiated TAC. Overall, 70 patients considered nVNS useful over a median time using nVNS of 47 (IQR, 66 – 18) months. The median time of using in patients whom did not found nVNS useful was 7 (IQR, 4 – 12) months. Twenty-three patients reported an adverse event (AE), while no serious treatment-related AEs occurred. Fifty-nine patients withdrew from using the device, including 11 patients that initially reported nVNS as useful. All groups considered nVNS more useful as preventive, while cluster headache and SUNCT/SUNA patients also considered it useful as acute treatment.

Conclusion: Our findings complement previous evidence of the effectiveness and tolerability of nVNS in CH in addition to other forms of TACs. Interestingly, nVNS seems to be more effective as preventive rather than as acute treatment in our cohort.

Fig. 1

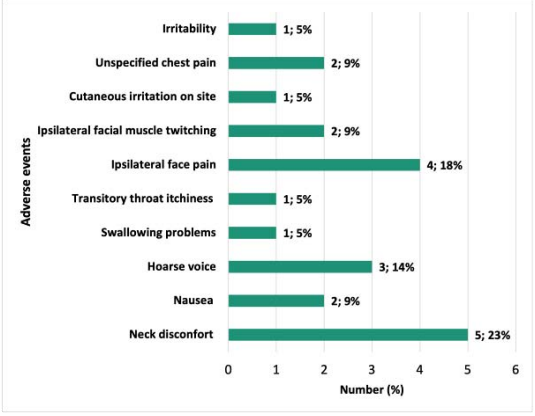


Fig. 2

TABLE 1 – Data summarized by the different TACs diagnosis at baseline

	eCH (n = 27)	cCH (n = 47)	PH (n = 10)	HC (n = 15)	SUNCT/SUNA (n = 7)	UND TACs (n = 2)	P value
DEMOGRAPHICAL DATA							
MALE, n (%)	25 (93%)	28 (60%)	1 (10%)	4 (27%)	3 (43%)	1 (50%)	< 0.001 [a]
Age, years, mean (SD)	55 (15)	51 (13)	50 (16)	53 (13)	58 (10)	65 (17)	0.474 [c]
CLINICAL CHARACTERISTICS							
Attack frequency, daily, median (IQR)	4 (5)	6 (5)	7 (12)	3 (7)	21 (117)	2 (-)	< 0.001 [a]
Attack duration, minutes, median (IQR)	60 (60)	90 (135)	20 (45)	120 (1440)	12 (17)	53 (-)	< 0.001 [a]
Coexisting ICHD-3 headache, n (%)	13 (48%)	29 (62%)	7 (70%)	5 (33%)	7 (100%)	1 (50%)	0.069 [b]
Psychiatric comorbidities, n (%)	2 (7%)	5 (11%)	1 (10%)	2 (13%)	1 (14%)	-	0.980 [b]
Number previous preventives failures, median (IQR)	3 (3)	5 (4)	5.5 (4)	4 (4)	7 (5)	5 (1)	0.060 [c]
Number of concomitant preventives, median (IQR)	1 (1)	1 (1)	1 (1)	1(2)	1 (2)	1 (0)	0.682 [c]
nVNS DATA							
General useful, n (%)	20 (74%)	30 (64%)	5 (50%)	11 (73%)	4 (57%)	0 (0%)	0.275 [b]
Preventive useful, n (%)	15 (56%)	26 (64%)	4 (80%)	11 (100%)	3 (75%)	-	0.432 [b]
Acute useful, n (%)	8 (30%)	18 (38%)	2 (40%)	3 (27%)	2 (50%)	-	0.372 [b]
AEs, n (%)	2 (7%)	8 (17%)	4 (40%)	8 (53%)	1 (17%)	0 (0%)	0.009 [b]
Withdrawal, n (%)	9 (33%)	28 (60%)	6 (60%)	8 (53%)	6 (86%)	2 (100%)	0.078 [b]

Abbreviations: AEs, adverse events; CH, Cluster Headache; HC, Hemicrania continua; IQR, interquartile range; N, number; nVNS, non-invasive Vagus Nerve stimulation; PH, Paroxysmal headache; SD, standard deviation; TACs, Trigeminal Autonomic Cephalalgias; UND, Undifferentiated.

[a]Kruskal-Wallis Test [b]Fisher's Exact Test

P310

Efficacy of TDCS in chronic migraine

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Objective: Chronic migraine (CM) make up the largest proportion of patients referring to specialized headache clinics. Patients with CM, are mostly resistant to medical therapy. Non-pharmaceutical therapies for chronic migraine might provide new opportunities for chronic headache treatment. Transcranial direct current stimulation (tDCS), a non-invasive neurostimulation method, is generally considered a safe form of neuromodulation with minimal severe side effects, utilizing constant, low direct current. In this clinical trial, we assessed the efficacy of tDCS in chronic migraine.

Methods: to investigate the efficacy of TDCS in the treatment of CM with and without MOH.

The anodal stimulation was applied on the right DLPFC and the cathodal stimulation on the occipital cortex. TDCS was applied for 3 consecutive days per week for 2 weeks and then once a week for another 6 weeks. During each session, a current of 2mA was delivered for 20 min, with a fade-in/fade-out period of 30 s.

We assessed the efficacy of this tDCS stimulation protocol based on the mean variation in the number of migraine headache days, the mean headache intensity and the mean headache duration, comparing the baseline pre-interventional period to the 8 week post-interventional period.

Results: Of the total 30 CM patients, the co-diagnosis of MOH was found in 56.7% of patients. The data analysis showed significant ($p < .05$) reductions in headache frequency until week four (in 70% of cases). The intensity of headache, the number of severe headaches, awakening headache and headache duration were all improved after 6 sessions (week 2). The best response to TDCS was seen in total headache duration and total severe headaches per week. No serious side effect was reported by the patients.

Conclusion: With the applied protocols of the present study, tDCS can be used as an effective intervention

for the prophylactic and therapeutic treatment of chronic migraine and offers a ray of hope for patients suffering from this debilitating disease.

P311

Occipital nerve stimulation in patients with refractory chronic cluster headache: Long term follow-up

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Objective: To describe the evolution of patients with Refractory Chronic Cluster Headache (RCCH) treated with Occipital Nerve Stimulation (ONS).

Methods: A retrospective longitudinal study of patients treated with ONS at a tertiary hospital headache unit. The primary outcome was the change in attacks per week at 3 and 12 months and at the last follow-up. Secondary variables included side effects and complications.

Results: Twenty-five patients (52.63% male, mean age 50 ± 8.79 years) were included. Six (24%) showed no response after provisional ONS implantation. The median follow-up was 3.83 years (1.16–16.31 years). The median number of attacks per week was: before implantation, 21 (14–28); at 3 months, 5.5 (0.44–19.25); at 12 months, 7 (0.44–14); and at the last follow-up, 10 (2.5–17.5). The reduction was statistically significant ($p<0.05$). Patients achieving >30% reduction were: 61.1% at 3 months, 72.2% at 12 months, and 63.15% at the last follow-up. Treatment was discontinued in six patients (five for inefficacy, one for side effects) after 4 ± 1.89 years. Four required reimplantation, with three recovering prior improvement. Wound infections occurred in 4 cases (21%), and electrode migration in 2 (10.5%).

Conclusion: ONS is an effective therapeutic alternative for RCCH, with long-term effects.

Fig. 1

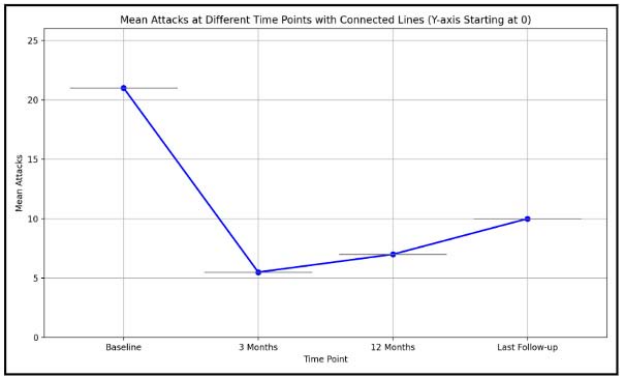
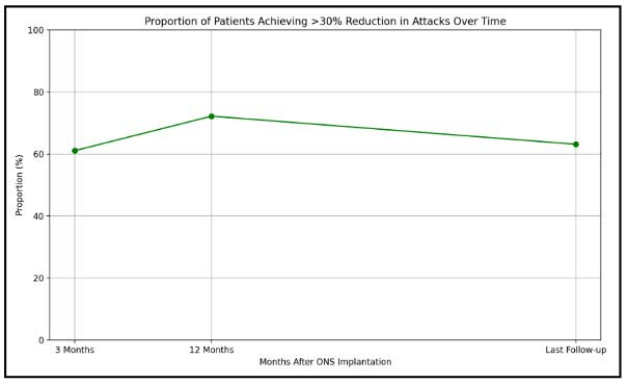


Fig. 2



P312

Ventral Tegmental Area (VTA) Deep Brain Stimulation (DBS) in refractory chronic cluster headache: Our experience of 4 cases

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Objective: Patients with refractory chronic Cluster Headache (rcCH) have limited therapeutic options. VTA DBS has shown effectiveness with a safety profile. We present our series of 4 patients.

Methods: Our multidisciplinary team has expertise in DBS for Parkinson Disease, Essential Tremor, Dystonia, Epilepsy and Psychiatric Diseases. Over the last 10 years, an average of 60 DBS interventions are performed by our functional neurosurgery team every year. Moreover, in our Headache Unit all patients with Cluster Headache are instructed to record daily attacks, the intensity and the duration. We calculate the Average Weekly Attack (AWA) of the 3 months previous to DBS surgery, of the interval from surgery to the day before starting the stimulation, and after 1, 3, 6, 12, 18 and 24 moths from stimulation. Headache Burden Index (BI = weekly attacks × intensity (Visual Analogic Scale/10) × duration (min)) is also available.

In our protocol, bilateral DBS is started 4 weeks after surgery and parameters of stimulation are modified every 2 weeks after achieving control of the attacks.

Results: Results and outcome of our 4 patients are shown in the table.

Conclusion: VTA DBS in Refractory Chronic Cluster Headache is very effective and should not be delayed in centers with expertise in DBS for other neurological diseases.

Fig. 1

Table: Data of our 4 patients with Refractory Chronic Cluster Headache treated with DBS

	Patient 1	Patient 2	Patient 3	Patient 4
Age (yo)	58	40	32	34
Sex	Male	Male	Female	Male
Years from CH onset	24	14	1.5 (chronic onset)	1.5 (chronic onset)
Years since CH chronification	2	12	-	-
AWA[1] of last 3 months before DBS Surgery Burden Index[2]	28 2100	21 4410	28 8400	28 11760
Date DBS Surgery	December 2022	July 2023	February 2025	March 2025
Device implanted	Medtronic Percept PC	Medtronic Percept PC	Medtronic Percept RC	Medtronic Percept RC
Side Effects/Morbidity	None	None	None	None
AWA from Surgery to DBS Stimulation Burden Index	3 720	35 3675	3 720	8 1440
Date of DBS Stimulation	January 2022	August 2023	April 2025	April 2025
AWA 1st month Burden Index	0 0	14 1260	0 0	7 1470
AWA 3rd month Burden Index	0 0	0 0	0 0	2 420
AWA 6th month Burden Index	0 0	0 0	- -	- -
AWA 12th month Burden Index	0 0	2 240	- -	- -
AWA 18th month Burden Index	0 0	3 252	- -	- -
AWA 24th month Burden Index	0 0	4 (till 22nd month) 360	- -	- -

[1]Average Weekly Attacks; [2] Weekly attacks x intensity of attack (Visual Analogic Scale/10) x duration of attack (min)

P313

External electrical stimulation with NERIVIO: Our experience in 3 cases of New Daily Persistent Headache (NDPH)

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Objective: NDPH is a disable primary headache with unclear pathophysiology and limited therapeutic options. NERIVIO is an external electrical device stimulator with proven evidence of its efficacy as a preventive treatment and alleviating attacks in migraine patients.

We aim to evaluate the effectiveness of NERIVIO in NDPH patients.

Methods: Three NDPH patients have been followed in our Headache Unit for more than 3 years. Exhaustive work-up tests ruled out secondary causes and all of them were refractory to anesthetic block of Great Occipital Nerve and Sphenopalatine Ganglion, Onabotulinumtoxin A (PREEMPT protocol), anti-CGRP monoclonal antibody and more than five oral preventive drugs. They were offered NERIVIO for 3 months. Estimulation paradigm was electrical stimulation on the arm during 45 minutes every 48h. The maximal intensity was manually set by the patient at an inframaximal pain threshold.

Results: All patients had a history of continous daily intensity pain of more than 8 up to 10 in Visual Analogic Scale. During the first month of NERIVIO Stimulation, one patient described some relief of pain for 2 weeks: archiving a pain intensity scale of 6. This improvement was transient during the 3 month stimulation and she did not wanted to continue. The other 2 patients did not present any changes in their pain patern and intesity.

Conclusion: NDPH is a frustrating disease refractory to all treatments including NERIVIO Stimulation in this small series.

P314

Preliminary effects of visual and motor cortex tDCS on EEG and clinical outcomes in migraine: A multicenter, double-blind, sham-controlled study

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Objective: Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation method for migraine. Evidence on its EEG effects remains limited. We examined clinical and EEG outcomes of a dual-site tDCS protocol targeting the left motor (M1, anodal) and visual cortex (O1, cathodal) in episodic migraine.

Methods: In this multicenter, randomized, double-blind, sham-controlled trial, 20 patients were enrolled. The active group received 2 mA tDCS for 20 minutes/day over 3 days; the sham group received identical placement, but stimulation was stopped after 30 seconds. EEG was recorded at baseline, post-stimulation, and 1-month follow-up. The power spectral density (PSD) was analyzed across the delta, theta, alpha, beta, and gamma bands. Clinical assessments included the Visual Analog Scale (VAS), Headache Impact Test (HIT-6), Montreal Cognitive Assessment (MoCA), Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI). EEG data were processed using a standardized protocol across centers.

Results: Only VAS scores improved significantly in the active group at 1-month follow-up (mean change: 3.7 vs. 1.8; $p < 0.05$). No significant differences were found for MoCA, BDI, or BAI. At the 1-month follow-up, EEG analysis revealed increased delta power in the left frontal, temporal, and occipital regions ($p < 0.05$, $r = 0.55–0.70$), as well as increased alpha power in the central and right parieto-occipital regions. Immediately after stimulation, a transient suppression of alpha activity was observed in frontal-temporal areas. Sustained increases in beta and gamma power

were detected in right parieto-occipital regions at 1-month follow-up.

Conclusion: Simultaneous tDCS to visual and motor cortices led to pain relief and lasting EEG modulation. Paradoxical increases in alpha, beta, and gamma—contrary to typical interictal patterns—may reflect normalization of cortical excitability. These findings support dual-site tDCS as a promising neuromodulatory strategy.

Fig. 1

Table 1. Delta Frequency Changes Following tDCS - Between-Group Comparison

Region	Group	N	Post-tDCS (Mean± SD)	1-Month Post-tDCS (Mean± SD)	Delta 1 Month -Post (Mean± SD)	Group Difference Mann-Whitney U	Effect Size (r) (Rank biserial correlation)	p
L_F _ PostPost EO delta	A	10	0.058 ±0.048	0.096±0.038	0.0383±0.058	15.0	0.700	0.007
	B	10	0.094±0.125	0.068±0.0041	-0.0258±0.0902			
L_T _ PostPost EO delta	A	10	0.051 ±0.026	0.068±0.060	0.0169 ±0.034	22.5	0.550	0.041
	B	10	0.09±0.079	0.06±0.0053	-0.0304±0.0595			
O1 _ PostPost EO delta	A	10	0.059 ±0.041	0.082±0.049	0.0234±0.0283	22.5	0.680	0.011
	B	10	0.078±0.049	0.075±0.0071	-0.0027±0.0885			

Note. /1 values indicate the change in mean delta power between immediate post-tDCS and the 1-month follow-up. Effect sizes are expressed as rank biserial correlation coefficients.
Based on Mann-Whitney U analyses, significant between-group differenees were found in delta frequency changes at the Left Frontal (L_F), Left Temporal (L_T), and Occipital (O1) regions ($p < .05$). A significant increase in delta activity was observed in Group A compared to Group B across all three regions.

Fig. 2

Table 2. Group Comparisons for VAS and MoCA Scores

Independent Samples T-Test

		Statistic	p	Mean difference	SE difference		Effect Size
VAS_PrePost	Mann-Whitney U	19.5	0.021	-2.000		Rank biserial correlation	0.610
MOCA	Mann-Whitney U	43.5	0.647	1.000		Rank biserial correlation	0.130

Note: H_a: μ A ≠ μ B. Effect sizes are reported as rank biserial correlations. * VAS: Visual Analog Scale** MoCA: Montreal Cognitive Assessment

Following stimulation, a reduction in pain intensity (VAS scores) was observed in both groups, with a more pronounced decrease in Group A. Between-group comparison using the Mann–Whitney U test indicated a statistically significant difference in VAS change scores ($U = 19.5$, $p = 0.021$, $r = 0.610$), favoring Group A. In contrast, no significant difference was found in MoCA scores between the groups ($U = 43.5$, $p = 0.647$, $r = 0.130$).

Table 2. Descriptive Statistics for VAS and MoCA by Group

	Grup	N	Mean	Median	SD	SE
VAS_PrePost	A	10	-3.70	-4.00	1.77	0.559
	B	10	-1.80	-1.50	1.62	0.512
MOCA	A	10	22.10	21.50	3.45	1.090
	B	10	21.40	21.50	2.95	0.933

* VAS: Visual Analog Scale** MoCA: Montreal Cognitive Assessment

P315

Assessment of the effectiveness of sphenopalatine ganglion blockade in the treatment of episodic migraine

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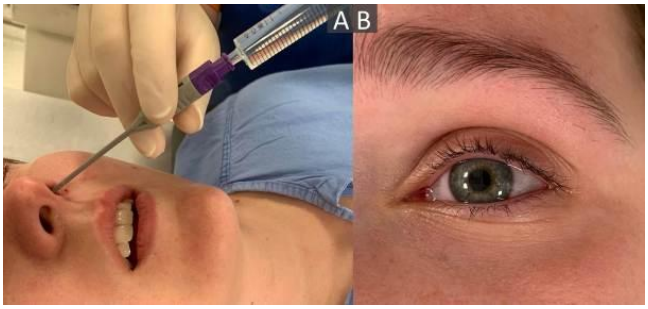
Objective: The objective of this study was to evaluate the effectiveness of sphenopalatine ganglion (SPG) blockade using 4% lidocaine in patients with episodic migraine (EM) who had an inadequate response to conventional pharmacological treatments. The study aimed to assess both the analgesic and preventive effects of repeated SPG blocks on headache intensity, migraine-related disability, and quality of life.

Methods: The study included 31 patients (26 women and 4 men) within an age range diagnosed with episodic migraine. Participants were aged 22–55 years, with a median age of 35 years. The SPG block was performed using a soft, needleless Sphenocath applicator (Curonix) with 4% lidocaine. The same procedure was performed in each patient after 6 weeks. Each patient was assessed using three scales: the VAS pain scale, the MIDAS (Migraine Disability Assessment) scale, and the HIT-6 (Headache Impact Test-6). Patients rated their pain in VAS score and impact of headache on daily functioning as measured by the HIT-6 scale before the block, six weeks after the first block, six weeks after the second block, and six months after the second block. Moreover, the impact of migraine on a person's daily functioning and level of disability was assessed using the MIDAS scale 6 weeks after the second blockade and again 6 months after the second blockade.

Results: SPG blockade significantly reduced pain intensity (VAS), migraine-related disability (MIDAS), and headache impact (HIT-6). After two procedures, the number of monthly migraine and headache days decreased by over 60%. The therapeutic effect was sustained at 6-month follow-up.

Conclusion: Preliminary results of analyses show that blockade of sphenopalatine ganglion can be an effective method of treating episodic migraine. For patients who suffer from migraine headaches, it may be an alternative or complement to pharmacological treatment.

Fig. 1



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Effectiveness of tDCS combined with aerobic exercise on pain and conditioned pain modulation in patients with migraine without aura. A case report

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Objective: Migraine is the most prevalent primary headache, affecting more than 5 million people in Spain. It has a major socioeconomic impact and significantly affects patients" quality of life, being the second leading cause of disability worldwide. The therapeutic landscape for migraine treatment has expanded to include novel pharmacological approaches. However, the chronic nature of migraine has raised interest in non-pharmacological strategies, leading to the development of therapies such as non-invasive brain stimulation, with transcranial direct current stimulation (tDCS) standing out. Likewise, aerobic exercise has strong scientific support as a treatment for migraine, showing evidence of improving headache frequency, pain intensity and headache duration, disability, and quality of life in patients with episodic migraine.
The aim of this study is to assess the effects of tDCS combined with aerobic exercise on pain and conditioned pain modulation in patients with migraine without aura.
Methods: A case report was conducted following the STROBE guidelines, consisting of 10 sessions over 2 weeks, combining an aerobic exercise protocol with tDCS. Pre- and post-intervention assessments were performed, along with follow-ups at 1 and 3 months after the intervention. The participant included in the study had to present a medical diagnosis of migraine without aura, according to ICHD-III criteria, and meet the inclusion and exclusion criteria established for the study.
Results: After 10 intervention sessions and during follow-ups, a trend toward improvement was observed in pain intensity, frequency and duration of headache episodes, conditioned pain modulation, pressure pain threshold, as well as disability and quality of life associated with headache, measured with MIDAS and HIT-6.
Conclusion: The combination of tDCS and aerobic exercise is effective in reducing pain and disability associated with migraine, in addition to improving pain processing in the short and medium term.

Fig. 1



Fig. 2

	Pre-Intervention	Post-Intervention	1 month follow-up	3 month follow-up
Pain Intensity (0-10)	9	4	3	3
Frequency headache	11	3	4	5
Duration headache	24	18	12	4

Fig. 3



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Primary cough headache – Botulinum toxin protocol treatment with a new indication?

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Objective: Primary cough headache (PCH) is a rare disorder characterized by sudden-onset, explosive headache triggered by Valsalva maneuvers (e.g., coughing or straining), without underlying intracranial abnormalities. Up to two-thirds of patients may present associated symptoms such as vertigo, nausea, or sleep disturbances. Indomethacin is the first-line treatment, but alternatives like acetazolamide or cerebrospinal fluid drainage have shown benefit in refractory or contraindicated cases.
Methods: A 69-year-old woman with a history of hypertension, esophageal hernia, solitary kidney, and menstrual migraine reported a new headache pattern, triggered exclusively by coughing and sneezing. She

described sudden, severe headaches, peaking within one minute and lasting less than two hours, without visual changes or jaw claudication. Initial treatment with flunarizine was ineffective. Brain Angio-MRI excluded vascular or structural abnormalities suggesting intracranial hypertension, and fundoscopy was normal. Lab tests including CRP, ESR, and renal function were unremarkable. A diagnosis of PCH was made. Given the solitary kidney, NSAIDs like indomethacin were avoided, and acetazolamide was prescribed, leading to clinical improvement. However, treatment was stopped due to renal impairment.

Results: Trials with amitriptyline and propranolol were unsuccessful. A PREEMPT protocol with botulinum toxin was initiated, resulting in a reduction in headache frequency to 15 days/month after the first cycle, and fewer than 5/month after the second, with sustained improvement.

Conclusion: Botulinum toxin is a safe and effective therapeutic option for PCH, especially in patients unresponsive to or intolerant of standard pharmacological treatments.

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Headache as a secondary manifestation of obstructive sleep apnea: A systematic review

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Objective: This study analyzed headache characteristics associated with obstructive sleep apnea (OSA) and the Impact or therapeutic Interventions, distinguishing morning headache from headache secondary to OsA.

Methods: A systematic review was conducted according to the cochrane Handbook for Systematic Reviews of Interventions. The search included PubMed, Cochrane Library and Lilacs, using descriptors connected to OSA, headache and treatments. Primary studies (clinical trials, cohort studies, observational studies) and systematic reviews were selected. Studies without full text, narrative reviews and those that did not address headache as a primary or secondary outcome were excluded. The analysis followed the PRISMA criteria.

Results: A total of 243 studies were identified, including 26 by manual search. After eligibility criteria, 8 were included in the final analysis. The findings indicated that morning headache is the most frequently associated manitestation of OSA, especially in severe cases. Interventions such as the use of CPAP have shown efficacy in reducing the prevalence and severity of headache. The review revealed that headache can be influenced by factors such as sleep fragmentation, daytime sleepiness, and respiratory symptoms.

Conclusion: OSA is significantly associated with morning headache. Therapeutic interventions, especially CPAP, appear to be effective in reducing this symptom. However, the methodological heterogeneity of the studies suggests the need for more standardized research to better understand the relationship between OSA and headache. Keywords: Obstructive sleep apnea Secondary headache, CPAP, Systematic review.

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Peripheral immune and metabolic dysregulation in migraine, Ménière's disease, and vestibular migraine: A single-cell atlas study

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Objective: Although immune microenvironment-related cells are crucial for cross-disease pathogenesis, their cellular mechanisms remain unclear, such as Migraine (MI), Ménière"s disease (MD) and vestibular migraine (VM).

Methods: We utilized a single-cell RNA sequencing dataset of peripheral blood mononuclear cells from ight patients with MI, five patients with MD, five patients with VM, and six healthy controls. A cross-disease cell atlas was constructed by analyzing cellular heterogeneity and dynamic changes in cell abundance. Further investigations focused on the heterogeneous characteristics of metabolic reprogramming, and differential expression analysis was performed across the groups. The core regulatory pathways were identified using gene set enrichment and pathway analyses. Additionally, pseudotime analysis was employed to infer the evolutionary trajectories, identifying key genes associated with differentiation.

Results: We firstly identified five cell types: T cells, B cells, dendritic cells, natural killer cells, and monocytes. Among these, T cell abundance significantly increased, whereas monocytes are essential for metabolic reprogramming.Notably, the upregulated MAPK signaling pathway was identified as the core regulatory pathway. T cell trajectory analysis revealed two differentiation pathways originating from CD8+ T cells that diverged into CD4+ T cells and naïve T cells. *PRKCA* was significantly upregulated during differentiation, being highly expressed in the disease groups.

Conclusion: This study delineated the immune cell cluster characteristics of MI, MD, and VM, revealing dynamic T cell imbalances within the immune microenvironment. Highly expressed *PRKCA* is a key regulatory node driving pathological processes through the MAPK signaling pathway,providing a foundation for subsequent research into novel therapeutic targets and theoretical insights.

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Alterations in the expression of histone deacetylases 1 and 6 genes and proteins in migraine patients

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Objective: The mechanisms of pathogenesis of migraine are poorly understood. Except for a few rare migraine variants, the roles of genetic and epigenetic mechanisms in migraine pathogenesis remain largely unknown. The aim of this study was to evaluate the expression of histone deacetylases 1 and 6 (HDAC1 and HDAC6) genes, which are enzymes that epigenetically regulate gene expression, in the blood of migraine patients and healthy controls. Both HDCA1 and HDCA6 may facilitate chromatin relaxation, potentially contributing to increased gene expression. Additionally, HDCA6, through the acetylation of non-histone proteins, is involved in cytoskeletal dynamics and protein quality control.
Methods: This study included 32 low-frequency episodic migraine patients and 28 controls without headaches. Blood samples were collected during the interictal phase of migraine. The expression of the HDCA1 and HDCA6 genes was determined by real-time qPCR, and the levels of HDCA1 and HDCA6 proteins were assessed using the ELISA test.
Results: We observed a decrease in HDCA1 expression in migraine patients compared to controls ($p < 0.01$). No difference was noted for HDCA6. Similar trends were observed for the HDCA1 and HDCA6 proteins. We observed several correlations between HDCA1 expression and migraine characteristics, including migraine intensity, headache frequency, and the mental state of migraine patients.
Conclusion: Migraine patients may be characterized by lower expression of specific genes regulated by HDCA1, which could be further investigated in future research. Overall, our study suggests that epigenetic control may represent an important factor in migraine pathogenesis and, therefore, could be considered in its therapy, with HDCA1 potentially targeted to enhance its expression. However, bioinformatic, experimental, and clinical studies are necessary to clarify how HDCA1 might serve as a therapeutic target in migraine.

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Pipeline for DNA methylation analysis using Illumina EPIC Beadchip arrays in complex polygenic diseases

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Objective: Genes associated with epigenetic changes in polygenic, complex diseases, such as migraine, tend to be overlooked given their small individual effects and high sample heterogeneity. Moreover, the substantial influence of technical artifacts and the absence of standardized methodologies for EWAS studies further reduce the power to detect potential epigenetic signals. We propose a pipeline for DNA methylation data analysis in migraine, combining two different versions of the Illumina EPIC array.
Methods: Data was split into training and test, leveraging the existent split in the two versions of the array and ensuring a proper distribution of cases and controls. After quality control and preprocessing, the M-values were used in four different batch-corrected pipelines. Using feature selection techniques, the most significant CpGs for each methodology were obtained evaluating their outcome predictive ability.
Results: Data was collected from 259 samples; training set with 194 individuals (66% cases, 34% controls), and test set with 67 individuals (54% cases, 46% controls). Cell-type composition was estimated and included–along with statistically significant covariates–in the batch-corrected linear models that identified differentially methylated CpGs. Permutation tests were applied to determine the optimal p-value threshold, then combined with random forest-based feature selection. The AUC of each model was compared to identify the best-performing pipeline.
Conclusion: The complex methodology described highlights the need for robust and standardised pipelines for methylation data analysis in the context of complex diseases. Such approaches are essential to minimise the false discovery rate and to improve the identification of novel biomarkers.

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Autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and headaches

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Objective: Introduction: CADASIL is the most common hereditary angiopathy. It occurs due to a mutation in the NOTCH3 gene, located on chromosome 19. The gene encodes a protein that acts mainly in the maintenance of vascular functional stability. CADASIL carriers have a higher risk of developing headache, especially migraine with aura, suffering from successive attacks throughout life.
Methods: Analysis of the prevalence of headache in patients diagnosed with CADASIL.
Results: Headache attacks are frequent and initial manifestations, affecting 20-40% of patients. CADASIL carriers present repetitive attacks, usually beginning in adolescence. The relationship between migraine and CADASIL can be justified by the identification of genetic anomalies in chromosome 19 in familial hemiplegic migraine and episodic ataxia. The first episodes of migraine may occur before the age of 20 and precede or be associated with early radiological changes (punctate hyperintensities in the deep or periventricular white matter) that may also be present in some individuals with primary migraine. Treatment remains a challenge to be solved. Gene therapy has shown promising approaches such as antisense oligonucleotides and short hairpin RNA (shRNA).
Conclusion: Migraine with aura events constitute the most characteristic and earliest initial symptom of patients with CADASIL. The lack of treatments that can interfere with the pathogenesis

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Polygenic risk score analysis in a portuguese cohort sheds light on migraine genetics

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Objective: Migraine is a common, polygenic neurovascular disorder whose pathophysiology remains partially understood. This study aimed to develop a polygenic risk score (PRS) based on genome-wide association study (GWAS) data to identify genetic variants associated with migraine and explore their potential relevance in disease mechanisms.
Methods: We analyzed GWAS data from a Portuguese cohort of 380 individuals (190 migraine patients and 190 controls) recruited from Centro Hospitalar Universitário de Santo António (CHUdSA) and CGPP-i3S. Quality control and PRS calculation were performed using PLINK software. The PRS was constructed using the clumping + thresholding (C+T) method across multiple p-value thresholds. SNPs were analyzed for association strength, linkage disequilibrium, and known clinical significance.
Results: The optimal PRS models were obtained at lower p-value thresholds, reflecting the limited sample size and increased noise at broader thresholds. No previously identified migraine-associated SNPs surpassed genome-wide significance ($p < 5\times10^{-8}$), though several variants of unknown significance (VUS) with strong effect sizes were identified. SNPs such as rs117797734 and rs75485498 showed significant associations and warrant further investigation. While the model shows potential for distinguishing cases from controls, overfitting remains a concern due to sample size limitations.
Conclusion: Our findings support the polygenic nature of migraine and underscore the value of PRS in uncovering novel genetic contributors. Though not yet clinically applicable, the PRS framework holds promise for improving migraine pathophysiology. Larger cohorts and in vivo validation are essential for advancing these models toward clinical relevance.
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P324

Phenotypic description of a multigenerational family with PRRT2 gene mutation: A case series of six members affected by hemiplegic migraine and paroxysmal events

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Objective: Mutations in the *PRRT2* gene have been identified as the cause of a spectrum of disorders, including paroxysmal kinesigenic dyskinesia (PKD) and benign familial infantile epilepsy. Recent evidence suggests its potential role in migraine phenotypes, particularly in cases presenting with complex aura. We present a case series from a single multigenerational family in which six heterozygous carriers of the *PRRT2* c.649dup mutation, exhibit migraine and/or paroxysmal neurological events.

Methods: Clinical data were retrospectively collected from six family members through outpatient neurological evaluations, headache diaries, neuroimaging, and genetic testing. The analysis focused on age of migraine onset, aura characteristics, attacks frequency and neurological comorbidities, including movement disorders and early-life paroxysmal events.

Results: All six individuals reported a history of migraine with or without aura. The mean age of onset was 13.5 ± 7.3 years (range 6–28). Four subjects experienced recurrent episodes fulfilling criteria for hemiplegic migraine, one reported only a single motor aura episode and one had migraine without aura. The frequency of migraine attacks ranged from less than 1 to 15 episodes/month, with a mean of 6.2 ± 4.8 monthly migraine days. One subject presented with PKD; two individuals reported childhood paroxysmal events. Brain MRIs were unremarkable in all subjects.

Conclusion: This case series highlights the phenotypic variability of the *PRRT2 c.649dup* variant within a single multigenerational family. The presence of motor aura in five out of six individuals suggests that *PRRT2* mutations may contribute to a broader spectrum of migraine phenotypes than previously recognized. The coexistence of migraine with aura and other paroxysmal neurological manifestations highlights the need for a comprehensive clinical-genetic approach. Our findings support the inclusion of *PRRT2* in gene panels for hemiplegic and complex aura migraine.

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Familial clustering of visual snow syndrome

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Objective: Visual snow syndrome (VSS) is a neurological disorder marked by persistent visual static alongside various visual and non-visual symptoms. Although it substantially impairs quality of life, treatment options are limited. This study describes a family with VSS to characterize phenotypic variability and to examine potential genetic and environmental contributions.

Methods: Following a report of familial clustering by an index patient, we conducted detailed clinical assessments of his family. Structured interviews documented age of onset, symptom patterns, triggers, and comorbidities across affected individuals spanning three generations. Written informed consent was obtained from the participating family members.

Results: Six family members across three generations were diagnosed with VSS. Eight family members reported visual symptoms not meeting full VSS ICHD-3 criteria. Clinical presentation of VSS varied markedly within the family, i.e. in age of onset (early childhood, n=3; later in life, n=3) and potential triggers. However, visual and non-visual symptom patterns overlapped among first-degree relatives. Visual snow was reported as the most disturbing symptom by all affected individuals. Palinopsia occurred equally in VSS patients and family members with few symptoms. No individual reported progression from isolated visual symptoms to full VSS. Non-visual symptoms included migraine with (n=3) and without aura (n=1), anxiety (n=4), depression (n=1), and tinnitus (n=2).

Conclusion: This cluster of family members with VSS and the observed overlap in symptoms support a hereditary component. However, considerable differences in age of onset and symptom patterns among relatives suggest that environmental factors may also influence disease expression in genetically predisposed individuals. Thus, trigger identification and avoidance are as crucial as elucidating the underlying genetic mechanisms.

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Novel headache frequency association with ESR2 dysfunction: A pilot study

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Objective: Based on the biological hypothesis that polymorphisms of genes involved in sex-hormone pathways may influence course of migraine, the aim of this study was to evaluate genetic variants in genes involved in hormone metabolism in connection with headache clinical characterictics.

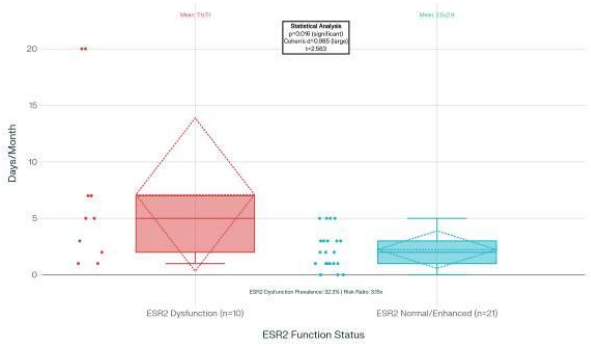
Methods: We investigated 8 polymorphisms implicated in hormone metabolism (AR, CYP19A1, ESR1, ESR2, SHBG, SRD5A2, COMT, PGR) in a cohort of 41 subjects (31 with migraine without aura [90% females] and 10 controls without headache [80% females]). Genotyping was conducted using the Allele company's pyrosequening system. Genotype/allele frequencies and haplotype analysis were determined using the SNPator web tool. Statistical comparisons of the clinical data and single-nucleotide polymorphisms were performed using JASP Software.

Results: The reduced expression of ESR2 gene (C/T and T/T variants of NC_000014.9:g.64233098C>T) was associated with 3.15 higher risk for frequent headaches. ESR2 dysfunction affects 32.3% of migraine patients (10/31). 60.0% patients with ESR2 dysfunction develop frequent headaches (≥5

days/month), while only 19% patients with normal or enhanced expression of ESR2 gene suffer from frequent migraines. In ESR2 dysfunction group mean frequency of headache days was 7.1 ± 7.1 days/month, while in ESR2 normal/enhanced group it was 2.5 ± 2.9 days/month ($p = 0.016$, $r = 0.430$, Cohen's $d = 0.985$) (Figure 1. Headache frequency by ESR2 status).

Conclusion: ESR2 dysfunction represents a novel genetic marker for headache frequency with strong statistical evidence, large effect size, and clear clinical relevance. The knowledge that ESR2 receptors expressed in trigeminal ganglion and regulates estrogen effects on neuroinflammation can explain its influence on pain chronification. Genetic screening for reduced expression of ESR2 gene could identify patients with high-risk of frequent headache. Future studies on large samples should confirm this observation.

Fig. 1



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Behavioural characterisation of a codeine-induced medication overuse headache model in mice: Focus on pain-related behaviour and cognitive impairment

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Objective: Medication overuse headache (MOH) is a chronic headache disorder caused by the overuse of analgesics in patients with primary headaches. Drugs associated with the highest risk of MOH are triptans and opioids. Even though opioid use is discouraged for headache management, codeine is a common component in combination products intended for mild-to-moderate pain (including headaches). The aim of this study was to characterise a codeine-induced MOH model and compare it to the established sumatriptan MOH model, by examining pain-related behaviours and cognitive dysfunction (which is increasingly being recognised as a feature of chronic headaches).

Methods: MOH was induced in male C57BL/6 mice by oral administration of codeine (15 mg/kg/day) or sumatriptan (10 mg/kg/day) for 10 days, followed by a 12-day drug-free period. Periorbital and hindpaw allodynia were regularly assessed during this period using von Frey filaments. On day 8, cognitive performance was assessed using the Novel Object Recognition Test (NORT). After the 12-day drug-free period (day 21), we assessed the development of periorbital allodynia following application of a low nitroglycerin dose.

Results: Compared to vehicle treatment, codeine and sumatriptan caused comparable levels of drug-induced periorbital and hindpaw allodynia during the drug administration period. During the drug-free period, periorbital allodynia resolved at a similar rate for codeine and sumatriptan, whereas hindpaw allodynia resolved more rapidly in codeine-treated mice (Fig 1). Both drugs produced cognitive impairment and reduced NORT discrimination index values (Fig 2). Lastly, application of nitroglycerin induced a recurrence of periorbital allodynia in both codeine and sumatriptan-treated mice (Fig 3).

Conclusion: Codeine induced cutaneous allodynia and cognitive impairment in mice, with effects comparable to those of sumatriptan. These results support the idea of codeine-induced model of MOH as a promising preclinical tool for studying MOH and its consequences.

Fig. 1

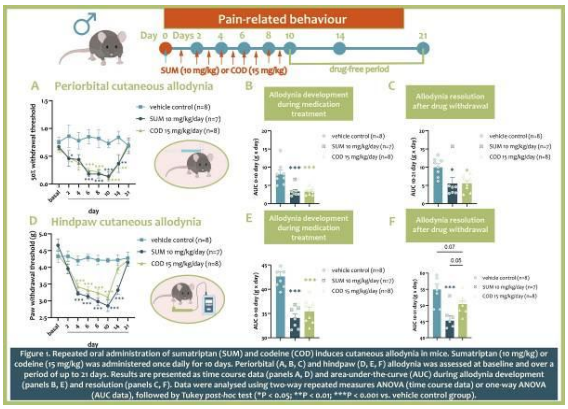


Fig. 2

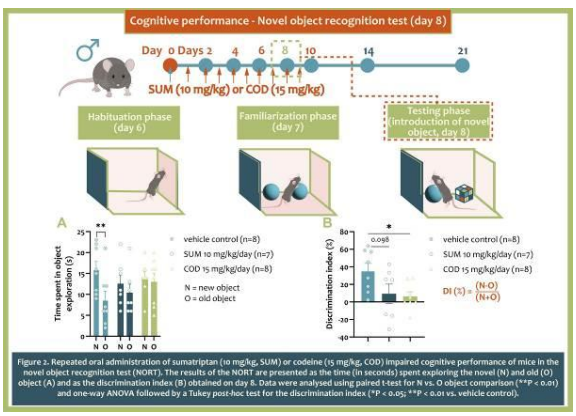


Fig. 3

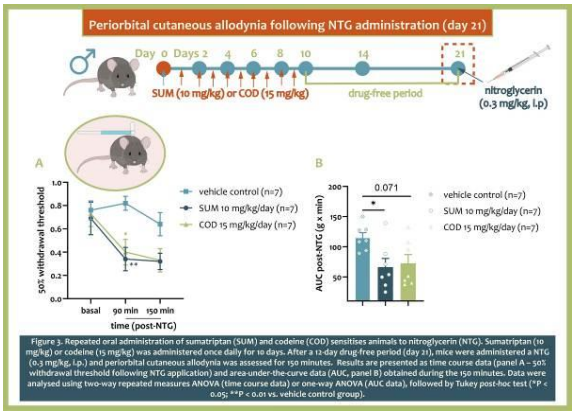


Figure 3: Repeated oral administration of sumatriptan (SUM) and codeine (COD) sensitises animals to nitroglycerin (NTG). Sumatriptan (10 mg/kg) or codeine (15 mg/kg) was administered once daily for 10 days. After a 12-day drug-free period (day 21), mice were administered a NTG (0.3 mg/kg, i.p.) and periorbital cutaneous allodynia was assessed for 150 minutes. Results are presented as time course data (panel A – 50% withdrawal threshold following NTG application) and area-under-the-curve data (AUC, panel B) obtained during the 150 minutes. Data were analysed using two-way repeated measures ANOVA (time course data) or one-way ANOVA (AUC data), followed by Tukey post-hoc test (*P < 0.05; **P < 0.01 vs. vehicle control group).

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Evolution of nitroglycerin-triggered premonitory symptoms in participants with migraine

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Objective: While the hypothalamus is reliably shown with functional neuroimaging to be active in the premonitory phase of migraine, other areas including visual, brainstem, and limbic areas may also be seen. To understand how the premonitory phase evolves, the temporal chronology of premonitory symptoms (PS) triggered by nitroglycerin (NTG) was evaluated.

Methods: Fifty-three subjects with migraine and a history of spontaneous PS were exposed to NTG infusion (0.5 mcg/kg/min;1° visit, V1). Participants who developed PS and migraine-like headache were invited to be re-exposed to NTG for a maximum of three triggered visits (V2 *n*=29; V3 *n*=11). The frequency and chronology of PS were collected for all the visits (*n*=93). The median time of onset in minutes of each symptom was recorded for all subjects during V1 (*n*=53).

Results: PS were triggered in 92 out of 93 (99%) of visits. The 5 most common PS were: photophobia (77%), fatigue (74%), neck stiffness (63%), difficulty concentrating (62%), and yawning (50%). The premonitory phase started with one PS in 40% (*n*=37) of the cases, and more than one in the remainder. Neck stiffness (38%), photophobia (38%), and fatigue (33%) were the most common PS occurring as the first symptom across all 93 NTG infusions. In contrast, thirst (14%), food cravings (2%), and yawning (13%) occurred as the first PS in a minority of cases. The median time of onset [IQR] of the most common PS (frequency≥35%) during V1 were: neck stiffness 10 minutes (6–16), photophobia 11 minutes (8–20), thirst 19 minutes (10–81), fatigue 20 minutes (10–46), difficulty concentrating 20 minutes (10–34), and yawning 40 minutes (16–69).

Conclusion: Neck stiffness and photophobia are the earliest PS to arise during NTG-triggered migraine attacks. Symptoms that are attributed to the hypothalamus typically begin after. These results may suggest an early dysmodulation of the thalamus, while the hypothalamus could be a later structure involved in the migraine attack, rather than be involved in attack initiation.

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Human assumed central sensitization in interictal migraine: A systematic review and meta-analysis

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Objective: Signs of human assumed central sensitization (HACS) including enhanced pain sensitivity and impaired pain processing can be established using static and dynamic quantitative sensory testing (QST). QST findings suggest HACS occurs in ictal migraine patients. However, its presence interictally and its relationship with headache characteristics remain unclear. Therefore, this study assessed the presence of HACS in interictal episodic (EM) and chronic migraine (CM) patients.

Methods: A comprehensive search was conducted in September 2024 across three databases. Studies examining HACS using static or dynamic QST measures in adults with interictal migraine were included. Two independent, blinded researchers performed study selection, data extraction, risk of bias and quality of evidence assessment. Meta-analysis was performed in Review Manager.

Results: Seventy-one articles were included in the qualitative analysis and 38 in the meta-analysis. Results were clustered by headache frequency and QST type. Lower pain thresholds for mechanical and thermal stimuli were found in the (extra-)trigeminal, and pain-free areas of both EM and CM ($p \leq .01$). Additionally, EM showed a larger area under the curve for blink reflex R2 threshold compared to pain-free controls ($p < .001$). Differences between EM and CM were only observed for dynamic QST.

Conclusion: Enhanced local and widespread pain sensitivity reflects the presence of HACS in interictal EM and CM, suggesting a need for multimodal treatment focused on desensitizing the central nervous system. The evidenced is provided through

various static and dynamic QST methods. While different QST profiles may affect HACS development, headache frequency has a limited influence.

P330

Neurophysiological correlates of Anti-CGRP therapy response in chronic migraine: A pilot study using quantitative sensory testing and conditioned pain modulation

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Objective: To explore longitudinal changes in migraine burden, sensory processing, and central pain modulation in women with chronic migraine treated with anti-CGRP monoclonal antibodies.

Methods: This pilot prospective cohort study enrolled women with chronic migraine under anti-CGRP monoclonal antibody therapy (fremanezumab). Evaluations included: clinical outcomes - migraine days, acute medication use, HIT-6, MIBS-4, CSI, ASC-12, PCS; biomarkers - blood CGRP levels; and neurophysiological testing - quantitative sensory testing (von Frey filaments, pressure algometry) and conditioned pain modulation (CPM) using sequential and simultaneous paradigms.

Results: Ten women were included (mean age 33.5 ± 8.3 years). At 3- and 6 months, migraine days/month significantly reduced (15.3±8.7 → 5.5±3.3 → 2.6±2.4), and acute medication use/month decreased (12.4±6.0 → 5.1±3.4 → 3.6±2.5). HIT-6 decreased significantly (68.8±5.0 → 53.5±12.2 → 44.0±29.7), as did CSI and PCS. MIBS-4 and ASC-12 improved not statistically.

At 6 months, pressure pain thresholds increased modestly at the trapezius (1.77±0.62 → 1.91±0.71 kg/cm²), but not at frontal or tibial sites. Mechanical detection thresholds rose slightly at frontal and trapezius (1.65±0.43 → 1.74±0.44; 1.84±0.46 → 1.90±0.57 log g), with no change at tibial sites. CPM showed improvement at trapezius (sequential: 20.1% → 31.3%; simultaneous: 22.4% → 59.9%) and tibial sites (sequential: 9.2% → 17.7%; simultaneous: 24.6% → 28.0%).

Conclusion: Anti-CGRP monoclonal antibodies significantly reduced migraine frequency and disability at both 3- and 6-month evaluations. However, only at 6-months follow-up were modest improvements observed in pressure and mechanical thresholds as well as in descending pain inhibition. These findings support further investigation into personalized approaches to migraine treatment based on neurophysiological profiling.

P331

TXNIP alleviates central sensitization via GLUT3-mediated glucose uptake in NTG-induced chronic migraine model of mice

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Objective: Chronic migraine (CM) is increasingly recognized as a metabolic vulnerability disorder; however, the role of aberrant neuronal glucose metabolism in CM remains poorly understood. TXNIP is a negative regulator of GLUT3, the neuron-specific glucose transporter. This study aims to investigate the role of TXNIP in a mouse model of CM.

Methods: The CM model was induced in mice via repeated intraperitoneal injections of nitroglycerin (NTG). We examined the effects of the TXNIP inhibitor SR37330 and adeno-associated virus-mediated neuronal-specific overexpression of GLUT3 on pain behaviors and central sensitization. Whole-brain glucose uptake was assessed using ^{18}F-FDG PET/CT. Tissues from the trigeminal nucleus caudalis (TNC) were subjected to immunofluorescence, co-immunoprecipitation, molecular docking, Western blot and RT-qPCR, transcriptome and metabolome sequencing, transmission electron microscopy, and 2-NBDG fluorescence imaging.

Results: CM mice exhibited reduced whole-brain glucose uptake. Glucose uptake in the TNC region was primarily mediated by neurons, not glial cells. Furthermore, the oxidative phosphorylation pathway was significantly downregulated, and TXNIP expression was significantly upregulated in the TNC neurons of CM mice. Neuronal-specific GLUT3 overexpression in TNC region and inhibiting TXNIP improved whole-brain glucose uptake, reversed mechanical allodynia in the hindpaws and periorbital regions, and reduced the frequency of mEPSCs and c-FOS expression in CM mice. Molecular docking and co-immunoprecipitation confirmed the interaction between TXNIP and GLUT3. TXNIP inhibition restored the downregulated GLUT3 expression in CM mice.

Conclusion: This study reveals for the first time impaired neuronal glucose uptake in CM mice. The TXNIP inhibitor SR37330 alleviates central sensitization in CM mice by restoring GLUT3-mediated glucose uptake.

Fig. 1

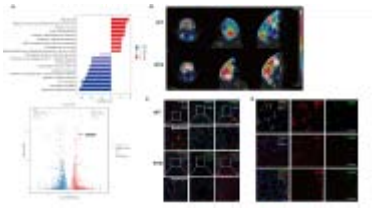
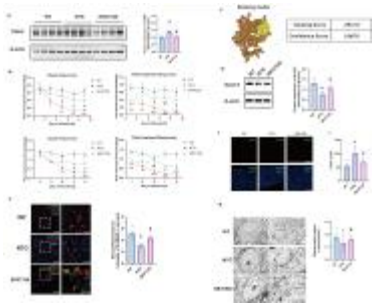


Fig. 2



P332

Regional neurovascular uncoupling as a mechanism for aura initiation and propagation

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Objective: While it is well established that the aura phenomenon originates from a hyperexcitable and hyperconnected visual cortex, the mechanisms underlying the brain's predisposition to initiate cortical spreading depolarization (CSD) in patients with migraine remain debated. Likewise, the neural substrates responsible for the propagation of aura from visual to somatosensory and motor areas—manifesting in complex aura phenotypes—have only been partially elucidated. It is hypothesized that an inadequate vascular supply to meet heightened demand—neurovascular uncoupling—may contribute to aura initiation and propagation.

Methods: Forty patients with migraine with aura (21 with simple visual aura and 19 with complex aura), 30 with migraine without aura, and 22 healthy controls (HCs) underwent a 3-Tesla MRI scan. A surrogate estimate of regional neurovascular coupling was obtained for each subject by calculating the correlation coefficient between z-scored ReHo and z-scored cerebral blood flow maps (obtained by multidelay arterial spin labelling).

Results: A significantly reduced neurovascular coupling was observed in the primary visual cortex parcels of the large-scale visual network in patients with both simple and complex aura, compared to both patients with migraine without aura and HCs. Additionally, patients with complex aura exhibited reduced neurovascular coupling in the posterior cingulate cortex/precuneus of the default mode network, compared to all other groups.

Conclusion: Neurovascular uncoupling in the primary visual cortex may represent a critical link between exposure to trigger factors and the initiation of the aura phenomenon. While physiological vascular oversupply may compensate for resting neurovascular demand, it becomes insufficient when energy requirement increases—such as during trigger exposure—thus facilitating aura onset. Furthermore, impaired neurovascular coupling in the PCC/precuneus may play a key role in facilitating propagation of aura beyond the visual cortex.

Fig. 1

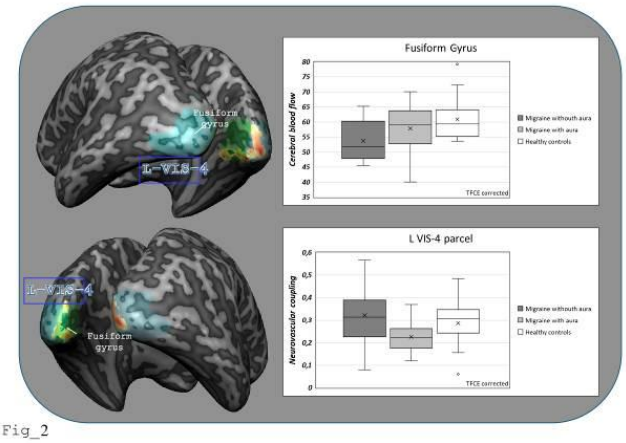


Fig_2

P333

Energy metabolism in chronic migraine: An overlooked hub of pathophysiology

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Objective: Despite advances in migraine research, the metabolic underpinnings of chronic migraine (CM) remain poorly understood. To explore metabolic mechanisms understudied in chronic migraine (CM), we performed multi-omics analysis to identify energy metabolism as a preventive therapeutic axis.

Methods: Plasma samples from 355 CM patients and 142 controls underwent multi-omics profiling (RNA-

seq + LC-MS/MS). Random forest prioritized DAMs and hub biomarkers via variable importance scores. KEGG enrichment and KGML interactome mapping identified shared pathways and hub nodes connecting DAMs and DEGs.

Results: A multi-omics integration of 355 CM patients with 142 controls was performed. The transcriptomics revealing OXPHOS ↓ (respiratory chain complex I/III/IV/V activity ↓, ATP synthase ATP6/CYTB dysfunction ↓) and coordinated down-regulation of mtDNA coding subunits (ND1/ND2/ND5/ND6 ↓) in humans. Comprehensive multi-omics analyses further demonstrated disruption of convergent pathways: downregulation of metabolic pathways such as OXPHOS, insulin signaling and central carbon metabolism.

Conclusion: This multi-omics study suggests metabolic dysregulationnd may represent pathophysiological drivers. Highlighting the potential to prioritize metabolic resilience, these findings provide a data-driven framework for advancing precision therapies and updating clinical guidelines.

Fig. 1

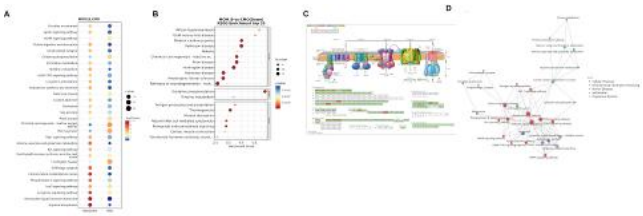
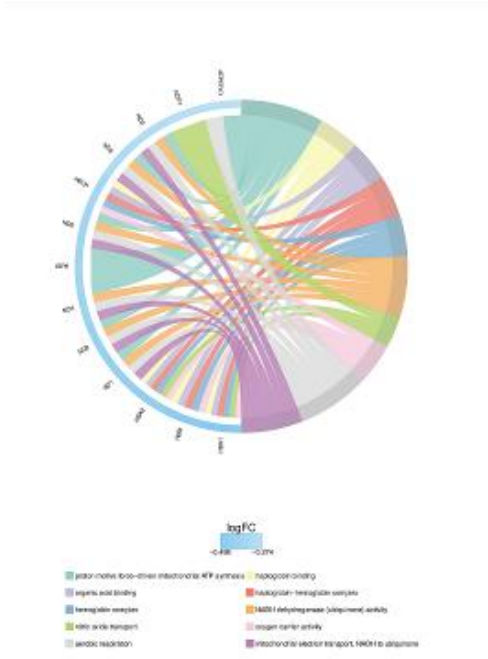


Fig. 2



P334

The influence of blood pressure on susceptibility to spreading depolarization

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Objective: Previous epidemiological studies suggest a bidirectional association between hypertension and migraine. Despite this association, the underlying mechanisms remain elusive. This study aims to elucidate the potential roles of systemic blood pressure (BP) and long-term antihypertensive therapy in migraine pathophysiology.

Methods: Spontaneously hypertensive (SHR) and normotensive Wistar-Kyoto (WKY) rats were subjected to KCl-evoked cortical spreading depolarization (SD) to assess the effects of systemic BP on cortical excitability. To examine the interplay between migraine susceptibility and chronic modulation of BP, both SHR and WKY rats were treated for three weeks with agents of distinct clinical profiles: amlodipine (antihypertension+; migraine prevention-), topiramate (migraine prevention+; antihypertension-), and candesartan (migraine prevention+; antihypertension+). For each condition, a corresponding vehicle group was included as control.

Results: SHR rats exhibited significantly higher SD susceptibility compared to WKY rats. In WKY rats, SD susceptibility was positively correlated with mean arterial pressure, whereas no such correlation was observed in SHR rats (figure 1). Compared to their respective vehicle-treated controls, candesartan significantly reduced BP and SD susceptibility in SHR and WKY rats. Topiramate did not affect BP in either strain but significantly reduced SD susceptibility in WKY rats, with no effect in SHR rats. Amlodipine markedly lowered BP in both strains and reduced SD susceptibility only in SHR rats, with no significant changes in WKY rats (figure 2).

Conclusion: Our findings highlight a link between BP and cortical excitability, which may mediate the clinical association between hypertension and increased migraine susceptibility. Modulating BP may reduce SD susceptibility, suggesting that optimizing BP control in patients with migraine may contribute to improved therapeutic outcomes, particularly in individuals with comorbid hypertension.

Fig. 1

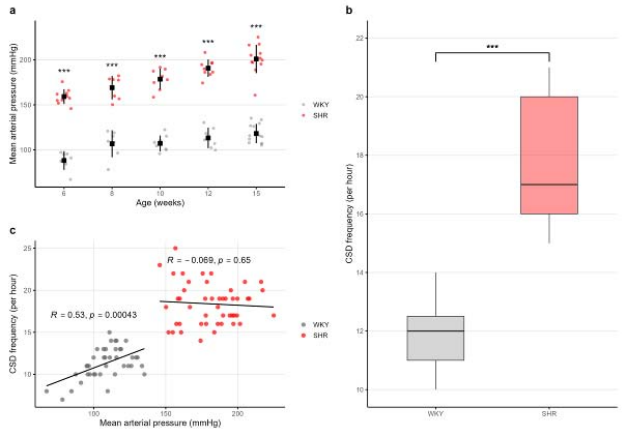
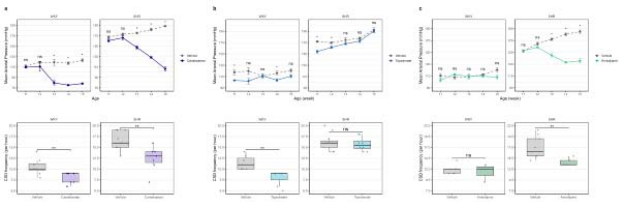


Fig. 2



P335

Pathophysiology of migraine with aura: A systematic review of current evidence

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Objective: Understand the complex mechanisms involved in the pathophysiological process (PTP) of migraine with aura(MGA),analyzing factors that influence its susceptibility, such as environmental exposure and genetic predisposition, which may contribute to chronification and worsen the condition over time. Additionally, it seeks to examine the main therapeutic and prophylactic approaches, as well as the relationship between the underlying PTP and current clinical treatments, aiding in the development of new therapies and improving existing techniques through a deeper understanding of MGA.

Methods: This work is a systematic Literature review of a quantitative nature. For its development, a guiding question was formulated following the PICOT strategy: "In individuals with MGA, what are the pathophysiological mechanisms involved based on current evidence, according to studies published in the last 10 years? "Subsequently, studies were searched in the Pubmed and SciELO databases. The selected studies address topics related to the guiding question and are available in English.

Results: From the 3.013 studies identified through the database, after full-text evaluation a total of 6 articles included in the final analysis.

Conclusion: Based on the analyzed data, the complexity of the pathophysiology of MGA became evident, extending beyond the clinical manifestation of headache. Understanding Cortical Spreading Depression (CSD) as the initial event, along with the activation of the trigeminovascular system and the involvement of inflammatory mediators, highlights the need for a deeper examination of the neural and vascular processes related to the disease. Therefore this study reinforces the importance of continuing scientific investigations into the pathophysiology of MGA. Integrating current knowledge with innovative therapeutic approaches has the potential to significantly improve patients QoL, while also contributing to the reduction of the social and economic burden caused by this prevalent neurological condition.

P336

Trigeminal autonomic cephalalgia as the initial presentation of a cerebral cavernous malformation: A rare case report

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Objective: We report the case of a patient presenting with trigeminal autonomic cephalalgia (TAC)-like headache as initial symptom of familial cerebral cavernous malformations (CCMs) associated with a pathogenic microdeletion in the KRIT1 gene.

Methods: A 49-year-old man with no prior neurological history developed a subacute onset of brief, strictly unilateral, left-sided retro-orbital headaches related to ipsilateral cranial autonomic symptoms—like conjunctival injection and eyelid ptosis—recurring up to 10–15 times per day. Upon evaluation at the Headache Center, a diagnosis of Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT) was considered. However, brain MRI revealed a cavernoma with signs of prior hemorrhage and hemosiderin deposits in the left insular region, along with multiple additional supratentorial and infratentorial cavernous malformations—findings consistent with familial CCM. These findings prompted genetic testing.

Results: Molecular analysis (MLPA confirmed by NGS) identified a heterozygous microdeletion affecting exons 10–11 of the KRIT1 gene, classified as

pathogenic and consistent with autosomal dominant familial CCM. Based on the headache phenotype, lamotrigine was initiated at a dose of 50 mg twice daily, leading to complete resolution of attacks within approximately two weeks. The absence of hemorrhage, along with the positive response to lamotrigine, suggest a mechanism of altered neuronal functioning rather than a structural or hemorrhagic cause, leading to activation of trigemino-autonomic pathways.

Conclusion: This case underscores the importance of considering secondary etiologies in patients with headache and features consisting with a diagnosis of TAC. Familial CCM due to KRIT1 mutations, should be included in the differential diagnosis when characteristic clinical features and imaging findings coexist.

P337

Cervical meningioma underlying facial episodic paresthesia, tinnitus and vertigo

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Objective: We studied the case of a 62-year-old woman with a 1-year history of progressively worsening occipital headache without neurovegetative symptoms, previously diagnosed with tension-type headache and treated with amitriptyline without benefit.

Methods: On admission, further clinical history revealed persistent right-sided tinnitus, intermittent dizziness, and paraesthesia in the right mastoid and mandibular regions. Physical exam was normal; neurological exam showed mild difficulty in tandem gait and hypoesthesia in the right great auricular nerve area (C2–C3). A cervical spine MRI with and without gadolinium revealed pathological tissue with intense and heterogeneous enhancement in the right parasagittal intra-canal and extra-dural space from C2 to C4–C5, extending into the extra-foraminal paravertebral area at C2–C3. The lesion appeared poorly dissociable from the C3–C4 roots, with signs of bone remodeling. The right vertebral artery was incorporated but without affecting flow signal. Based on clinical and imaging findings, a diagnosis of cervicogenic headache was suggested,according with the third International Classification of Headache Disorders.

Results: Morphological features indicated a probable C3 nerve root schwannoma, and a neurosurgical procedure was performed. Intraoperative histology suggested meningioma; final histology confirmed a WHO grade I meningotheliomatous meningioma (negative for S100 and GFAP). At 1-month follow-up, the patient reported marked improvement in neck pain, tinnitus, and vertigo. Follow-up MRI showed no residual or recurrent tumor.

Conclusion: Meningiomas are the second most common primary intradural extramedullary spinal tumors, typically slow-growing and often presenting with sensory symptoms and radicular pain. MRI is the gold standard for diagnosis. This case highlights the need to consider spinal tumors in patients with neck pain, tinnitus, vertigo, and cranial paraesthesia.

P338

Altered brain structure and function in migraine: Preliminary findings from 5.0T ultra-high-field MRI

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Objective: Migraine involves complex brain network dysregulation, and ultra-high-field 5T MRI enables enhanced detection of subtle structural and functional alterations. This study aimed to characterize brain abnormalities in migraine using 5T MRI and explore their clinical correlations.

Methods: Thirty-three episodic migraine patients and 30 age- and sex-matched healthy controls (HCs) underwent 5T MRI, including high-resolution T1-weighted anatomical imaging and resting-state functional MRI (rs-fMRI). Standard preprocessing of rs-fMRI data was performed, including slice timing correction, motion correction, spatial normalization to MNI space, and spatial smoothing.

Results: Compared to healthy controls, migraine patients exhibited increased ReHo values in the right middle frontal gyrus (involced in pain modulation and cognitive control) and decreased ReHo in the right calcarine cortex (primary visual area) and left superior temporal gyrus (STG, auditory/language network). Left STG ReHo negatively correlated with migraine duration ($r = -0.403$, $p = 0.033$).

Conclusion: Migraine is associated with concurrent functional and structural brain abnormalities: frontal hyper-synchrony as compensatory mechanism, sensory region hypo-synchrony as dysfunction, and GMV increases potentially reflecting neuroplastic adaptation or disease burden.

P339

Neurophysiological effects of atogepant in episodic migraine: The ATOM project

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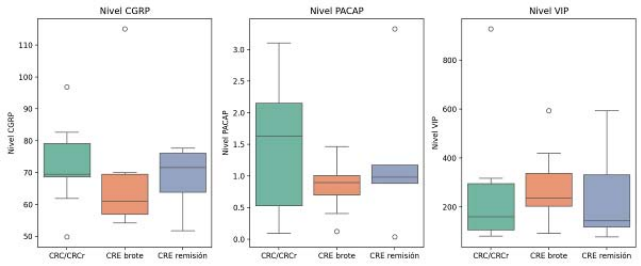
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Objective: Our study aims to describe the neurophysiological mechanisms underlying the effect of atogepant in the prevention of high-frequency episodic migraine (HFEM). We assessed changes of central sensitization and habituation after three months of atogepant treatment.
Methods: This is a prospective study enrolling subjects with HFEM (8-14 monthly migraine days-MMDs). During the interictal phase, we performed a neurophysiological evaluation assessing central sensitization and habituation, by means of the lower limb nociceptive withdrawal reflex (single stimulus threshold–RTh, temporal summation threshold–TST), the nociceptive blink reflex (nBR), and visual evoked potentials (VEPs). Participants were assessed at baseline (T0) and after three months of atogepant 60 mg intake (T1). Responders achieved a reduction of at least 50% in MMDs at T1.
Results: We enrolled 22 subjects with HFEM (age 37.7±11.8 years, 16 females). At T0, they presented a mean of 10.2±2.0 MMDs, with a MIDAS of 45.4 ± 29.4. Atogepant determined a reduction in both MMDs and MIDAS score (MMDs T1 4.8±3.7, p<0.001 vs. T0; MIDAS T1 8.6±10.4, p<0.001 vs. T0). Responder rate at T1 was 68.2% (15/22).
At T1, we found an increase in RTh (T0: 13.3±5.7 vs. T1: 15.8±6.7, p<0.001), but not in the TST (T0: 9.3±4.6 vs. T1: 10.3±4.6, p<0.389). nRB assessed at 0.3Hz and 0.5Hz showed a baseline habituation, also confirmed at T1 (p<0.001 for all comparisons). At 0.2Hz, we observed a reduction in the area of the first block at T1 (T0: 1.48±0.9 µVxms vs. T1: 1.0±0.5 µVxms, p=0.045) with a modulation of the habituation phenomenon (p=0.001). PEV evaluation showed a lack of habituation both at T0 and T1 (habituation index: T0: 92.2 ± 22.1 vs. T1 93.2 ± 13.1, p=0.794).
Conclusion: Our findings suggest that after a 3-month atogepant treatment there is an improvement in central sensitization mechanisms and a modulation of the habituation pattern.

P340
Cluster-BIO: Cross-sectional study of plasma biomarkers (CGRP, PACAP-38, and VIP) in cluster headache patients
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Objective: The pathophysiology of cluster headache (CH) involves multiple neuropeptides. This study aimed to analyze plasma concentrations of calcitonin gene-related peptide (CGRP), pituitary adenylate cyclase-activating polypeptide-38 (PACAP-38), and vasoactive intestinal peptide (VIP) in patients with different CH phenotypes to assess their potential as differential biomarkers.
Methods: A cross-sectional study was conducted in patients diagnosed with CH according to ICHD-3 criteria, including episodic CH in interictal bout (ECH-bout), episodic CH in remission (ECH-remission), and chronic CH (CCH). Plasma concentrations of CGRP, PACAP-38, and VIP were measured using ELISA. Differences between subgroups were analyzed using non-parametric tests.
Results: Twenty-three patients were included: 5 ECH-remission, 8 ECH-bout, and 10 CCH. Mean±SD or median [IQR] CGRP levels were: ECH-remission, 68.21±10.63 pg/mL; ECH-bout, 61.05 [56.98–69.52] pg/mL; CCH, 72.17±12.66 pg/mL. For PACAP-38: ECH-remission, 1.28±1.22 ng/mL; ECH-bout, 0.83±0.4 ng/mL; CCH, 1.52±1.06 ng/mL. For VIP: ECH-remission, 253.15±213.70 pg/mL; ECH-bout, 284.93±156.86 pg/mL; CCH, 160 [106.66–295.61] pg/mL.
A trend toward higher CGRP levels was observed in CCH vs. ECH-bout (*p*=0.4, post hoc *p*=0.09). No significant differences were found in PACAP-38 (*p*=0.13) or VIP (*p*=0.66) between subgroups.
Conclusion: Plasma CGRP levels suggest its potential role as a phenotypic biomarker in CCH. No phenotypic differences were observed in PACAP-38 or VIP levels.

Fig. 1



P341
To explore the mechanism of glucagon-like peptide-1 receptor (GLP-1R) in migraine
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Objective: Migraine is a serious neurological disorder and one of the most common types of primary

headaches. However, the exact mechanisms behind migraine onset are not fully understood. Activating GLP-1R can alleviate pain by regulating autophagy and activating inflammatory pathways. However, it remains unclear how GLP-1R interacts with key molecules or signaling pathways in the pathogenesis of migraine. In this study, we investigated the intrinsic molecular mechanisms by which GLP-1R exerts its analgesic effects in a migraine mouse model.

Methods: To induce chronic migraine in mice, repeated intraperitoneal injections of nitroglycerin were administered. The mechanical pain threshold of the periorbital and plantar areas was continuously monitored. To determine the role of GLP-1R in the chronic migraine model, we administered different concentrations (125ug/kg, 250ug/kg, 400ug/kg, and 800ug/kg) of the GLP-1 selective agonist (Liraglutide). The optimal concentration was selected using immunofluorescence staining, Western blotting, and real-time quantitative PCR to investigate the potential pathways through which GLP-1 improves pain.

Results: In the chronic migraine model induced by glyceryl trinitrate in mice, the expression of GLP-1R protein in the caudal nucleus of the trigeminal nerve (TNC) increased, and GLP-1R was co-localized with neurons within TNC. Administering 400ug/kg of liraglutide reduced the baseline mechanical hyperresponsiveness in chronic migraine mice and inhibited the upregulation of c-fos in TNC, thereby alleviating central sensitization in chronic migraine. In addition, activation of GLP-1R can improve chronic migraine by regulating autophagy through the AMPK/mTOR pathway.

Conclusion: Our results suggest that in a chronic migraine mouse model, activation of GLP-1R in neurons in TNC can improve chronic migraine by regulating autophagy via the AMPK/mTOR pathway.

P342

Migraine with visual aura, unilateral mydriasis and Takotsubo syndrome. random coincidence or common pathogenesis? The precarious balance of the autonomic nervous system and the complex relationship between brain and heart

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Objective: The examination of a woman who presented a migraine attack with visual aura and unilateral mydriasis, followed, a few days later, by an episode of Takotsubo cardiomyopathy, prompted us to review the existing literature correlating migraine and TS as well as the most recent studies regarding the association between Takotsubo Syndrome and neurological dysfunction. Our aim is to define the role of dysautonomia and the contribution of the Autonomic Nervous System in the pathogenesis of both diseases, also, to define the functional role of the hypothalamus in the both the determination of headache attacks and the onset of clinical manifestations in other organs and tissues.

Methods: Review of anatomy, physiology and neural regulation in both physiological and stress responses. Examination of the functional connections of the hypothalamus. Critical review of similar case reports.

Results: The coexistence of psycho-emotional stressors, endocrine/hormonal factors and a possible genetic predisposition might explain the pathophysiological overlap between these two distinct clinical manifestations.

Conclusion: The hypothalamus is functionally connected with all the pain-related brain regions and pathways and can be responsible for the clinical manifestations in both the nervous system and the cardiovascular apparatus. migraine is the most frequent chronic, early onset condition associated with TS.

P343

Can prophylactic single-pulse Transcranial Magnetic Stimulation (sTMS) treat motion sensitivity triggered by systemic CGRP or PACAP in a mouse model of vestibular migraine?

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Objective: In 2022, Lloyd et al. (PMID 35668368) showed that sTMS was an effective treatment of difficult-to-treat migraine causes such as vestibular migraine. Increased motion sensitivity correlates with the severity of vestibular migraine symptoms, and we had previously shown that systemic CGRP and PACAP exacerbate motion-induced nausea in wild-type C57B6/J (WT) mice and olcegepant, a CGRP receptor antagonist, can reverse CGRP"s effect. In this study, we wondered if prophylactic sTMS alone would be effective in reducing motion-induced nausea triggered by systemic CGRP or PACAP.

Methods: Eighteen mice were used in these studies (12 F/6 M). As a behavioral surrogate for motion-induced nausea, we performed motion-induced thermoregulation in male and female C57B6/J mice, with mice orbitally rotated for 20 minutes with head

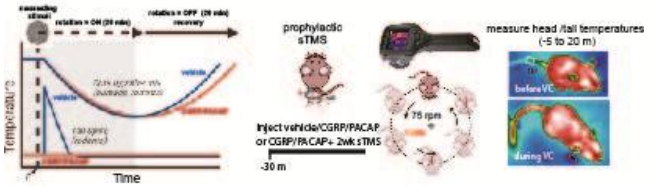
and tail temperatures monitored throughout. Mice were evaluated in these assays following intraperitoneal (IP) injections of i) vehicle control, ii) CGRP (0.5 mg/kg in females: 0.1 mg/kg in males), iii) PACAP (0.15 mg/kg in females: 0.3 mg/kg in males), or iv & v) the same concentration of CGRP (iv) or PACAP (v) in mice that had received two weeks of daily sTMS stimulation. The sTMS parameters were two pulses (~1 ms each) at 1T, delivered over the occipital cortex, mimicking stimulation parameters used in the *eNeura* SAVI Dual device.

Results: Our findings suggest that prophylactic sTMS does reduce motion-induced dizziness/nausea in wild-type C57Bl/6 mice after systemic CGRP or PACAP injection. sTMS reduced motion-induced dizziness to systemic PACAP in both male and female mice, whereas sTMS only partially rescued motion-induced dizziness to systemic CGRP.

Conclusion: This study suggests that sTMS may be an effective treatment to reduce motion-induced dizziness/nausea induced by systemic PACAP and, to a lesser extent, systemic CGRP.

We would like to acknowledge Ava Thierry for data analysis and grant support from NIH-R01DC017261 (AEL) and The Migraine Trust (APA).

Fig. 1



P344

Can botulinum toxin A (BoNT) treat motion sensitivity triggered by systemic CGRP or PACAP in a mouse model of vestibular migraine?

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Objective: Vestibular migraine is the most common cause of spontaneous episodic vertigo in adult patients and the second most common cause of vertigo in patients of all ages. In 2022, Goror et al. (PMID 333722518) showed that botulinum toxin A was an effective treatment for vestibular migraine. Increased motion sensitivity correlates with the severity of vestibular migraine symptoms, and we had previously shown that systemic CGRP and PACAP exacerbate motion-induced nausea in wild-type C57B6/J (WT) mice and olcegepant, a CGRP receptor antagonist, can reverse CGRP"s effect. In this study, we wondered if BoNT alone would be effective in reducing motion-induced nausea triggered by systemic CGRP or PACAP.

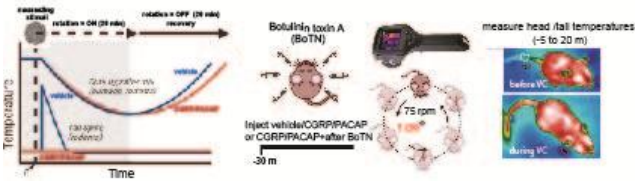
Methods: Eighteen mice were used in these studies (12 F/6 M). As a behavioral surrogate for motion-induced nausea, we performed motion-induced thermoregulation in male and female C57B6/J mice orbitally rotated for 20 minutes with head and tail temperatures monitored throughout. Mice were evaluated in these assays following intraperitoneal (IP) injections of i) vehicle control, ii) CGRP (0.5 mg/kg in females: 0.1 mg/kg in males), iii) PACAP (0.15 mg/kg in females: 0.3 mg/kg in males), or iv & v) the same concentration of CGRP (iv) or PACAP (v) in mice that had been injected in the facial area with BoNT (0.5 U/mouse) four to five days prior to testing. Mice were injected with BoNT in six bilateral sites: two behind the eyes, two in front of the ears, and two behind the ears/neck.

Results: Our findings suggest that BoNT injection does reduce motion-induced nausea in WT C57Bl/6 mice after systemic CGRP or PACAP injection. BoNT reduced motion-induced dizziness to both CGRP and PACAP in male mice more than in female mice.

Conclusion: This study suggests that BoNT injection may be an effective treatment to reduce motion-induced nausea induced by systemic CGRP or PACAP.

We acknowledge Ava Thierry for data analysis and grant support from NIH-R01DC017261 (AEL) and The Medical Research Foundation (APA).

Fig. 1



P345

Opening of ATP-sensitive potassium channels activates meningeal nociceptors: Implications for the origin of migraine headache

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Objective: Meningeal nociceptors within the trigeminal ganglion are important contributors to migraine pathogenesis because they transmit pain signals from the dura mater to the central nervous system. Dural ATP-sensitive potassium (KATP) channels have garnered increasing attention as potential modulators of meningeal nociception. Human studies show that intravenous infusion of levcromakalim, a KATP channel opener, induces migraine attacks in people with migraine. However, the anatomical site and mechanism of action remain unknown.

Methods: To address these gaps, we conducted in vivo single-unit electrophysiological recordings of 36 meningeal nociceptors (23 Aδ- and 13 C-fibers) in the trigeminal ganglion of anesthetized male and female rats. We measured spontaneous firing rates before and up to 4 hours after a 20-minute continuous intracarotid infusion of levcromakalim (1.43 mg/kg or 0.14 mg/kg) or vehicle (71.4% ethanol).

Results: Levcromakalim at 1.43 mg/kg activated 9 (69%) of 13 nociceptors, compared with 1 (11%) of 9 in the vehicle group (P = 0.012). Activation rates did not differ between Aδ-fibers (6 of 8, 69%) and C-fibers (3 of 6, 50%; P = 1.00), or between male (6 of 8, 75%) and female animals (3 of 5, 60%; P = 0.61). Moreover, levcromakalim at 0.14 mg/kg activated only 3 (21%) of 14 nociceptors.

Conclusion: Taken together, our findings demonstrate that KATP channel opening mediates activation of meningeal nociceptors, providing a mechanistic basis for previous observations in humans. The development of KATP channel blockers might therefore hold therapeutic promise for migraine by inhibiting meningeal nociceptors.

Fig. 1

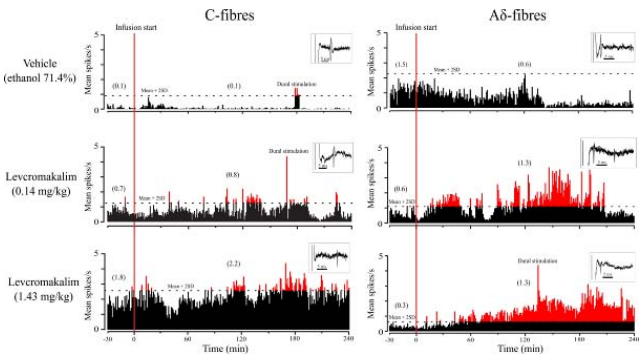
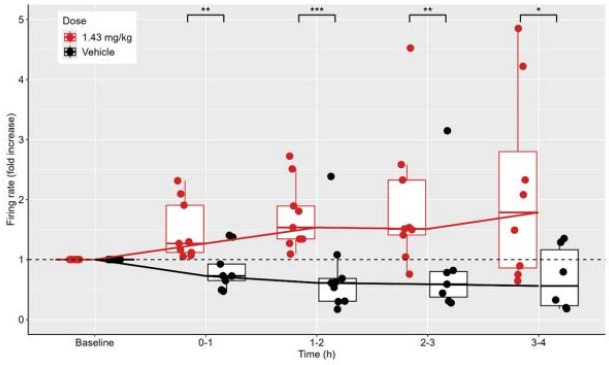


Fig. 2



P346

Activation and sensitization of meningeal nociceptors by PACAP-38: Implications for migraine headache

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Objective: Emerging evidence implicates pituitary adenylate cyclase-activating polypeptide-38 (PACAP-38) in migraine and other headache disorders. Systemic infusion of PACAP-38 induces migraine headache in people with migraine and mild headache in healthy adults. However, the precise mechanism and site of action remain poorly characterized. To address this gap, we assessed whether PACAP-38 elicits headache by activating meningeal nociceptors.

Methods: In vivo single-unit electrophysiological recordings were obtained from C- and Aδ-meningeal nociceptors in the trigeminal ganglion of anesthetized male and female rats. Spontaneous firing rates and mechanical responses to dural indentation with von Frey filaments were recorded before and for 4 hours after a 20-minute intracarotid infusion of PACAP-38 (1 µg/ml/kg, 10 µg/ml/kg, and 100 µg/ml/kg) or vehicle (isotonic saline).

Results: At the human-equivalent dose (10 µg/ml/kg), PACAP-38 activated 15 of 30 (50%) neurons, compared with none after vehicle (P < 0.01). Activation rates did not differ between C-fibers (7 of 17; 41%) and Aδ-fibers (8 of 13; 61.5%). The lowest dose of PACAP-38 (1 µg/ml/kg) activated 3 of 9 (33%) neurons, whereas the highest dose (100 µg/ml/kg) activated all four tested neurons, including two C-fibers and two Aδ-fibers.

Conclusion: These results suggest that PACAP-38 induces headache through peripheral activation of

meningeal nociceptors rather than exerting direct central effects within the spinal trigeminal nucleus.

Fig. 1

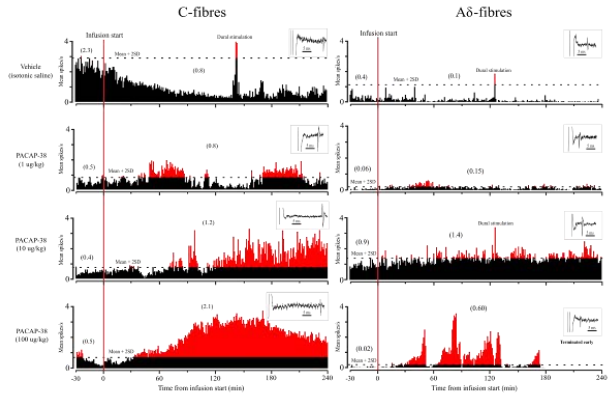
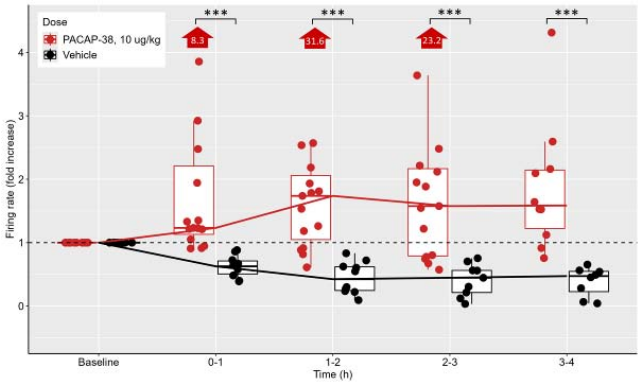


Fig. 2



P347

Shared neural signatures of photophobia in migraine and post-traumatic headache: A task-based fMRI study

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Objective: Persistent post-traumatic headache (PTH) and migraine frequently present with photic hypersensitivity that exacerbates headache symptoms. We sought to determine whether persistent PTH is associated with altered brain responses to visual stimuli and to explore shared neural mechanisms of photophobia with migraine.

Methods: This cross-sectional functional magnetic resonance imaging (fMRI) study included 80 adults with persistent PTH, 261 with migraine, and 143 healthy controls (HCs). All participants underwent visual stimulation using a flickering checkerboard during a 3T fMRI session. Blood oxygen level-dependent (BOLD) responses were examined using whole-brain and region-of-interest (ROI) analyses. All analyses were adjusted for age and sex.

Results: Whole-brain analysis revealed no significant BOLD differences across the full persistent PTH, migraine, and HC groups. However, participants with persistent PTH who experienced photophobia during the scan (n = 41) showed greater activation in the anterior and mid-cingulate cortex compared with HCs (*P*FWE = 0.010). ROI analyses identified greater activation in the anterior cingulate, mid-cingulate, and insular cortices in both photophobic participants with persistent PTH and ictal participants with migraine, relative to HCs (all $P < 0.05$). No significant differences were found between photophobic participants with persistent PTH and ictal participants with migraine

Conclusion: Photophobia in persistent PTH is associated with greater activation in cortical regions implicated in pain processing. These patterns parallel those observed during migraine attacks, indicating shared neural mechanisms between the two headache disorders.

P348

Shaken and stirred: CGRP stability endorses pragmatic clinical and research sampling

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Objective: Calcitonin gene-related peptide (CGRP) is a pivotal peptide in the pathophysiology and therapy of migraine. Pharmacological and clinical research increasingly focuses on the effects of inhibiting the CGRP pathway. Striking inter-individual differences fuel the question of biological CGRP variability or the influence of analytical pitfalls. We analyzed the stability of CGRP in human plasma and provide evidence-based recommendations for sample preprocessing.

Methods: In this analytical measurement study, blood samples from 40 healthy volunteers were collected and processed at predefined time points (6–180 minutes) under varying conditions (immediate and delayed centrifugation). CGRP concentrations were quantified using a validated sandwich ELISA. Statistical analyses included repeated measures ANOVA (adjusted for age and sex) and paired t-tests.

Results: Median CGRP values showed a slight numerical increase over time, with a tendency for higher levels in females. However, repeated measures ANOVA revealed no significant effect of processing delay on CGRP concentrations (P = 0·326). The

interaction between time and sex was significant (partial eta squared = 0·069, P = 0·040), but subgroup analyses did not yield significant within-subject effects. Immediate versus delayed centrifugation (30 and 60 minutes) did not significantly affect CGRP levels.

Conclusion: CGRP in human plasma is stable across a range of delayed processing and centrifugation protocols. Technical artifacts contribute minimally to interindividual variability, supporting the feasibility of multicenter studies and routine clinical sampling for CGRP biomarker research.

Fig. 1

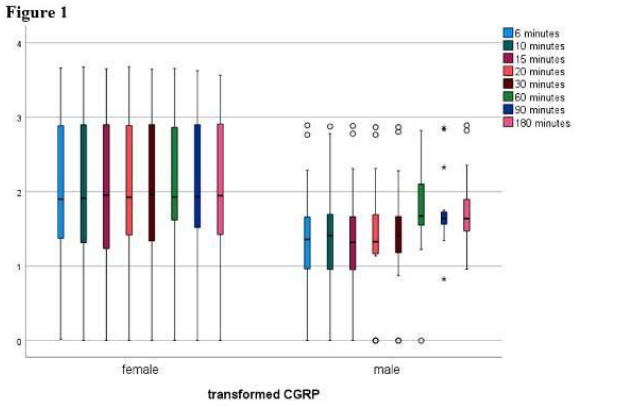


Figure: Box-Plots of transformed CGRP over time
CGRP values showed high interindividual differences between subjects, with female subjects presenting tendencial higher values. Overall the measurements showed no relevant degradation up to 180 minutes.

Fig. 2

Table 1 Estimated CGRP levels separated by sex

	Transformed CGRP		CGRP[1]	
	Female	Male	Female	Male
Time point	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
6 minutes	1·97 (1·52 – 2·43)	1·32 (0·84 – 1·80)	92·97 (31·98 – 266·19)	20·04 (5·94 – 62·7)
10 minutes	1·95 (1·47 – 2·43)	1·34 (0·86 – 1·82)	87·72 (28·35 – 266·86)	20·98 (6·24 – 65·69)
15 minutes	1·93 (1·47 – 2·43)	1·32 (0·84 – 1·80)	84·90 (26·76 – 264·97)	19·84 (5·95 – 61·64)
20 minutes	2·01 (1·56 – 2·45)	1·37 (0·89 – 1·84)	100·16 (35·04 – 283·14)	22·28 (6·75 – 68·80)
30 minutes	2·06 (1·65 – 2·46)	1·43 (0·99 – 1·87)	113·29 (43·87 – 290·05)	25·98 (8·81 – 73·11)
60 minutes	2·11 (1·73 – 2·50)	1·75 (1·39 – 2·12)	128·72 (52·25 – 315·18)	55·49 (23·46 – 129·60)
90 minutes	2·09 (1·69 – 2·49)	1·76 (1·47 – 2·04)	122·03 (48·22 – 306·79)	56·02 (28·64 – 108·80)
180 minutes	2·03 (1·60 – 2·46)	1·77 (1·48 – 2·06)	104·93 (38·47 – 283·88)	58·16 (29·45 – 113·83)

Estimated marginal means of (transformed) CGRP with 95% confidence intervals (CI) from repeated measures ANOVA. [1] Re-calculated CGRP values.

Fig. 3

Table 2 Effect of immediate vs. non-immediate centrifugation on transformed CGRP levels

	F	P	η^2_p[1]
Immediate vs. non-immediate centrifugation	0·091	0·765	0·003
Time	2·155	0·151	0·058
Time * age	0·703	0·407	0·020
Time * sex	5·365	0·027	0·133
Immediate vs. non-immediate centrifugation * age	0·294	0·591	0·008
Immediate vs. non-immediate centrifugation * sex	3·853	0·058	0·099

Within-subject effects from repeated measures ANOVA. [1] Partial eta squared.

P349

Ion channel plasticity in trigeminal neurons following acute and chronic infraorbital nerve injury

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Objective: The trigeminal system is responsible for transmitting pain signals in the craniofacial region. Primary headache disorders are characterised by dysfunction and sensitization of these neurons, leading to amplified and sustained pain symptoms.
This study examined the electrophysiological properties of trigeminal neurons, following acute and chronic infraorbital nerve (ION) injury, in order to understand how peripheral nerve damage may contribute to changes in trigeminal excitability.

Methods: Whole-cell patch-clamp recordings were conducted on trigeminal ganglion neurons isolated from female Wistar rats subjected to acute or chronic ION injury, alongside naive controls. Voltage-clamp protocols were used to assess sodium and potassium currents, while current-clamp experiments evaluated neuronal firing properties and spontaneous activity.

Results: Acute ION injury led to heightened neuronal activity, evidenced by increased sodium currents and increased spontaneous activity. In contrast, chronic injury resulted in reduced sodium and potassium currents and diminished excitability, indicating a distinct neurophysiological phenotype.

Conclusion: These findings suggest that acute peripheral trigeminal insult induces hyperexcitability, while chronic injury leads to a transition toward a more stable but maladaptive state. These stage-dependent changes may help inform targeted therapeutic strategies for acute versus chronic headache disorders.

P350

Occipital headache unveiling cerebral venous sinus thrombosis: A hypothesis linking sleep deprivation, elevated creatine kinase, and neuroinflammation

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Objective: This case aims to analyze the potential pathophysiological interplay between acute sleep deprivation, elevated serum creatine kinase (CK) levels, and the emergence of headache as a clinical manifestation of cerebral venous sinus thrombosis (CVST). It seeks to highlight the possibility that sleep deprivation-induced neuroinflammation may serve as a contributing factor or early indicator of underlying cerebrovascular pathology.

Methods: A 22-year-old male presented with a one-week history of occipital headache, followed by acute onset of nausea, vomiting, and sensory aphasia.

Neurological assessment prompted urgent cranial CT and CT venography, which revealed small corticalized lesions in the left temporal lobe with cortico-subcortical edema, as well as thrombosis of the right transverse sinus, sigmoid sinus, and internal jugular vein. Laboratory testing showed a marked elevation in serum CK levels (2700 U/L), in the absence of trauma, seizures, or muscular overexertion. The patient reported significant sleep deprivation in the days preceding symptom onset.

Results: The unexplained CK elevation, combined with neuroimaging findings and the anatomical correlation between occipital pain and sigmoid sinus thrombosis, supported a mechanistic hypothesis linking sleep deprivation to neural stress. Literature suggests that acute sleep loss may trigger oxidative and inflammatory pathways, leading to neuronal injury and the release of markers such as CK-BB and neuron-specific enolase. These mechanisms may contribute to or amplify headache, particularly in secondary causes such as CVST.

Conclusion: This case underscores the potential role of acute sleep deprivation in promoting neuroinflammation and unmasking cerebrovascular pathology. Elevated CK in this setting may reflect neuronal stress. In young adults with atypical headache, recent sleep loss, and unexplained hyperCKemia, clinicians should maintain a high index of suspicion for CVST and consider early neuroimaging.

The patient gave his consent.

P351

Evolution of cerebral autoregulation, cerebral vasoreactivity, and baroreflex in certain and probable reversible cerebral vasoconstriction syndrome (RCVS), from acute stage to remission

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Objective: Demonstrating the reversibility of cerebral artery stenoses is a major diagnostic criterion for RCVS, but evidence of cerebral artery stenosis at the onset of the disease could be challenging . Therefore, additional diagnostic tools would be helpful to support the diagnosis of early RCVS. We evaluated cerebral autoregulation, cerebral vasoreactivity, and baroreflex sensitivity in patients with confirmed RCVS (with intracranial artery stenoses) and probable RCVS (without visible stenosis).

Methods: Patients presenting with suspected RCVS at the Toulouse University Hospital were included from January 2023 to December 2024. Cerebral blood flow velovities were assessed using transcranial Doppler ultrasound and blood pressure and heart rate using photopletysmography. We assessed cerebral autoregulation using the Mx index, cerebral vasoreactivity with the breath-holding index (BHI), and baroreflex sensitivity (BRS). Monitoring was repeated at one month and three months.

Results: A total of 50 patients were included: 19 with confirmed RCVS, and 31 were classified as probable RCVS. Initial Mx index was significantly higher in the RCVS group compared to controls [RCVS: 0.31 (0.25), control: 0.13 (0.17), p = 0.003], one month Mx index was higher in RCVS [RCVS: 0.34 (0.31), control: 0.13 (0.17), p = 0.003], three months Mx index was similar in RCVS and controls [RCVS: 0.20 (0.26), control: 0.13 (0.17), p = 0.128]. There were no differences in BRS or BHI between patients and controls. There were no differences in Mx between confirmed RCVS compared to probable RCVS [confirmed RCVS: 0.34 (0.24), probable RCVS: 0.29 (0.26), p = 0.513], however, BHI was significantly lower in confirmed RCVS [confirmed RCVS: 1.64 (0.62), probable RCVS: 1.83 (0.55), p = 0.009]. An Mx ≥ 0.38 was highly specific (95.5%) but had low sensitivity (44%) for RCVS diagnosis.

Conclusion: Cerebral autoregulation was impaired in early RCVS up to one month. A high Mx index is specific but not sensitive for diagnostic of RCVS.

Fig. 1

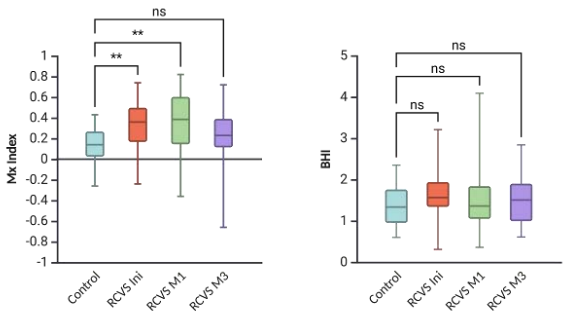


Fig. 2

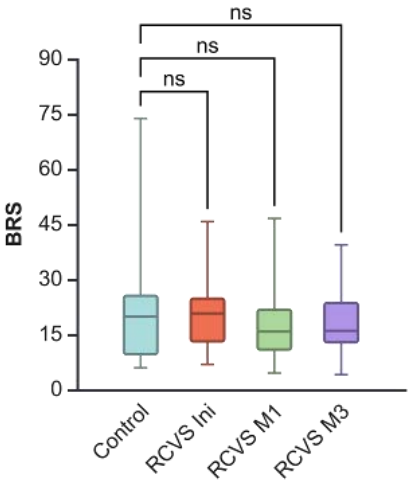
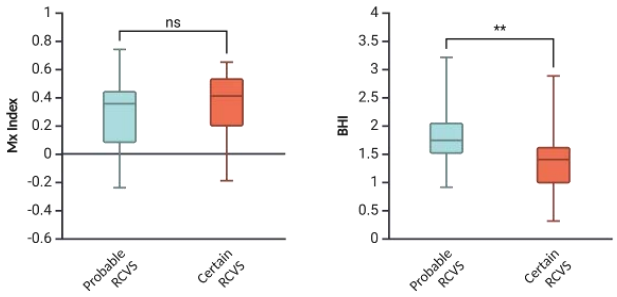


Fig. 3



P352

Presentation and treatment determinants in cerebrospinal fluid hypotension syndrome: A case series

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Objective: Cerebrospinal fluid hypotension (CSFH) is typically caused by spontaneous/traumatic spinal dural tears or subarachnoid-venous system communications. They may heal naturally or require medical therapy. We intended to characterize phenotypes and therapy response factors in a CSFH population.

Methods: Case series - patients admitted in our center between 2018-2025

Results: 13 patients (12 female, mean age 46 years) were included. 38,5% reported cervical/thoracic trauma (car, sport accidents; massage). 12 had orthostatic headache, 6 had nausea/vomiting, 3 had diplopia (2 horizontal, 1 combined horizontal-vertical - the latter being the only case without headache), 3 had tinnitus and 3 had either vertigo, ear fullness or reduction of sound perception. All patients performed brain MRI, and spinal cord MRI, CT/MRI myelography and/or subtraction digital myelography when appropriate. 9 had CSFH imaging signs (pachymeningeal enhancement, subdural effusions, pituitary enlargement, cisternal obliteration, brainstem sagging, cerebellar tonsil ectopy). 5 had cystic spinal nerve root dilations: 4 at multiple cervicodorsal levels, 1 of which also lumbar; and 1 primarily sacral. 2 others had cervicodorsal CSF-venous fistulas (CSF-VF), without overt cysts. 10 patients underwent epidural blood patch (BP), 8 of which lumbar BP. We found a second BP was needed only in 3 patients, all with cervicodorsal multifocal cystic dilations, 2 of which directed at thoracic segments. In these patients, full recovery was later only achieved after multiple BPs and multimodal therapy (I.V. caffeine, vitamin A, steroids, subarachnoid saline, sphenopalatine ganglion/occipital nerve blocks).

Conclusion: Our series demonstrates some classic signatures of CSFH. Though most patients responded to only one BP, cervical/dorsal dural leaks (suggested by aggregation of multiple nerve root cysts) appeared more refractory, in contrast with isolated CSF-VF. Limited sample size/imaging need be addressed for future more conclusive research.

P353

Inhibiting the peripheral degradation of anandamide reduces trigeminal hyperalgesia in a model of dural neurogenic inflammation via a CB1/CB2-independent mechanism

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Objective: The recent availability of CGRP-targeting drugs has improved migraine management, although it is now clear that many patients are CGRP-resistant. Inhibition of the degradation pathway of endocannabinoids may represent a new therapeutic target. Indeed, the inhibition of fatty acid amide hydrolase (FAAH), the main catabolic enzyme of anandamide, and of N-acylethanolamine-hydrolysing acid amidase (NAAA), which hydrolyses palmitoylethanolamide, may exert analgesic and anti-inflammatory effects. The aim of the study was to investigate and compare the effects of peripheral FAAH inhibition (URB937) and NAAA inhibition (ARN726) on trigeminal hyperalgesia induced in the animal model of migraine based on dural neurogenic inflammation.

Methods: Migraine-like dural inflammation was induced in male rats via infusion of inflammatory soup (IS) onto the dura. Animals were treated i.p. with ARN726 or URB937, or vehicle. To further investigate the URB937 effects, additional groups were treated with cannabinoid (CB) 1 or CB2 receptor antagonists (AM251 or AM630) in combination with URB937 treatment. Trigeminal nocifensive behavior was assessed using the orofacial formalin test (OFT) 2h after IS infusion.

Results: IS infusion produced a significant increase in trigeminal hyperalgesia compared to controls. Such increase was significantly reduced by URB937 treatment, while ARN726 had no effect. Antagonism of CB1 or CB2 receptors did not reverse URB937 anti-hyperalgesic effect.

Conclusion: The combination of IS infusion with OFT shows that inflammatory mediators in the meninges activate and sensitize the nociceptive terminals of the trigeminal nerve. Peripheral inhibition of FAAH through URB937 significantly reduces IS-induced trigeminal hyperalgesia, whereas inhibition of NAAA does not produce similar effects. These findings

suggest a prominent role for anandamide in the pain modulation in this model of neurogenic inflammation. URB937 anti-hyperalgesic effects appear to be CB1/CB2 receptor independent activation.

P354

Network-level brain connectivity alterations in an animal model of migraine and the effects of olcegepant treatment

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Objective: Migraine is a neurological disorder involving disrupted brain connectivity during attacks. While CGRP-targeted therapies are clinically effective, their impact on brain networks is unclear. We previously showed that nitroglycerin (NTG) induces thalamic and subcortical connectivity changes in male rats, mimicking migraine-like network disruption. Here, we examine how CGRP receptor antagonism affects brain connectivity in this NTG-based model.

Methods: Seven rats received NTG followed by vehicle (NTG + vehicle), and 8 received NTG followed by olcegepant (NTG + OLC) one hour and 30 min later. Resting-state fMRI was acquired two hours post-NTG under isoflurane anaesthesia. Resting-state fMRI was acquired two hours post-NTG under isoflurane anaesthesia. Data were pre-processed and parcellated into 232 regions of interest (ROIs) using the SIGMA atlas. Functional connectivity matrices were computed via Spearman correlations between ROI time series. Graph-theoretical measures, nodal degree, clustering coefficient (CC) and global efficiency, were derived using the Brain Connectivity Toolbox in MATLAB. Key regions of the rat pain matrix were selected for their role in nociception and migraine-related dysfunction.

Results: Compared to NTG + vehicle, NTG + OLC rats exhibited reduced nodal degree in the left striatum, bilateral cingulate, and insular cortices, indicating decreased hub centrality. The left amygdalo-hippocampal area showed reduced degree and CC, reflecting dampened limbic integration. Thalamic CC and global efficiency were significantly reduced, consistent with attenuated thalamocortical signaling. Notably, left cingulate degree declined from 22.14 to 13.63 ($p = 0.007$), and thalamic CC from 0.074 to 0.069 ($p = 0.008$).

Conclusion: Olcegepant significantly modulated connectivity within the pain matrix towards greater efficiency and reduced hubness in regions such as the thalamus, insula, and cingulate cortex, to restore migraine-related impairments in connectivity.

P355

Cluster headaches and changements on MRI at hypophyseal region

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Objective: Cluster headaches are one of the rare types of primary headaches. According to ICHD 3rd edition they are presented with strictly unilateral headache, lasting 15-180 minutes , associated with autonomic symptoms on the side of the pain.

Main aim of our study was to evaluate such called "atipic" cases of cluster headache and any changements at hypophyseal region on MRI

Methods: We included 188 patients (126 women/ 62 men) addressed at Neurology Department of YSMU during period from May 2024 till May 2025, from which 25 (21 men/ 4 women) was diagnosed with cluster headache. Age of participants was 18-65 years. All patients were diagnosed by headache specialist according to ICHD -3 diagnostic criteria. All patients with cluster headache was undergone MRI, MRA 3 tesla.

Results: Data analysis revealed that from 25 patients with cluster headache, 4 men diagnosed chronic cluster headache. From 10 men 6 patients has photophobia during attack, 2 men with chronic cluster describe shift of the site of pain after several months, in 2 cases duration of attack was more than 3 hours. In those 10 cases we found changements on MRI at hypophysis region– in 3 microadenoma of hypophysis , 4 Ratke cysts, 3 Intrusion of the suprasellar cistern into the sella turcica correspondingly.

Conclusion: Summarizig data we suggest that changements at the hypophyseal region can be the cause of non standard presentation of cluster headache and we need to realise more studies with bigger amount of patients and probably discuss some changements at diagnostic criteria.

P356

Analysis of the structure of migraine according to the neurological clinic in Russia

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Objective: Introduction: Headaches remain one of the major public health problems worldwide. Assessment of the prevalence and structure of headaches is a fundamental step for the effective organization of medical care for patients with cephalgia.

Methods: A single-center retrospective study was conducted with the analysis of electronic medical records of patients who had an outpatient

appointment with a neurologist at the Russian Center of Neurology and Neurosciences with headache in the period from 01.01.2022 to 31.12.2022. Patients with diagnoses of G43 (Migraine) and G44 (Other headache syndromes) according to ICD-10, verified according to ICD-3 criteria, were included.

Results: In total 22,445 patients applied to a neurologist, of which 2,830 (12.6%) were diagnosed with headache, and 1,325 (5.9%) had migraines. *Characteristics:* women - 80%; age from 30 to 49 years – 58.49%, average age – 38.85±14.99 years old. The total experience of migraine is 17.10±8.22 years. The majority of patients did not receive preventive treatment for migraine. *Types*: without aura (G43.0) – 697 people (52.61%), with aura (G43.1) – 287 (21.66%), other – 111 (8.37%), unspecified – 211 (15.93%), complicated (G43.3) – 19. (1.43%). *Frequency:* rare episodic - 552 people (37.05%), frequent episodic - 282 (21.28%), chronic – 491 (41.67%). The average frequency is 17.60±6.91 days/month. *Preventive therapy* was prescribed to 1,137 people (85.8%): monotherapy: 453 people (34.18%); 2 groups of drugs – 432 (32.60%); 3 groups – 198 (14.94%), 4 and more groups – 54 (4.07%). *Number of visits*: once – 897 people (67.7%), 2 visits – 262 (19.77%); 3 visits – 103 (7.77%), more than 4 visits - 62 (4.67%)

Conclusion: Migraine accounts for 5.9% of neurological treatment requestsand is prevalent in women aged 30 to 49 years. Patients with chronic migraines, who are prescribed multicomponent preventive therapy for migraines, turn to a neurologist.

P358

Photophobia and visual triggers in vestibular migraine

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Objective: We investigated the correlation of photophobia during the VM attack with interictal photosensitivity and visually triggering dizziness in patients with VM.

Methods: We enrolled patients diagnosed with VM, with or without photophobia, across seven specialized vertigo and headache clinics in China. Healthy individuals were also included as a control group. Using a cross-sectional survey design, we collected data related to light intensity and dizziness frequency triggered by flicker, glare, and eyestrain using the Headache Triggers Sensitivity and Avoidance Questionnaire.

Results: A total of 366 patients were recruited. The photosensitivity and frequency of dizziness induced by flicker, glare, and eyestrain observed in patients with VM and photophobia were significantly elevated compared with those in patients without photophobia and control participants ($P < 0.001$). A significant positive correlation was observed between photosensitivity levels and dizziness frequency triggered by flicker, glare, and eyestrain in patients with VM and photophobia ($P < 0.001$).

Conclusion: This study unequivocally established a positive association of ictal photophobia with interictal photosensitivity and visually triggering dizziness, strongly advocating the need for further research on exposure-based therapies for managing VM.

Fig. 1

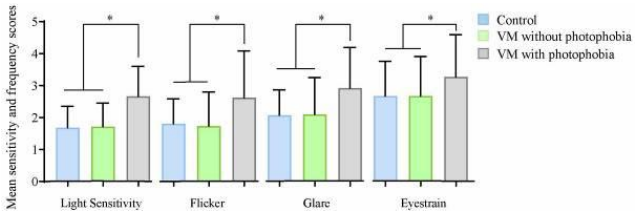


Fig. 2

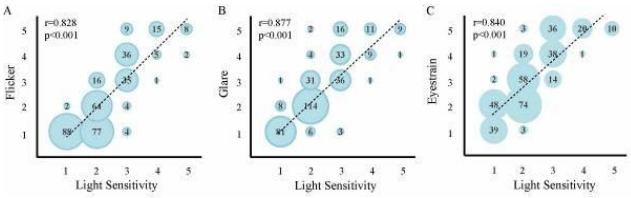
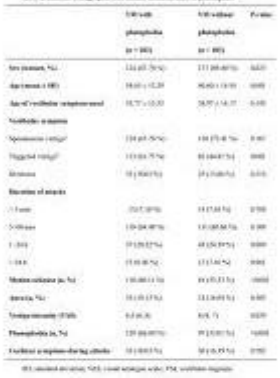
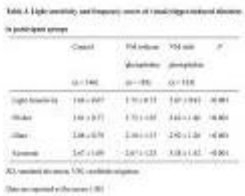


Fig. 3







P359

Prevalence and characteristics of Visual Snow symptoms in migraine: A cohort study in patients with and without aura

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Objective: Visual symptoms are common in migraine**,** yet their prevalence and relation to migraine subtype and aura frequency remain insufficiently characterized. We assessed the prevalence and features of visual symptoms, focusing on visual static and other symptoms associated with Visual Snow Syndrome (VSS), in migraine with aura (MA) and without aura (MO).

Methods: A cross-sectional survey in the Leiden Migraine Cohort, a web- and clinic-based sample, captured migraine characteristics and visual phenomena, including visual static, palinopsia, afterimages, photophobia, nyctalopia, and entoptic phenomena. Outcomes included prevalence, episodic versus continuous course, and intensity of visual static, with logistic regression and correlation analyses assessing subgroup differences and relationships with aura frequency.

Results: Among 441 participants (34% MA, 66% MO), visual static was reported by 24%, predominantly as episodic phenomenon (92%). Aura frequency correlated positively with visual static intensity ($r = 0.33$, $p < 0.001$), but overall prevalence of visual static did not differ between MA and MO (24% vs 24%; OR 1.0, 95% CI [0.6–1.5]). Other visual symptoms were common: palinopsia/afterimages (32%), afterimages of light sources (32%), entoptic phenomena (22%), self-light of the eye (32%), interictal photophobia (68%), and nyctalopia (25%). The point prevalence of VSS was 2.0% (95% CI [0.7–3.3]).

Conclusion: Episodic visual static is common in migraine, and its intensity increases with aura frequency. While up to one-third of participants report episodic VSS-like symptoms, continuous visual snow and full VSS are rare.

P362

Artificial intelligence for stroke risk and care in migraineurs: A scoping review

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Objective: To map and synthesize existing evidence on the use of artificial intelligence (AI) for predicting stroke risk, incidence, and timing in patients with migraine.

Methods: We conducted a scoping review. PubMed, Embase, Scopus, Web of Science and grey literature were searched from inception to August 2025. Eligible studies applied AI or machine learning or deep learning to migraine populations to assess stroke risk, incidence, or in managing acute stroke care in migraineurs.

Results: Nine studies met inclusion criteria. Three large cohort studies used AI enhanced electrocardiography (AIECG) and found migraine with aura to have higher risk of atrial fibrillation and consequent vascular outcomes, especially stroke, compared to migraine without aura (P<0.001). A telestroke study found AI imaging support software reported high user satisfaction. Four predictive modeling studies showed high performance (accuracy generally higher than 90%) for stroke prediction in migraine populations. Migraine subtype, comorbidities, and medication use were identified as important predictors.
Conclusion: AI methods show promise in identifying migraine patients at elevated risk of atrial fibrillation and stroke and in supporting acute stroke care. Current evidence, however, is heterogeneous and exploratory. Future research should prioritize large-scale, prospective multicentric validations to assess the reliability, generalizability, and clinical utility of these approaches.

P364

Investigating the clinical features predicting the development of resistant and refractory migraine – A machine learning model based upon the REFINE study data

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Objective: Can machine learning techniques be used to identify clinical predictors of progression to Resistant or Refractory Migraine?
Methods: We used the REFINE dataset, collected prospectively across 15 European headache centers, where patients were classified at baseline into three groups (NRNRM, ResM, RefM) based on European Headache Federation criteria. The aim was to identify predictors of progression over a 3–6 month follow-up. After preprocessing (handling of missing/outlier values and undersampling), we applied feature selection using both correlation analysis and Random Forest importance. Selected variables were used to train and compare classification models. Model performance was evaluated using accuracy and F1-score, and SHAP analysis was applied to the best-performing model to interpret feature contributions.
Results: Key predictors of diagnostic change included baseline EHF diagnosis (r = 0.63), presence of ≥8 debilitating headache days/month (r = 0.55), HIT-6 score (r = 0.35), and HURT item 4 (medication days/month, r = 0.33). Random Forest-based selection further highlighted migraine days over 3 months, number of treatment failures, HALT score, and triptan use. Gradient Boosting achieved the best performance (based on F1-score) and SHAP analysis confirmed the clinical relevance of the selected features.
Conclusion: This study highlights the potential of machine learning approaches in identifying clinical variables that influence migraine progression to resistant or refractory forms. These findings could help clinicians in the early recognition of patients at high risk for preventive treatment failures, allowing for targeted and timely interventions

P365

Forecasting migraine with machine learning from mHealth data

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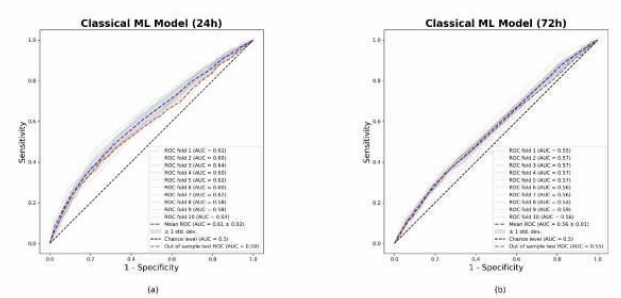
Objective: To develop and evaluate machine learning (ML) models to forecast headache days using mobile health (mHealth) data from a migraine biofeedback treatment app.

Methods: This was a ML study of data from the BioCer clinical trial (NCT05616741) evaluating app-based biofeedback for preventive treatment of episodic migraine. Participants completed three months of daily biofeedback sessions with wearables measuring trapezius muscle tension, heart rate variability and peripheral skin temperature. Input data for the models included these parameters as summary metrics from the biofeedback sessions and daily headache entries. The outcomes of interest were the presence of a moderate-to-intense headache (defined as an VAS intensity of 4 or higher on a scale of 0-10) within a 24-hour and 72-hour window the following day. The dataset was randomly split into train and test sets. A long range of ML architectures, foundation models (Tab-PFN), and time-series models (GRU-D) were trained and optimized using the area under the receiver operating characteristics curve (AUC). The best model identified during training was applied on the unseen test set.

Results: 146 individuals, with a total of 26209 headache days were included in the forecasting models. For 24-hour window predictions, the top performing decision tree classifier achieved a test set AUC of 0.59. The Tab-PFN model and GRU-D model scored 0.58 and 0.51. For the 72-hour forecasting window, the test set performances were 0.55, 0.54, and 0.51, respectively (Fig. 1, Table 1). The most important features were self-reported headache entries, duration of headache and previous neuromuscular conditions (Fig. 2).

Conclusion: Despite the large scale of the available dataset, precisely and prospectively captured data, and extensive model testing, we were not able to forecast headache days with more than modest accuracy. Probably individual level autonomous nervous system parameters are too heterogeneous to be used to forecast migraine attacks on a group level.

Fig. 1



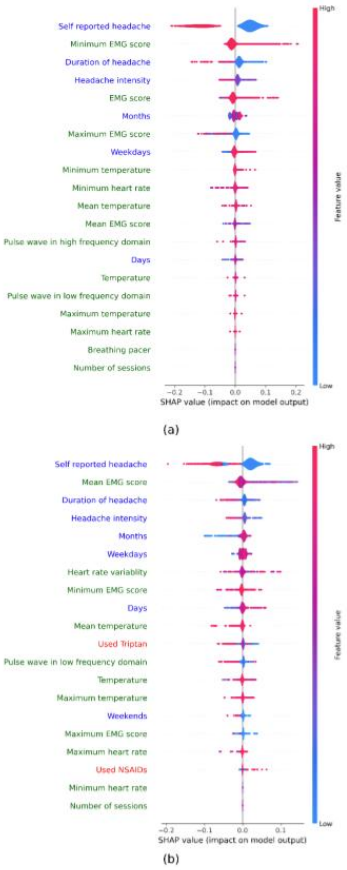
Receiver operating characteristics (ROC) curve with training and test set performance for the top performing model for (a) 24h, and (b) 72h time window

Fig. 2

Table 1. Forecasting model results. For the training set the mean of all 10 folds ± 1 standard deviation is reported. For the test set the bootstrapped 95% confidence interval is reported

	Performance Metrics	24h train (SD)	24h test (95% CI)	72h train (SD)	72h test (95% CI)
Classical ML Models (decision tree classifier)	AUC	0.61 (0.02)	0.59 (0.56-0.61)	0.56 (0.01)	0.55 (0.53-0.56)
	Balanced accuracy	0.58 (0.02)	0.58 (0.56-0.60)	0.54 (0.01)	0.54 (0.52-0.55)
	Sensitivity	0.67 (0.01)	0.62 (0.58-0.63)	0.58 (0.03)	0.56 (0.54-0.57)
	Specificity	0.72 (0.01)	0.66 (0.64-0.67)	0.68 (0.08)	0.70 (0.68-0.71)
Foundation Model (TabPFN)	AUC	0.55 (0.03)	0.58 (0.56-0.60)	0.52 (0.02)	0.54 (0.52-0.56)
	Balanced accuracy	0.51 (0.04)	0.50 (0.50-0.51)	0.50 (0.03)	0.53 (0.52-0.54)
	Sensitivity	0.53 (0.06)	0.51 (0.50-0.53)	0.52 (0.02)	0.52 (0.51-0.54)
	Specificity	0.52 (0.02)	0.52 (0.51-0.54)	0.53 (0.06)	0.51 (0.50-0.53)
Time-series ML Models (GRU-D)	AUC	0.61 (0.02)	0.51 (0.47-0.55)	0.54 (0.02)	0.51 (0.47-0.55)
	Balanced accuracy	0.56 (0.01)	0.52 (0.47-0.54)	0.54 (0.02)	0.53 (0.49-0.54)
	Sensitivity	0.50 (0.01)	0.46 (0.40-0.49)	0.52 (0.03)	0.49 (0.48-0.51)
	Specificity	0.68 (0.08)	0.65 (0.48-0.82)	0.66 (0.08)	0.64 (0.58-0.68)

Fig. 3



SHAP summary plot of the 20 most important features with the top performing model for (a) 24h, and (b) 72h time window

P366

Toward predictive migraine care: Development of a 24-hour risk model from daily patient diaries

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Objective: Predicting migraine attacks creates opportunities for early intervention and may help individuals with migraine maintain control over their daily lives. The aim of this study was to develop and internally validate a model to predict 24-hour attack risk in patients with episodic migraine.

Methods: In this cohort study, individuals with episodic migraine completed a validated e-diary for at least 3 and up to 12 months, recording headache characteristics, triggers, and lifestyle factors (e.g., sleep, exercise, stress) on a daily basis. A generalized linear mixed-effect model with 23 literature-based predictors was first used to forecast whether a new attack would occur within 24 hours based on factors from the previous 24 hours. The final model was then derived from the significant predictors of this initial model together with 60 additional candidate predictors, which were subjected to LASSO variable selection. LASSO is a regression-based statistical method that performs both variable selection and regularization to improve model prediction and interpretability.

Results: A total of 88,921 diary entries, including 9,820 migraine onset events, were collected from 348 participants with migraine. The initial model showed moderate discrimination (AUC= 0.63) and good calibration (intercept=0.29,slope=1.15). Risk-increasing factors were natural menses, sleep-deprivation, stress, and intense physical activity; lower risk was linked to a recent attack, skipping meals, and reduced stress. In the final model (AUC=0.62, Intercept=0,slope=1), variable selection added pain coping, well-being, and severe hangover as predictive factors.

Conclusion: Diary-based factors allow moderate prediction of 24-hour migraine risk, and future use of advanced AI models may improve accuracy by capturing more complex patterns.

P367

Enhancing clinical decision-making in migraine: Development and preliminary validation of an artificial intelligence model predicting CGRP-mAb treatment response at 3 months

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Objective: This study aimed to predict 3-month responses to anti-CGRP monoclonal antibodies (CGRP-mAbs) in migraine patients using artificial intelligence (AI), based on baseline clinical characteristics before the first treatment. We also assessed whether the AI could practically assist physicians in decision-making.

Methods: Phase 1: We developed an AI model using retrospective data from 100 patients (80 for training, 20 for testing) receiving CGRP-mAbs. The model predicted whether patients would achieve ≥50% reduction in monthly migraine days at 3 months. **Phase 2:** Using the test dataset, three general neurologists first predicted outcomes without AI, then with AI guidance, including AI confidence scores (0–100%). Performance metrics were compared between predictions with and without AI.

Results: Phase 1: For the test dataset, the AI model achieved 68.9% sensitivity and 62.2% specificity. **Phase 2:** Physicians" median performance without AI was 63.5% sensitivity and 60.1% specificity. With AI

assistance, these improved to 69.7% sensitivity and 63.7% specificity.
Conclusion: AI support enhanced physicians" ability to predict CGRP-mAb treatment outcomes. While external validation is needed, this model shows promise for personalized migraine care and optimized use of CGRP-mAbs.

P368

Developing an artificial intelligence-based headache diagnostic model using Japanese cohort and external validation for Italian cohort

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Objective: Misdiagnoses of headache disorders are a serious issue. Therefore, we previously developed an artificial intelligence (AI)-based headache diagnosis model using a large questionnaire database in a specialized headache clinic in Japan. However, its external validation in other cohorts abroad has not been performed. Therefore, we validated its utility using an Italian cohort.
Methods: We previously developed an AI-based headache diagnosis model in Japan (PMID: 37596885) using a headache questionnaire at the initial consultation based on a retrospective investigation of 6058 patients diagnosed by a headache specialist. The model was a 5-class classification model. As for the diagnostic performance, sensitivity and specificity were both 84.2%. Using the AI-based headache diagnosis model, we tested its utility using the Italian cohort consisting of 411 medical students with headache disorders with 17 variables of headache characteristics. The prediction was migraine or non-migraine headache disorders, and the ground truth was based on the neurologists" diagnosis.
Results: Of the 411 medical students with headache disorders, 245 (59.6%) had migraine, and others had non-migraine headache disorders. The sensitivity was 91.8% and the specificity was 62.3%.
Conclusion: AI developed using the Japanese cohort had different performance for the Italian cohort. Given the model's limitations based on the data from a single clinic in Japan and the skewed cohort of Italian medical students, our results suggested that an AI-based diagnosis model should be developed depending on the clinical settings in each country.

P369

Clinical-genotype machine prescription for migraine – A HUNT study

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[2]NTNU Norwegian University of Science and Technology, Department of Neuromedicine and Movement Science, Trondheim, Norway
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[4]University College London, UCL Queen Square Institute of Neurology, London, United Kingdom
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[10]St. Olavs University Hospital, Neuroclinic, Trondheim, Norway
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Objective: Migraine is highly heritable, yet no machine learning (ML) models for predicting treatment responses have incorporated genetic data. We aimed to develop ML models including both

genetic and clinical information to predict treatment responses of migraine preventives and triptans.

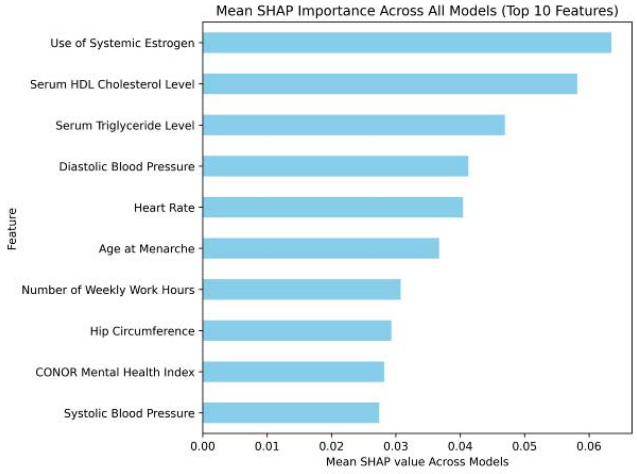
Methods: Data came from the population-based Trøndelag Health Studies (HUNT) and national prescription records. Clinical features included demographics, serum metabolic measures, comorbidities, mental health and lifestyle factors. Genetic features included 108 migraine risk loci. Preventive response was defined as ≥50% reduction in triptan use after first preventive dispensation, and triptan response as ≥3 dispensations. The dataset was split into training (70%), validation (10%) and test set (20%). A series of standard and causal ML architectures were trained and optimized on the training and validation set, and the best model was evaluated on the held-out test data. SHAP (Shapley Additive exPlanations) values identified key predictors.

Results: In total, 475 participants tried a preventive (amitriptyline, beta-blocker, candesartan or topiramate) and 565 a triptan (371 sumatriptan) during the project period. Using only clinical features, the best models achieved area under curve (AUC) of 0.56-0.69 for the preventives (0.56 for triptans). When combining clinical and genetic data, the AUCs were unchanged or reduced in all cases except for amitriptyline (AUC 0.80) and sumatriptan (AUC 0.55). The most important predictors were hormone-related features, lipid levels and hemodynamic parameters (Figure 1).

Conclusion: We developed models that predicted treatment responses to amitriptyline, beta-blockers, candesartan and topiramate with modest accuracy. Incorporating genetic data did not enhance performance, although the limited sample size prevents firm conclusions.

Figure 1. SHAP bar blot of ten most important clinical features across all four preventive models

Fig. 1



P370

Migraine disability, and depression in Brazilian medical students: A cross-sectional study

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Objective: To evaluate the burden of headache-related disability and depression comorbidity among a high-risk population of medical students.

Methods: This cross-sectional study was approved by the local ethics committee. Sociodemographic data, lifestyle, comorbidities, and headache characteristics were assessed using an online self-administered questionnaire (125 items), which included the clinical tools HIT-6, MIDAS, BECK, and ASC-12. Inclusion criteria: medical students aged ≥18 years recruited first to last year of graduation. Exclusion: incomplete answers. A convenience sample was collected between October 15, 2024, and March 29, 2025. Chi-square tests and t-tests were conducted in JASP to assess group differences (headache vs. non-headache), with p-values < 0.05 considered statistically significant.

Results: A total of 134 participants were included, with a mean age of 22.1 years; 81 were women (60.5%). Headache prevalence was 59.7%, with a mean age of onset of 13.9 years. Eighty participants reported active headaches, predominantly migraine subtypes: probable migraine without aura (40.5%), migraine without aura (28.4%), and episodic tension-type headache (18.9%). HIT-6 test revealed a substantial/severe impact in 38.1% of migraines without aura and 37.5% of migraines with aura. MIDAS test showed moderate disability in 26.7% and severe disability in 28.1% of participants with headache. Individuals with headache had higher rates of moderate or severe depression (19% vs. 13.3%), though the difference was not statistically significant ($p > 0.05$).

Conclusion: This study showed a high prevalence of headaches among medical students, with a predominance of probable migraine without aura. Moderate and severe depression were also more frequent in those with headaches. The HIT-6 and MIDAS tools highlighted a substantial functional impact. These findings emphasize the need for targeted strategies for mental health and disability assessments in this academic population.

P371

AI-powered personalized therapy for migraine patients: Transforming treatment approaches

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Objective: Millions of people throughout world suffer from migraines, which frequently derail life. Many patients find little help despite several therapies since treatments are not customized to their specific needs. Analyzing genetics, environment, and lifestyle, this review investigates how artificial intelligence can design tailored migraine treatments that will eventually raise patient pleasure and results

Methods: From 2015 to 2023, we examined more than 50 peer-reviewed papers drawn from reliable databases including PubMed, Scopus, and IEEE Xplore. Our interest was on how artificial intelligence and machine learning assess clinical, genetic, and lifestyle information to enhance migraine treatment. We examined how early diagnosis, prediction of successful treatments, and monitoring of progress all depend on artificial intelligence. We also looked at how wearables and mobile applications powered by artificial intelligence provide real-time input and automatically adapt medicines

Results: By employing machine learning to forecast migraines based on triggers including environment and genetics, artificial intelligence is revolutionizing migraine treatment. By determining the optimum drugs for every patient, it customizes treatments and lowers side effects while increasing efficacy. Tracking migraine patterns with artificial intelligence powered wearables also allows real-time treatment changes that lower attack frequency and improve quality of life

Conclusion: Personalized treatments powered by artificial intelligence are revolutionizing migraine control. Although there are privacy and clinical application problems, increasing evidence suggests that artificial intelligence may help to raise standards of care. Better outcomes will result from future research that concentrates on perfecting these models so treatment may be made more targeted and effective

Fig. 1

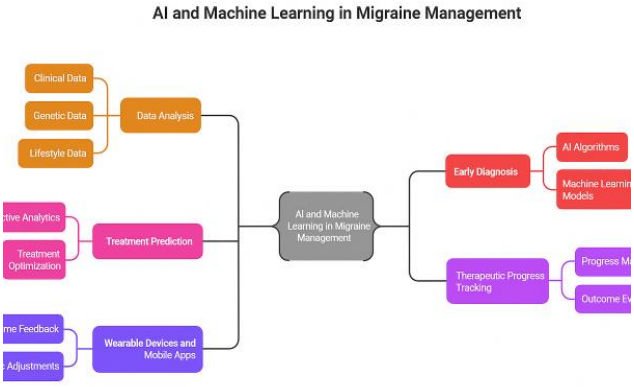
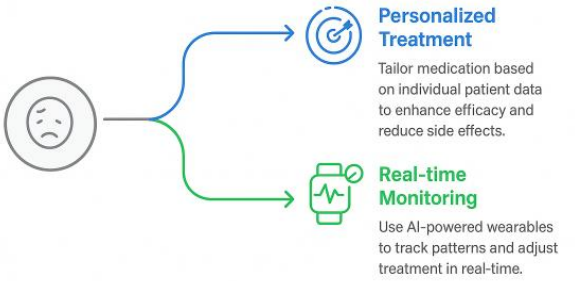


Fig. 2



P372

Integrating machine learning into headache medicine: Towards personalized therapeutic strategies

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Objective: Headache disorders are getting trickier to understand, and it"s become clear that one-size-fits-all treatments just don"t cut it. People respond differently to the same medication or therapy, which makes personalized care more important than ever. This review takes a close look at how machine learning (ML) might help us move in that direction — predicting how someone might respond to treatment, identifying different headache subtypes, and helping doctors make more tailored care plans

Methods: We dug through recent research published from 2015 to 2025, using databases like PubMed, Scopus, and Web of Science. We focused on studies that used supervised, unsupervised, or deep learning models to diagnose or predict outcomes for common headache types such as migraines and tension-type headaches. From each study, we pulled details about the kind of ML model used, the size of the dataset,

what patient features were analyzed, and how the models were validated

Results: The research so far looks promising. Models like random forests, support vector machines, and neural networks have been used to spot individual headache patterns and predict which treatments might actually work. When researchers combined data from multiple sources — things like clinical records, brain scans, and wearable devices — the predictions got even sharper. Still, there are some real hurdles: data quality varies a lot, sample sizes are often small, and many ML models are hard to interpret in a clinical setting

Conclusion: Machine learning could completely change how we approach headache care, making it more data-driven and personalized. But for that to happen, we need models that are not just accurate, but also transparent and easy for clinicians to trust. Building these systems will take teamwork doctors, data scientists, and policy experts all working together to turn experimental algorithms into practical tools that genuinely improve patient care

Fig. 1

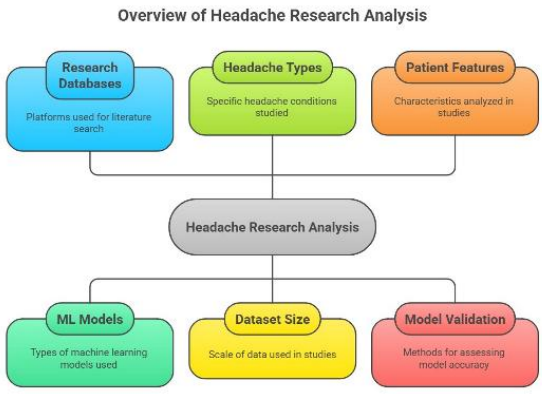
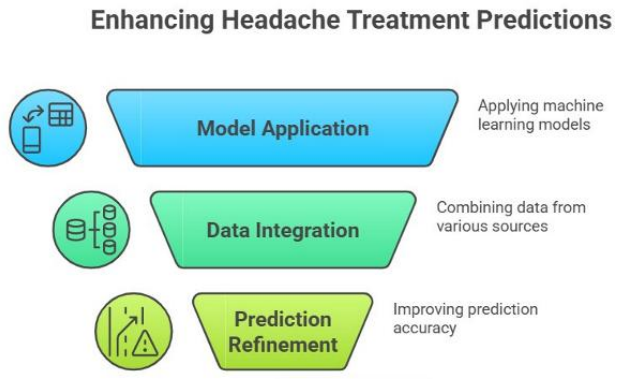


Fig. 2



P374

Case report: Retinal involvement in recurrent painful ophthalmoplegic neuropathy with reversible color vision impairment

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Objective: To report a case of recurrent painful ophthalmoplegic neuropathy (RPON) with reversible color vision abnormalities and explore potential pathogenic mechanisms.

Methods: A 23-year-old male had episodic headaches ＞8 years and left ptosis with diplopia ＞ 4 years. Headaches featured left periorbital/temporal distending pain, nausea, vomiting, photophobia and phonophobia, lasting 4-24 hours. Four years post-onset, transient left dyschromatopsia and ipsilateral oculomotor nerve palsy developed 1d post-attack, resolving spontaneously ≤1 week. Steroids were ineffective. Recent persistent left mydriasis noted. The patient gave him consent to publish his details in an open access journal.

Results: Fundus was normal. MRI showed left oculomotor nerve enhancement during attacks resolving in remission. The Farnsworth-Munsell 100-hue test demonstrated reversible left-eye color vision impairment during attacks (Total Error Score 168). Pattern electroretinogram (PERG) revealed significantly higher P50 and N95 wave amplitudes in remission versus attack phase. Acute treatments (rizatriptan, ibuprofen, loxoprofen, rimegepant) failed; only indomethacin provided relief. Interictal IV nitroglycerin failed to induce migraine-like headache.

Conclusion: RPON is reclassified as a neuralgia in ICHD-3. By inhibiting cyclooxygenase (COX), indomethacin suppresses prostaglandin synthesis, reducing prostaglandin-mediated sensitization of trigeminovascular afferents, suggesting trigeminovascular afferent sensitization in RPON. Furthermore, RPON pathophysiology may involve retinal neuronal networks beyond the oculomotor nerve, supported by PERG amplitude changes implicating inner retinal layer pathology, indicating pathogenesis distinct from classical cranial neuropathies.

Fig. 1

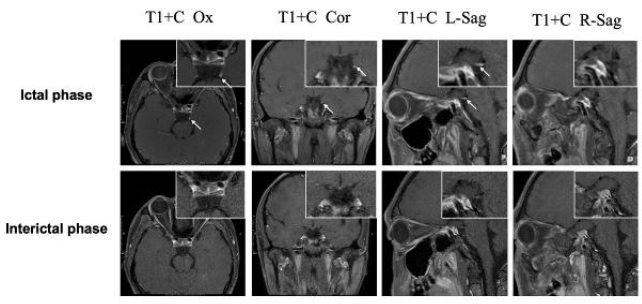


Figure 1. MRI showed left oculomotor nerve enhancement (white arrow) during ictal phase resolving in interictal phase.

Fig. 2

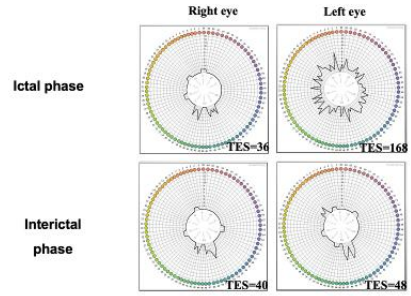


Figure 2. The Farnsworth-Munsell 100-hue test demonstrated reversible left-eye color vision impairment during ictal phase (TES=168). TES: Total Error Score

Fig. 3

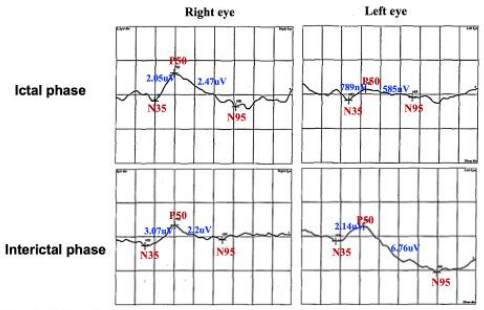


Figure 3. Pattern electroretinogram (PERG) revealed significantly higher P50 and N95 wave amplitudes in interictal phase versus ictal phase.

P375

New trends in migraine management: Transcending the traditional divide between acute and preventive treatments

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Objective: Migraine treatment is divided into acute and preventive methods. Acute treatment aims to quickly relieve headache and symptoms with minimal side effects, helping patients return to normal. Preventive treatment focuses on reducing the frequency, severity, and disability of attacks, and improving response to acute therapy. Guidelines usually address these separately. With the discovery of calcitonin gene-related peptide (CGRP) and its role in migraine, CGRP receptor antagonists like rimegepant have been developed and approved for both acute and preventive treatment.

Methods: Emerging researches showed a strong link between migraine acute and preventive treatments. Acute medications like lasmiditan and rimegepant not only relieve symptoms quickly but also lower attack frequency and disease impact over time.

The AMPP study found that better acute treatment lowers the risk of migraine progression, aligning with the goal of preventive treatment. Additionally, preventive medications can have immediate effects and improve acute treatment"s effectiveness. These findings suggest that acute treatment may also prevent migraine chronicity, while preventive treatment can act quickly and enhance acute therapy. This model transcends traditional divide between acute and preventive treatments and offers a novel perspective for managing migraine.

Results: Some patients who qualify for prevention can control migraines well with optimized acute treatment alone, avoiding daily medication and reducing their burden.

Conclusion: Clinicians should understand that acute and preventive treatments are linked goals to improve management and prevent progression. Personalized plans are needed to enhance both treatments and lessen the overall impact on patients.

P376

Friend or foe? A literature review of GLP-1 RA therapy and its emerging links to migraine and intracranial hypertension

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Objective: This literature review examines whether glucagon-like peptide-1 receptor agonists (GLP-1 RAs)used in type 2 diabetes mellitus (T2DM) are linked with increased migraine incidence and explores emerging evidence connecting GLP-1therapies with idiopathic intracranial hypertension (IIH). Although GLP-1 RAs improve glycemic control, their neurovascular effects remain uncertain.

Methods: A systematic search was conducted in PubMed and Web of Science. In PubMed, 76 articles were retrieved; we excluded 33 reviews, 3 book chapters, 5 studies not related to GLP-1 or headache, and 3 non-English/unpublished papers. In Web of Science, 99 articles were identified; after excluding 32 reviews, 25 unrelated studies, and 25 duplicates, 49 unique articles remained. These were categorized into four domains: migraine risk, therapeutic comparisons, mechanistic insights, and IIH-related studies.

Results: Twenty-two articles show that T2DM patients on GLP-1 RAs have a significantly higher prevalence of migraine diagnoses and increased use of migraine-specific medications (e.g., triptans and CGRP antagonists). Fourteen comparative studies indicate that, compared with DPP-4 inhibitors and SGLT2 inhibitors, GLP-1 RAs exhibit the strongest association with headache outcomes. Eight mechanistic studies suggest that GLP-1 signaling may influence migraine via altered neurovascular tone, modulation of inflammatory mediators, and changes in neuronal excitability. In five IIH-related studies, GLP-1 RAs showed potential to lower intracranial pressure and improve cerebrospinal fluid dynamics, although evidence is preliminary.

Conclusion: GLP-1 RAs offer significant metabolic benefits in T2DM but may have mixed neurovascular effects—namely, an increased migraine risk alongside potential benefits in IIH. These findings underscore the need for careful clinical evaluation and further prospective research to clarify the dual role of GLP-1 signaling in neurovascular regulation.

Fig. 1

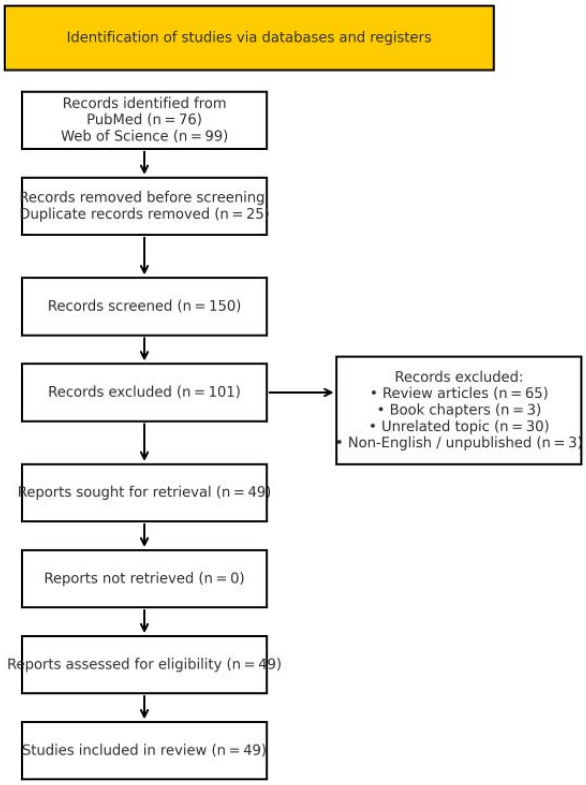
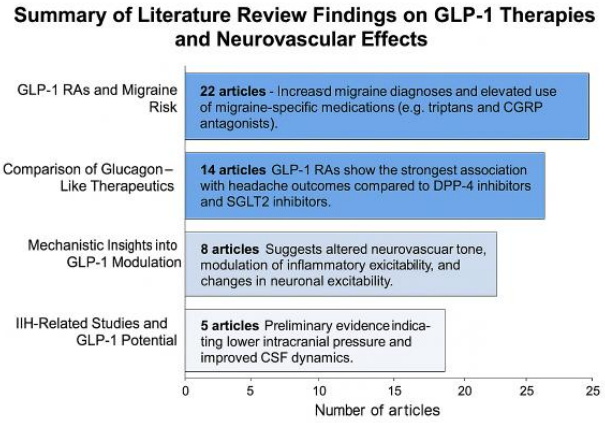


Fig. 2



P377

Assessing the effectiveness of personalized migraine treatment – A 22-year N-of-1 study

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[2]Hospital da Luz, Lisbon, Neurology, Lisbon, Portugal

Objective: Migraine exhibits significant clinical variability, both between individuals and within the same patient over time. This variability reflects genetic, environmental, and pharmacological factors, influencing attack frequency, duration, intensity, phenotype, and therapeutic response. We aimed to analyze this variability in a single patient treated with multiple preventive drugs in monotherapy over 22 years.

Methods: This retrospective analysis examined prospectively collected data from a 65-year-old man with obsessive-compulsive personality disorder and a long history of migraine without aura, evolving into chronic migraine with triptan overuse. Continuous daily headache calendars from 2002–2024 recorded headache days and zolmitriptan use. Each preventive was used alone for ≥6 weeks, allowing isolated comparison of the six months before and after initiation. No relevant external changes (lifestyle, health, or medication) occurred during the observed valproate loss of efficacy. No significant adverse effects were reported

Results: Topiramate (2006) was ineffective (+8.3% headache days); amitriptyline (2008) increased headache days (+20.4%) but reduced zolmitriptan use (−37.7%). Valproate (2013–2020) provided a sustained benefit (−63% headache days, −68% zolmitriptan), but efficacy declined from age 59 despite dose escalation. Erenumab (2020–2021) worsened both metrics (+4.1%, +37.8%). Flunarizine (2023) had modest benefit (−17%), and oxitriptan (2023–2024) had minimal effect. Despite long-term triptan overuse, the patient never developed medication-overuse headache, and zolmitriptan remained effective throughout

Conclusion: We report a case of chronic refractory migraine with long-term triptan overuse but without evidence of medication-overuse headache. This case raises the question of whether pharmacological resistance to preventives may be linked to preserved responsiveness to acute treatments

P379

Improving headache self-management through a digital pathway: Post-market survey results from an Estonian primary care centre

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[3]Tartu University Hospital, Department of Neurology, Tartu, Estonia

Objective: This survey-based evaluation aimed to assess patient and clinician experiences with the Migrevention™ Digital Headache Clinic during a pilot in an Estonian primary care center. The goal was to evaluate its impact on patient self-management, perceived health outcomes, clinical usability, and workflow efficiency.
Methods: In December 2024, a structured survey was conducted among 43 patients and 3 nurses at Pealinna Perearstid, who had used the digital headache care pathway for at least three months. Patient responses were collected via nurse-led telephone interviews with Likert-scale and open-ended questions, assessing symptom burden, awareness, confidence in self-management, app usability, and continued use intent. Nurses provided feedback on care quality, timeliness, and digital tool relevance. All participants gave verbal informed consent in line with ethical standards.
Results: Of the patients surveyed, 61.9% reported reduced headache frequency/intensity, and 72.1% noted improved awareness of triggers, medication use, and prevention. The app received high satisfaction scores: ease of use (4.79/5), technical stability (4.55/5), and relevance (4.86/5); 97.6% would recommend it, and 88.4% wished to continue. Most common improvement request was medication entry (77.8%). Nurses reported faster (4.33/5) and higher-quality (4.67/5) care, and reduced need for in-person visits. Qualitative feedback was exploratory due to the pilot's scale.
Conclusion: The digital care pathway improved patient-reported awareness and self-management, with high satisfaction and strong intention to continue. Clinicians noted improved care efficiency and reduced burden, supporting the feasibility of digital headache management in primary care.

P380

Temporal fluctuations of premonitory symptoms in vestibular migraine

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[1]King's College London, London, United Kingdom

Objective: To investigate the temporal dynamics of symptom fluctuations around acute dizziness exacerbations in vestibular migraine (VM), we conducted a time-locked analysis centered on dizziness spikes.
Methods: We analysed 1-month prospective diary data from the NitroVest mechanistic study at King"s College London. Symptoms were scored by participants on a 1–10 scale. Participants with dizziness reporting on ≥5 distinct days were included. Dizziness spikes were defined as a ≥2-point increase compared to prior day. Per spike, a 7-day window (day −3 to +3) was constructed, and symptom scores were aligned to the spike and averaged across events and participants. Linear mixed-effects models assessed the effect of day-relative-to-spike on symptom scores, with participant ID as a random intercept. Analyses were conducted in R (v4.5.0) & RStudio (24.12.0).
Results: Twenty-two participants . Headache, movement sensitivity, photophobia, and osmophobia significantly increased during the spike. Headache and osmophobia followed a biphasic W-shaped pattern, while movement sensitivity and photophobia remained elevated post-spike. These latter symptoms, along with osmophobia, dropped below average one day before the spike. Phonophobia and nausea showed a biphasic sine-like pattern peaking post-spike, though not significantly. Among non-canonical symptoms, fatigue and tinnitus dropped pre-spike and peaked on day 0. Pallor rose with the spike and persisted for a day, while micturition decreased during and polyuria increased after the spike. Subjective happiness declined in the 3 days pre-spike and remained low post-spike.
Conclusion: Symptom dynamics around dizziness spikes in VM point to central autonomic and sensory dysregulation. Pre-spike sensory improvement may reflect false recovery before decompensation. Changes in pallor, urinary function, and mood suggest hypothalamic or brainstem involvement, likely monoaminergic. These findings support a premonitory phase in VM and may offer a window for early intervention.

P381

Migraine-based subtyping of Ménière's disease: Implications for personalized diagnosis and therapy

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Objective: Can the identification of a migraine-associated subtype refine our understanding and management of Meniere's disease (MD)? we will addresses this question by synthesizing evidence on MD heterogeneity, with a specific focus on subtyping based on migraine comorbidity, to assess its clinical, diagnostic, and therapeutic relevance.
Methods: A systematic analysis of the literature was conducted to evaluate subtyping approaches for MD, including those based on clinical symptoms, comorbidities, immune profiles, genetic markers, and imaging findings. Emphasis was placed on studies utilizing migraine as a key classifier, incorporating clinical criteria, cluster analysis, and cytokine profiling to define the "MD with migraine" subgroup.

Results: Approximately 45% of MD patients experience migraine during vertigo attacks. Migraine-based subtyping identifies a distinct patient subgroup characterized by younger onset age, higher headache frequency, and frequent coexistence with autoimmune disorders. Cluster analyses have consistently delineated a "MD with migraine" subtype (e.g., Type 4), which exhibits elevated proinflammatory cytokines (e.g., IL-1β), earlier bilateral involvement, and unique genetic predispositions. These patients may respond differently to conventional MD therapies but show potential benefit from migraine prophylactic measures, such as lifestyle modifications and nortriptyline

Conclusion: The identification of a migraine-associated subtype in Meniere"s disease holds significant clinical importance, highlighting shared neurovascular and inflammatory pathways between the two disorders. This subtyping approach facilitates more personalized management strategies, improves prognostic accuracy, and guides targeted therapeutic interventions. Future research integrating multimodal biomarkers is essential to validate and refine this classification, ultimately advancing toward precision medicine in MD care

Fig. 1

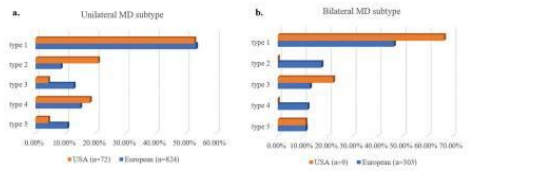


Figure 1. The comparison of MD subtypes distribution between European and USA cohorts. Bar chart comparing percentages of Ménière's disease (MD) subtypes reported by Crossley J et al [96] in US population and Frejo et al [92, 93] in a European population, respectively. a, unilateral Meniere's disease subtypes distribution. Type 1, sporadic MD without migraine and autoimmune disease; type1 delayed MD; type 3, familial MD; type 4, MD with migraine; type 5, MD with autoimmune disease. b, bilateral Meniere's disease subtypes distribution. Type 1, bilateral MD with metachronic hearing loss; type 2, bilateral MD with synchronic hearing loss; type 3, familial MD; type 4, MD with migraine; type 5, MD with autoimmune disease.

Fig. 2

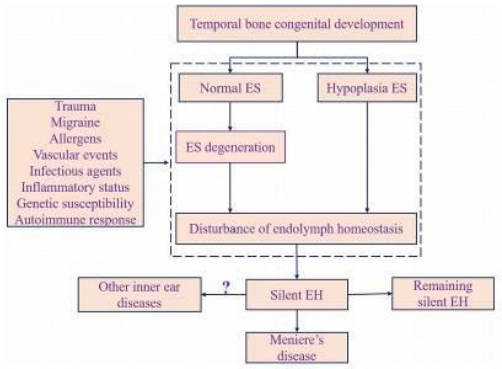


Figure 2. A pattern diagram of Meniere's disease occurrence. ES, endolymphatic sac; EH, endolymphatic hydrops.

P382

Comparative efficacy and safety of prednisolone versus conservative management in treating post-dural puncture headache: A systematic review and meta-analysis

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[1]King Edward Medical University, Lahore, Pakistan
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Objective: This review aims to compare the efficacy and safety of prednisolone versus conservative management in treating post-dural puncture headache (PDPH).

Methods: PubMed, Embase, Scopus, Web of Science, Cochrane Library, and ClinicalTrials.gov were searched from inception to September 4, 2025 for randomised controlled trials (RCTs) comparing prednisolone to conservative management in treating PDPH. Data analyses were performed using RevMan v5.4.1. Dichotomous outcomes were pooled as risk ratios (RR) and continuous outcomes as mean differences (MD), with 95% confidence intervals (CI). Primary outcome was reduction in pain Visual Analogue Scale (VAS) scores post-treatment from baseline. Secondary outcomes were need for epidural blood patch (EBP), adverse event rate and diclofenac consumption.

Results: Three studies were included, comprising 183 patients (64.8% female, mean ages 28.5 ± 4.3 to 47.33 ± 10.44 years). Prednisolone use was associated with significantly greater reductions in VAS scores at Day 1 (MD -0.67, 95% CI -1.02 to -0.32), Day 3 (MD -2.18, 95% CI -3.59 to -0.77) and Day 4 (MD -3.74, 95% CI -4.06 to -3.42) post-treatment. However, non-significant differences were seen at 12 hours and Day 2 post-treatment. Adverse event rates were lower with prednisolone use (RR 0.3, 95% CI 0.18-0.51), and also mean diclofenac consumption (MD -3.48, 95% CI -3.85 to -3.1). However, no significant differences were observed for EBP need.

Conclusion: Prednisolone demonstrated greater short-term pain relief, lower adverse event rates, and reduced analgesic use compared to conservative management for PDPH, though no difference was observed in epidural blood patch requirements. These findings suggest potential benefit, but confirmation in larger, high-quality trials is required for confident integration into clinical practice.

Fig. 1

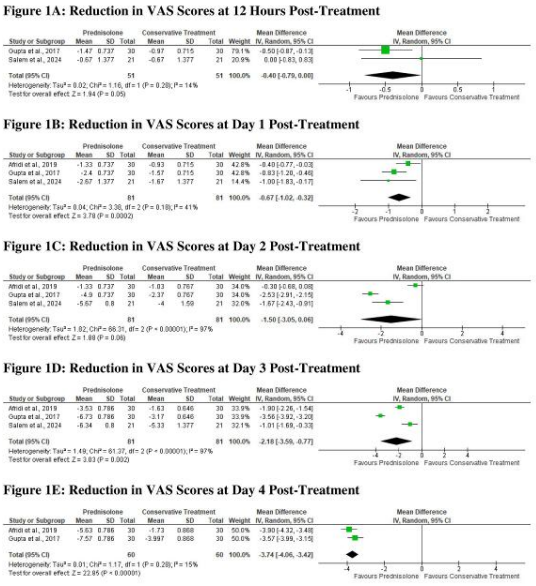
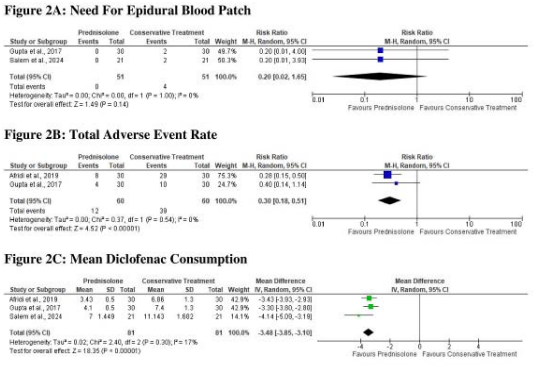


Fig. 2



P384

Efficacy and safety of almotriptan for treatment of menstrual migraine: A systematic review

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Objective: This study aims to evaluate the efficacy and safety of almotriptan for treating menstrual migraine.

Methods: We systematically searched PubMed, Scopus, Embase, Cochrane Library, and ClinicalTrials.gov from inception to August 21, 2025. We included randomised controlled trials (RCTs) evaluating effectiveness of almotriptan in treating menstrual migraine.

Results: Three randomized controlled trials involving 469 women with menstrual migraine were included (mean ages 36.2 to 37 years). In a large trial (n=255), almotriptan 12.5 mg and zolmitriptan 2.5 mg were compared and both demonstrated comparable efficacy. At 2 hours pain relief rates were similar (67.9% versus 68.6%), with no significant differences in recurrence, rescue medication use, or adverse events. Another placebo-controlled crossover trial (n=147) found almotriptan significantly more effective than placebo, with higher rates of 2-hour pain freedom (RR 1.81, 95% CI 1.28-2.57) and sustained pain freedom up to 24 hours (36.1% versus 17.2%). Rescue medication use was reduced (39.3% versus 59.8%), while recurrence rates and adverse events were similar. In a third trial (n=67) comparing almotriptan and frovatriptan, both achieved comparable rates of 2-hour pain relief (41% versus 36%) and pain freedom (29% versus 19%), but recurrence was lower with frovatriptan at 24 and 48 hours. Across studies, almotriptan was well tolerated, with adverse events generally mild and similar to comparator drugs or placebo.

Conclusion: Almotriptan is effective and well tolerated for the acute treatment of menstrual migraine, showing superiority over placebo and comparable efficacy to other triptans. Frovatriptan may reduce recurrence more effectively, but larger, dedicated trials are needed to confirm these findings.

P385

Traumatic experiences and their implications for core clinical features of nociplastic pain conditions

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Objective: Traumatic experiences (TEs) have been implicated in the development of central sensitization (CS) and in altered mind–body regulation. While such mechanisms are established in fibromyalgia (FM), they may also contribute to the course of chronic migraine (CM). The present study explored the impact of TEs on CS and on health outcomes in FM, CM, and their comorbidity (CM+FM).

Methods: The sample included 97 CM, 130 FM, 91 CM+FM participants with diagnoses confirmed by specialists, and 141 healthy controls (HC). TEs were measured with the Traumatic Experiences Checklist, CS with the Central Sensitization Inventory, and health-related quality of life with the SF-36. Group differences were analyzed with ANCOVA and MANCOVA. A moderated mediation model tested whether CS mediated the relationship between TEs and health outcomes and whether effects differed by group.

Results: FM and CM+FM patients reported more severe TEs, particularly emotional neglect and physical

threats, compared with CM and HC. CS severity increased progressively across groups (HC < CM < FM < CM+FM), paralleling reductions in physical and mental health. The predictive effect of TEs on CS was stronger in FM and CM+FM than in CM. Mediation analyses confirmed that CS fully explained the association between TEs and impaired quality of life, especially in FM and CM+FM.

Conclusion: Traumatic experiences contribute to CS and reduced quality of life in chronic pain conditions, with the strongest effects in FM and CM+FM. These findings highlight the relevance of trauma-informed and integrative psychotherapeutic approaches for patients with chronic pain.

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P386

Chronic cluster headache coexisting with primary headache associated with sexual activity: A case report

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Objective: Chronic Cluster headache is defined as attacks occurring for one year or longer without remission, or with remission periods lasting less than 3 months. The attacks are of severe, unilateral pain, lasting 15-180 minutes and occurring from once every other day to eight times a day. The pain is associated with ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, forehead and facial sweating, miosis, ptosis and/or eyelid oedema, and/or with restlessness or agitation. Primary headache associated with sexual activity is headache precipitated by sexual activity,starting as a dull bilateral ache as sexual excitement increases and suddenly becoming intense at orgasm. Both headaches are more prevalent in males than in females. However, their co-existance has rarely been reported.

Methods: To describe a clinical case of two co-existing primary headaches in one and the same patient.

Results: A 38-year-old man, with long-standing (>20 years) *de novo* chronic cluster headache presenting with severe, strictly right-sided occipital, orbital and temporal pain, intensity of VAS=10, with accompanying conjunctival injection, nasal congestion, and restlessness; lasting from 5 min to 3 hours, with a frequency of 2 to 3 attackes per 24 hours, mostly appearing at night. The patient has never had remissions longer than 1.5 months. Five years after the onset of his chronic cluster headache, attacks with the same characteristics, but shorter in duration (around 30 min only) started to appear during sexual intercourse, just before or at orgasm.

Conclusion: There is some limited clinical evidence describing that sexual activity may trigger cluster headaches attacks in some patients. However, in this particular case there is no temporal relation between the onset of both headache types, suggesting two distinct co-existing headache types in the same individual. Further research is needed to look for possible common pathophysiological mechanisms between these two primary headache disorders.

P387

Comparative analysis of efficacy between sumatriptan and naratriptan in the abortive treatment of migraine

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Objective: To compare the efficacy of oral Naratriptan and Sumatriptan in migraine prevention.

Methods: This is a study based on a bibliographic search conducted in the SciELO and PubMed databases, using the descriptors "Migraine," "Prophylaxis," "Sumatriptan," and "Naratriptan." Articles in Portuguese and English, published within the last five years, were selected.

Results: Sumatriptan (SMT) 100mg exhibits a faster response time, achieving 45% pain freedom at 4h, while Naratripta (NRT) 2.5mg achieved 31% within the same time interval. However, at higher doses, NRT 10mg shows quite similar effects to SMT, reaching 65% pain freedom at 4h. Regarding potency, NRT 10mg is more potent than SMT in initial pain relief, with even a longer duration of effect. NRT demonstrates a lower recurrence rate of attacks, especially at higher doses, with less need for rescue medication. As for adverse effects, NRT 2.5mg has a lower rate, while higher doses of 7.5 and 10mg show a higher rate of adverse effects, but still lower than SMT.

Conclusion: Sumatriptan and Naratriptan are both effective in the abortive treatment of oral migraine; however, they possess distinct characteristics. Therefore, factors such as time to pain relief, duration of effect, recurrence rate of attacks, and cardiovascular adverse effects should be considered. Thus, the choice between the two medications should be made based on the patient's profile and clinical needs for attack control, considering both efficacy and safety profile.

P388

When migraine meets maternity: A case highlighting the risks of non-selective β-blockers in pregnancy

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Objective: Migraine often improves during pregnancy, but close monitoring remains important to protect maternal and fetal health. Non-drug approaches and nerve blocks are preferred. If medication is needed, risks should be weighed and discussed. β-blockers are used during pregnancy but may cause intrauterine growth restriction (IUGR), particularly non-selective agents like propranolol. β1-selective blockers carry a lower risk. Propranolol should be discontinued late in pregnancy due to potential neonatal effects. Fetal growth and neonatal health should be closely monitored.

Methods: Clinical case description.

Results: A healthy 30-year-old woman with migraine without aura since age 20, previously on propranolol 40 mg/day for prophylaxis and sertraline 50 mg/day, had propranolol continued during the preconception period - following a risk-benefit discussion - due to frequent migraine attacks. At 21 weeks of an otherwise uncomplicated pregnancy, the fetus was growing along the 50th percentile, and the patient reported a reduction in migraine frequency. In this context, a gradual taper of propranolol to 20 mg/day was initiated. However, at 27 weeks, while still on 20 mg/day, routine ultrasound revealed severe intrauterine growth restriction (IUGR), with fetal growth falling to below the 1st percentile. Propranolol was discontinued immediately. A follow-up scan 15 days later showed recovery to the 10th percentile. Delivery occurred at 33 weeks and 5 days, with the infant weighing at the 15th percentile and reaching the 50th percentile by one month of age, remaining healthy with appropriate growth. Neonatal monitoring included regular growth and heart rate assessments.

Conclusion: Preconception counseling is vital to provide safe treatment for headache disorders during pregnancy. This case highlights the need for individualized treatment planning. In cases using non-selective agents like propranolol, fetal risks - particularly IUGR - must be considered and monitored carefully.

P389

Refractory chronic cluster headache: A new therapeutic option

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Objective: Cluster headache is the most common of the trigeminal autonomic cephalalgias. The prevalence of refractory chronic cluster headache is unknown, and in the face of failure of preventive therapies, alternative options are urgently needed.

Methods: A 54-year-old woman with hypertension began, at age 46, experiencing very intense (10/10) stabbing facial pain that started in the left nostril and radiated retro-ocularly and to the ipsilateral forehead, a few hours after sleep onset, accompanied by ipsilateral ocular autonomic signs and agitation, lasting between 1 and 2 hours. Secondary causes, as well as comorbid migraine, were excluded. Acute therapy with oral zolmitriptan 5 mg, subcutaneous sumatriptan 6 mg, and oxygen were used, with moderate effect. Preventive treatment included prednisolone and occipital nerve block during exacerbations, and verapamil, both as monotherapy and in combination with topiramate and lithium in various regimens. Nevertheless, a profile of therapeutic resistance persisted, with rare pain-free periods. The addition of botulinum toxin, following the PREEMPT protocol, yielded only a partial response. In the presence of up to six episodes per day, invasive neuromodulation was considered when, in January 2025, off-label use of atogepant administered once daily at a dose of 60 mg was proposed.

Results: The patient responded with approximately a 90% reduction in headaches to date (no more than one per week), experiencing anorexia and constipation as adverse effects, symptoms considered tolerable relative to the functional gain and pain relief.

Conclusion: Treating refractory chronic cluster headache is challenging, as it is highly disabling for the patient. Although other therapies targeting CGRP have not shown clear benefit in clinical trials, especially in chronic forms, atogepant may offer a promising alternative.

P390

Efficacy of oral and non-oral migraine prophylactic treatment on self-reported subjective sleep quality in migraine patients with sleep problems: A review and meta-analysis

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Objective: To investigate the effects of oral and non-oral migraine prophylaxis on subjective sleep quality in migraine patients with sleep problems. Possibly, prophylactic treatment of migraine aiming at a reduction of migraine attack frequency can also positively affect the quality of sleep for patients with migraine with sleep problems.

Methods: PubMed, Cochrane, Embase and CINAHL databases were searched in March 2022 for studies evaluating prophylactic treatment of migraine and the impact on perceived sleep quality (Pittsburgh Sleep Quality Index or Insomnia Severity Index). A systematic review using the McMaster Tool and a random-effects meta-analysis (effect size Cohen's d) were conducted.

Results: Seven studies were identified, including 989 participants, of which 844/989 (85.3%) female, with a mean (SD) age of 41.3 (12.1) years. In 6/7 (85.7%) studies, monthly migraine days improved ($p < 0.002$). Five out of six (83.3%) studies presented a relevant improvement in quality of sleep ($p < 0.05$), and one study reported a clinically meaningful improvement in the treatment group (Insomnia Severity Index change >7, in >50% of participants). The meta-analysis showed a large effect size of 1.09 (95% confidence interval 0.57-1.62; overall $p < 0.001$; Cochran's Q < 0.0001) for migraine prophylaxis on improving sleep quality.

Conclusion: In conclusion, prophylactic migraine treatment improves sleep quality in patients with migraine and sleep problems, as measured with self-reported questionnaires Pittsburgh Sleep Quality Index and Insomnia Severity Index. Unfortunately, some included studies used prophylactic treatment that is not in current (international) guidelines. The evidence for this improvement in quality of sleep is strong, and seems a generic effect of migraine prophylaxis.

Fig. 1

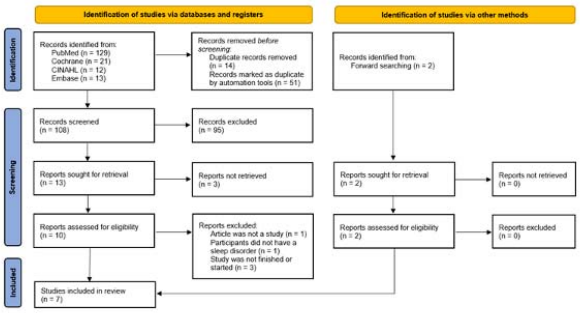
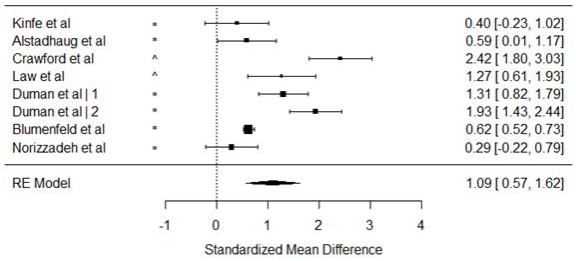


Fig. 2



P391

Migraine worsening after excellent initial response to galcanezumab

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Objective: Migraine is reportedly a major cause of disability in the global population and several medications can be used to treat it (both abortive and preventive). More recently, anti-CGRP antibodies have been used to improve headaches and even though they're associated with a good outcome, not all of the patients show sustained improvement.

Methods: Case report and literature review.

Results: The first patient, 40-year-old female with a medical history of hereditary angioedema and diagnosed with chronic migraine. Several prophylactics were tried (topiramate, amitriptyline, and atogepant) with no improvement. She was medicated with Galcanezumab resulting in a good initial response with improvement of migraine frequency and severity. However, in the last few months of treatment, she experienced recrudescence of symptoms – she's now awaiting treatment with eptinezumab. The second one, 41-year-old male with medical history of Gilbert syndrome and diagnosed with chronic migraine combined with medication-overuse headache. While he tried several preventive medications (topiramate, amitriptyline, venlafaxine and valproic acid), he was also medicated with corticosteroids. Despite the prescribed medications, no pain control was attained so he started treatment with Galcanezumab, which initially significantly improved his migraine's symptoms. In the last months of treatment he also started to experience frequent and severe migraine episodes, returning to his basal state - he's now being treated with botulinum toxin.

Conclusion: Recent literature and medical experience refer to Galcanezumab as a good sustained treatment to refractory migraine. However, these cases highlight

the situations in which, despite the initial response being great, there's no prolonged effect on pain relief.

P392

Correlation between cardiovascular risk factors, subclinical atherosclerosis and hemodynamic changes in patients with episodic migraine

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Objective: Recent studies suggest correlations between patients with cardiovascular-risk-factors(CVRFs) and migraine.The aim of the study is to evaluate the subclinical-atherosclerosis(intima-media-thickness(IMT) and hemodynamic-changers(Left-Ventricular-Ejection-Fraction(LVEF)) in patients with CVRFs and episodic migraine(EM) versus patients with CVRFs without EM.
Methods: We included in the study 90 patients aged 18-65 years with CVRFs, with/without EM, without cardiovascular-disease/stroke. We compared the results of the 43(47.8%) patients with EM versus 47(52.2%) patients without EM. They underwent clinical-examination, blood pressure(BP), heart-rate(HR), body-mass-index(BMI), glycemia/lipid-profile(total/LDL-cholesterol, triglycerides) and in patients with AF we calculate CHA2DS2-VA-score. We measured IMT using a carotid-duplex-scan and LVEF using echocardiography in both groups of patients.
Results: LVEF significant decreased and left/right-IMT, SBP, LDL-cholesterol/triglycerides significand increased in patients with EM and CVRFs compared with patients without EM with CVRFs($p<0.05$). From 43(47.8%) patients with EM there were 15(16.67%) patients with atrial-fibrillation(AF) and 28(31.12%) patients without AF. SBP and total-cholesterol significant increase in patients with EM and AF versus patients with EM without AF($p<0.05$). From 31(34.44%) AF patients included in the study, patients with AF and EM had significant higher rates of left/right-IMT, LDL-cholesterol and triglycerides ($p<0.05$) and higher rates of CHA2DS2-VA-score versus patients with AF without EM.
Conclusion: EM patients with CVRFs may have a greater degree of IMT, SBP, associated lipid-profile changes and lower degree of LVEF compared to CVRFs patients without EM. Evaluation of subclinical-atherosclerosis and identification the presence of hemodynamic-changes in correlation with AF, CHA2DS2-VA-score and lipid-profile changes, are very important in patients with EM and CVRFs.

P393

Efficacy and safety of valproate versus topiramate in migraine prophylaxis: A systematic review and meta-analysis

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Objective: This study aims to compare the efficacy and safety of Valproate and Topiramate, which are two drugs used for migraine prophylaxis.
Methods: We systematically searched the PubMed, Scopus, Embase, Web of Science, Cochrane, and ClinicalTrials.gov databases from inception to June 12, 2025. Relevant controlled vocabulary terms and keywords were used. We included randomised controlled trials (RCTs) comparing valproate to topiramate for migraine prophylaxis in adults. Meta-analysis was performed using Review Manager v5.4.1. Continuous and dichotomous outcomes were presented as mean differences (MD) and risk-ratios (RR) respectively, with 95% continuous intervals (CI). Inter-study heterogeneity was evaluated with I2 statistics. Outcomes evaluated were frequency of migraine, severity of migraine, duration of migraine attack, MIDAS score, responder rate, and adverse events (nausea, paresthesia, memory disturbance, tremors, diarrhea, weight loss, and hair loss).
Results: A total of seven RCTs were included, comprising 1003 participants in total. Topiramate significantly reduced migraine frequency compared to valproate (MD 0.25, 95% CI 0.08 to 0.43). No significant differences were observed in migraine severity, duration, MIDAS score, or responder rate. For adverse events, incidence of hair loss was significantly higher with valproate (RR 4.82, 95% CI 1.91 to 12.14), while weight loss was more frequent with topiramate (RR 0.08, 95% CI 0.01 to 0.60). No significant differences were observed in other adverse events.
Conclusion: Topiramate and valproate demonstrated comparable efficacy in migraine prophylaxis, though topiramate was associated with greater reduction in migraine frequency. Safety profiles differed, with more hair loss reported with valproate and more weight loss with topiramate.

Fig. 1

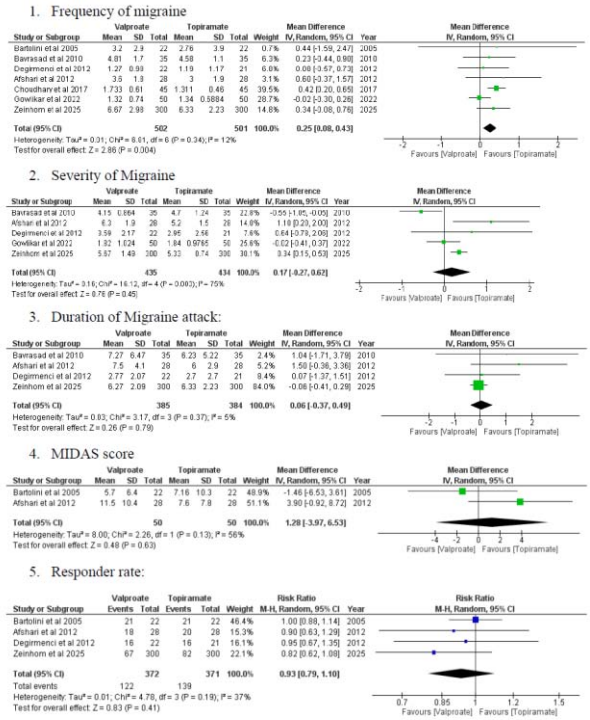
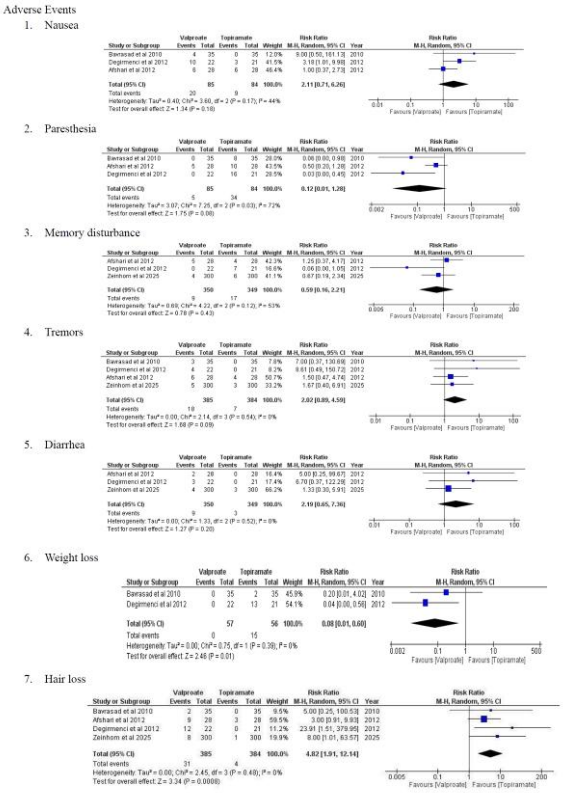


Fig. 2



P394

Examination of perceived barriers to physical activity participation according to functional status in individuals with migraine: A pilot study

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Objective: This study aimed to examine perceived barriers to physical activity according to functional status in individuals with migraine.

Methods: Forty-six migraine patients (median age: 26.78±10.55 years) participated. Functional disability was assessed via the Migraine Disability Assessment Scale (MIDAS). Participants were classified as low-disability (LD, n=22) or high-disability (HD, n=24). Pain intensity, physical activity level, and perceived barriers were evaluated with the Visual Analog Scale (VAS), International Physical Activity Questionnaire (IPAQ-7), and Self-Perceived Barriers for Physical Activity Scale (SPB-PAS), respectively.

Results: The study results showed that the HD group had significantly higher scores in terms of body image/physical-social anxiety (p=0.047) and pain intensity (VAS) (p=0.002), compared to the LD group. No significant differences were found between the groups in the variables of fatigue/laziness (p=0.717), responsibilities/time constraints (p=0.179), environment/facilities (p=0.081) and physical activity levels (p=0.575).

Conclusion: Individuals with HD migraine perceived greater barriers related to body image and physical-social anxiety, and reported higher pain intensity. However, physical activity levels were not significantly influenced by disability status. These findings highlight that factors influencing participation in physical activity are not limited to functional impairments, but also encompass psychosocial elements, pain perception, and individual coping strategies. It is important to consider these multidimensional barriers. Personalizing patient education and self-management strategies accordingly can enhance the effectiveness of interventions supporting behavioral change.

P395

Nationwide expansion of headache care in Russia: Training physicians and establishing 60 clinics via a Tiered educational program

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Objective: To address Russia's limited headache specialty clinics coverage (primarily in Moscow/St. Petersburg) by training physicians nationwide and establishing regional headache clinics.

Methods: Since 2018, the Institute of Interdisciplinary Medicine (Moscow) has hosted a 3-level seminar

series "How to Open a Headache Clinic?" for neurologists/GPs: **Basic level:** Practical training in ICHD-3 diagnostic criteria, EHF consensus (Diagnosis and management of migraine in ten steps), and management of primary headaches: migraines, TTH, cluster headaches, and trigeminal neuralgia using case-based learning (group/pair work). **Participants receive patient interview algorithm, guidelines for establishing a headache clinic and promoting it to both physicians and patients. Second level:** Migraine comorbidities (cardiovascular disease, hormonal influences, contraceptive interactions); therapeutic applications of CGRP monoclonal antibodies and gepants; current IHS and EHF guidelines for: acute migraine treatment and evidence-based preventive therapies; hands-on workshops: Botulinum toxin therapy and biofeedback techniques. **Third level: supervised clinical assessments of real patients for differential diagnosis of secondary headaches and treatment optimization.** All the seminars are accredited in the national system of continuous medical education.

Results: • 280+ physicians trained over 8 years. • 60 multidisciplinary headache clinics established nationwide (from Kaliningrad to Vladivostok) (picture 1) • A dedicated physician chat facilitates knowledge exchange. • Trainees presented at 100+ local/national conferences.

Conclusion: The program successfully decentralized headache care in Russia, significantly improving patient access to specialized treatment. Ongoing peer networking ensures sustained clinical expertise development.

Fig. 1



P396

Insurance status and its impact on treatment compliance in Korean patients receiving anti-calcitonin gene-related peptide monoclonal antibody therapy: A real-world study

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Objective: This study investigated the effect of Korea's strict National Health Insurance Service (NHIS) coverage on treatment compliance and explored factors associated with long-term persistence in a real-world Korean setting.

Methods: This retrospective multicenter study at four hospitals included adult migraine patients (≥18 years) treated with anti-CGRP mAbs. Patients were grouped according to NHIS coverage. Compliance was assessed by persistence (treatment duration), persistence rate (patients remaining on treatment at 6 and 12 months), and adherence (proportion of days covered, PDC). Factors associated with long-term persistence were analyzed.

Results: A total of 140 patients were included: 12 (8.6%) covered and 128 non-covered. Prior CGRP mAb use was noted in 3 (25.0%) and 23 (18.0%), respectively. Monthly headache days were higher in the covered group (median 25.5 [IQR 14.0–28.0]) vs. non-covered (median 15.0 [IQR 10.0–20.0]; p = 0.027). More covered patients had ≥26 headache days/month (50% vs. 18%; p = 0.018). Discontinuation rate was lower in the covered group (50.0% vs. 73.4%; p < 0.001), with more non-covered patients receiving receiving fewer than six injections. At 6 months, persistence rate was higher in the covered group (80.0% vs. 63.8%; p = 0.002); at 12 months, it remained higher (66.7% vs. 47.2%), but not significant (p = 0.912). Near-daily headache (≥26 days/month) independently associated with lower long-term persistence (OR = 0.021; p = 0.004), while prior CGRP mAb use was associated with higher persistence (OR = 4.093; p = 0.035).

Conclusion: The proportion of patients receiving NHIS coverage was very low. While NHIS coverage may improve persistence, headache burden and prior anti-CGRP mAb use also affect long-term persistence. Further nationwide research is needed to evaluate the clinical and economic impact of expanding insurance support to improve compliance and outcomes.

Fig. 1

Table 1. Comparison of Clinical Characteristics by Insurance Coverage Status for Anti-CGRP mAbs Therapy (n=140)

	Covered (n=12)	Non-covered (n=128)	*P* value
Age, mean (SD)	43.6 (±15.7)	44.7 (±11.8)	0.902
Sex, female	10 (83.3)	106 (82.8)	0.662
BMI, mean (SD)	22.7 (±4.2)	22.2 (±3.3)	0.783
Hypertension	4 (33.3)	13 (10.2)	0.060
DM	0	3 (2.3)	0.637
Migraine subtype, n (%)			
without aura	11 (91.7)	120 (93.8)	0.127
with aura	1 (8.3)	8 (6.3)	
chronic migraine	11 (91.7)	80 (62.5)	
PMM	0	7 (5.7)	0.540
MRM	0	12 (9.7)	
Baseline headache characteristics, median (IQR)			
Monthly headache days	25.5 (14.0-28.0)	15.0 (10.0-20.0)	**0.027**
Monthly medication days	13.0 (3.0-25.0)	10.0 (6.0-20.0)	0.856
Monthly headache days ≥ 26, n (%)	6 (50.0)	23 (18.0)	**0.018**
Age of onset, mean (SD)	20.9 (±10.3)	27.1 (±12.7)	0.152
Disease duration before CGRP, mean (SD)	19.2 (±20.0)	15.9 (±11.2)	0.876
Questionnaires			
HIT-6	60.9 (±7.9)	61.4 (±7.8)	0.654
GAD7	5.5 (2.8–9.8)	5.0 (2.0–8.8)	0.436
PHQ9	8.5 (5.0–13.3)	7.0 (4.0–9.0)	0.150
Anti-CGRP mAbs type, n (%)			
galcanezumab	6 (50.0)	53 (41.4)	0.792
fremanezumab	6 (50.0)	75 (58.6)	
Prior anti-CGRP mAbs treatment, n (%)	3 (25.0)	23 (18.0)	0.391

Fig. 2

Table 2. Comparison of Treatment Compliance Based on Insurance coverage

	Covered (n=12)	Non-covered (n=128)	P value
Total number of injection, median (IQR)	7.5 (4.3-11.0)	5.0 (3.0-9.0)	0.140
Interval of injections, days, median (IQR)	32.1 (30.7–33.9)	31.9 (30.0–36.0)	0.867
Anti-CGRP mAbs discontinuation, n (%)	6 (50.0)	94 (73.4)	**< 0.001**
Adherence, % (IQR)	86.7 (57.5-100)	79.9 (43.3-100)	0.595
Days Covered (IQR)	225 (127.5-330.0)	150 (90.0-270.0)	0.140
Adherent, n (%)	8 (66.7)	64 (50.0)	0.212
Persistence			
Duration of treatment, days (IQR)	313.0 (120.3-374.0)	177.0 (91.3-358.7)	0.214
At 6 month			
Follow up, n (%)	10 (83.8)	94 (73.4)	< 0.001
Persistence rate, %	8 (80.0)	60 (63.8)	0.002
At 12 month			
Follow up, n (%)	9 (75.0)	72 (56.3)	0.063
Persistence rate, %	6 (66.7)	34 (47.2)	0.912

Fig. 3

Table 3. Logistic Regression Analysis of Factors Influencing Treatment Persistence at 6 and 12 Months

Variable	B	OR	p-value	95% CI (Lower-upper)
At 6 months				
Age	0.033	1.034	0.644	0.897-1.192
Onset Age	0.047	1.048	0.495	0.915-1.201
Disease duration before treatment	0.001	1.001	0.990	0.875-1.145
Sex (female)	-0.384	0.681	0.527	0.207-2.239
Migraine Subtype(chronic migraine)	0.156	1.168	0.769	0.413-3.302
Previous anti-CGRP treatment	0.372	1.451	0.551	0.427-4.926
Headache Days (Baseline)	-0.002	0.998	0.971	0.896-1.112
Medication Days (Baseline)	0.045	1.046	0.247	0.970-1.127
NHIS covered	1.542	4.672	0.135	0.620-35.192
Monthly headache days ≥26	-2.200	0.111	**0.026**	0.016-0.764
At 12 months				
Age	-0.278	0.757	0.212	0.489-1.172
Onset Age	0.037	1.359	0.165	0.881-2.097
Disease duration before treatment	0.325	1.384	0.140	0.899-2.132
Sex (female)	0.886	2.425	0.304	0.448-13.114
Migraine Subtype(chronic migraine)	0.631	1.879	0.321	0.540-6.532
Previous anti-CGRP treatment	1.409	4.093	**0.035**	1.106-15.144
Headache Days (Baseline)	0.079	1.082	0.195	0.960-1.220
Medication Days (Baseline)	0.037	1.038	0.421	0.948-1.136
NHIS covered	0.466	1.594	0.673	0.183-13.903
Monthly headache days ≥26	-3.859	0.021	**0.004**	0.002-0.290

P397

Bridging the gap from pharmacy to hospital in headache diagnosis and treatment in a lower-middle-income country: The community pharmacist expert in headache pilot project from Thailand

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Objective: In Thailand, the over-the-counter drugs are commonly prescribed to patients with headaches by community pharmacists. Thus, pharmacists played a vital role in screening and referring complicated patients to the hospital. The Community Pharmacist Expert in Headache (CPEH) program, a pilot initiative to empower community pharmacists in Thailand with the skills to assess, manage, and triage patients was employed to evaluate the feasibility and effectiveness in the healthcare system..

Methods: The CPEH project was conducted between June–November 2024 across 87 participating community pharmacies from various regions in Thailand. Pharmacists underwent targeted online headache training. Data collection sheet and referral notes were collected prospectively (Figure 1). Pharmacists initially gave the pharmacotherapy and/or referred to specialists via public hospital networks or telemedicine consultation with a neurologist, the SMILE migraine® application.

Results: A total of 23 patients from 5 community pharmacies (response rate 5.7%) were evaluated (91% female; mean age 41.1 years). The majority (69.6%) reported severe pain (Pain scale ≥7), and 30.4% could not perform work (Table 1). Pharmacists performed 100% adherence to ICHD-3 diagnostic criteria, red-flag (SNOOP4) screening, and MOH. NSAIDs were the most commonly prescribed abortive medication, followed by ergotamines and triptans. The preventive medications pattern by headache frequency was summarized in Table 2. Four patients were referred, with two completing teleconsultation.

Conclusion: CPEH demonstrated that community pharmacists can be effectively upskilled to provide structured and guideline-based headache care. This model has the potential to reduce healthcare burden and improve access to headache services in primary care settings. Further improvement and implementation on a larger scale are needed.

Fig. 1

Figure 1 Thai version (A) and translated English version (B) of case record of migraineur provided to the community pharmacy.

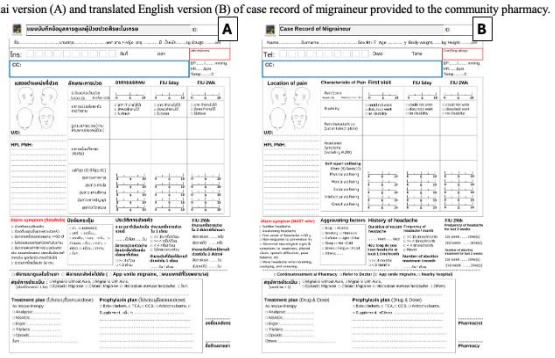


Fig. 2

Table 1 Demographic data, headache characteristics, abortive medication, and preventive medication of enrolled participants

	All (N = 23)
Demographic data	
Age, years (mean)	41.1
Sex – Female (%)	21 (91.3%)
Body mass index, kg/m² (mean)	24.66
Headache characteristics	
Pain score	
Mild (0-3)	1 (4.3%)
Moderate (3-6)	6 (26.1%)
Severe (7-10)	16 (69.6%)
Disability	
Could not work	7 (30.4%)
Disturbed work	14 (60.9%)
No disability	2 (8.7%)
Number of headache days per month	
≥ 15	5 (21.7%)
4-14	3 (13.0%)
< 4	15 (65.2%)
Alarming symptoms (SNOOP4)	1 (4.3%)
Medication overuse headache	1 (4.3%)
Trigger factors	
Drug	0 (0%)
Alcohol	2 (8.7%)
Smoking	2 (8.7%)
Hormone	2 (8.7%)
Caffeine	1 (4.3%)
Light	9 (39.1%)
Odor	4 (17.4%)
Sleep problem	7 (30.4%)
Hot	12 (52.2%)
Cold	4 (17.4%)
Stress	13 (56.5%)
Fatigue	2 (8.7%)
Food	0 (0%)
Others	3 (13.0%)
Medication patterns	
Number of abortive use per month (mean)	5.89
Type of abortive medication	
Paracetamol 500 mg	2 (8.7%)
Naproxen 250 mg	9 (39.1%)
Diclofenac sodium 50 mg	12 (52.2%)
Ibuprofen 400 mg	2 (8.7%)
Sumatriptan 50 mg	6 (26.1%)
Ergot derivatives	12 (52.2%)
Type of preventive medication	
Amitriptyline	3 (13.0%)
Flunarizine	9 (39.1%)
Propranolol	1 (4.3%)
Topiramate	1 (4.3%)
Magnesium	1 (4.3%)

Fig. 3

Table 2 Preventive Medication Use by Headache Frequency

Headache Days/Month	Patients (N)	Received Prophylaxis (%)	Medications Used (frequency)
<4	15	6 (40.0%)	Flunarizine (4) Amitriptyline (2)
4–14	3	3 (100.0%)	Flunarizine (2) Propranolol (1)
≥15	5	4 (80.0%)	Flunarizine (3) Amitriptyline (1) Topiramate (1) Magnesium (1)

P398

Absenteeism in an outpatient headache clinic at a tertiary care hospital

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Objective: Headache is among the neurological disorders most associated with years lived with disability, imposing a substantial burden on healthcare systems. However, Headache Clinics often report high rates of patient absenteeism. This study aimed to characterize the population of patients who fail to attend their first Neurology/Headache consultation, in order to develop strategies to mitigate this issue.

Methods: A retrospective, single-center observational study involving consecutive patients scheduled for a first Neurology/Headache consultation at Hospital Egas Moniz between 2022 and 2023. Demographic data, as well as information regarding source and reason for referral, were collected through the review of medical records.

Results: Of 821 scheduled first Neurology/Headache consultations during this period, 231 (28%) were missed, with some patients missing more than one appointment. A total of 211 patients were included, of whom 77% were female, with a mean age of 40 years. Migraine was the presumptive diagnosis in 68% of patients. Most referrals came from the Emergency Department (44%) with refractoriness to preventive therapy being the main reason for referral. We found that 143 (68%) patients did not meet the criteria for follow-up in this consultation, according to newly established referral criteria. Patients with a diagnosed psychiatric disorder missed significantly more appointments (Mann-Whitney test: Z=3.555; p<0.001). No association was found between absenteeism and referral appropriateness or initial diagnosis.

Conclusion: Absenteeism in Neurology/Headache consultations is a significant issue influenced by both patient-related variables—such as comorbid psychiatric conditions—and external factors, including lack of awareness regarding appropriate referral criteria for this consultation.

P399

Adherence to treatment guidelines for monoclonal antibodies against calcitonin gene-related peptide in migraine prophylaxis – A register-based cohort study

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Objective: This study aimed to estimate adherence to treatment guidelines during the national introduction of CGRP inhibitors (CGRPi) in Stockholm, Sweden.
Methods: In this register-based cohort study, individuals with a migraine diagnosis or migraine drug dispensation in the Stockholm region were followed during the period January 1993 to June 2022. CGRPi treatment guidelines were evaluated across four categories: patient eligibility, prescriber qualifications, treatment evaluation, and monitoring/reporting. Kaplan-Meier estimates were used to assess CGRPi persistence, and treatment switching and discontinuation patterns were illustrated using a Sankey diagram.
Results: Among 89 344 eligible individuals, 2184 (2%) had at least one CGRPi dispensation, while 87 160 (98%) did not. Most individuals with CGRPi (90%) had a prior migraine diagnosis at the first CGRPi dispensation, and 72% had been prescribed at least two previous migraine prophylactic medicines. In most cases (97%), the initial and subsequent CGRPi prescriptions were issued by neurologists or physicians at specialized migraine clinics. Median persistence on CGRPi was 6.1 months (Interquartile Range: 9.3 months), although some individuals continued treatment uninterrupted for over two years, and switching between different CGRPi types was common.
Conclusion: Prescribers in the Stockholm region adhered reasonably well to CGRPi treatment guidelines, with prescriptions generally supported by a medical rationale, suggesting that CGRPi therapies have been appropriately integrated into clinical practice.

Fig. 1

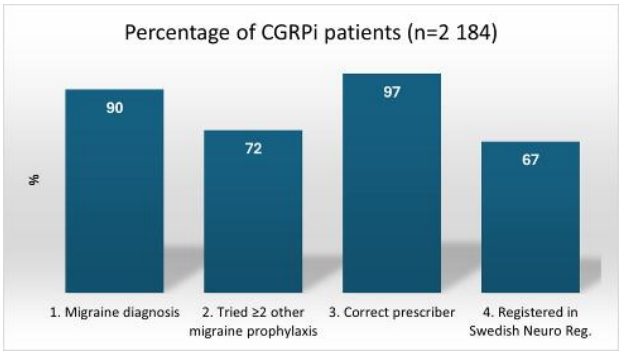


Fig. 2

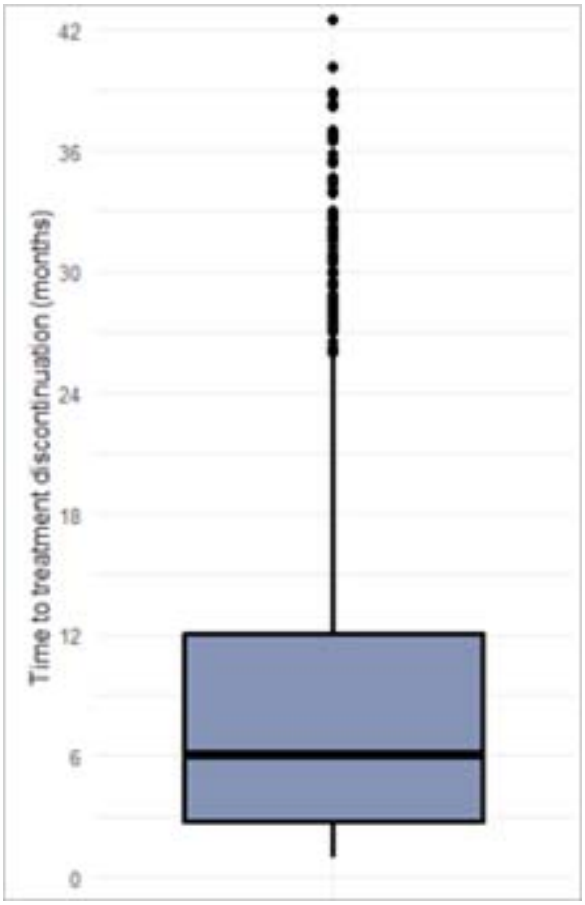
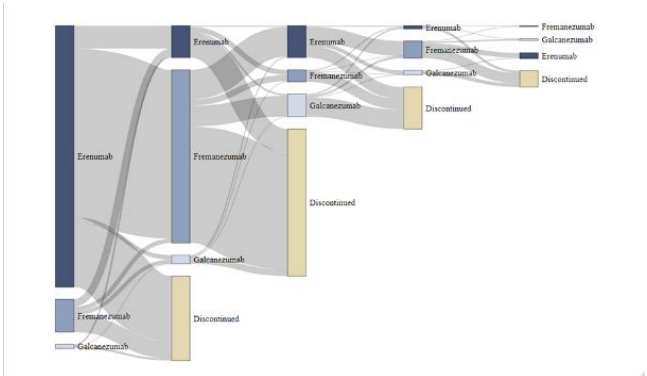


Fig. 3



P400

Characterisation of demographics, migraine severity and quality of life in Malaysia: Highlighting disparities in access to care

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Objective: To characterise demographics, migraine severity, quality of life and to examine associations between sociodemographic factors and migraine severity.

Methods: Observational cross-sectional study at Hospital Sultan Abdul Aziz Shah, from January 2024 to July 2024. The study population consisted of migraine patients attending the Neurology Clinic, who underwent comprehensive clinical assessments and completed two self-administered questionnaires (Migraine Disability Assessment (MIDAS) score and the Migraine-Specific Quality of Life Questionnaire (MSQ).

Results: There were 47 patients who participated, comprising of 34 female (72.3%) and 13 male (27.7%) patients, with a mean age of 36.5 years. Majority of them had normal body mass index (40.4%) and mean blood pressure (Table 1). Most of them suffered from episodic migraine (44.7%), followed by chronic migraine without aura (27.7%) and chronic migraine with aura (14.9%). Most of the patients required at least two prophylactic drugs (70.2%) and 42.6% required at least two reliever drugs (Fig 1). The MIDAS score reflects the disability due migraine with grade four having severe disability. Majority of patients were in grade four (38.3%), followed by grade three (29.8%) and grade two (17.9%). The MSQ score reflects the quality of life, with higher scores showing better quality of life. The patients reported the worst scores in domains indicating restriction in daily activities and emotional disturbances due to migraine (mean score 60.2 and 71.4 respectively). However, there was no significant association between migraine severity and demographic variables, age, headache days, or number of medications taken (Table 2).

Conclusion: There was no association between demographics and migraine severity, but results reflect the suboptimal medication use, with excessive reliance on relievers despite severity of migraine. This highlights the need to address limited access to adequate prophylactic drug and newer migraine therapies.

Fig. 1

Table 1: Sociodemographic characteristics of respondents

Variables	Patients (n=47)
Age, mean (years)	36.5
Gender, n (%)	
Female	34 (72.3%)
Male	13 (27.7%)
Education, n (%)	
Secondary	11 (23.4%)
Tertiary	36 (76.6%)
Type of migraine, n(%)	
Chronic migraine with aura	7(14.9%)
Chronic migraine without aura	13 (27.7%)
Episodic migraine	21 (44.7%)
Others	6(12.8%)
Headache days per month, n (%)	
0-10	32 (68.1%)
11-20	10 (21.3%)
21-30	5(10.6%)
Anthropometric data	
Weight (mean, kg)	68.8
Height (mean, cm)	157.6
BMI (kg/m²), n (%)	
Underweight <18.5	4 (8.5%)
Normal 18.5-24.9	19 (40.4%)
Overweight 25-29.9	14 (29.8%)
Obese >30	10 (21.3%)
Blood pressure (mean, mmHg)	
Systolic blood pressure	119.9
Diastolic blood pressure	77.4
Medication, n (%)	
Reliever (number of drugs)	
None	10 (21.3%)
1-2	20 (42.6%)
3-4	17 (36.2%)
Prophylaxis (number of drugs)	
None	12 (25.5%)
1-2	33 (70.2%)
3-4	2 (4.3%)
MIDAS score, n (%)	
Grade I	8 (17.0%)
Grade II	7 (14.9%)
Grade III	14 (29.8%)
Grade IV	18 (38.3%)
MSQ score (mean)	
Role function restrictive (RFR)	60.2
Role function preventive(RFP)	74.8
Emotional function (EF)	71.4
Total score mean	206.4

Fig. 2

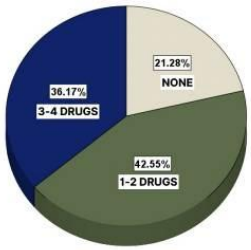


Figure 1(a) Number of reliever medications required for migraine

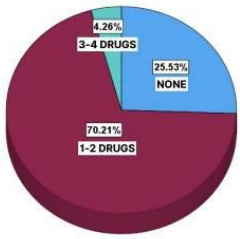


Figure 1(b) Number of prophylactic medications required for migraine

Fig. 3

Table 2. Association between sociodemographic and migraine severity

Variable	Grade I n (%)	Grade II n (%)	Grade III n (%)	Grade IV n (%)	p-value
Age					0.821
<33 years	2 (13.3)	2 (13.3)	6 (40.0)	5 (33.3)	
≥33 years	6 (18.8)	5 (15.6)	8 (25.0)	13 (40.6)	
Gender					0.741
Male	2 (15.4)	3 (23.1)	4 (30.8)	4 (30.8)	
Female	6 (17.6)	4 (11.8)	10 (29.4)	14 (41.2)	
Education					0.573
Secondary	3 (27.3)	1 (9.1)	2 (18.2)	5 (45.5)	
Tertiary	5 (13.9)	6 (16.7)	12 (33.3)	13 (36.1)	
Blood Pressure	3 (16.7)	1 (5.6)	5 (27.8)	9 (50.0)	0.703
Optimal					
Normal	2 (11.8)	4 (23.5)	6 (35.3)	5 (29.4)	
At risk	1 (14.3)	2 (28.6)	2 (28.6)	2 (28.6)	
Stage 1 HPT	2 (40.0)	0 (0.0)	1 (20.0)	2 (40.0)	
BMI					0.380
Underweight	1 (25.0)	0 (0.0)	3 (75.0)	0 (0.0)	
Normal	4 (21.1)	4 (21.1)	3 (15.8)	8 (42.1)	
Overweight	1 (7.1)	1 (7.1)	6 (42.9)	6 (42.9)	
Obese	2 (20.0)	2 (20.0)	2 (20.0)	4 (40.0)	
Relievers					0.467
None	3 (30.0)	2 (20.0)	4 (40.0)	1 (10.0)	
1–2 drugs	2 (10.0)	3 (15.0)	6 (30.0)	9 (45.0)	
3–4 drugs	3 (17.6)	2 (11.8)	4 (23.5)	8 (47.1)	
Prophylaxis					0.432
None	1 (8.3)	3 (25.0)	3 (25.0)	5 (41.7)	
1–2 drugs	7 (21.2)	3 (9.1)	10 (30.3)	13 (39.4)	
3–4 drugs	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)	
Headache Days					
0–10	7 (20.6)	6 (17.6)	10 (29.4)	11 (32.4)	0.655
11–20	1 (10.0)	1 (10.0)	4 (40.0)	4 (40.0)	
21–30	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	

P401

Influence of chronic migraine reimbursement policies on onabotulinumtoxinA treatment retention: A retrospective longitudinal study

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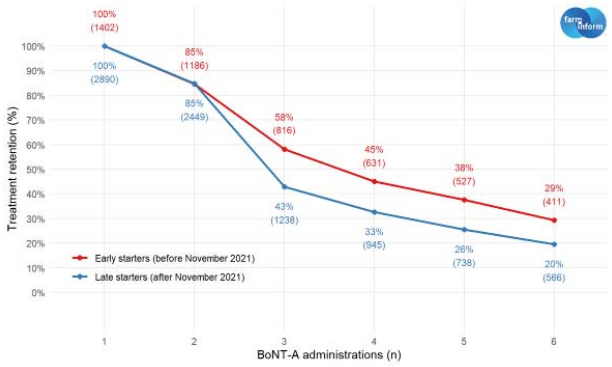
Objective: OnabotulinumtoxinA (BoNT-A) injections can relieve chronic migraine (CM) attacks. In the Netherlands, CM patients are eligible for reimbursement of CGRP(receptor) inhibitors after failing conventional prophylactics, including two administrations of BoNT-A. Some patients experience discomfort, accompanied by unnecessary costs, and long waiting times for CGRP inhibitors. We investigated the retention of BoNT-A treatment in CM, before and after the implementation of the CM reimbursement policy.

Methods: We conducted a longitudinal, retrospective study, including CM patients from all hospitals in the Netherlands. BoNT-A administration expenses for CM are claimed through the Diagnosis Treatment Combinations and the BoNT-A medication costs (Add-Ons). Within the claims data, the use of BoNT-A for CM can accurately be selected and tracked over time for individual patients. Farminform received the hospitals' declaration-data over a period of six years from its partner DHD (LBZ, 2019–2024, DHD, Utrecht, The Netherlands). Patients starting BoNT-A were tracked for 18 months. Starters of BoNT-A treatment were defined based on their history.

Results: 4292 CM patients starting BoNT-A from 56 hospitals were included and divided in starters before (early starters, n=1402) and after (late starters, n=2890) the introduction of the CGRP reimbursement policy. Figure 1 (BoNT-A treatment retention curves: early vs. late starters) shows retention (%) of BoNT-A treatment by number of administrations. Retention from the second to the third administration was 58% in early starters versus 43% in late starters.

Conclusion: The results indicate CGRP reimbursement policies in CM influence treatment retention after the initial two administrations of BoNT-A. This may reflect a shift in the patient profile initiating BoNT-A since CGRP reimbursement in CM. A limitation is the lack of defined reasons for treatment discontinuation, limiting generalizability and omitting context on BoNT-A's impact on CM frequency and severity.

Fig. 1



P402

Cost-effectiveness of adding mindfulness to standard care for chronic migraine with medication overuse

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Objective: Chronic Migraine with Medication Overuse Headache (CM-MOH) leads to significant healthcare and productivity costs. A recent study showed that adding a mindfulness-based program to treatment as usual (TaU+MIND) improved outcomes compared to TaU alone. This study evaluates the cost-effectiveness of this combined approach.

Methods: Patients with CM-MOH completed a cost-assessment protocol covering the three months prior to treatment, including direct healthcare, non-medical, and indirect costs. Repeated measures analysis compared cost reductions between groups, and independent-sample t-tests assessed differences in cost changes post-treatment.

Results: 154 patients completed the 12-month follow-up. In the TaU group, costs dropped from €2620 (95% CI: €2146–3094) to €1603 (95% CI: €1182–2023). In the TaU + MIND group, costs fell from €2978 (95% CI: €2293–3656) to €752 (95% CI: €539–965). The interaction analysis showed a significant group*time effect ($F = 2.953,149$; $p = .035$) with a moderate effect size (partial $\eta^2 = 0.056$). The largest part of cost reduction was due to indirect cost (i.e. related to reduction in productivity) which in the TaU+MIND group fell from €2,487 (95% CI: €1,902-3,071) to €573 (95% CI: €215–930), the same figures being €2,148

(95% CI: € 1,563-2,732) and € 1,419 (95%CI: €1061-1,777) respectively in the TaU group. The average annual cost saving was €2582 in favor of the TaU + MIND group—well above the €57 reimbursement per patient for mindfulness sessions by the Lombardia Region Health System

Conclusion: Adding six weekly group mindfulness sessions to standard care is a cost-effective strategy for managing CM-MOH.

P403

Cost-effectiveness and resource allocation in migraine management: Real-world economic burden in lebanon

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Objective: To quantify the economic burden of migraine in Lebanon and assess implications for cost-effectiveness and resource allocation.

Methods: A cross-sectional study of 337 adults (≥18 years) with migraine receiving treatment ≥6 months was conducted. Data included sociodemographics, insurance coverage, direct out-of-pocket (OOP) costs (hospitalizations, day cases, neurology consultations, diagnostic tests, nursing/home help, transportation), indirect costs (sick leave, income loss, work impairment), and household income. Costs were collected over 3 months, winsorized at the 99th percentile, and annualized.

Results: Mean age was 32.8 years; 78.0% were female, 36.2% uninsured, and 61.7% employed. Over 3 months, 13.7% reported hospital admission, 16.6% a day case, 26.7% a neurology visit, and 27.6% diagnostic testing. Mean OOP cost was $217.8 (median $40; IQR $0–260), equivalent to ~$872 annually, with investigations ($79.1), admissions ($42.5), and consultations ($37.0) as main drivers. Productivity loss was notable: 32.3% reported sick leave (mean 2.8 days/quarter; median 1), and 14.5% reported wage loss, averaging $19.5/month overall, rising to $134 (median $74) among those affected. Work impairment averaged 3.7/10. Combined economic burden was ~$245 per quarter (~$980 annually). Vulnerability was high: 77.8% earned <$1,500/month and 11.6% <$500/month.

Conclusion: Migraine care imposes a substantial burden (~$1,000/patient/year), disproportionately affecting uninsured and low-income groups. Current approaches are unsustainable. Resource allocation should prioritize preventive therapies, streamlined diagnostics, subsidies for essential services, and workplace interventions to reduce productivity loss, supported by economic evaluation frameworks to optimize outcomes under constrained resources.

P404

The "Chronic Headache Project" of the Veneto region: A new opportunity to bring hidden cases to light and optimize patient management through a network-based organizational strategy and continuous training

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Objective: The Veneto Region recognized chronic primary headache as a widespread and disabling condition with a significant socio-economic burden. A regional pilot project called the "Chronic Headache Project" was developed thanks to funds made available following the approval of Italian law 81/2020, with the aim of improving care and management of adult and pediatric patients suffering from chronic primary headache.

Methods: Approximately €922,000 were allocated by the Ministry of Health over a two-year period (2023–2024). The funds were designated for the following initiatives: 1) mapping of third-level Headache Centers and assessment of their quality; 2) developing alternative follow-up and treatment methods through telemedicine; 3) multiprofessional training involving neurologists and other specialist physicians, general practitioners, pediatricians, nurses and pharmacists; 4) standardization of patient management by Headache Centers; 5) development of a multidisciplinary care model involving neuroscience-trained nurses ("case managers"), pain therapists, gynecologists, dietitians/nutritionists, and psychologists; 6) organization of awareness events for

the general public, including schools; 7) creation of a validated digital population screening tool (app); 8) involvement of patients" associations; 9) information campaigns.
Results: Results will be measured using the following indicators: number of individuals participating in the population screening, number of dedicated prescriptions for chronic headache, waiting times, number of telemedicine services provided, number of trained nurse case managers, number of training courses organized and number of their participants.
Conclusion: The "Chronic Headache Project" aims to improve the care and management of adult and pediatric chronic primary headache patients. The project was supported by ministerial funding, based on a specific Italian national law — an initiative that is unique in Europe.

P405

Evaluating a rapid-access headache pathway for trigeminal autonomic cephalalgias: A service-based review

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Objective: Trigeminal autonomic cephalalgias (TACs) are a group of primary headache disorders often requiring urgent specialist input due to their severity and impact. To address this, a dedicated rapid-access headache service was implemented to provide timely assessment, advice, and treatment. This evaluation assesses the effectiveness and outcomes of this service model.
Methods: A retrospective review was conducted of 419 consecutive consultations for 190 patients seen in the rapid-access TAC service between February 19, 2018, and July 29, 2024. Data were extracted from clinic letters and summarized using percentages or medians with interquartile ranges (IQR).
Results: The median patient age was 49 years (IQR: 38–58), with 67% being male. The majority of referrals occurred in March (11.5%) and November (9.8%), with 19% representing new patients. The distance to patients" home ranged from 1 - 423 Km (median 32, IQR: 8 - 103). Most cases were diagnosed with cluster headache (79%), followed by other primary headaches (20%) and secondary headaches (1%). Among TAC patients, the median duration of the headache bout at the time of review was 3 weeks (IQR: 1–8). Interventions included treatment adjustments (51%), greater occipital nerve (GON) injections (13%), a combination of both (24%), or advice only (11%). Clinical benefit was reported in 62% of patients following intervention.
Conclusion: A dedicated rapid-access TAC headache service is a clinically effective model for managing patients with primary headache disorders, particularly cluster headache. This approach facilitates timely, targeted treatment and reduces reliance on emergency care services.

P406

Early efficacy of fremanezumab in children and adolescents with episodic migraine

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Objective: The SPACE study (NCT04458857) evaluated the efficacy and safety of fremanezumab in children and adolescents with episodic migraine (EM). Here we present the efficacy of fremanezumab at different timepoints during the 3-month double-blind period (DBP).
Methods: In this multicenter, Phase 3 trial, participants (aged 6–17 years) with a migraine diagnosis for ≥6 months and history of ≤14 headache days/month were randomized to monthly fremanezumab (120 mg, <45kg; 225 mg, ≥45kg) or placebo for 3 months. Primary endpoint: least-squares (LS) mean change from baseline in average monthly migraine days (MMD) during the 3-month DBP. Other efficacy outcomes: LS mean changes from baseline in average monthly and weekly migraine days (WMD) and monthly headache days of at least moderate severity (MHD) and ≥50% MMD response rates (RRs).
Results: Of 237 randomized participants, 234 (fremanezumab: n=123; placebo: n=111) were

included in the efficacy analysis. Mean changes from baseline in MMD were greater for fremanezumab (–2.5) versus placebo (–1.4) during the 3-month DBP (p=0.0210) and at each month (**Fig. 1**), with a trend favoring fremanezumab observed from Week 1 (**Fig. 2**). Reductions in MHD were numerically greater at each month with fremanezumab versus placebo (**Fig. 3**). The ≥50% MMD RRs were numerically higher for fremanezumab versus placebo at Month 1 (41.5% vs 23.4%), Month 2 (49.6% vs 30.6%) and Month 3 (53.7% vs 37.8%).

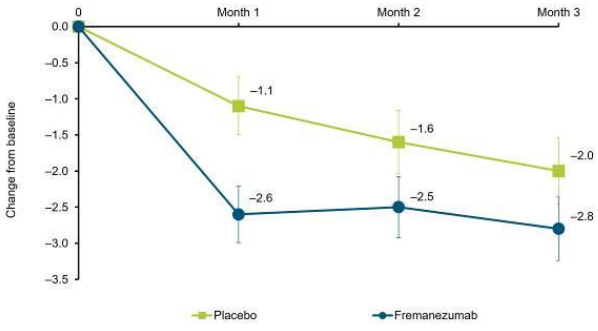
Fig. 1 LS mean change from baseline in average MMD at Months 1, 2, and 3

Fig. 2 LS mean change from baseline in average WMD at Weeks 1, 2, 3, and 4

Fig. 3 LS mean change from baseline in average MHD at Months 1, 2, and 3

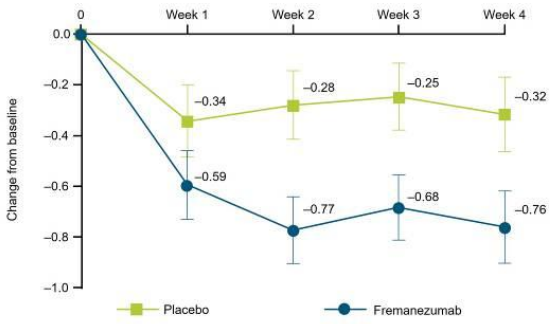
Conclusion: Compared with placebo, fremanezumab led to numerically greater reductions in MMD and MHD within 1 month of initiating treatment in children and adolescents with EM, with reductions in WMD observed by Week 1.

Fig. 1



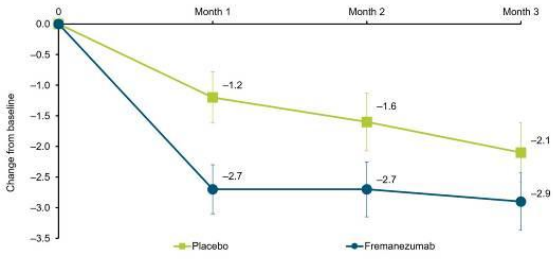
LS means (±SE) are shown from a MMRM.
LS, least squares; MMD, monthly migraine days; MMRM, mixed-effects model for repeated measures; SE, standard error.

Fig. 2



LS means (±SE) are shown from a MMRM.
LS, least squares; MMRM, mixed-effects model for repeated measures; SE, standard error; WMD, weekly migraine days.

Fig. 3



LS means (±SE) are shown from a MMRM.
LS, least squares; MHD, monthly headache days of at least moderate severity; MMRM, mixed-effects model for repeated measures; SE, standard error.

P407

OnabotulinumtoxinA in the management of refractory migraines in adolescents: A prospective clinical study

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Objective: Migraine is a common and disabling neurological condition in adolescents, particularly when it becomes chronic or refractory to standard treatments. OnabotulinumtoxinA (BOTOX®) has proven efficacy in adults with chronic migraine, but data in the paediatric population are limited. This study aimed to evaluate the effectiveness and tolerability of Botulinum toxin in adolescents with treatment-resistant migraine.

Methods: This prospective study included all patients who received BOTOX treatment between 2018 and 2025 at our tertiary paediatric headache clinic. Diagnoses were made according to the ICHD-3. BOTOX was administered following the PREEMPT injection protocol (155 units). Treatment response was evaluated 6–12 weeks post-injection. A "good response" was defined as a sustained reduction in headache frequency and/or severity for more than four weeks, "partial response" as transient improvement lasting less than four weeks, and "no response" as no meaningful clinical improvement. Tolerability and adverse effects were also recorded.

Results: Thirty-seven patients aged 13–17 years (mean 15 years), 84% female, underwent 70 treatment sessions (1–4 per patient, mean 1.9). The majority (97%) were diagnosed with chronic migraine, one patient had high-frequency episodic migraine. All had failed standard preventive treatments, with an average of 5 medications tried per patient. Of 65 evaluable sessions, 35 (54%) resulted in a good response, 7 (11%) in a partial response, and 23 (33%) showed no response. Adverse effects were reported in 16 sessions (23%), most commonly procedural anxiety and pain. No serious complications were observed.

Conclusion: Botulinum toxin appears to be a safe, well-tolerated, and effective treatment for adolescents with refractory migraine. Over half of treatment sessions provided sustained symptomatic relief. These findings support the inclusion of OnabotulinumtoxinA as a therapeutic option within a multidisciplinary approach to paediatric migraine management.

P408

Efficacy and safety of melatonin for migraine in pediatrics and adolescents: A systematic review and meta-analysis of randomized controlled trials

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Objective: Circadian rhythm misalignment due to hypothalamic disruptions is a proposed contributor to migraines. This systematic review and meta-analysis aimed to assess the efficacy and safety of melatonin, a hypothalamic neuropepetide, for migraines in pediatric and adolescent populations.

Methods: This review followed PRISMA guidelines. A systematic search was conducted across Cochrane Library, Embase, PubMed, and Science Direct. Screening was done using Rayyan; analysis through RevMan; and quality assessment via the Cochrane Risk of Bias tool. Mean differences (MD), risk ratios (RR), and odds ratios (OR) with 95% confidence intervals (CI) were calculated using a random effects model. Outcomes were presented using forest plots. PROSPERO ID: CRD420251045377.

Results: Five studies involving 318 patients were included. Risk of bias ranged from low to moderate. Melatonin did not significantly reduce headache frequency (MD = 1.52, 95% CI [-2.72, 5.76]) or intensity (MD = 0.96, 95% CI [-1.62, 3.53]). However, PedMIDAS scores showed significant reduction in disability (MD = 13.20, 95% CI [8.13, 18.27], $p < 0.0001$). Melatonin showed no significant difference from control in total adverse events (RR = 1), serious adverse events (RR = 0.81), or dropouts. Reported adverse events included worsened headache, nausea, elevated heart rate, fatigue, and rash.

Conclusion: Based on the individual trials, melatonin is relatively safe and effective in the management of migraine in pediatric and adolescent populations; however, to establish its clinical safety and efficacy, more robust clinical trials with larger number of subjects are required as the overall efficacy and safety remains inconclusive.

Fig. 1

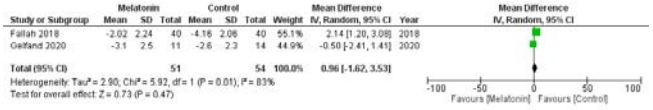


Fig. 2

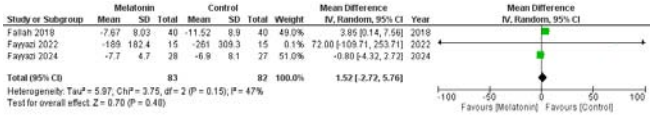
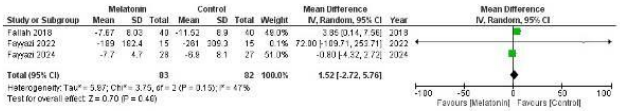


Fig. 3



P409

Suggestions for managing adolescents with unspecified headaches

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Objective: Headaches among adolescent children often lead to school absenteeism. Headaches among adolescent children can be difficult to pinpoint physical causes, which may cause difficulties for parents. This study aims to clarify the characteristics associated with headaches in junior high school students to facilitate support strategies when no clear cause is evident.

Methods: This study is a secondary analysis of a survey administered to junior high school students aged 12 to 13 years. A total of 98 students who completed the online Lifestyle Attitudes, blood pressure measurements, and the Japanese version of the Abbreviated Impulsiveness Scale (JABIS), with all data available, were included in the analysis. The university's ethics committee approved the study and the principal of the affiliated junior high school issued an information notice to parents. As children are often unable to clarify a headache, morning discomfort was considered equivalent to a headache. Students were divided into two groups: those who felt

uncomfortable and those who did not, and were compared.

Results: Thirty-five individuals felt uncomfortable upon arrival at the school. No significant differences were observed in average sleep duration, blood pressure, or Attentional Impulsiveness. Statistically significant differences were identified between the two groups in Nonplanning Impulsiveness (p=0.043) and Motor Impulsiveness (p=0.073). It is important to note that JABIS had a higher average score for Nonplanning Impulsiveness compared to university students at the time of the scale's development.

Conclusion: In Japan, when students experience headaches, they are frequently provided with general lifestyle advice that lacks specific directives. Our research suggests that offering targeted guidance on planning school life could help reduce stress-related headaches among Japanese adolescents, who are obligated to handle large amounts of information and multitask daily basis.

P410

Diagnostic accuracy of the timed up and go test in children and adolescents with migraine

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Objective: Altered balance and gait have been observed in adults with migraine, often reflected in longer Timed Up and Go (TUG) test times. This study aimed to assess whether the TUG test can distinguish children and adolescents with migraine from healthy controls

Methods: A total of 102 participants aged 6 to 16 years were included, comprising 51 children with migraine and 51 age-matched healthy controls. Demographic data were collected from all participants, and clinical data from the migraine group. All participants performed the TUG test three times, with a one-minute interval between trials; the shortest time was used for analysis.

Results: Children with migraine had significantly longer TUG times (mean ± SD 6.76 ± 0.9 s) than controls (5.37 ± 0.5 s; $p < 0.001$). The ROC analysis demonstrated good discriminatory ability (AUC = 0.787; 95% CI: 0.694–0.880), with an optimal cutoff of 5.96 seconds. At this threshold, sensitivity was 82.4% and specificity 76.5% (Table 1).

Table 1: Diagnostic accuracy of the Timed Up and Go test in children and adolescents with migraine and controls (n = 102).

Cutoff	5.965
AUC (95% CI)	0.787(0.694; 0.880)
Sensitivity (%) (95% CI)	82.4(69.1; 91.6)
Specificity (%) (95% CI)	76.5(62.4; 87.2)
LR+ (95% CI)	4.3(2.4; 8.0)
LR - (95% CI)	0.3(0.2; 0.5)
PPV (%) (95% CI)	81.3(70.2; 88.9)
NPV (%) (95% CI)	77.8(67.7;85.4)

95% CI, 95% confidence interval; AUC, area under the curve; LR−, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

Conclusion: The TUG test showed good diagnostic accuracy for identifying children and adolescents with migraine, supporting its use as a practical screening tool for balance-related impairments. Its simplicity and functional nature (encompassing standing, walking, and sitting) enhancing its applicability in pediatric evaluations, potentially aiding in the detection of subtle functional deficits often missed in this population.

P411

Idiopathic intracranial hypertension in children and adolescents: A retrospective study in a third level center

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Objective: This retrospective study analyzes clinical presentation, radiological findings,and outcomes of pediatric idiopathic intracranial hypertension (IIH), a rare disorder marked by elevated intracranial pressure (ICP) without intracranial pathology

Methods: We reviewed 68 pediatric cases (36 females, 32 males) referred between January 2007 and March 2024. Patients were stratified into <8 years (prepubertal) and ≥8 years (pubertal/postpubertal) due to different anthropometric and clinical profiles.

Results: Symptoms varied by age and sex. Headache dominated in pubertal patients (80.9%), especially females (87%), while prepubertal males more often had diplopia (11.4%) and fewer headaches. Diplopia with sixth nerve palsy was the second most common sign (29.4%), followed by nausea/vomiting (23.5%), visual obscurations or loss (19.5%), photophobia/phonophobia (17.6%), vertigo (11.7%), and neck pain (4.4%). Mean CSF opening pressure was 40.5 cmH_2O (SD 13.6), higher in pubertal patients (42.6 vs. 33.4 cmH_2O) and in those with headache plus

diplopia (54.9 cmH_2O, P<0.01). Papilledema was almost universal; 7.4% were asymptomatic, detected via screening.

MRI abnormalities were present in 79.6% of 54 imaged patients: perioptic sheath distension (70%), empty sella (37.2%), tortuous optic nerves (16.3%), and transverse sinus stenosis (4.6%). Visual evoked potentials were often abnormal with cranial nerve involvement, while electroretinograms were normal.

Acetazolamide was the main therapy, lasting on average 5.4 months. Treatment usually continued for about one month beyond fundus normalization.

Conclusion: Pediatric IIH shows distinct patterns: prepubertal males frequently present with diplopia without headache, while pubertal females more often exhibit headache and obesity. Early recognition and treatment are essential to prevent visual damage.

P412

Stigma and healthcare transition for headache disorders: A mixed-methods survey of young adults in three countries

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Objective: Headache disorders are a leading source of care-sensitive disability worldwide. The transition from adolescent to adult healthcare is an important juncture for effective management. This study examined associations between stigma and headache care continuity for emerging adults.

Methods: A convergent mixed-methods design was used in this online observational survey of young adults aged 18–25 from the United States, United Kingdom, and Canada. Of 784 individuals screened, 309 reported recurring headache, and 260 (84.1%) completed measures including the Headache Impact Test, Migraine-Related Stigma questionnaire, and open-ended items on transition care, supplying over 1000 free text comments. Logistic regression examined factors associated with a source of headache care; narrative thematic analysis explored manifestations of stigma in care trajectories.

Results: Respondents (median age 23 [22-24], 67.3% female; 67.7% non-White, 58.1% migraine) had a median of 7 [5-12] monthly headache days, with 73.1% experiencing substantial-to-severe functional impact. Overall, 31.5% lacked a headache provider. Nearly half (45.4%) reported their pain had been doubted or dismissed by healthcare professionals. In multivariable modeling, transition services (aOR 2.17, 95% CI 1.71–2.84), transition skills (aOR 1.38, 95% CI 1.12–1.71), and perceived headache burden minimization by others (aOR 1.12, 95% CI 1.01–1.25) were associated with having a headache provider (pseudo R^2=0.30). Yet early qualitative analysis indicates stigma's harmful role in transition: eroding therapeutic relationships, delaying care-seeking, prompting provider switching, and diminishing confidence in treatment when headache is delegitimized as a neurologic condition.

Conclusion: Many individuals with functionally impactful headache fail to establish adult care. Pervasive stigma undermines care continuity. Findings demonstrate underuse of structured transition frameworks and call for embedded stigma-focused strategies across healthcare systems.

Fig. 1

Study Participants (n=260)	n (%) or median [IQR]
DEMOGRAPHICS	
Age, years	23 [22 - 24]
Gender	
Female	175 (67.3)
Male	64 (24.6)
Non-binary	21 (8.1)
Race/Ethnicity	
White	84 (32.3)
Black	54 (20.8)
Asian	45 (17.3)
Mixed	43 (17.3)
Other	32 (12.3)
CLINICAL CHARACTERISTICS	
Self-reported headache diagnoses	
Migraine	151 (58.1)
Tension-type headache	125 (48.1)
Cluster headache	38 (14.6)
Other	34 (13.1)
Monthly headache days	7 [5 – 12]
Headache Impact Test score	62 [59 – 65]
Reported healthcare stigma	118 (45.4)
Migraine-related stigma score	
Minimizing burden subscale	7 [5 – 10]
Secondary gain subscale	7 [3 – 13]
Source of Headache Care	
None	82 (31.5)
Adult primary care	119 (45.8)
Adult neurology	16 (6.9)
Adult pain medicine	21 (8.1)
Pediatric primary care	9 (3.5)
Pediatric specialty care	3 (1.2)

Fig. 2

Transition Preparation, Stigma and Adult Headache Care Engagement

	Has Headache Provider	Lacks Headache Provider	Δ	Ratio
SERVICES RECEIVED				
Was helped to find an adult provider	42%	7%	34%	5.70
Received clear explanations of diagnosis & treatment	57%	15%	43%	3.92
Was offered preventive strategies	55%	17%	37%	3.19
Was offered rescue strategies	65%	27%	38%	2.41
Was oriented to practice operations	71%	43%	29%	1.67
SKILLS ACHIEVED				
Communicated with care team	63%	28%	35%	2.25
Filled or refilled Rx	73%	44%	29%	1.66
Viewed health information via portal or app	88%	56%	32%	1.56
Scheduled appointment	88%	61%	27%	1.45
Completed pre-visit forms	79%	67%	12%	1.18
STIGMA PERCEIVED				
Others view as easily treatable	47%	37%	10%	1.28
Others lack understanding of pain	53%	34%	19%	1.54
Others lack understanding of burden	28%	15%	13%	1.85
Prompts hiding or concealing pain	18%	14%	4%	1.31

Fig. 3

Stigma-Specific Themes in Young Adult Headache Care Transition

Theme	Representative quotes
Invalidation compromising therapeutic relationships	*The worst part about transition is "finding doctors willing to actually help you and not make you the villain."* *"Try to be assertive as you will often be ignored if you are quiet and indirect."* *"Sometimes there's a sense of hesitation from the healthcare providers and I have to fight a little bit harder to prove them wrong."* *"It's critical to make the initial impression as true to reality as possible. Find a doctor who validates your experience.* *"As you age, there are things that you cannot tell the physician out of shame."*
Stigma leading to delayed care-seeking and provider switching	*"I've never gone to a professional because I'm afraid they won't take it seriously. My sister had similar headaches and they didn't do anything about it and she's still suffering "* *"Don't be afraid to speak up when you feel like your provider's not listening to you and being sympathetic to your needs. It's okay to switch care providers until you find a good match."* *"After my experiences when I was younger, I have an instinctive aversion to healthcare visits, even though I know it is important to have yearly checkups."* *The hardest part has been the uncertainty in finding the right provider who understands my history with headaches."* *"Keep switching until they believe you and don't just blame your pain on work or life."*
Lack of confidence in care due to diagnostic delegitimization	*"My migraines that severely impact my life just get brushed off as stressed-based, or I'm told to sleep more... even though I'm already very proactive in matters I can control."* *"Advocate for yourself. They told me that I may just be being dramatic."* *"They told me it was just anxiety, but I felt they were telling me that because I am a woman."* *"As a child I was regularly told I was making it up for attention, then as an adult I was accused of drug-seeking behaviour even though I was open to any method of solution."* *"I have had a primary care doctor say that my headaches (now diagnosed as chronic migraines) could just be solved by reducing stress."*

P413

Specialist transition headache clinic from an UK perspective: From children to young adults

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Objective: The transition from paediatric to adult care for young people with headache disorders can often be fragmented. The UK National Institute for Health and Care Excellence set out a quality standard identifying this as a high-priority area for quality improvement. We established a dedicated transition headache clinic to support young adults moving from the Headache Team at Great Ormond Street Hospital (GOSH) to the adult service within King"s Health Partners (KHP).

Methods: We developed a joint clinic with GOSH Specialist Headache Nurses and adult headache specialists to facilitate a smooth transition for young adults with complex headache disorders. The process begins as they approach their 17th birthday, a period that coincides with significant academic pressures in the UK. The GOSH team initiates this, and cases are discussed in a multidisciplinary meeting. During the appointment, parents are asked to step out for the history and examination, encouraging the young person to become accustomed to the adult clinic setting and advocate for themselves.

Results: Thirty-eight patients were seen in the KHP Transition headache clinic, 13 continued their adult care in King"s College Hospital, 24 in Guy"s and St Thomas" Hospital. The main diagnosis was migraine (*n*= 37), of which 27% had aura. The most common preventive treatments tried were pizotifen, propranolol and amitriptyline. In this cohort, 92% received unilateral GON (greater occipital nerve) injections. For those who turned 18 years old, four patients started on gepants, seven patients started on CGRP mAbs, and two patients were initiated on botulinum toxin type A by PREEMPT.

Conclusion: A structured transition headache clinic can successfully bridge the gap and provide continuity of care during a pivotal time in the young adult"s lives, both academically and developmentally. As more patients access novel treatments in adulthood, continued follow-up will be crucial to assess long-term outcomes.

P414

Effectiveness and tolerability of anti-CGRP monoclonal antibodies for the prevention of migraine in pediatric patients in real world

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Objective: To analyze the effectiveness and tolerability of anti-CGRP monoclonal antibodies (anti-CGRP mAbs) in pediatric patients with resistant migraine in a real-world setting

Methods: Prospective observational study including patients under 18 years with resistant migraine (≥3

prior preventive treatment failures), treated with anti-CGRP mAbs under compassionate use. Demographic data, efficacy variables (monthly headache days – MHD; monthly migraine days – MMD), and adverse events were collected. Response to anti-CGRP mAbs was defined as a ≥50% reduction in MHD. Effectiveness and tolerability were analyzed at 3 months (M3).

Results: Of the 15 patients included, 10 had reached M3: median age 15 [14, 16] years, 7 females (70.0%), 7 with chronic migraine (70.0%), and 3 with high-frequency episodic migraine. Types of mAbs: erenumab 140 mg (50.0%), fremanezumab 125 mg (30.0%), galcanezumab 120 mg (20.0%). Mean baseline frequency: 19.1 ± 6.9 MHD, 16.0 ± 6.8 MMD. At 3 months, 50.0% were responders, with a mean reduction in MHD of −8.5 ± 6.7 (p=0.03) and in MMD of −9.2 ± 5.6 (p=0.03). No adverse events or treatment discontinuations were reported during the first 3 months.

Conclusion: Anti-CGRP mAbs in adolescents with resistant migraine in real world are well tolerated, with effectiveness similar to that observed in the adult population during the first 3 months of treatment. Our data support the use of anti-CGRP mAbs as a therapeutic option in the pediatric population.

P415

The associations of neck discomfort in children and adolescents with chronic migraine

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Objective: We have previously presented data on the premonitory manifestations of neck discomfort, vertigo and allodynia in migraine, and suggested that these may share neurobiological central sensitisation mechanisms. We aimed to study the associations of neck discomfort in our paediatric chronic migraine patients.

Methods: Chronic migraine patients seen within the Children's Headache Clinic at Great Ormond Street Hospital for Children from January 2022-February 2023 were identified (*n*=76). Extended phenotypic data was collected from the first clinic consultation letter and analysed (IBM SPSS *v* 31). Migraine symptoms were coded as dichotomous variables (present/absent). Descriptive statistics were used to summarise patient demographics (Table1). The co-associations of neck discomfort were analysed using Cohen"s kappa. A binomial logistic regression model with logit link function was used to identify variables of interest that may be associated with neck discomfort: vertigo, age, aura, allodynia, sex and monthly headache days.

Results: Patients were aged 5-17 years (median 14, IQR 12-15), and 75% were female. Aura was reported by 37%. The median number of monthly headache days was 30 (IQR 26-30). Neck discomfort was reported by 32%. The percentage agreement between the reporting of allodynia and neck discomfort was 71%, with fair agreement (kappa 0.26, *P*=0.02), and between vertigo and neck discomfort was 58%, with fair agreement (kappa 0.23, *P*=0.01). The presence of allodynia was significantly associated with neck discomfort (OR 4, 95% CI 1-17, *P*=0.04). There were no other variables of significance (for vertigo; OR 3.3, 95% CI 0.9-12, *P*=0.07), Table 2.

Conclusion: Neck discomfort and allodynia may be mediated via shared thalamic and brainstem sensitisation mechanisms, even in the absence of migraine headache during the premonitory phase. The association between neck discomfort and vertigo has been demonstrated in our adult patients, and warrants future exploration in larger numbers of paediatric patients.

Fig. 1

Age (range, median, IQR)	5-17 years, 14, 12-15
Sex	57 female, 19 male
Disease duration (range, median, IQR)	1-11 years, 4, 2-7
Monthly headache frequency (range, median, IQR)	15-30, 30, 26-30
Aura (%)	28/76 (37%)
Current preventive use (%)	31/76 (41%)
Vertigo	48/76 (63%)
Allodynia	16/76 (21%)
Neck discomfort	24/76 (32%)

Fig. 2

Variable	*B*	SE	Wald	OR	95% CI for OR	*P*
Age	1.2	3.5	0.1	3.3	0-3466	0.7
Sex	-0.8	0.7	1.4	0.4	0.9-1.0	0.3
Vertigo	1.2	0.7	3.2	3.3	0.9-12.0	0.07
Allodynia	1.5	0.7	4.4	4.3	1.1-17.0	0.04
Aura	-0.9	0.6	2.0	0.4	0.1-1.4	0.2
Monthly headache frequency	-3.0	2.7	1.2	0.05	0-10.4	0.3

P416

A structured pediatric headache registry: Enhancing documentation, patient outcomes, and research capacity in Canada

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Objective: Despite the high prevalence and disease burden of pediatric headaches, diagnosis and management practices remain variable, in part due to inconsistent clinical documentation and inadequate longitudinal data. This study will establish a registry

that generates real-time standardized clinic notes for pediatric patients (<18 years) with primary headache disorders. We will evaluate how structured documentation potentially shortens visit duration, improves note completeness, and enhances clinician and patient satisfaction.

Methods: This prospective observational study will begin recruitment in June 2026, with an anticipated sample size of 350-450 patients from the Comprehensive Pediatric Headache Centre in London, Ontario. Data collection includes headache and medical history, neurological examination findings, comorbidity screening, laboratory investigations, and brain imaging results per standard of care, as well as patient-reported headache diaries and response to treatment. Registry-generated notes will have distinct formats for initial consults versus follow-up appointments.

Results: All analyses will be conducted in SPSS v.30, with statistical significance set at $p < 0.05$. The primary outcome will be the reduction in patient visit duration before and after implementation of structured note generation. Regression models will be used to compare time metrics while adjusting for clinician, patient age, diagnosis complexity, and visit type (new consult versus follow-up). Secondary outcomes including note completeness and registry utilization will be modeled with logistic regression. Clinician usability will be assessed using the SUS, with subgroup analyses stratified by role and experience. Patient and caregiver satisfaction will be evaluated through surveys and summarized descriptively.

Conclusion: Through standardized notes and longitudinal data collection, this registry aims to improve the workflow and quality of routine care and establish a foundation for future pediatric headache research.

P417

Childhood migraine chronification: Is there a role for prophylactic treatment?

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Objective: Chronic migraine (CM) is a very debilitating condition and the transformation to CM typically occurs over months. We investigated the effect of prophylactic therapy on childhood migraine chronification and predictive factors of chronification.

Methods: We included 165 pediatric patients with migraine evaluated at Bambino Gesù Children"s Hospital from May 2021 to May 2023. All had headache frequency > 4 per month (i.e. "high frequency"), anxiety (GAD-7) and depression (PHQ-9) screening, no ongoing preventive treatment at baseline visit (T0). Demographic and clinical data were recorded at T0. Headache frequency, the use of attack and prophylactic treatment were recorded at follow-up T1 (approximately 4 months) and T2 (approximately 12 months). The sample was divided in two groups based on exposure or not to prophylaxis in order to compare the chronification frequency. Subsequently, we divided our cohort in two groups based on progression or not to CM to identify features associated to chronification using multivariate logistic regression analysis.

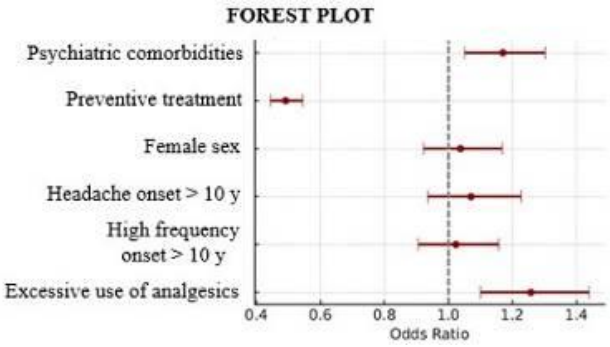
Results: Chronification frequency was significantly lower in the treated group: 14% vs 88.9% (Odds-Ratio 0.023, 95% CI 0.0079-0.052, p<0.001), suggesting a protective role of prophylaxis against migraine chronification. We divided our cohort in two groups based on progression or not to CM to identify features associated to chronification. At multivariate logistic regression analysis, we found that the independent variables significantly associated to progression to CM were excessive use of analgesics ($p = 0.001$) and psychiatric comorbidities ($p = 0.005$), while it was confirmed the protective role of preventive treatment ($p < 0.0001$).

Conclusion: Clinicians should consider pharmacological treatment in children with increasing headache frequency to prevent CM. It may be beneficial to routinely screen children and adolescents with migraine for anxiety and depression and to educate the patient and parents on the correct use of analgesics.

Fig. 1

Multivariate logistic regression analysis		
	Dependent variable: chronification	
Independent variable	OR [95%CI]	*p*
Psychiatric comorbidities	1.17 [1.05–1.30]	**0.005**
Preventive treatment	0.49 [0.44–0.54]	**< 0.001**
Female sex	1.04 [0.92–1.17]	0.5361
Headache onset > 10 y	1.07 [0.94–1.23]	0.313
High frequency onset > 10 y	1.02 [0.90–1.16]	0.714
Excessive use of analgesics	1.26 [1.10–1.44]	**0.001**

Fig. 2



P418

Stress-related behavior and headache among women in Slovenia

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Objective: Headache is a common and debilitating condition that places a significant burden on the healthcare system. It can negatively affect psychological and social well-being. In Slovenia, psychosocial factors associated with headaches, particularly among women, remain insufficiently explored. Identifying high-risk population groups is essential for developing targeted prevention strategies.

Methods: This study is based on data from a national survey conducted as part of the CINDI program. A self-administered postal questionnaire was used. Multiple logistic regression analysis was performed to assess the impact of gender, age, education level, employment status, self-assessed social class, residential environment, perceived stress, coffee consumption, and sleep patterns on headache prevalence.

Results: The results showed significantly higher odds of headaches among individuals experiencing high stress levels (OR yes vs. no = 1.99; P < 0.001), those with insufficient sleep (OR <6 vs. 8 hours/day = 1.23; P < 0.001), and coffee drinkers (OR >1 cup vs. no cups/day = 1.58; P < 0.001). Furthermore, the highest odds were observed among women (OR women vs. men = 1.99; P < 0.001), individuals aged 25–29 years (OR 25–29 vs. 70–74 = 6.10; P < 0.001), and those with the lowest educational attainment (OR primary vs. postgraduate = 1.34; P = 0.082).

Conclusion: In Slovenia, women in intellectual or leadership positions, particularly those aged 25–29 years, represent the highest-risk group for frequent headache disorders, which are strongly associated with stress-related behaviors. These findings highlight the need for targeted stress management related to gender and workplace well-being interventions.

P419

Migraine in men – Differences in phenotype and treatment patterns: Results from the migraine in Poland cross-sectional national survey

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Objective: The "Migraine in Poland" study is a large-scale nationwide cross-sectional online survey that assessed symptomatology, consulting, diagnosis, treatment, and burden of migraine in Poland. The purpose of this analysis is to define migraine phenotype and patterns of care for Polish men.

Methods: The questionnaire evaluated healthcare system utilization, headache features, history of diagnosis, comorbidities, burden, as well as the use of acute or preventive treatment. The survey included questions that allowed for diagnosis according to the ICHD-3.

Results: 3225 individuals aged 13 to 80 (mean age 38.9) responded to the survey (87.1% were women). Migraine without aura diagnosis was confirmed in 1679 (52.7%) of patients, and this group was included in further analysis. The current study group consisted of 244 men (14.6%) and 1431 women (85.4%). Men tended to experience fewer types of headaches compared to women (p<0.001) and were significantly less likely to report visual and sensory symptoms accompanying the worst headache than women (p<0.001). Warning symptoms preceding the onset of headache were more likely, and the time required to return to normal functioning was longer in men than in women (median 24 and 10 hours, respectively; p<0.001). The use of acute treatment was significantly higher in men, regarding both physician-prescribed medications (80.3% vs 69.3%; p<0.001) and OTC medications (p<0.001), as well as natural-based or alternative remedies (p<0.001). Men were more likely to use combination drugs (66% vs 57,9%; p=0.017) and often fulfilled the criteria for medication overuse (29,5% vs 22%;p=0.01). Prophylactic treatment was less frequently used in men (21.7% vs. 38%; p<0.001). Men reported spending more money on medications monthly than women (p<0.001).

Conclusion: Our study confirms the existence of significant gender differences in the course of migraine, both in terms of clinical characteristics of the disease and patterns related to health behaviors and access to medical care.

P420

Men in the headache clinic: Characterization and sex comparison

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Objective: Headaches are more prevalent in women, leading to underrepresentation of men in related studies. This study aimed to characterize male headache patients and explore sex differences.
Methods: This retrospective observational study was conducted at headache consultations of both a public and a private hospital. Clinical data from medical records were entered into a uniform, sex-stratified database, including sociodemographics, ICHD-3 diagnosis, neuroimaging, family history and treatment.
Results: Out of 700 patients, 112 were men (16.0%), comprising 12.2% of the public and 26.3% of the private hospital samples (p<0.001). Men reported later symptom onset compared to women (36.0 vs 26.4 years old, p<0.001) and were older at the 1st appointment (48.2 vs 42.6 years, p<0.001), regardless of hospital setting (p=n.s). Men were less likely to have a fully established diagnosis (10.7% vs 8.3%, p<0.001), and, when Medication Overuse Headache was excluded, they had more trigeminal autonomic cephalalgias (20.4% vs 1.3%, p<0.001), secondary headaches (11.5% vs 8.0%, p=0.006), such as headaches related to vascular (4.4% vs 1.1%, p<0.001) and homeostasis disorders (1.8% vs 0.3%, p<0.001), and neuralgias/facial pain (9.0% vs 2.9%, p=0.003). Men used fewer preventive drugs, more often taking none (36.6% vs 21.4%, p=0.001), and were less likely to use 2 or more preventives (17.9% vs 27.9%, p=0.001). They also showed lower analgesic overuse (10.5% vs 28.1%, p<0.001). Migraine was the most common diagnosis (42.0% of men vs 73.3% of women), with chronic migraine being less frequent in men (16.7% vs 37.6%, p=0.004).
Conclusion: These results highlight sex differences among headache clinic patients, particularly regarding type of diagnoses, likelihood of having secondary headaches and prescribed treatment. These differences should be considered by clinicians in the approach of these patients and reinforce the need for future studies considering sex.

P421

Sex-related disparities in migraine diagnosis and treatment: Insights from a tertiary headache center

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Objective: Migraine is a prevalent and disabling neurological disorder that is often underdiagnosed and undertreated, especially in early care. Sex-related factors may contribute to this gap. This study examines sex differences in migraine diagnosis and management before and after presentation at a tertiary headache center and explores whether disparities are linked to clinical presentation.
Methods: In this retrospective, cross-sectional study conducted at the tertiary headache center of Charité - Universitätsmedizin Berlin, we included patients diagnosed with migraine between December 2015 and January 2023. We examined sex-related differences in prior diagnoses, clinical presentation, and treatment strategies, both before and after tertiary center evaluation.
Results: Among 1,168 migraine patients, men were significantly less likely than women to have received an accurate migraine diagnosis prior to presentation at the tertiary center (54.3% vs. 71.6%, p < 0.01, OR 0.54, 95% CI 0.36 - 0.81). The diagnosis at our headache center was made in 99.6% of cases according to the ICHD-3 criteria. In men, the clinical presentation of migraine attacks did not differ between those correctly diagnosed and those missed at prior care. In contrast, women with prior accurate diagnoses reported significantly more migraine-associated symptoms and subjective trigger factors than women with missed diagnoses or men (p < 0.01). No sex differences were found in drug treatment for acute and preventive care, neither prior to nor after presentation at our center.
Conclusion: Men with migraine are substantially less likely than women to receive a correct diagnosis in routine care. Higher diagnostic accuracy in women appears to be driven by more recognizable symptom patterns, whereas underdiagnosis in men may stem from limited awareness of less canonical clinical presentations. Enhancing early detection calls for sex-sensitive clinical training and increased recognition of the diverse manifestations of migraine.

P422

Detailed migraine symptoms: Patterns and sex-related differences in patients at a tertiary headache center

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Objective: Existing literature describes a higher migraine burden in females. However, there are limited data on sex differences in detailed symptomatology. We sought to characterize differences in headache features and associated symptoms between males and females.
Methods: We queried prospectively collected data from the Mayo Clinic Headache Database (2000-2023) derived from intake questionnaires completed before or during a headache clinic visit.

Results: Among 17,824 patients, there were 13,078 females (73.4%) and 4,746 males (26.6%). 84.8% of patients reported at least 1 trigger (87.7% females, 77.1% males). Most common triggers were psychological stress (62.2% F, 46.4% M), lack of sleep (49.3% F, 34.8% M), and weather changes (43.7% F, 24.7% M). Physical exertion was identified with similar frequency (12.4% F vs 12.6% M). 16.0% of patients (17.9% F, 11.0% M), endorsed a prodrome before headache onset, commonly fatigue (10.9%), excessive yawning (2.1%), and food craving (1.5%). Migraine onset was unilateral in 34.1% of patients, bilateral in 19.5%, and alternating between either in 46.4%. Bilateral onset was more frequent in males (26.2%) vs females (17.0%). Pressure characteristic was endorsed more by males (73.8%) vs females (72.9%). Photophobia was the most common migraine-associated symptom (80.6% of patients; 84.3% F vs 69.6% M), followed by nausea (73.9%), phonophobia (72.6%), and osmophobia (41.9%). 57.1% patients reported cranial autonomic symptoms (CASs). Nasal congestion, rhinorrhea, and conjunctival injection were more prevalent in males compared to females (18.4% vs 17.5%, 12.9% vs 12.1%, and 12.3% vs 8.0%).

Conclusion: Female patients more commonly report triggers, prodrome, and associated symptoms, while male patients more commonly report cranial autonomic symptoms, bilateral headache, and a pressure quality. Heightened sympathetic responses to stress and a male-specific mechanism of trigeminal ganglion sensitization may help explain the high frequency of CASs in males.

Fig. 1

Characteristics	Total (N=17824)	Female (N=13078)	Male (N=4746)	Trends	P-value
Demographics: Mean (SD)					
Age at presentation	44.3 (15.4)	43.2 (14.9)	47.6 (16.1)	M > F	<0.001
Age of headache onset	23.4 (15.0)	21.6 (14.3)	28.3 (18.9)	M > F	<0.001
Height (m)	1.69 (0.10)	1.65 (0.07)	1.79 (0.07)	M > F	<0.001
Weight (kg)	81.2 (21.9)	77.1 (21.2)	92.1 (20.3)	M > F	<0.001
BMI (kg/m^2)	28.4 (7.1)	28.3 (7.6)	28.5 (5.0)	M > F	<0.001
Triggers	14934/17601	11336/12934	3598/4667	F > M	<0.001
Number of respondents: 17601	(84.8%)	(87.7%)	(77.1%)		
Psychological Stress	10199 (57.9%)	8034 (62.2%)	2165 (46.4%)	F > M	<0.001
Lack of Sleep	8007 (45.5%)	6382 (49.3%)	1625 (34.8%)	F > M	<0.001
Weather Changes	6803 (38.7%)	5652 (43.7%)	1151 (24.7%)	F > M	<0.001
Strong Smells	4962 (28.2%)	4285 (33.1%)	677 (14.5%)	F > M	<0.001
Missed Meals	4903 (27.9%)	4017 (31.1%)	886 (19.0%)	F > M	<0.001
Flickering Lights	4347 (24.7%)	3539 (27.4%)	808 (17.3%)	F > M	<0.001
Alcohol	3351 (19.0%)	2593 (20.1%)	758 (16.2%)	F > M	<0.001
Fatigue	2934 (16.7%)	2328 (18.0%)	606 (13.0%)	F > M	<0.001
Certain Foods	2841 (16.1%)	2285 (17.7%)	556 (11.9%)	F > M	<0.001
Too Much Sleep	2197 (12.5%)	1747 (13.5%)	450 (9.6%)	F > M	<0.001
Physical Exertion	2190 (12.4%)	1804 (12.4%)	586 (12.6%)	M = F	0.782
Loud Sounds	2165 (12.3%)	1727 (13.4%)	438 (9.4%)	F > M	<0.001
Coughing	889 (5.1%)	659 (5.1%)	230 (4.9%)	M = F	0.655
Medications	625 (3.6%)	483 (3.8%)	142 (3.0%)	F > M	0.001
Chewing	519 (2.9%)	418 (3.2%)	101 (2.1%)	F > M	<0.001
Orgasm	388 (2.2%)	277 (2.1%)	111 (2.4%)	M = F	0.345
Menstruation	-	3697 (28.6%)	-	-	-
Other	2700 (15.3%)	1951 (15.1%)	749 (16.1%)	M = F	0.117
Prodromal Symptoms	2250/14085	1814/10117	436/3968	F > M	< 0.001
Number of respondents: 14085	(16.0%)	(17.9%)	(11.0%)		
Fatigue	1538 (10.9%)	1264 (12.5%)	274 (6.9%)	F > M	< 0.001
Excessive Yawning	295 (2.1%)	255 (2.5%)	40 (1.0%)	F > M	< 0.001
Euphoria	221 (1.6%)	168 (1.7%)	53 (1.3%)	M = F	0.163
Food Craving	214 (1.5%)	187 (1.9%)	27 (0.7%)	F > M	< 0.001
Reduced Libido	94 (0.7%)	71 (0.7%)	23 (0.6%)	M = F	0.423
Neck Pain	38 (0.3%)	33 (0.3%)	5 (0.1%)	F > M	0.039
Aura	8140 (45.7%)	6345 (48.5%)	1795 (37.8%)	F > M	< 0.001
Number of respondents: 17824					
Visual	6781 (38.0%)	5334 (40.8%)	1447 (30.5%)	F > M	<0.001
Sensory	3468 (19.5%)	2727 (20.9%)	741 (15.6%)	F > M	<0.001
Motor	1529 (8.6%)	1206 (9.2%)	323 (6.8%)	F > M	<0.001
Headache Laterality at Onset					
Number of respondents: 17808, F: 13064, M: 4744					
On one side	6075 (34.1%)	4547 (34.8%)	1528 (32.2%)	F > M	0.0014
On both sides	3465 (19.5%)	2224 (17.0%)	1241 (26.2%)	M > F	< 0.001
Sometimes one side, sometimes on both sides	8268 (46.4%)	6293 (48.2%)	1975 (41.6%)	F > M	< 0.001

Fig. 2

Headache Location at Onset					
Number of respondents: 17807, F: 13064, M: 4743					
Front of the head	6292 (35.3%)	4575 (35.0%)	1717 (36.2%)	M = F	0.145
Side of the head	4437 (24.8%)	3386 (25.9%)	1051 (22.2%)	F > M	< 0.001
Back of the head	3937 (22.1%)	2888 (22.1%)	1049 (22.1%)	M = F	0.999
Throughout entire head	2127 (11.9%)	1505 (11.5%)	622 (13.1%)	M > F	0.003
Top of the head	1014 (5.7%)	710 (5.4%)	304 (6.4%)	M > F	0.013
Average Intensity: Mean (SD) Over past 4 weeks, Scale 1-10 Number of respondents: 17794	6.7 (2.21)	6.8 (2.1)	6.3 (2.3)	F > M	< 0.001
Headache description					
Number of respondents: 17531, F: 12894, M: 4637					
Pressure	12823 (73.1%)	9399 (72.9%)	3424 (73.8%)	M > F	0.021
Throbbing	10562 (60.3%)	8134 (63.1%)	2428 (52.4%)	F > M	< 0.001
Jabbing	9394 (53.6%)	7123 (55.2%)	2271 (48.9%)	F > M	< 0.001
Migraine-associated symptoms					
Number of respondents: 16714, F: 12464, M: 4250					
Photophobia	13469 (80.6%)	10511 (84.3%)	2958 (69.6%)	F > M	< 0.001
Nausea	12351 (73.9%)	9941 (79.8%)	2410 (56.7%)	F > M	< 0.001
Phonophobia	12129 (72.6%)	9618 (77.2%)	2511 (59.1%)	F > M	< 0.001
Osmophobia	7010 (41.9%)	6078 (48.8%)	932 (21.9%)	F > M	< 0.001
Vomiting	5959 (35.7%)	4936 (39.6%)	1023 (24.1%)	F > M	< 0.001
Cranial autonomic symptoms	10038/17565	7434/12903	2604/4662	F > M	0.004
Number of respondents: 17565	(57.1%)	(57.6%)	(55.9%)		
Lacrimation	3205 (18.3%)	2350 (18.2%)	855 (18.3%)	M = F	0.847
Nasal Congestion	3119 (17.8%)	2260 (17.5%)	859 (18.4%)	M > F	0.039
Rhinorrhea	2166 (12.3%)	1565 (12.1%)	601 (12.9%)	M > F	0.041
Ptosis	2086 (11.9%)	1543 (12.0%)	543 (11.7%)	M = F	0.574
Conjunctival Injection	1609 (9.2%)	1037 (8.0%)	572 (12.3%)	M > F	< 0.001
Facial Flushing	1288 (7.3%)	1031 (8.0%)	257 (5.5%)	F > M	< 0.001
Facial Sweating	679 (3.9%)	516 (4.0%)	163 (3.5%)	M = F	0.127
Eyelid edema	397 (2.3%)	321 (2.5%)	76 (1.6%)	F > M	< 0.001
Miosis	273 (1.6%)	210 (1.6%)	63 (1.4%)	M = F	0.191
Headache Exacerbation Factors					
Number of respondents: 17615, F: 12941, M: 4674					
Exertion	11610 (65.9%)	9076 (70.1%)	2534 (54.2%)	F > M	< 0.001
Strain (Valsalva, coughing, sneezing)	9983 (56.7%)	7811 (60.4%)	2172 (46.5%)	F > M	< 0.001
Mental Activity	4862 (27.6%)	3763 (29.1%)	1099 (23.5%)	F > M	< 0.001
Cold exposure	3063 (17.4%)	2513 (19.4%)	550 (11.8%)	F > M	< 0.001
Menstruation	-	5309 (41.0%)	-	-	-
Headache-related disability to daily functioning over past 4 weeks					
Scale 0-3 (0: No headache, 1: Mild headache, no effect on functioning, 2: Moderate headache, normal activity possible with difficulty, 3: Severe headache, normal activity not possible)					
Number of respondents: 17812, F: 13069, M: 4743					
No headaches	313 (1.8%)	200 (1.5%)	113 (2.4%)	M > F	< 0.001
Mild headache	1265 (7.1%)	778 (6.0%)	487 (10.3%)	M > F	< 0.001
Moderate headache	9952 (55.9%)	7309 (55.9%)	2643 (55.7%)	M = F	0.808
Severe headache	6282 (35.3%)	4782 (36.6%)	1500 (31.6%)	F > M	< 0.001

P423

Efficacy and safety of fremanezumab for the preventive treatment of episodic and chronic migraine in children and adolescents: Outcomes from two randomized, double-blind, placebo-controlled, phase 3 studies

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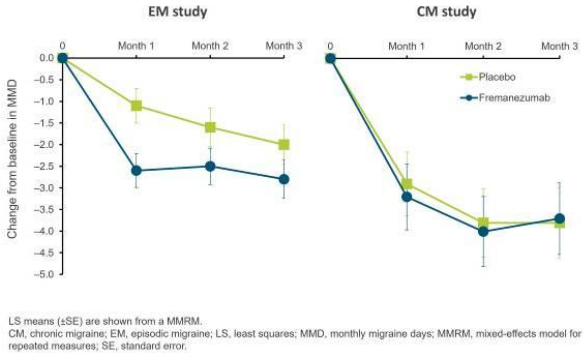
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Objective: To evaluate the efficacy and safety of fremanezumab in children and adolescents with episodic (EM; NCT04458857) or chronic migraine (CM; NCT04464707).
Methods: In two identically designed, multicenter, double-blind, parallel-group, Phase 3 trials, eligible participants (aged 6–17 years; migraine diagnosis for ≥6 months; history of ≤14 [EM] or ≥15 headache days/month [CM]), were randomized 1:1 to monthly fremanezumab (<45kg, 120 mg; ≥45kg, 225 mg) or placebo for 3 months. Primary endpoint: least squares (LS) mean change from baseline in average monthly migraine days (MMD) during the 3-month double-blind period. Secondary endpoints included mean change from baseline in monthly headache days of at least moderate severity (MHD) and ≥50% MMD response rates. Safety assessments included adverse event (AE) reporting.
Results: In total, 234 and 289 participants from the EM and CM studies, respectively, were included in the efficacy analyses. Fremanezumab significantly reduced MMD versus placebo (–2.5 vs –1.4; p=0.0210) in the EM study; no significant difference was observed between treatment groups in the CM study (–3.8 vs –3.7; p=0.8484; Fig.1). In the EM study, MHD reduction was significantly greater with fremanezumab versus placebo (–2.6 vs –1.5; p=0.0172), as was the ≥50% MMD response rate (47.2% vs 27.0%; p=0.0016). Across both studies, the proportion of participants reporting ≥1 AE was similar for fremanezumab and placebo (EM: 55% vs 49%; CM: 58% vs 54%). Serious AEs (≤3%) and AEs leading to discontinuation (<1%) were infrequent.
Fig. 1 LS mean change from baseline in average MMD at Months 1, 2, and 3 in children and adolescents with EM and CM
Conclusion: Treatment with fremanezumab led to significant reductions in MMD and MHD in children and adolescents with EM. The primary endpoint was not met in the CM study; further evaluation in this population is ongoing. Fremanezumab demonstrated favorable safety and tolerability profiles in both studies, consistent with those observed in pivotal adult trials.

Fig. 1



LS means (±SE) are shown from a MMRM.
CM, chronic migraine; EM, episodic migraine; LS, least squares; MMD, monthly migraine days; MMRM, mixed-effects model for repeated measures; SE, standard error.

P424

Long-term effectiveness of monoclonal antibodies targeting CGRP in migraine patients

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Objective: Monoclonal antibodies are a new therapeutic strategy for episodic and chronic migraine prophylaxis. Their target is the calcitonin gene-related neuropeptide, which is a strong vasodilator for meningeal arteries and arterioles by activating endothelial adenylyl cyclase, which seems to be involved in the beginning of inflammation and headache. However, long-term effectiveness of these drugs are still scarce.
We aim to evaluate the effectiveness of 3 anti-CGRP subcutaneous monoclonal treatments (erenumab, galcanezumab and fremanezumab) over 2 to 3 years.
Methods: Observational, retrospective study involving 334 patients. The collected variables before treatment, and after 6, 12, 24 and 36 months, were the following: days of migraine and headache, and punctuation in HIT-6 and MIDAS scores. Potentially confusing factors such as cardiovascular risk, psychiatric history, chronic pain and fibromyalgia, were considered.
Results: After starting treatment, there was a total decrease of the frequency of headache of 4.9, 7.32 and 7.36 days after 36 months of treatment with erenumab, galcanezumab and fremanezumab, respectively; being the decrease in frequency of migraine almost identical among them. The score in HIT-6 scale decreased 4.77, 5.88 and 13.44 points. MIDAS score decreased 86.18, 65.37 and 75.92 points. All of these items showed a more noticeable improvement within 6 months of treatment, stabilizing over time until 36 months or increasing slightly, probably due to missing data from more than

half of the patients (ongoing study). Patients' characteristics at the start of the study among all of the groups, including confusing factors, showed no statistical differences.

Conclusion: Monoclonal antibodies showed a remarkable decrease in the frequency of headaches and migraine, as well as the score in MIDAS and HIT-6 scales, not being influenced by the mentioned confusion factors. This improvement is more noticeable during the first 6 months of treatment, but is stable over time until 36 months.

P425

Improvement in headache frequency does not alter pain sensitivity in chronic migraine treated with flunarizine

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Objective: Pain sensitivity has been previously found to be related to headache frequency and treatment outcomes. In this study, we are particularly interested in whether improvement in headache alters pain sensitivity.

Methods: We included patients with chronic migraine who were responders of three-month flunarizine. Pain sensitivity over the left supraorbital area, including cold, heat, punctate, and pressure pain thresholds (CPT, HPT, MPT, PPT), was assessed using quantitative sensory testing (QST). All the subjects kept an eDiary throughout the study period. QST sessions were performed before and after treatment. Migraine Disability Assessment Scale (MIDAS) and Yale-Brown Obsessive-Compulsive Scale (YBOCS) were used to assess disability and analgesic obsession. Treatment responders were defined as a ≧50% reduction in headache frequency in the third month compared to baseline.

Results: Fifty treatment responders (35.0± 8.9yrs., 72%F) were included in the analysis. After treatment, the headache frequency (17.3±7.0 vs. 5.1±3.5 days, p<0.001), MIDAS (39.8±37.5 vs. 15.2±17.3, p<0.001), and YBOCS (8.1±6.6 vs.5.3±6.2, p=0.001) significantly improved. On the other hand, neither HPT, MPT, nor PPT improved accordingly. Moreover, CPT became even higher (18.8±8.2℃ vs. 21.3±8.5℃, more sensitive) after treatment.

Conclusion: Our findings indicate that although flunarizine significantly reduces headache frequency and related disability, it does not concurrently reduce pain sensitivity. Despite clinical improvement, the unchanged HPT, MPT, and PPT and increased CPT suggest persistent central sensitization or hypersensitivity. These findings align with our previous EEG results, demonstrating persistent abnormal occipital power despite clinical improvement. The dissociation between improved headache profiles and alterations in pain sensitivity deserves further investigation, whether altered pain threshold in migraine is an intrinsic character rather than a symptom of migraine.

P426

Treatment switching after first Anti-CGRP MAb failure in migraine: Gepants or another MAb?

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Objective: To compare the effectiveness, tolerability, and persistence of switching to a gepant versus switching to another monoclonal antibody (mAb) in patients with migraine who failed to a first anti-CGRP mAb.

Methods: This retrospective observational study included patients from a tertiary Headache Unit who switched to a gepant (atogepant or rimegepant) or to a second mAb following the failure of a first mAb between May 2024 and March 2025. Demographic and baseline clinical characteristics were collected. Response rates, reduction in monthly migraine days [MMD], adverse events and discontinuation rates were assessed at 3 months and compared between groups.

Results: A total of 46 patients were included (mean age 49 years; 89% female), of whom 21 switched to a gepant and 25 to another mAb. Baseline MMD was 15 and 16, respectively. Baseline characteristics were comparable. At 3 months, ≥30% reduction in MMD was observed in 38% of gepant switchers versus 28% of mAb switchers (p=0.54); ≥50% reduction was seen in 14% and 8%, respectively (p=0.65). Median MMD reduction was 2 days (IQR 0.5–5.0) with gepants and 1 day (IQR –0.5–5.5) with mAbs (p=0.27). Adverse events occurred in 23.8% (gepants) and 32% (mAbs)(p=0.74), with constipation being the most frequent (14% vs. 24%). Treatment discontinuation was 23.8% in the gepant group (19% inefficacy; 4.8% intolerance) versus 16% in the mAb group (all due to inefficacy)(p=0.71).

Conclusion: Switching to a gepant or another mAb after failure of a first mAb shows similar overall outcomes. However, a trend towards a higher clinical

response and better tolerability was observed in the gepant group, warranting further confirmation in prospective comparative studies.

Fig. 1

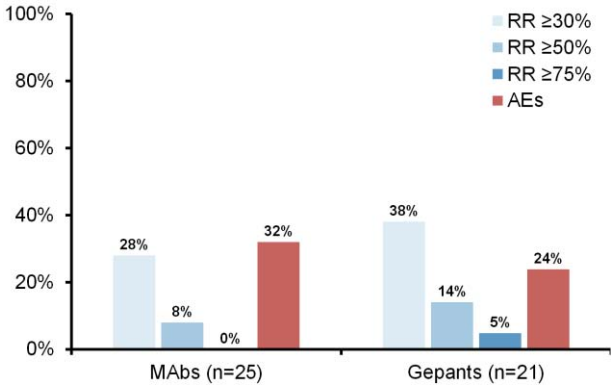
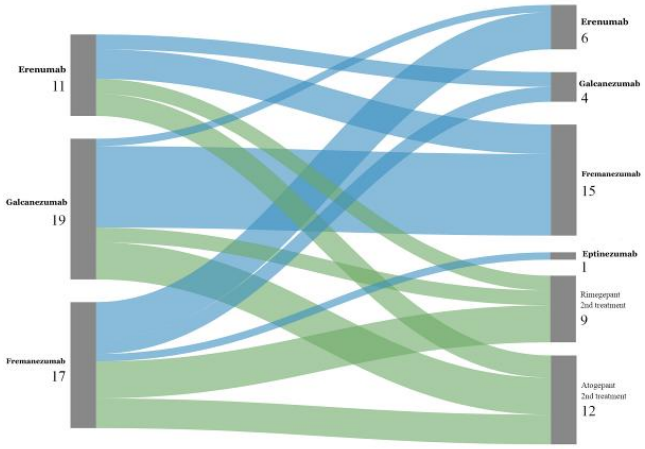


Fig. 2



P427

Treatment pattern and reasons for discontinuing preventive treatment in cluster headache: A prospective cohort study

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Objective: Pharmacological prevention of cluster headache aims to reduce the frequency and intensity of attacks, but its long-term effectiveness and tolerance remains uncertain. The aim of this study was twofold: first, to quantify the discontinuation rates of prophylactic therapeutics due to adverse effects; and second, we assessed the proportion of verapamil responders who maintained its prophylactic effectiveness at follow-up**.**

Methods: In total, 596 patients with cluster headache fulfilling the ICHD-criteria (the baseline cohort) completed a semi-structured interview between 2017 and 2023. Of these, 430 were re-interviewed after a median time of 4.6 years, forming the follow-up cohort.

Results: Of the baseline cohort, 457 patients (77%) had taken preventive medicine. Among these, 123 (27%) had discontinued treatment due to adverse effects. The discontinuation rate first-line treatment verapamil was 18%. Proportionally, the second-line treatments with lithium or topiramate were discontinued due to intolerance in nearly half of the patients. The odds of discontinuing lithium or topiramate therapy were four times higher than for verapamil ($p<0.0001$).

In the follow-up cohort, only 33%, i.e. 143 patients received prophylactic medicine at the time of the second interview. Of the initial 131 verapamil responders, 77 patients continued the use of verapamil, and 54 patients had discontinued due to remission. At the time of the second interview, 91 patients were treated with verapamil and 55% of them were 50% responders. Adverse effects were the cause for discontinuation of verapamil in 17% between the first and second interview.

Conclusion: Effective therapeutic prevention of cluster headache is hindered by intolerance and insufficient efficacy of the preventatives. Verapamil remains effective over time for a subgroup of initial responders, but our findings underscore the need for more tolerable and effective prophylactic medicine in the treatment of cluster headache.

P428

Audit / service evaluation Verapamil : Clinical and ECG monitoring in patients with cluster headache

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Objective: Verapamil remains the first-line preventive therapy for cluster headache, despite limited evidence of efficacy and cardiac risks. Although there is no consensus on how ECG monitoring should be undertaken, guidelines suggest that an ECG should be done prior to starting treatment, 10-14 days after each dose increase, and at regular intervals after reaching a stable dose. Our audit aims to assess the cardiac safety of verapamil, focusing on ECG abnormalities and variations in clinician practices, with the goal of developing a regional prescribing pathway for cluster headache.

Methods: We conducted a retrospective review of 61 cluster headache patients treated with verapamil at a

specialist neurology hospital between March 2020 and November 2023. Prescriptions were made by 13 neurologists across general and headache clinics. The review focused on safety gaps in prescription, dose escalation, ECG monitoring, and follow-up.

Results: Cardiac side effects included bradycardia (3 patients), complete heart block (1 on 640mg/day), Wenckebach phenomenon (1 on 160mg TDS), and other ECG changes (2). Six patients required hospitalization or cardiology consultation. Other side effects included rash (2), leg swelling (5), and dizziness. Variability in prescribing practices and ECG monitoring was noted, with gaps in communication, documentation, and follow-up. One patient required 19 visits for dose titration and monitoring.

Conclusion: Our study highlights the need for safer, more consistent verapamil prescribing. We are developing a regional pathway, checklist, and dedicated clinics for new patients.

Fig. 1

Verapamil table of recommendations and evidence

VERAPAMIL	STANDARD	GUIDELINES AND SOURCES
EFFICACY INDICATION	Despite low evidence, verapamil remains the drug of choice for treatment of cluster headache.	Clinical preventive treatment of CH with verapamil is based on 2 randomized controlled studies and 3 open-label studies. In total, 183 CH patients participated. Verapamil 360 mg/day was used in both controlled studies. Half of the chronic patients experienced benefit from verapamil treatment, and the attack burden of episodic patients was, on average, reduced by 1 attack/day (**R. Jensen, Headache, 2019**) **EAN guidelines 2023**: Verapamil is medication of choice for ECH and CCH, 80% responder rate
DOSE	The dose of verapamil required for treatment of CH is approx. double the dose required in cardiovascular treatments.	**EAN guidelines 2023**: Start 80mg 3-4 times/day and increase in 80mg steps every 3-4 days **Goadsby, Practical Neurology 2019**: start 80 mg tds and increase in 80 mg steps every 2 weeks (table), max recommended dose 320 tds (960)
CARDIAC TOXICITY	Treatment of CH with verapamil is limited by cardiac toxicity, which is not necessarily time or dose dependent.	**EAN guidelines 2023**: 1/3 bradycardia, 1/5 AV conduction abnormalities **Goadsby, Practical Neurology 2019**: 1/5 cardiac arrythmia, bradycardia or long PR A small found that 75% of patients who presented with ECG abnormality did so with a delayed onset of >2 years Lanteri-Minet et al, The Journal of Headache and Pain, January 2011)
ECG MONITORING	ECG monitoring is necessary.	**EAN guidelines 2023**: baseline, then after every 160mg increase above 480mg **Goadsby, Practical Neurology 2019**: baseline, then every 10-14 days as dose is increased. After reaching a stable dose, do ECG every 1-2/12 (for how long?), then every 6/12 **BASH**: baseline and at every increase, then every 6/12 **OUCH website**: baseline and after every increase

P429

Real-world trajectories following discontinuation of Anti-CGRP monoclonal antibodies in migraine patients

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Objective: Discontinuation of anti-CGRP monoclonal antibodies (mAbs) is a common challenge in clinical practice, yet data on outcomes of patients following treatment discontinuation remains scarce. This study aims to describe the characteristics and post-discontinuation outcomes of patients who stopped anti-CGRP mAb therapy for migraine.

Methods: Unicentric, retrospective, observational study of migraine patients who discontinued anti-CGRP mAbs. Collected data included treatment duration, monthly headache days (MHD) before starting therapy and at discontinuation, reasons for stopping, and timing of treatment reintroduction.

Results: We analysed 12 patients (83% female, mean age 48 years, mean MHD 10.5±8.0), two of whom discontinued treatment twice, totalling 14 treatment cycles. Reasons for discontinuation included sustained efficacy (n=10), pregnancy planning, unplanned pregnancy, Raynaud"s phenomenon, and switch to oral anti-CGRP. Mean treatment duration at discontinuation was 20 months, while mean MHD was 5.3±7.6. Among the 10 patients who discontinued due to sustained efficacy, 7 restarted treatment: 4 within 3 months, 1 within 6 months, and 2 after 6 months. All patients who did not restart had <2 MHD at discontinuation (mean: 0.9±0.8), compared to only 1 of the 7 who did restart (mean: 7.0±10.4). Patients who did not restart had no other oral preventives at discontinuation. Upon reintroduction, response was comparable to the initial cycle (average MHD at 3 months: 9.0±11.9 vs. 9.2±11.8).

Conclusion: Most discontinuations occurred due to sustained efficacy. However, many patients resumed treatment, reflecting a need for continued preventive therapy in a significant subset of migraneurs. Those who did not restart had excellent migraine control at the time of discontinuation. Importantly, treatment interruption did not impair response upon reinitiation in our cohort. These findings underscore the need for personalized treatment strategies and close follow-up in migraine management.

P430

Chronology of response to Anti-CGRP mAbs in migraine: The CRONOS-CGRP study

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Objective: To characterize the temporal dynamics of response to anti-CGRP monoclonal antibodies (mAbs) using survival analysis over a 12-month period, and to identify the optimal time to switch therapy in non-responders and clinical predictors of response.

Methods: We conducted a single-center prospective cohort study including 462 patients with episodic or chronic migraine treated with erenumab, galcanezumab, or fremanezumab between February 2021 and November 2024. The baseline period was defined as the month preceding treatment initiation. Response was defined as a ≥50% reduction in monthly headache days (MHDs). Cumulative and instantaneous probabilities of response were estimated using Kaplan-Meier curves. A subgroup analysis compared anti-CGRP mAb-naïve patients with those who switched due to lack or loss of effectiveness, in order to evaluate the optimal switching time. Cox regression was used to identify predictors of response.

Results: Median baseline MHDs was 18.5 (IQR 12.3–30.0); 76.6% had chronic migraine. Among 301(72.0%)

responders, 252(83.7%) achieved response within the first 3 months. Cumulative probability of response plateaued at 72.0% by month 10. Instantaneous hazard peaked in month 1 (36.1%) and dropped below 10% after month 3. Naïve patients showed higher cumulative response (78.7%) and earlier hazard peaks than switchers (49.9%). A crossover in hazard curves suggested month 4 as the earliest point where switching offered a higher probability of response than continuing the initial mAb. In multivariable analysis, male sex was linked to a 32% lower response likelihood. Each additional headache day and prior preventive reduced response odds by 3.1% and 4.7%, respectively. Unilateral pain and photophobia increased the probability of early response by 30.6% and 63.9%

Conclusion: The probability of response to anti-CGRP mAbs is highest within the first 3 months. Switching may be most beneficial around month 4 in non-responders. Baseline clinical features may help predict early response.

Fig. 1

Table 1. Cohort characteristics	n=462
Demographics	
Age, mean ± SD	47.8 ± 12.0
Sex female, n (%)	401 (86.2)
Migraine features	
Chronic migraine, n (%)	356 (76.6)
Age at migraine onset, median (IQR; range)	14.0 (10–18; 2–68)
Duration of migraine, median (IQR; range)	33 (20–42; 2–70)
Aura, n/N (%)	141/459 (30.7)
Unilateral pain, n/N (%)	325/459 (69.9)
Photophobia, n/N (%)	391/444 (88.1)
Phonophobia, n/N (%)	358/444 (80.6)
Osmophobia, n/N (%)	219/444 (49.3)
Nausea, n/N (%)	359/459 (78.2)
Trigeminal autonomic symptoms, n (%)	139/440 (31.6)
Tearing, n/N (%)	84/440 (19.1)
Conjunctival injection, n/N (%)	65/440 (14.8)
Nasal congestion, n/N (%)	39/440 (8.9)
Ptosis, n/N (%)	30/440 (6.8)
Periorbital edema, n/N (%)	27/440 (5.8)
Interictal symptoms, n (%)	238/462 (51.2)
Photophobia, n/N (%)	132/462 (28.4)
Phonophobia, n/N (%)	104/462 (22.5)
Osmophobia, n/N (%)	80/462 (17.3)
Allodynia, n/N (%)	95/462 (20.4)
Baseline migraine burden	
Monthly headache days, median (IQR; range)	18.5 (12.3–30; 3–31)
HIT-6, median (IQR; range)	67 (63–71; 43–78)
Comorbidities	
Hypertension, n/N (%)	69/455 (15.2)
Anxious-depressive syndrome, n/N (%)	236/458 (51.5)

Abbreviations: N, number of participants with available data for each variable; SD, standard deviation; IQR, interquartile range

Fig. 2

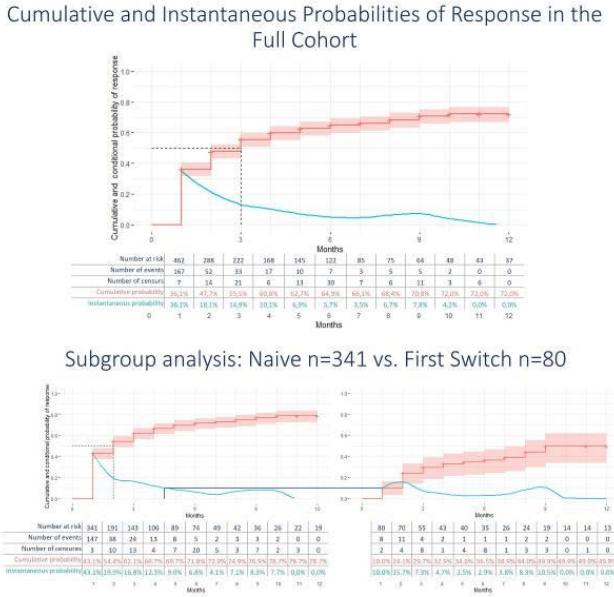
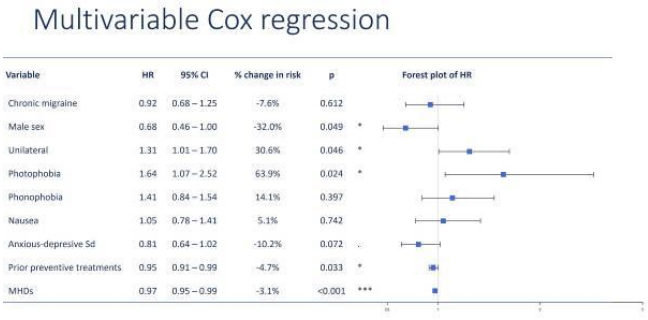


Fig. 3



P431

Predictors of response to antiCGRP monoclonal antibodies in real-world: Czech Migraine Registry (ReMig)

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Objective: To identify predictors of treatment response to anti-CGRP monoclonal antibodies (mAbs) in patients enrolled in the Czech Registry of Migraine Patients on Biological Treatment (ReMig).

Methods: This was a prospective, multicenter study utilizing data from the ReMig database, aimed at evaluating the impact of clinical and sociodemographic factors on the efficacy of all 4

mAbs. Patients were classified as responders (R) if they experienced a ≥50% reduction in monthly migraine days (MMD), and as non-responders (NR) if the reduction was <50%. Logistic regression analysis was used. Data collection spanned from January 2021 to July 2024.

Results: A total of 3285 patients (87.4% female) were analysed. Of these, 2422 (73.7%) were classified as R and 863 (26.3%) as NR. Female patients had a 29% lower likelihood of treatment failure. No significant differences were observed in terms of age, age at diagnosis, or disease duration. Patients with chronic migraine had a 40.1% higher risk of NR. Previously failed prophylactic treatments did not differ significantly between groups (mean 2.2; median 2.0). Medication overuse headache (MOH) did not negatively impact treatment outcomes (R: 34.9%; NR: 36.8%, p=0.423). Response to triptans was associated with a 27% lower risk of treatment failure. Higher education was significantly more prevalent among R (p=0.004). Part-time employment or disability pension status was associated with a 54.6% and 51.5% risk of NR respectively. No comorbidities, psychiatric included (p=0.693), significantly influenced treatment outcomes. However, each unit increase in body mass index (BMI) was associated with a 1.9% increase in the risk of treatment failure.

Conclusion: Chronic migraine, poor response to triptans, higher BMI, lower educational attainment, and male sex may be associated with reduced efficacy of anti-CGRP mAb therapy. In contrast, disease duration, prior prophylactic treatment failures, MOH, and comorbidities did not significantly impact treatment response in this cohort.

P432

Retrospective evaluation of safety and tolerability of fremanezumab in patients with vascular risk factors

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Objective: The objective of this retrospective evaluation was to assess the safety and tolerability of fremanezumab (Ajovy) in patients with cerebrovascular risk factors.

Methods: We currently have over 2000 patients on Ajovy at the Walton Centre NHS Trust. We retrospectively reviewed the notes for 1000 patients from November 2020 until October 2023, identifying any patients with potential cerebrovascular risk factors, in particular, diabetes, hypertension, hypercholesterolaemia, previous strokes and cerebral bleeds.

Results: We analysed the notes of 986 patients as we were unable to access the notes for 14/1000 patients who were managed in Welsh satellite clinics.

Majority of the patients we reviewed were young female patients (F:M 800 187) with no cerebrovascular risk factors.

178 (18%) of the evaluated patients had at least one identifiable vascular risk factor. 97 (54.5%) of these patients remain on Ajovy.

These included 29 patients (3%) over 75 years old, 42 (4%) with diabetes, 90 (9%) with hypertension, 63 (6%) hypercholesterolemia, 15 (1.5%) with previous strokes, 3 (0.3%) with previous myocardial infarction and 10 (1%) with history of cerebral bleeds.

The remaining 81 patients (45.5%) stopped treatment for various reasons, majority of which (37.04%, 30 patients).

6 patients (7%) (0.6% of the total number of patients evaluated) discontinued due to vascular risk factors, which included uncontrolled HTN (5%, 4 patients), post stroke (2%, 2 pts). 3 (4%) passed away while on treatment.

21 patients (25.93%) were lost to follow up and 7 patients (9%) reconsidered continuing treatment.

Conclusion: We evaluated 986 patients, 178 (18%) of whom had vascular risk factors. Overall, only 6 patients (0.6%), discontinued treatment due to cerebrovascular risk factors.

Therefore, in our experience fremanezumab can be safe, to be used in patients with cerebrovascular risk factors.

We aim to review our remaining 1000 patients to add further power to our data.

P433

Atogepant for vestibular migraine: Preliminary clinical experience in two patients

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Objective: Vestibular migraine (VM) is the second most common cause of recurrent vertigo. It shares migraine pathophysiology but presents with episodic vertigo, dizziness, and balance disturbances. Treatment is often extrapolated from general migraine prevention strategies. The role of gepants (CGRP receptor antagonists) in VM remains unclear despite their proven efficacy in classic migraine. The objective is to describe clinical outcomes in two patients with VM treated preventively with atogepant, providing initial evidence to support its potential role in VM management.

Methods: Two patients (one male, one female; aged 35 and 44 years) with neurologist-andENT-confirmed VM were assessed using validated instruments, including the Headache Impact Test (HIT-6) and Patient Global Impression of Change (PGIC). Data were prospectively collected on monthly headache days, vestibular symptom severity, and functional

disability before and after one month of atogepant 60 mg daily. Ongoing prospective follow-up is planned to assess long-term treatment outcomes and tolerability.

Results: Both patients showed marked clinical improvement in migraine attack intensity and frequency after one month of daily atogepant. HIT-6 scores decreased by 19 and 13 points (scores of 67 and 61 initially reduced to 54 and 42) indicating substantial reductions in headache impact. PGIC scale reporting much improved and very much improved, respectively, reflected significant global improvement. Monthly headache days decreased from daily attacks at baseline to 1 and 3 days per month. Vestibular symptoms also improved, with fewer vertigo episodes and better balance function. Both patients reported no side effects.

Conclusion: Atogepant showed promising efficacy in reducing migraine burden and vestibular symptoms in these VM cases. These preliminary findings suggest potential for CGRP receptor antagonists in VM management, but larger controlled studies are needed to establish definitive efficacy and safety in this population.

P434

People with migraine and two years treatment with anti-CGRP therapies. First results from the prospective national registry "Hercules"

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Objective: Novel agents targeting the CGRP pathway constitute a novel mechanism-based treatment for migraine that has revolutionized the therapeutic landscape. Our aim was to document their long-term efficacy and safety outcomes in Hellas.

Methods: The "HERCULES" is a patient-centered, national, multicenter, longitudinal, prospective, observational, non-interventional study supported by the Hellenic Headache Society.

Results: So far, 322 subjects with migraine and prior failure to at least 3 repurposed anti-migraine prophylactic treatments attending 7 headache centers in Greece have been recorded, of whom 141 (43.7%) completed the 2-year treatment with anti-CGRP agents [17/141 (12%) subjects with erenumab; 18/141 (12.7%) with galcanezumab; and 106/141 (75.2%) with fremanezumab] while 51/322 (15.8%) participants discontinued treatment [fremanezumab 26/322 (8%); galcanezumab 17/322 (5.3%); 7/322 (2.2%) erenumab; eptinezumab 1/322 (0.3%)], due to failure [40/322 (12.4%)], adverse events (AE) [9/322 (2.8%)], or complete remission of migraine [2/51 (0.6%)]. The most common AE recorded were constipation [41/322 (12.7%)] and injection site reactions [40/332 (12.4%)]. Only one severe AE has been recorderd [1/322 (0.3%)] during intravenous infusion of eptinezumab (allergic reaction). After 24 doses of anti-CGRP monoclonal antibodies (anti-CGRP mAbs), 120/141 subjects (85.1%) recorded a greater than 50% reduction in monthly migraine days (MMDs) compared to before administration of anti-CGRP mAbs. More than 75% or 100% reduction in MMDs were recorderd in 38/141 (26.9%) and 9/141 (6.4%) subjects.

Conclusion: Anti-CGRP mAbs are effective, safe, and well tolerated after long-term administration and should be considered as a first-line prophylactic treatment for migraine.

P435

Eptinezumab 100 mg infusion every one or two months in the prevention of severe chronic migraine : A faisability study in a French headache centre

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Objective: Since 2021, eptinezumab, has been indicated in France for patients experiencing more than eight migraine days per month and who have failed at least two oral preventive treatments. Marketing authorization recommends quarterly hospital-based administration of either 100 mg or 300 mg. However, current reimbursement policies for day hospitalizations only cover the 100 mg dose. We hypothesized that administering 100 mg of eptinezumab every 4to8 weeks could be feasible and beneficial in routine clinical practice, in a subset of patients with severe migraine.

Methods: We conducted a retrospective descriptive study to evaluate the reasons for shortened dosing intervals of eptinezumab for migraine treatment in the neurology department of Montpellier University Hospital. Secondary objectives included assessing efficacy (monthly number of migraine days, use of acute treatments), tolerability, and changes in HAD and HIT6 scores.

Results: A total of 20 patients (mean age 39.95 years, mean number of mensual migraine days 22.15 days) received 100 mg of eptinezumab every 4 to 8 weeks.

In 80% of cases, the decision to shorten the interval was based on a partial (n=9) or absent (n=7) response to the quarterly regimen. Overall, a significant reduction in monthly migraine days was observed (–6.65 days at 3 months and –8.9 days at 6 months), comparable to literature data for the 300 mg quarterly dose. Mean HAD and HIT-6 scores also decreased (HAD from 19.6 to 16.53; HIT-6 from 70.8 to 66.47). Tolerability was satisfactory. Comparison between the 13 responders and 7 non-responders revealed no significant differences. In non-responders, switching to a shortened regimen helped confirm the refractory nature of their migraine to eptinezumab.

Conclusion: Administering 100mg of eptinezumab every 4to8 weeks appears to be a relevant alternative for patients who are partial or non responders to the quartely regimen. Recognition of this practice in France could support its broader implementation, allow for controlled studies

P436

Trigeminal neuralgia in multiple sclerosis: Epidemiology and long-term outcomes in a tertiary neurology centre in the UK

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Objective: Despite its severe impact on quality of life, data on long-term management and treatment escalation of TN in MS remain scarce. We aim to describe the epidemiology and long-term outcomes of trigeminal neuralgia(TN) in patients with multiple sclerosis (MS) referred to Leeds Neurosciences.

Methods: We screened consecutive MS patients from the West Yorkshire MS register between 1994 and 2025**.** Demographics, clinical phenotype, medications and surgical interventions were included. TN severity was graded using a 3-point Treatment escalation score (TES:1 drug(1), ≥2drugs (2),inpatient/surgical intervention(3). Descriptive data was analyzed using Microsoft Excel and statistical analysis was performed on STATA, with linear regression used for categorical outcomes

Results: From 2,004 MS patients, we included thirty-four patients (1.7%) with MS and TN, mean age 56.9 years (SD±12.2) with a mean follow-up of 10.5 years (SD±7.7). 91.3% had TN diagnosed after MS (only 2 cases TN as first symptom of MS and 3 had a neurovascular conflict on symptomatic side). 91.2% unilateral TN and 54.8% right-sided. 85% had positive imaging findings (pons lesions) Relapsing-remitting MS in55.9%. 75% required oral/intravenous steroids for exacerbations and 4 had nerve blocks. 61.8% tried ≥1oralmedication(CBZ in 35.3%, GBP 26.5%). 1/3 of patients were MS disease-modifying treatments.44.1% had ≥1 surgical procedure(10 had ≥1 thermocoagulation, 1 cryotherapy, 7 gamma-knife). 50% currently treated with carbamazepine. 50% had severe TN with TES 3. 61.8% (21 patients) had a good outcome complete relief or manageable.Age of MS or TN diagnosis and duration of treatment with MS DMTs didn''t have a significant effect on TN prognosis

Conclusion: More than half of our cohort achieved good TN pain control and required significant treatment escalation (TES3) . Further research into novel treatments and long-term outcomes is needed to determine the best regimes to manage TN in MS patients.

P437

Local cutaneous complications of CGRP monoclonal antibodies: A case series

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Objective: To characterize the frequency, clinical features, management, and implications of local cutaneous adverse reactions associated with subcutaneous anti-CGRP monoclonal antibodies in resistant migraine patients.

Methods: Retrospective case series of resistant migraine patients followed at a headache outpatient clinic between November 2023-June 2025. All received subcutaneous anti-CGRP monoclonal antibodies and developed mild to moderate injection-site reactions. Demographic, clinical data, treatment response, management were collected from records and analyzed descriptively. **Patients gave their consent to publish their details in an open access journal.**

Results: Nine women treated with subcutaneous anti-CGRP monoclonal antibodies developed mild/moderate local cutaneous reactions (mainly erythema, induration, edema, and pruritus) representing 5% of all treated patients (n=190; fremanezumab 88, galcanezumab 75, erenumab 27). Reactions appeared after first dose in five patients and between the second and fifth in four. Mean age was 45.9 years (SD 3.2), and six (66.7%) had a history of allergy. Seven cases occurred with fremanezumab (8% of those exposed). Two continued therapy with supportive measures (local cooling, topical corticosteroid cream, pre/post-injection antihistamines, and rotation of injection site to abdominal area), while five required switching due to persistent reactions with or without lack of efficacy: two to atogepant, one to erenumab then

eptinezumab, and one directly to eptinezumab; one discontinued. Of the remaining, one switched from galcanezumab to erenumab and one from erenumab to eptinezumab, both with good tolerability

Conclusion: Local cutaneous reactions to subcutaneous anti-CGRP monoclonal antibodies occurred in nearly 5% of patients and were generally mild. Supportive measures allowed continuation in some cases, but most required switching to another monoclonal antibody or a gepant. Monitoring and proactive management are essential to minimize treatment discontinuation.

P438

Use of corticosteroid containing greater occipital nerve injections in pregnancy, breastfeeding and peri-conception

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Objective: Service evaluation to review our practice of methylprednisolone-containing greater occipital nerve (GON) injections given for the management of primary headache disorders in peri-conception, pregnancy, and breastfeeding.

Methods: A retrospective service evaluation (2016-2025) of patients aged 18 and over who received GON injections in headache clinics at King"s College Hospital London whilst trying to conceive, during pregnancy or in the post-partum period was performed. Individuals were followed up as part of their ongoing clinical care to address pregnancy and foetal outcomes. Clinical data, including effectiveness, migraine characteristics and frequencies, were collected via review of clinical notes.

Results: Females (*n*=25), 2 of which over multiple pregnancies with a median (IQR) age of 33 (30.75-36) years were injected; 17 during pregnancy, and 4 solely whilst breastfeeding. Of the 6 who received injection whilst trying to conceive, 4 conceived naturally. Methylprednisolone (80mg) was used alongside lidocaine 2% in all but one patient reviewed. Eight received an injection in their third trimester. Pregnancy or neonatal complications included: gestational diabetes (*n*=2), pre-term delivery (*n*=2), pre-eclampsia (*n*=1), NICU admission (*n*=3), small for gestational age (*n*=1). There was one stillbirth in the context of antiphospholipid syndrome and recurrent miscarriage, and one medical termination of pregnancy for complex foetal abnormalities at the 20-week scan. Efficacy was comparable to benefit demonstrated by studies of lidocaine only injections in this setting. The GON injection was helpful in reducing severity or frequency of migraine in 85% (*n*=23).

Conclusion: In this retrospective cohort of patients who received mixed constituent GON injection, there were no relative safety signals and offer an effective treatment for women during this journey when they have limited migraine treatment options. We intend to continue to monitor the service prospectively to evaluate further this method.

P439

Long-term efficacy and predictors of response of cgrp monoclonal antibodies in migraine prevention: A real-world service evaluation

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Objective: Monoclonal antibodies (mAbs) targeting calcitonin gene-related peptide (CGRP) have been used for migraine prevention for five years. We conducted a service evaluation to assess their long-term efficacy.

Methods: Patients receiving CGRP-mAbs at King"s College Hospital, London, were sent a questionnaire. Clinical data were extracted from records as part of a service evaluation. Data were summarized using percentages or medians with interquartile ranges (IQR). A generalized linear model with binomial distribution and logit link function was used to identify predictors, with >30% response as a binary outcome.

Results: Patients (*n*=223) responded (median age 48, IQR 35–57; 82% female), with diagnoses of chronic migraine (*n*=138, 62%), episodic migraine (*n*=65, 29%), and new daily persistent headache with migraine phenotype (*n*=20, 9%). Median age at mAb initiation was 45 (IQR 33–55); migraine duration 26 years (IQR 13–36).

Most first received fremanezumab (*n*=157, 70%) or erenumab (*n*=65, 29%); one received galcanezumab. A >30% response to the first mAb was reported in 77% (*n*=50) on erenumab and 80% (*n*=125) on fremanezumab.

Most (*n*=179, 80%) received one mAb only; some required switching to a second (*n* =36, 16%) and 8 (4%) received a third. Ongoing benefit >30% was reported by 59/82 (72%) with erenumab, 137/176 (78%) with fremanezumab, and 9/12 (75%) with galcanezumab. (Table 1)

A model predicting response to the first mAb (χ^2=40.87, df = 22, *P*=0.009) showed higher odds with triptan responders (OR=5.98, *P*=0.002) and later age at initiation (OR=1.08, *P*=0.01). More premonitory symptoms (OR=0.88, *P*=0.049), failed prior

preventives (OR= 0.70, *P*=0.002), and longer migraine duration (OR=0.93, *P*=0.03) predicted lower odds.

Conclusion: CGRP-mAbs are effective for most patients. Response is more likely in triptan responders and those starting later. Poorer outcomes with longer migraine duration, more premonitory symptoms, and prior failure of preventives support early initiation of mAbs for a better outcome.

Fig. 1

	Response				Median duration of effect (Weeks) [IQR]	Total Duration of follow up
	<30%	>30% but lost efficacy	30-50%	>50%		
Erenumab	13 (16%)	10 (12%)	3 (4%)	56 (68%)	190 [116-297]	304 weeks (5.9 years)
Fremanezumab	25 (14%)	14 (8%)	18 (10%)	119 (68%)	100 [30-218]	195 weeks (3.6 years)
Galcanezumab	1 (8%)	2 (17%)	2 (17%)	7 (58%)	222 [189-287	71 weeks (1.4 years)

Table 1: Overall response to CGRP monoclonal antibody treatments.

P440

Impact of CGRP monoclonal antibodies on the most bothersome non-pain symptom in migraine: A service evaluation

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Objective: Monoclonal antibodies (mAbs) targeting Calcitonin Gene-Related Peptide have been in use as migraine preventives for five years. We conducted a service evaluation to assess their efficacy and the impact on the most bothersome non-pain symptom (MBS).

Methods: Patients currently on mAbs at King"s College Hospital, London completed a questionnaire, and clinical and efficacy data were collected from patient records. Data were summarized as percentages or as medians with interquartile ranges (IQR). Associations between categorical variables were assessed using Pearson Chi-Square tests.

Results: Patients (*n*=223) responded (median age 48, IQR 35–57; 82% female), with diagnoses of chronic migraine (*n*=138, 62%), episodic migraine (*n*=65, 29%), and new daily persistent headache with migraine phenotype (*n*=20, 9%).

Fatigue was the most frequent MBS (*n*=44, 20%), followed by brain fog (*n*=38, 17%), neck stiffness (*n*=31, 14%), nausea (*n*=26, 12%) and photophobia (*n*=21, 9%).

More than 30% improvement in headache with the current mAb was reported by 191 (88%), however, only 107 (56%) of those who reported headache improvement noted an improvement in the MBS. Improvement of the MBS had a statistically significant positive association on headache improvement (χ^2 = 7.77, *P* = 0.005). Type of mAb did not have a significant effect on the improvement of MBS (χ^2 = 1.29, *P* = 0.53).

Of those who reported headache improvement with mAbs, the majority of those who identified fatigue (56%), brain fog (58%), photophobia (67%) and nausea (77%) as the MBS reported improvement and only 46% of those who identified neck stiffness as the MBS reported improvement.

Conclusion: Fatigue, brain fog and neck stiffness are the most common non-pain symptoms among migraine patients. Despite improvement in headache, a significant proportion of patients continue to be affected by their most bothersome non-pain symptom. Nausea and photophobia may respond well to mAbs, while neck stiffness may have a lesser benefit.

P441

CGRP monoclonal antibodies in migraine: Do premonitory symptoms persist without headache? – A service evaluation

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Objective: Monoclonal antibodies (mAbs) targeting calcitonin gene-related peptide (CGRP) have been in use for migraine prevention for five years. We conducted a service evaluation focusing on efficacy and the effect of CGRP-mAbs on premonitory symptoms (PreS).

Methods: Patients currently receiving mAbs at King"s College Hospital, London completed a questionnaire, including data on PreS. Clinical data were extracted from patient records. Data were summarised as percentages or medians with interquartile ranges (IQR). Associations between categorical variables were assessed using Pearson Chi-Square tests.

Results: Patients (*n*=223) responded (median age 48, IQR 35–57; 82% female), with diagnoses of chronic migraine (*n*=138, 62%), episodic migraine (*n*=65, 29%), and new daily persistent headache with migraine phenotype (*n*=20, 9%).

Overall, 188 patients (84%) recognised PreS, with a median of 6 symptoms (IQR 2–9). Most common PreS were fatigue (67%), neck stiffness (58%) and brain fog (58%). Symptoms which were more frequent in the premonitory phase than in the headache phase were yawning (76% vs. 61%), food cravings (57% vs. 50%)

and euphoria (56% vs. 13%). Although present in the premonitory phase, all other symptoms were more frequent during headache.
Build-up of PreS that did not evolve into headache was reported by 114 (53%), which included 54% (*n*=104) of patients with >30% improvement in headache and 38% (*n*=10) of those with <30% improvement. Median number of PreS in this group was 5 (IQR 3–7). Brain fog (60%), fatigue (54%), and neck stiffness (51%) were most common and the duration of PreS was 1–24 hours in most (67%). The type of mAb did not have a significant association with the occurrence of PreS without headache (χ^2 = 0.71, df=2, *P* = 0.70).
Conclusion: Premonitory symptoms are recognised by a significant majority of migraine patients. Over half of those responding to mAbs continue to experience premonitory symptoms without headache, supporting a central mechanism in migraine pathophysiology.

P442

Superiority of candesartan over topiramate in the treatment of migraine: A comparative cohort study

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Objective: To compare the tolerability and effectiveness of candesartan versus topiramate using real-world data.
Methods: In this longitudinal cohort study at the Leiden Headache Center, data were collected via a validated E-diary. The 28 days before treatment served as baseline. The primary endpoint was medication discontinuation within 6 months. Secondary endpoints included ≥50% response rate, and changes in monthly migraine days (MMD), headache days (MHD), acute medication days (MAMD), and HIT-6 score. Patients received a propensity score based on baseline MHD, MMD, HADS, and prior preventive treatment failures. Discontinuation was assessed via Kaplan-Meier and Cox regression, adjusting for propensity score. Secondary outcomes were analyzed using adjusted regressions. Sensitivity analyses with optimal matching were also included.
Results: 661 patients were included. Discontinuation was lower for candesartan (29.7%) vs. topiramate (67.3%; HR 2.5 [95% CI: 1.9–3.3], p<0.001). Candesartan also showed a higher ≥50% response rate (47% vs. 29%; OR 0.6 [95% CI: 0.4–0.8], p=0.004) and greater reduction in MHD (-1.1 days [95% CI: -2.2 to -0.01], p=0.04). No significant differences were seen in MMD, MAMD, or HIT-6 after adjustment. Sensitivity analyses confirmed the results.
Conclusion: Candesartan appears better tolerated and more effective than topiramate. These findings suggest a need to revise treatment guidelines to avoid exposing patients to less tolerable and less effective therapies.

P443

Satisfaction rates and self-reported adverse events of antiCGRP therapies for migraine prevention – Focus on patient perspectives

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Objective: Anti-CGRP therapies are an important breakthrough in migraine prevention because of increased efficacy, specific mechanism of action and better tolerability that renders patient adhesion to these treatments much higher. Real world data showed more side effects than in clinical trials but nevertheless these drugs are well tolerated. We present the results of a study on self -reported efficacy and adverse effects of a large sample of patients on anti-CGRP therapies.
Methods: Single-center observational study assessing the self-reported efficacy and adverse effects of anti-CGRP therapies via online surveys, over the past 12 months.
Results: 277 online questionnaires were fulfilled by 142 patients, 91% women, mean age 48.8 years. 4% of questionnaires corresponded to patients on Atogepant, 9.3% on Erenumab , 24.4% on Eptinezumab, 29% on Galcanezumab and 32% on Fremanezumab. Duration of treatment ranged from 1 to 48 months.22,1% stated that were "much better" (7 in the Patient Global Impression of Change scale - PGIC) and 35.3% were "better with a real and useful difference" scoring 6 in PGIC. 55.9% reported one or more adverse events caused by the medication. Most frequent side effects included: 34.8% gastrointestinal symptoms, mainly obstipation as expected but also diarrhea (3%), and 12.8% local skin reactions. Less frequent complaints were: 11.7% weight gain, 10.8% dizziness, 9.3% fatigue, 4.9 % depressed mood and 4.4% referred high blood pressure during treatment. 10.3% of patients complained of chest pain or palpitations.
Conclusion: More than half of our patients reported significant improvement with antiCGRP therapy. Self-reported adverse events were more frequent (56%) than previously reported. Most frequent, were gastrointestinal symptoms and local skin reactions. Nevertheless, some other complaints were not expected such as weight gain, dizziness, palpitations and chest pain arising in more than 10% of patients, showing the need for maintaning recent therapies adverse events surveillance

P444

Anxiety affects all aspects of quality of life in medication overuse headache patients

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Objective: Anxiety among medication overuse headache (MOH) patients was assessed . The primary objective of this study was to examine the relationship between anxiety and health related quality of life among medication overuse headache (MOH) patients in group of 600 new diagnosed MOH patients.

Methods: prospective clinical study

Results: The study showed a positive correlation between the anxiety and duration of MOH. Anxiety is showed as a risk factor for development of MOH. Anxiety was singled out as a risk factor for the overall aspect of health in MOH sufferers ($p = 0.05$). The study found that the duration of the earlier chronic headache positively correlated with the impact of MOH ($r = 0.327$, $p = 0.003$). The impact of MOH as well as anxiety were on all domain of health and assessed as significant, correlating with the duration of the MOH ($p \leq 0.05$)

Conclusion: Assessment of anxiety in MOH patients could be important for improving their quality of life

P445

Exploring sensory sensitivities in autism and migraine: A cross-sectional survey analysis of atypical sensory processing and its impact on migraine-specific quality of life

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Objective: The relationship between autism and migraine has emerged as a significant area of study over the past decade. Atypical sensory processing has been proposed as a shared feature of both conditions. In this cross-sectional observational study, we hypothesised that there is a greater burden of atypical sensory processing in autistic and migraine groups, which in turn negatively affects the migraine-specific quality of life (QoL).

Methods: We conducted a survey using validated questionnaires including the Migraine Screening Questionnaire, the Glasgow Sensory Questionnaire (GSQ) and Migraine Specific QoL Questionnaire (MSQ). Funding was provided by Brighton and Sussex Medical School. Data was collected from the Qualtrics platform and analysed using Python software. Data from a total of 201 participants were collected. Statistical analyses included chi-squared tests, regression analysis and analyses of variance to examine the data.

Results: We found an overarching relationship between autism, migraine and higher sensory sensitivity scores. Results indicate that migraine is more prevalent in autism ($p<0.05$) and that autistic individuals with migraine have the highest sensory sensitivity scores. There was a statistically significant negative correlation between sensitivity scores (GSQ) and the MSQ ($p<0.0001$), indicating that increased sensory sensitivities reduces the QoL of those with migraine regardless of the presence of autism ($p>0.5$).

Conclusion: These findings identify sensory sensitivity as an important predictor of QoL in migraine. Clinically, there should be greater awareness of migraine as a comorbidity of autism, with sensory sensitivity as a key therapeutic target. Further research is needed to support the growing evidence of the relationship between autism, migraine and sensory sensitivity.

P446

A preliminary study on the effects of vestibular migraine, Ménière's disease and comorbidities on emotional status and cognitive function

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Objective: To compare emotional status and cognitive function in vestibular migraine (VM), Meniere's disease (MD), and their comorbidity (VMMD), and to analyze factors influencing cognition.

Methods: This cross-sectional study included 96 outpatients (32 males, 64 females, 21–73 years) at Union Hospital, Tongji Medical College, from Dec 2022–Dec 2023: 31 VM, 36 MD, 29 VMMD, plus 32 controls. Cognitive function was assessed with the Montreal Cognitive Assessment (MoCA); emotional and somatization symptoms were evaluated using the GAD scale, PHQ-9, SCL-90, and SS scale. Multiple linear regression explored factors affecting cognition.

Results: The VMMD group had lower MoCA scores (26.0 [24.5–28.0]) than controls (28.0 [27.0–29.0]) and MD patients (28.0 [26.0–30.0]) ($P=0.006$). VMMD showed deficits in visuospatial/executive function, delayed recall, and orientation ($P<0.05$). VM, MD, and VMMD groups had higher anxiety, depression, and somatization compared with controls ($P<0.05$), with VMMD showing the greatest distress. Regression analysis indicated education level and vestibular disease type as key factors: university education predicted higher MoCA scores ($P<0.001$), while VMMD was associated with cognitive decline ($P<0.01$).

Conclusion: Patients with VM and MD, especially VMMD, experience significant emotional distress. Cognitive impairment is evident in VM and VMMD,

affecting specific domains. These findings highlight the need to consider both emotional and cognitive aspects in clinical evaluation and management.

P447

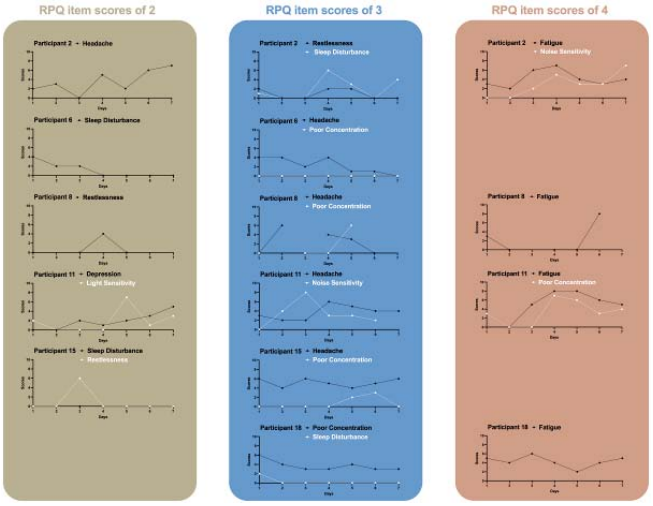
Daily symptom registrations reveal variability in post-traumatic headache and other persistent post-concussion symptoms

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Objective: Post-traumatic headache (PTH) is one of the most common and disabling persistent post-concussion symptoms (PPCS; symptoms lasting more than 3 months after a concussion). PTH is typically assessed using retrospective assessments, such as the Rivermead Post Concussion Symptoms Questionnaire (RPQ), which are prone to memory biases and do not capture the day-to-day variability of PTH.
Methods: In this study, we investigated how daily registrations of PTH and other PPCS relate to the RPQ and explored the variability of symptom trajectories over time. Nineteen participants registered PPCS for 28 days using an mHealth app and subsequently completed the RPQ. From the final 7 days of registrations, average, highest, and last-day symptom scores were calculated and correlated with corresponding RPQ items. Data from the full 28 days were used to compute within-person SD and mean squared successive difference (MSSD).
Results: Correlations between the RPQ and daily registrations were weak to moderate (range: 0.343–0.590). The respective RPQ item explained up to 35% of the variance in average daily registrations. For PTH, MSSD ranged from 0–18.05 and within-person SD from 0–3.01, highlighting considerable heterogeneity in PTH variability. Visual inspection showed that participants with identical RPQ scores often showed distinct PTH variability patterns, and that variability also differed across PPCS within the same individual (see Figure 1).
Conclusion: This study highlights the potential additional value of daily registrations for capturing the dynamic and fluctuating nature of PTH and other PPCS, which may be missed by retrospective questionnaires. PPCS vary both within and between individuals over time. Reducing this complexity to a single total score oversimplifies a nuanced reality.

Fig. 1



P449

German language adaptation of the Migraine Interictal Burden Scale (MIBS-4) – Preliminary results from an online pre-post survey

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Objective: The *Migraine Interictal Burden Scale* (MIBS-4) comprises four items to assess the disability and strain of persons with migraine during headache-free periods. The aim of this study is to develop a German version and to assess the psychometric properties of this version.
Methods: The MIBS-4 was translated into German by two headache experts and blindly back-translated by a professional translator. Subsequently, the MIBS-4 was tested for comprehensibility by eight persons with Migraine. Linguistic discrepancies were discussed in an expert panel and modifications were conducted to optimize the translation. To determine the psychometric properties, an online pre-post survey was conducted. Data (MIBS-4 and other measures) were collected before and four weeks after treatment (multimodal inpatient routine care at a specialized headache clinic). The current dataset comprises *N*=14

inpatients (age *M*=38.1, *SD*=16.5, 100% female, *n*=11 chronic migraine, *n*=3 episodic migraine).
Results: Reliability (McDonald's Omega: ω=0.89) was good. The Spearman correlations with similar measures were moderate to high (MIBS-4 and *Fear of Attacks in Migraine Inventory*, FAMI: ρ=.60, *p*=.023, MIBS-4 and *Headache impact test*, HIT-6: ρ=.62, *p*=.019), indicating good convergent validity. The comparison of pre- and post-values (MIBS-4, *n*=10) did not show any indication of a relevant change (Pre: *M*=7.71, *SD*=3.24, Post: *M*=7.41, *SD*=3.1, Wilcoxon signed-rank test: z=-0.782, *p*=0.434).
Conclusion: There is initial evidence of good psychometric properties of the German version of the MIBS-4. Evidence of sensitivity to change is still lacking, although additional data from a larger sample may provide such evidence. The MIBS-4 is likely suitable for the screening of interictal disability and strain in persons with migraine in German-speaking countries. A definitive assessment requires data from an adequately powered sample, which is planned.

P450

Association between sleep quality, stress and concentration levels among migraineurs

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Objective: Migraine is among the most common neurological disorders worldwide and is frequently linked to sleep disturbances. Stress is also widely recognized as a potential trigger of migraine attacks.
This study aimed to explore the associations between migraine characteristics, perceived stress, concentration levels, and sleep quality.
Methods: In this cross-sectional study, 41 individuals with migraine completed an anonymous online survey (LimeSurvey). Data collection included demographic and clinical information, as well as the Perceived Stress Scale (PSS-10), the Attention and Performance Self-Assessment (APSA-20), and the Pittsburgh Sleep Quality Index (PSQI).
Results: Migraine frequency was positively correlated with the PSQI sleep disturbances component (r = 0.41, p = 0.01). A moderate correlation was also observed between perceived stress and concentration levels (r = 0.38, p = 0.007). No significant associations were identified between migraine frequency or intensity and overall stress, concentration, or global PSQI scores.
Conclusion: These findings underline the link between subjective stress and concentration difficulties in individuals with migraine, while migraine-specific effects on stress and sleep quality remained inconclusive. Larger, controlled studies are warranted to clarify these relationships and inform targeted interventions.

P451

Light and odor hypersensitivity in migraine: Association with clinical characteristics, psychological aspects, and quality of life – A pilot study

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Objective: To analyze correlations between light and odor hypersensitivity and clinical headache, psychological, and quality-of-life factors in individuals with migraine.
Methods: This cross-sectional study included 27 individuals (18–51 years) with a clinical diagnosis of migraine. Light and odor hypersensitivity were assessed with the Utah Photophobia Symptom Impact Scale–version 2 (UPSIS-2) and the Chemical Odor Sensitivity Scale (COSS). Clinical measures: headache intensity and frequency, Headache Impact Test (HIT-6), and Allodynia Symptom Checklist (ASC-12). Psychological status: Hospital Anxiety and Depression Scale (HADS). Quality of life: Migraine-Specific Quality of Life Questionnaire (MSQ). Data were analyzed using Pearson correlation ($p<0.05$).
Results: UPSIS-2 score was associated with higher headache impact and poorer quality of life (Table 1). COSS score was associated with cutaneous allodynia and poorer quality of life (Table 2). A positive correlation was observed between UPSIS-2 and COSS scores (r=0.469; p=0.01).

Table 1. Correlations between UPSIS-2 and psychosocial and clinical aspects

Variables	**Correlation Coefficient**	**p**
Migraine Intensity	0.38	0.05
Migraine Frequency	−0.16	0.41
HIT-6	0.41	**0.03**
ASC-12	0.23	0.25
MSQ	−0.45	**0.02**
HADS		
HADS Depression	0.16	0.42
HADS Anxiety	0.23	0.24

Table 2. Correlations between COSS and psychosocial and clinical aspects

Variables	**Correlation Coefficient**	**p**
Migraine Intensity	0.23	0.25
Migraine Frequency	0.12	0.54

HIT-6	0.15	0.44
ASC-12	0.39	**0.04**
MSQ	−0.51	**0.01**
HADS		
HADS Depression	0.22	0.25
HADS Anxiety	0.10	0.61

Conclusion: This pilot study indicates that light and odor sensitivity in migraine are associated with greater disease burden and poorer quality of life. The association between odor hypersensitivity and cutaneous allodynia reinforce the hypothesis that osmophobia may represent a potential marker of central sensitization. Furthermore, the positive correlation between these sensitivities suggests a shared profile of sensory amplification.

P452

Response of migraine aura to CGRP-mAbs

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Objective: Phase 3 studies have shown that monoclonal antibodies targeting calcitonin gene-related peptide or its receptor (anti-CGRP mAbs) are effective in both migraine without aura (MwoA) and migraine with aura (MwA). However, the occurrence and clinical course of migraine aura have rarely been assessed as outcomes. Anecdotal and cohort studies suggest that aura may improve with CGRP-based treatments, although de novo aura has also been reported. It remains unclear why the cortical phenomenon of migraine aura should respond to peripherally acting treatment. This analysis investigates whether anti-CGRP mAbs influence migraine aura independently of headache and examines the occurrence of de novo aura.

Methods: We report data from the Austrian Migraine Registry on behalf of the Austrian Migraine Research Collaboration, comparing baseline and follow-up findings in patients with MWA treated with anti-CGRP mAbs. Changes in aura were compared with headache features, premonitory symptoms, and associated symptoms. Analyses will be performed using complete case analysis, and associations between clinical outcomes and predictors will be examined by linear regression.

Results: Out of 417 patients, 117 patients fulfilled criteria for MWA. At baseline (n=107), median aura frequency was 4 days/month (IQR 5), duration 30 minutes (IQR 45), and intensity 8 (IQR 4, NRS). At follow-up 1 (n=63), median aura frequency was 2 days/month (IQR 3), duration 35 minutes (IQR 60), and intensity 8 (IQR 9). At follow-up 2 (n=12), median aura frequency was 2.5 days/month (IQR 4.75), duration 40 minutes (IQR 105), and intensity 6 (IQR 9). Premonitory and accompanying symptoms (17-item composite) at baseline (n=105) showed a median of 25 (IQR 13). Mean intervals to follow-up 1 and 2 were 141.2 (±96.9) and 441.8 (±90.1) days. Comprehensive statistical analyses are ongoing.

Conclusion: Preliminary data suggests anti-CGRP mAbs may reduce aura frequency and duration, while intensity remains unchanged.

P453

Measuring what matters: Emotional well-being and the impact of headache-free days

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Objective: This study assess subjective emotional well-being in patients with episodic migraine (EM) or chronic migraine (CM), by evaluating positive and negative emotions experienced on the last day with migraine and on the last day without migraine.

Methods: A multicenter cross-sectional study was conducted across 13 Italian headache centers. Adults with EM or CM were enrolled and demographic and clinical variables were collected. All patients completed validated questionnaires assessing, on a 10 point Likert Scale, the Emotional Well-Being (EWB), calculated as the sum of positive affects (PA) and negative affects (NA) experienced on their most recent day with and without migraine. Disability was

measured with MIDAS and its correlation with EWB explored.
Results: A total of 436 patients were enrolled (F/M: 378/58; mean age: 44.5±13.5; EM/CM: 342/94; mean disease duration: 23.5±14.9 years; mean migraine frequency: 9.9±7.5); Of these, 55.5% were married or cohabiting; 49.5% held a university degree. PA was significantly higher on migraine-free days (p<*0.001*), while NA was significantly higher during migraine days (p<*0.001*), indicating reduced EWB in presence of migraine. Moreover, subjects with EM reported higher EWB values compared with those with CM (3.7±1.5 *vs* 3.2±1.9, *p<0.005*) on a migraine day, but no differences emerged between EM and CM on migraine-free days. MIDAS correlate with lower PA score (*p<0.001*), higher NA (*p<0.001*) and reduced EWB (*p<0.001*) on migraine days, but not on migraine-free days, suggesting that disability does not influence positive emotions when patients are free of headache.
Conclusion: CM is associated with significantly reduced EWB compared to EM. While migraine disability, as measured by MIDAS, predicts EWB during migraine days, it does not capture positive affects and EWB on headache-free days. These findings underscore the importance of integrating subjective well-being into migraine assessment to better address patients" quality of life beyond pain and disability.

P454

When aura does not always mean migraine: Visual aura from intracranial internal carotid artery aneurysms

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Objective: We present a rare case of migraine-like visual aura without headache, triggered by two large left intracranial internal carotid artery (ICA) aneurysms. Endovascular repair of these aneurysms led to ischemic strokes in the left posterior cerebral artery (PCA) territory, likely via a functional posterior communicating artery (PComA). To our knowledge, this is the first reported case of headache-free visual aura precipitated by intracranial ICA aneurysms.
Methods: A 46-year-old woman experienced stereotypical right visual field auras for 18 months. MRI revealed four intracranial aneurysms: two in the left ICA, one in the right ICA, and one small basilar artery aneurysm. Following endovascular repair of the left ICA aneurysms, she developed multiple PCA strokes, attributed to embolic events through a functional PComA.
Results: -
Conclusion: Cortical spreading depression (CSD), a self-propagating wave of neuronal and glial depolarization, underlies migraine aura. Cerebral microembolism, arising from hemodynamic changes or microthrombi in unruptured aneurysms, can trigger CSD. In this patient, a functional PComA likely facilitated thromboembolic transmission before and after intervention, causing recurrent visual auras and occipital ischemic injury.
This case illustrates that visual aura without headache does not always indicate migraine and may reflect underlying vascular pathology. Migraine-like aura associated with ICA aneurysms highlights the importance of considering secondary causes in atypical presentations. These findings support the role of cerebral microembolism in initiating CSD via a functional PComA, mimicking migraine aura. Prompt recognition and management of aneurysmal disease are essential to prevent ischemic complications.

P455

Construct validity of the central sensitization inventory in patients with migraine

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Objective: The aim of this study was to verify the construct validity, through hypothesis testing, of the Central Sensitization Inventory (CSI) in migraine population.
Methods: A total of 132 individuals diagnosed with migraine were included. According to hypotheses raised a priori to investigate the construct validity of the CSI, the questionnaire would correlate with the Allodynia Symptom Checklist (ASC-12), Headache Impact Test (HIT-6), Pain Catastrophizing Scale (BPCS), Tampa Scale of Kinesiophobia (TSK) and EQ-5D-5L-VAS questionnaires, as well as the Pressure Pain Threshold (PPT) of the temporalis, trapezius and suboccipital muscles. Pearson"s correlation was calculated for hypothesis testing between CSI and the other variables of this study.
Results: Weak correlations were found between the CSI and the frequency of migraine (r= 0.29; p=0.001), the HIT-6 questionnaire (r= 0.27; p=0.002) and the trapezius muscle PPT (r= -0.21; p=0.014). There were moderate correlations between the CSI and the ASC-12 (r= 0.36; p<0.001), the PCS (r= 0.36; p<0.001), the TSK (r= 0,47; p<0,001), the EQ-5D-5L (r= -0.44; p<0.001) and the suboccipital muscle PPT (r= -0.37; p<0.001).

Table 1 - Central Sensitization Inventory prediction variables (n=132).

n= 132	r	p-value
Migraine frequency	0.29	**0.001**
Migraine onset	0.41	**<0.001**
ASC-12	0.36	**<0.001**
HIT-6	0.27	**0.002**
PCS	0.36	**<0.001**
TSK	0.47	**<0.001**
EQ-5D-5L	-0.44	**<0.001**
Temporalis PPT	-0,13	>0,05
Trapezius PPT	-0.21	**0.014**
Suboccipital PPT	-0.37	**<0.001**

Conclusion: The results of this study provided sufficient evidence to validate the CSI questionnaire for patients with migraine.

P456

Psychometric properties of a new instrument collecting daily symptom data in trigeminal neuralgia: Trigeminal Neuralgia Electronic Diary (TnED©)

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Objective: Trigeminal neuralgia (TN) is an orphan chronic condition with severe facial pain attacks and significant unmet need. Given no validated instrument to record data on paroxysms, continuous pain, and their interference, the Trigeminal Neuralgia Electronic Diary (TnED©) was developed and its content validity demonstrated in previous study. Data collected from the controlled randomized withdrawal trial LIBRA (NOE-TGN-201, NCT05217628), assessing basimglurant safety and efficacy in patients with TN, was used to assess TnED"s© psychometric properties.

Methods: TnED© is a daily 3 or 5-question diary recording paroxysms (severity, frequency), continuous pain (CP, if present; severity, duration), and pain interference (from paroxysms and CP). In the LIBRA trial, patients completed TnED© daily throughout the trial, and Patient Global Impression of change (PGI-C), Penn-Facial Pain Scale-Revised (Penn-FPS-R), and Sheehan Disability Scale (SDS). The data from the LIBRA 8-week active run-in was analysed to assess TnED"s© psychometric properties e.g. test-retest reliability, internal consistency, construct validity, and clinically Meaningful Within Patient Change (MWPC).

Results: Data of 90 participants were analysed (54% purely paroxysmal, 46% with CP). Scatter plots of W7 and W8 data demonstrated test-retest reliability. Internal consistency showed paroxysm severity and CP severity strongly correlated with interference (Spearman"s Rank Correlation R>0.8). Correlations with Penn-FPS-R and SDS demonstrated construct validity, especially for paroxysms severity, CP severity, and interference. CP duration and paroxysms frequency showed weaker internal and external correlations. Paroxysms severity clinically MWPC was -2 points (range -1.5 to -2.5; -30% to -40%), with similar values for other measures.

Conclusion: The new TnED® has demonstrated satisfactory reliability and validity to serve as a clinical outcome assessment for TN, with paroxysm severity being highly correlated with other validated instruments.

P457

Anxiety, depression and premonitory mood disturbance in vestibular migraine

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Objective: Mood disorders are a common comorbidity with migraine and a cohort of patients also report premonitory mood disturbance. Data regarding the prevalence of premonitory mood disturbance and mood disorders specifically in vestibular migraine remain limited.

Methods: Participants were recruited as part of the NITROVEST mechanistic study via advertisement and clinician referral. Data were collected on age, sex, HADS-A and HADS-D scores and premonitory symptoms of mood fluctuation, depression, euphoria and irritability. Clinically significant anxiety and depression (CSAD) were defined as HADS scores of 8 or more. Statistical analysis using Fisher"s Exact Test was performed using IBM SPSS Statistical Software (v 29).

Results: In total, 34 participants with vestibular migraine completed HADS-A and HADS-D questionnaires. The median age was 36 years (IQR 31-44), with more women than men (71% vs 29%).

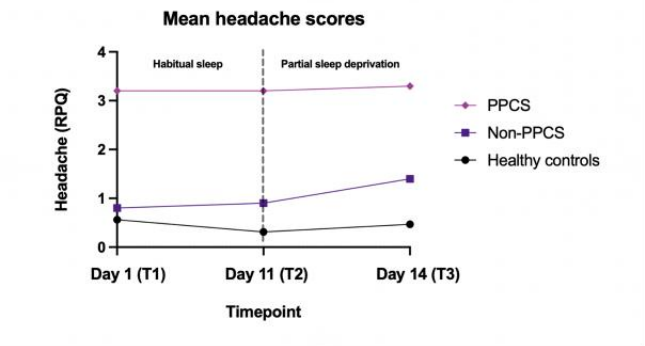
The median HADS-A score was 11 (IQR 7-14) with 71% patients having a score of 8 or more. The median HADS-D score was 8 (IQR 6-10) with 59% having a score of 8 or more. In total, 82% of patients reported having CSAD. The most commonly reported premonitory mood disturbance was irritability (26%), followed by mood fluctuations (21%), depression

(15%) and euphoria (6%). In total, 41% of patients reported premonitory mood disturbance.
Patients with CSAD were not more likely to report premonitory mood disturbance compared to patients without CSAD (39% with CSAD vs 50% without CSAD, *P* = 0.67).
Conclusion: Clinically significant anxiety and depression are highly prevalent in patients with vestibular migraine. The presence of premonitory mood disturbance was dissociated from clinically significant anxiety and depression, as determined by HADS-A and HADS-D scores, suggesting the biological mechanisms underpinning premonitory mood symptoms may be distinct from those of mood disorders.

P458
Preliminary data of an ongoing experimental study: The effect of partial sleep deprivation on post-traumatic headache
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Objective: Following a mild traumatic brain injury (mTBI), approximately 20% of individuals experience long-lasting symptoms, referred to as persistent post-concussion symptoms (PPCS). Post-traumatic headache (PTH) and sleep disturbances are among the most commonly reported complaints, but the interaction of these symptoms is poorly understood. The current study aims to examine if levels of sleep disturbances differ in people with and without PTH and how partial sleep deprivation affects headaches in people with and without PPCS. Preliminary data on headache burden before and after partial sleep deprivation will be presented.
Methods: The study includes three groups: 12 adults with mTBI and PPCS (mean age 33, 83.3% female), 15 adults with mTBI without PPCS (mean age 40, 53.3% female), and 38 adults as healthy controls (mean age 30, 44.7% female). The Rivermead Post Concussion Symptoms Questionnaire (RPQ; 0-4 scale) was used to measure headache burden at three separate times: day 1 (T1), day 11 (T2) and day 14 (T3). On day 11, participants were asked to sleep two hours less for three consecutive days, based on their mean sleep time measured by actigraphy.
Results: There was a significant difference in mean age between groups (*p*=.043). The PPCS group had the highest headache burden at all three timepoints compared with the other two groups: 3.2 (*SD* = 0.919) at T1, 3.2 (*SD* = 0.919) at T2, and 3.3 (*SD* = 0.68) at T3. The lowest mean score at each timepoint was found within the healthy control group, with 0.56 (*SD* = 0.77) at T1, 0.31 (*SD* = 0.58) at T2 and 0.47 (*SD* = 0.85) at T3 (Figure 1).
Conclusion: The descriptive statistics indicate a larger headache burden in the PPCS group, both before and after partial sleep deprivation. Data collection is ongoing, and larger samples and statistical analyses will be performed to determine whether there are within- or between-group effects of partial sleep deprivation on headache burden.

Fig. 1



P459
Side-shifting pattern of hemicrania continua: A rare variant
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Objective: Hemicrania Continua (HC) presents as unilateral headache associated with autonomic features. Prompt clinical diagnosis leads to early effective management of this entity. We present an interesting case of HC which mimicked migraine.
Methods: Single-patient case report with retrospective review of the clinical course, headache pattern, neurological examination, brain imaging, prior migraine treatments, and standardized indomethacin test (dose-escalation with withdrawal–rechallenge). Safety monitoring included renal and gastrointestinal profiles.
Results: A 42-year-old man had 2 to 3 years history of continuous daily headache that alternated between hemicrania over days–weeks. Exacerbations featured ipsilateral lacrimation, nasal congestion, and mild ptosis. Multiple migraine pharmaceutical regimens (propranolol, amitriptyline, triptans) yielded minimal benefit. Examination and MRI were normal. Indomethacin 25–50 mg t.i.d. produced complete relief within 48 hours; brief discontinuation precipitated prompt recurrence, and reinstatement

restored remission. The patient remained symptom-free on 25 mg b.i.d. with PPI cover at 6-month follow-up, without any adverse events.

Conclusion: Continuous headache with autonomic features should prompt consideration of HC even when laterality is not strictly side-locked. An indomethacin trial with withdrawal–rechallenge can confirm diagnosis and rapidly resolve symptoms, preventing years of ineffective migraine-directed therapy.

Fig. 1



P460

Intracranial hypotension: Three cases of clinical consideration

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Objective: Intracranial hypotension is an entity with distinct and well-defined clinical characteristics. The underline cause remains a diagnostic challenge, as does achieving an effective treatment. Herein, we present three intriguing cases of intracranial hypotension and their therapeutic management.

Methods: Clinical evaluation-neuroimaging-treatment.

Results: 1st case: A 57-year-old man, was presented with severe orthostatic headache accompanied by dizziness, nausea, tinnitus and horizontal diplopia (right abducens nerve palsy). Brain Magnetic Resonance Imaging (MRI) was initially performed and revealed pachymeningitis with gadolinium-enhancement and spinal-cord MRI revealed a subdural hygroma at the A6-level, suggestive of cerebrospinal fluid (CSF) leak(Figure 1). Conservative management(intravenous fluids-oral caffeine-analgesics) was administered, followed by epidural blood patch, which resulted in resolution of symptoms. **2nd case:** A 37-year-old male underwent suboccipital craniectomy for Chiari I malformation. Fifteen days postoperatively, he developed othrostatic headache, nausea and dizziness. Brain MRI demonstrated a supine CSF leak and hydromyelia of cervical spinal cord(Figure 2). The patient was treated with conservative treatment with improvement of symptoms over the following month. **3rd case:** A 49-year-old male precented with orthostatic headache, nausea and dizziness. Brain MRI demonstrated sinus venous enlargement and dura enhancement, while MRI of the spinal axis did not reveal any evidence of CSF leak(Figure3). Conservative management failed to achieve clinical improvement;epidural blood patch was performed leading to resolution of symptoms.

Conclusion: Although intracranial hypotension can be diagnosed clinically and supported by its characteristic MRI findings, determining the underlying etiology may be challenging and necessitates comprehensive imaging of the entire spinal axis. In many cases conservative management proves insufficient and treatment with epidural blood patch is required.

P462

Efficacy of eptinezumab during a migraine attack: Preliminary data from an Italian multicenter real-world experience (the BEFREE study)

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Objective: In the RELIEF study, eptinezumab significantly shortened time to headache pain freedom and to absence of most bothersome symptom when administered during a migraine attack, 0.5–1 hour following the start of infusion. The aim of this study was to observe the possible resolution of a migraine attack during eptinezumab infusion in a real-world setting, particularly exploring the first 30 minutes.
Methods: This is an ongoing multicenter Italian observational prospective study. Patients with episodic (EM) and chronic migraine (CM) receiving eptinezumab 100 mg or 300 mg during a migraine attack were enrolled. Eptinezumab was administered within 1–12 h of onset of the qualifying migraine. Migraine features were recorded at different timepoints after infusion start: 10 minutes (T10), 20 minutes (T20), 30 minutes (T30), 1h, 1.5h, 2.5h, 3h, 3.5h, and from 4h to 48 h.
Results: We enrolled 31 patients, mainly female (87%) with a mean age of 43.1±2.7 yrs; 68% had CM and 62% MO. The NRS score (baseline 6.2±1.9) progressively reduced at different timepoints, with the lowest value after 12 hours after the infusion (2.9±3.7). In the first 30 minutes of the infusion, NRS score significantly varied from T0 to T10 (p=0.011) and from 10 to 20 minutes (p=0.004). Photophobia was significantly lower at T10 (p=0.025) and at T20 (p=0.08) compared to baseline. The presence of phonophobia was significantly lower comparing baseline to T20 (p=0.005) and T30 (p=0.005). Osmophobia was also significant comparing baseline to T30 (p=0.046). Pain freedom was reported by 6.5% of patients at T10, 20% T20, 13.3% T30, 16.7% 1h, 19% 2h, 58% 12h, 35.3% 24 h and 31.3% 48 h. The achievement of pain freedom from T10 to T20 and from 4h to 12h was significant (p=0.046).
Conclusion: During the first 30 minutes of the infusion, eptinezumab demonstrated to induce a rapid resolution of migraine pain intensity and associated symptoms, suggesting a peripheral site of pharmacological action for CGRP blockade.

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Epidemiology of cluster headache: A systematic review and meta-analysis of global prevalence, incidence, and risk factors

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Objective: To synthesize global evidence on the prevalence, incidence, and risk factors of cluster headache (CH), and examine subgroup differences by sex, region, and diagnostic subtype.
Methods: We searched PubMed, Scopus, and Web of Science up to July 2025 for observational studies reporting on CH epidemiology among adults (≥18 years). Eligible studies used ICHD-2 or ICHD-3 criteria. Outcomes included CH prevalence, incidence, sex ratios, and risk factors.
Results: Sixty-seven studies (874,000+ participants) were included. Most focused on general populations (62 studies, 93.94%), with others on students, monks, and twins. Geographically, studies originated mainly from Europe (n=39), Asia (n=26), Africa (n=6), and North America (n=5), with none from South America or Oceania. Prevalence ranged from 0.01% to 1.7%, with key estimates of 124–151 per 100,000. Incidence was less reported, ranging from 2.5 to 6.4 per 100,000/year. Sex-specific data showed 29,380 male and 12,328 female CH patients (M: F = 2.38:1), with reported ratios from 0.42:1 to 29.4:1, typically 2–5:1. Settings included hospital-based (60%), community (25%), academic (10%), and specialized centers (5%). Data collection spanned 1935–2023, with most studies post-2010. Prevalence estimation periods ranged from 3 months to 20 years. Diagnostic criteria evolved: ICHD-3/3β (recent), ICHD-2 (2004–2015), and IHS (pre-2004). Risk factors included smoking (up to 70%), alcohol, and family history.
Conclusion: This systematic review offers a comprehensive synthesis of CH epidemiology. Despite its rarity, CH demonstrates consistent male predominance and associations with modifiable behavioral risks. Findings reveal global variation in data and diagnosis, highlighting the need for enhanced awareness and targeted healthcare planning.

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Prevalence of migraine and its neurological burden in Africa: A systematic review and meta-analysis of community-based studies

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Objective: Migraine is a disabling neurological disorder and a leading cause of years lived with disability. In Africa, community-based data on migraine remain limited. This review aimed to estimate the pooled prevalence of migraine and

summarize its neurological burden across African populations.

Methods: We systematically searched three major databases (PubMed, Web of Science, Scopus) in June 2025 for community-based studies reporting migraine prevalence in African countries.

Results: We included 49 studies with 113,022 participants from 14 African countries. Ethiopia (23.4%), Egypt (17.0%), and Nigeria (14.9%) were most represented. Most studies were urban-based; the largest samples came from the general population (59.8%) and students (12.0%). Sex distribution was nearly equal (50.5% female). Participants were mostly aged 20–40 years. Reported migraine prevalence ranged from 3.4% to 53.4%, with most studies between 5 and 17.3%. Some reported prevalence per 100,000, ranging from 6,400 to 50,600. Incidence was rarely assessed. Female predominance was common, with sex ratios often between 0.7 and 1.2:1 (M: F), though some studies showed male dominance. The ICHD criteria were most used for diagnosis, followed by the HARDSHIP and MIDAS tools. Tension-type headache and probable migraine were frequently reported. Common risk factors included female sex, family history, stress, poor sleep, menstruation, noise, sunlight, and dietary triggers.

Conclusion: Migraine prevalence in Africa shows wide variability, but consistent links to sex, psychosocial, and environmental factors. Greater awareness and targeted strategies are needed to address its burden across diverse African settings.

P465

Real wold experience of atogepant in 72 patients with chronic migraine and daily headache (AtoOnly Consortium)

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Objective: Chronic migraine patients with daily headache (CMDH) have been excluded from randomized clinical trials assessing the efficacy and safety of gepants. In the present study, we analyzed the tolerability and effectiveness of Atogepant in CMDH from a multicentric registry.

Methods: Multicenter (n=18) prospective cohort study. Study population: consecutive patients with High Frequency Episodic Headache (HFEH) and Chronic Migraine receiving Atogepant 60mg per day. According to the local guidelines, Atogepant is approved in patients with prior failure to three or more migraine preventive drugs, including onabotulinumtoxinA.

Patients were evaluated by headache experts and followed-up quarterly. Variables collected: demographics, mood disorder requiring treatment, painful syndromes, clinical situation and impact of migraine-

Good response (R50%) to atogepant was defined as the proportion of patients who achieved a reduction of at least 50% in the number of headache days per month, compared to the baseline period. Discontinuation due to Treatment Emergent Adverse Event was recorded. Data of follow-up at 3 months are presented. Patients with CMDH were compared to patients with CM or HFEM.

Results: In our registry of 574 patients, three month-follow-up was achived in 234, and 72 (30.8%) presented CMDH. Differences between groups are shown in the table. As expected, patients with CMDH had more Monthly Migraine and Headache days, more frequently chronic pain and mood disorders and had received OnabotulinumToxin A and anti CGRP Monoclonal antibody.

At 3 month follow-up, patients with CMDH has SR50 of 38.9% compared to 58.6% (p=0.001) in non CMHD. Moreover Atogrepant retention was lower in CMDH. Atogepant discontinuation concerning tolerability was no different among groups.

Conclusion: Patients with Chronic Migraine and Daily Headache has a poorer response to Atogepant,

athough more than one third achieved a good response at three months.

Fig. 1

Atogepant in Chronic Migraine with Daily Headache (CMDH): Three months follow-up

	CMDH n=72	Non-CMDH n=162	P value
Age (yo), mean (SD)	48.7 (12.2)	45.8 (13.3)	n.s.
Female (%)	83.8	85.0	n.s.
Migraine worsening, years [IQR]	10 [5-20]	10 [5-20]	n.s.
Chronic migraine (%)	97.3	68.3	0.001
Monthly Headache Days, baseline [IQR]	30 [30-30]	15 [12-21]	0.001
Monthly Migraine Days, baseline [IQR]	21 [15-30]	12 [10-16]	0.001
HIT6, baseline [IQR]	68 [65-74]	68 [63-72]	n.s.
Mood disorders (%)	48.0	36.6	0.01
Chronic pain (%)	19.6	14.1	0.001
Previous Onabotulinumtoxin A use (%)	95.0	81.5	0.001
Previous anti-CGRP MAB[1] use (%)	70.4	46.9	0.001
Three Months follow-up			
Good outcome (%)	38.9	58.6	0.005
Retention index (%)	69.4	85.2	0.005
Atogepant discontinuation due to TEAE[2] (%)	13.9	8.60	n.s.

[1]Monoclonal antibody; [2]Treatment Emergent Adverse Event

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Headache characteristics of patients diagnosed with Giant Cell Arteritis (GCA) in a UK District general hospital

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Objective: To assess headache characteristics in GCA as per the 2020 European Headache Federation recommendations for neurologists managing GCA.
Methods: We conducted retrospective data collection of initial presentation of 78 patients with GCA between 2018 to 2025 at Frimley Health NHS Trust. All patients were diagnosed by a rheumatologist in keeping with the ACR/EULAR 1990 or revised 2022 classification for GCA. We analysed headache characteristics and additional GCA features documented in clinical notes.
Results: 72% of the patients were female with a median age of onset 74 years (range 54-91 years). 81% of patients presented with a headache and 57 patients had a location documented. Some patients had a headache in more than one location, the majority of which was temporal in 75% of cases followed by frontal (23%) and occipital (21%). Other locations mentioned were global (11%), vertex (7%), retro-orbital (5%), central (2%) and parietal (2%). 27 patients had unilateral and 18 had a bilateral headache. Headache severity was documented for 15 patients; 60% reported severe (8-10/10), 20% moderate (5-7/10) and 20% mild (<5/10).Headache quality was documented for 30 patients of which 27% described neuralgia, 27% persistent or dull, and 20% a throbbing or pulsatile headache. Other descriptions included a "band-like sensation", "sore" or pain like "waves". 51% of patients reported visual disturbance and 50% also had jaw claudication.
Conclusion: Our data demonstrates the significant variability in the headache location, severity, and character seen in GCA. Further real world studies examining the headache characteristics in GCA patients are needed in order to guide clinicians to be more vigilant in patients presenting with new onset headache.

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A prospective real-world analysis of atogepant in refractory migraine patients

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Objective: The objective of this study was to evaluate the effectiveness, tolerability, and impact of atogepant in a real-world population of patients with medically refractory episodic and chronic migraine.
Methods: This prospective, single-centre audit included adults with episodic or chronic migraine who were refractory to ≥3 classes of preventive therapies and initiated on daily oral atogepant for 3 months.
Results: Of 153 patients treated, 78 (M/F: 14/64; mean age 48.3±1.6 years) who submitted 3-month headache diaries were included in the analysis. Patients had failed a mean of 8.3±0.3 preventive treatments prior to atogepant; 38% (N=30) had failed to respond or tolerate a CGRP monoclonal antibody (mAb). At 3 months, monthly migraine days were reduced by 8.7 days (P=0.001), and monthly headache days by 7.5 days (P<0.001). Mean HIT-6 scores dropped by 6.0 points (from 69.0±0.4 to 63.0±0.8, P<0.001). Atogepant achieved ≥50% reduction in migraine days in 63% of patients. Among those who previously failed a CGRP mAb, 70% (N=21) had ≥30% reduction in monthly migraine days. Patients reported a mean 54±3% benefit on the global impression of change scale. Adverse events were reported in 49% over 3 months. The most common were constipation (19%), decreased appetite/weight loss (13%), nausea/vomiting (12%), fatigue (12%), and dizziness (5%), all considered mild
Conclusion: Atogepant appears to be an effective and well-tolerated treatment for patients who are refractory to other preventive therapies, including those who failed to respond or tolerate previously a CGRP mAbs. These real-world findings support atogepant"s utility in complex clinical populations.

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Eptinezumab for migraine prevention: Initial experience from a Portuguese tertiary hospital

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Objective: Eptinezumab was recently approved in our hospital, with the first patient receiving treatment in August 2024. Given the limited European real-world data available, we aimed to describe the clinical profile of patients who initiated eptinezumab in our hospital.
Methods: Retrospective descriptive study of adult patients who initiated eptinezumab for migraine prevention in our tertiary headache clinic between August 2024 and May 2025. Demographic, clinical, and treatment-related data were retrieved from medical records.
Results: Eighteen patients initiated eptinezumab. Overall, 72% were female, and the mean age was 43.3 years (range: 20–63). Migraine was chronic in 10 patients (56%) and episodic in 8 (44%).
All patients had previously tried more than two oral preventive treatments (range: 3 to over 10). Prior anti-CGRP monoclonal antibody use was documented in 14 patients (78%), all of whom had previously received galcanezumab. Among them, 4 were also treated with fremanezumab, and 1 of these had additionally received erenumab. In total, 4 patients had been exposed to more than one monoclonal antibody (range: 1 to 3). Four patients (22%) started eptinezumab as their first anti-CGRP monoclonal antibody.
At the time of analysis, 17 patients were under active treatment: 10 (59%) were receiving eptinezumab with oral preventives (of whom 2 [12%] also received botulinum toxin); 1 (6%) was treated with botulinum toxin only; and 4 (24%) were on monotherapy. No patient was using another monoclonal antibody concurrently. One patient discontinued eptinezumab due to lack of efficacy and resumed fremanezumab.
Conclusion: Eptinezumab offers distinct advantages. Nonetheless, in this cohort, it was not frequently selected as a first-line option, being primarily used in patients with highly refractory migraine. Treatment adherence was high and further data are needed to assess long-term effectiveness and better define its role in clinical practice.

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The burden of high-frequency episodic migraine and chronic migraine in the population-based PopHEAD study

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Objective: Is there any difference between the disease burden and quality of life among individuals with high-frequency episodic migraine (HFEM) and chronic migraine (CM)?
Methods: PopHEAD is a population-based cross-sectional study in the Norwegian county of Vestfold and Telemark. 28,753 participants (18-70 years) were invited to fill in an electronic questionnaire. The questionnaire was a modified version of the HARDSHIP-questionnaire. HFEM was classified according to newly proposed criteria, and CM according to ICHD-3. Using linear regression for continuous variables and logistic regression for binary outcomes, we compared measures of disease burden and quality of life between participants classified with HFEM and CM. The analysis was conducted first with adjustment for age and sex, then with additional adjustment for monthly migraine days.
Results: Of 8,265 participants 225 had HFEM and 349 had CM. Compared to the HFEM group, the CM group had more monthly migraine days (17.9 vs. 9.7, $p < 0.001$) and headache days (20.8 vs. 9.9, $p < 0.001$). In analyses adjusted for age and sex, the CM group reported greater disease burden across nearly all measures, including work and social impairment, and had a lower quality of life ($p < 0.01$). With additional adjustment for monthly migraine days, no significant differences in disease burden were found between the two groups, except from days missed from household work ($p = 0.03$).
Conclusion: The higher disease burden observed in CM compared to HFEM was fully explained by the higher number of monthly migraine days in the CM group. This finding suggests that monthly migraine days, not monthly headache days, are the primary driver of burden and should form the basis for future revisions to the ICHD criteria.

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Eptinezumab and onabotulinumtoxinA in the treatment of chronic migraine: A real-world evidence study

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Objective: Migraine is a spectrum of disorders along a *continuum*, often evolving into a chronic condition, very debilitating and common in the global population. Results of previous studies from our group highlight under and late diagnosis in real-world context (1). The purpose of the present study is to address the questions dealing with the differences in efficacy of eptinezumab and onabotulinumtoxinA in an Italian real-world setting of chronic migraine and medication overuse headache (MOH).
Methods: The primary endpoint of efficacy is reduction of monthly migraine days (MMDs) after 3 and 6 months. The secondary endpoints are represented by reduction of MHDs, days in need for rescue medications and effects on pain intensity (VAS) and disability (MIDAS). The study is approved by Regional Ethics Committee and conducted at the Regional Headache Center. Statistical differences are evaluated through Two-way RM ANOVA, followed by Bonferroni or Sidak test.
Results: Forty chronic migraine patients refractory to standard treatments are observed, among whom 15 are over 50 and 4 over 65 years old. Eptinezumab and onabotulinumtoxinA are effective after 3 and 6 months on MMDs and MHDs. OnabotulinumtoxinA-treated group presents a trend to reduction of rescue medications after 3 months.
Conclusion: OnabotulinumtoxinA deserves investigation as useful as add-on therapy to monoclonal antibodies directed towards the signaling of the calcitonin-gene related peptide (CGRP) or its receptor antagonists, gepants, for chronic migraine, also in older patients, and MOH.
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P473

Real-world effectiveness of eptinezumab in participants in whom ≥1 prior anti-cgrp preventive treatment had failed: Results for the first 75 participants in an ongoing prospective study

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[2]Lundbeck, Deerfield, IL, United States
[3]H. Lundbeck A/S, Copenhagen, Denmark
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[6]Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland, OH, United States

Objective: To assess the real-world effectiveness of eptinezumab for preventive treatment of migraine in participants in whom ≥1 preventive calcitonin gene-related peptide antagonist (anti-CGRP) had previously failed.
Methods: INFUSE was an observational, prospective study with 190 participants potentially recruited from ≥100 United States infusion centers. Inclusion criteria included adults with a migraine diagnosis in whom ≥1 preventive anti-CGRP had failed (subcutaneous monoclonal antibodies and preventive oral gepants), with treatment failure defined by participants reporting that prior therapy was stopped due to a lack of effectiveness or side effects. Patient-reported outcomes were remotely collected on a digital app and assessed at month 6 (after 2 eptinezumab infusions), including Patient Global Impression of Change (PGIC); monthly headache days (MHDs) and 50% reduction in MHDs, both from the Migraine Disability Assessment (MIDAS); and "good days" (participant defined).
Results: Overall, most participants were female (67/75 [89%]) and White/Caucasian (63/75 [84%]), and 36/75 (48%) were 35–54 years old. Of 75 participants, 45 (60%) reported that **≥**3 anti-CGRPs had failed, with high disease burden recorded across measures at baseline. In the interim effectiveness analysis population (N=48) after 6 months of eptinezumab treatment, 33% (95% confidence interval [CI]: 22%–47%) of participants reported a rating of much or very much improved on the PGIC, and 71% (95% CI: 57%–82%) reported any improvement (minimally, much, or very much improved). The mean MHD reduction was 5.8 days/month (P<0.001; baseline: 19.0 MHDs) on MIDAS; a MIDAS-derived 50% reduction in MHDs was achieved by 42% (95% CI: 29%–56%) of participants; and an increase of 5.3 good days/month was reported (P<0.001; baseline: 10.0 days/month).
Conclusion: Participants for whom prior anti-CGRP therapies have failed experienced, on average, improvements across multiple participant-reported migraine outcomes after escalation to eptinezumab treatment.

P474

Burden of migraine in systemic lupus erythematosus patients of Europe: A systematic review and meta-analysis

***S. Arsalan Wasti**[1], A. Wasti[2]*
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[2]Continental Medical College, Lahore, Pakistan

Objective: This review aims to estimate the prevalence of migraine in systemic lupus erythematosus (SLE) patients of Europe.
Methods: We searched PubMed, Scopus, Embase, Web of Science and Google Scholar from inception to July 29, 2025 for studies reporting the prevalence of migraine in SLE patients in Europe. Statistical analyses were performed in R/RStudio (v2025.05.1+513). Prevalences were pooled as proportions, stabilized with double-arcsine transformations. Publication bias was assessed through Doi plot with Luis Furuya-Kanamori (LFK) index.
Results: Eighteen studies were included, with a total of 1094 participants. Pooled prevalence of migraine in SLE patients was calculated to be 32% (95% Confidence Interval [CI] 26% to 39%), with high heterogeneity (I2 = 77.1%). Subgroup analysis by country revealed highest prevalence in SLE patients of Italy (62%, 95% CI 47% to 75%) and lowest in Poland (7%, 95% CI 1% to 19%). Subgroup analysis by sub-region of Europe showed highest prevalence in Northern Europe (39%, 95% CI 34% to 43%) and lowest in Central Europe (7%, 95% CI 1% to 19%). No signs of publication bias were seen (LFK index 0.39).
Conclusion: Approximately one in three European patients with SLE experience migraine, with prevalence estimates ranging from 7% to 62% across countries. These findings highlight the need for improved clinical vigilance and region-specific research to better address this underrecognized comorbidity.

Fig. 1

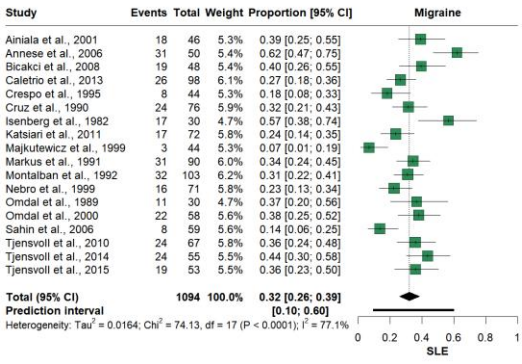


Figure 1: Forest Plot Showing Pooled Prevalence Of Migraine

Fig. 2

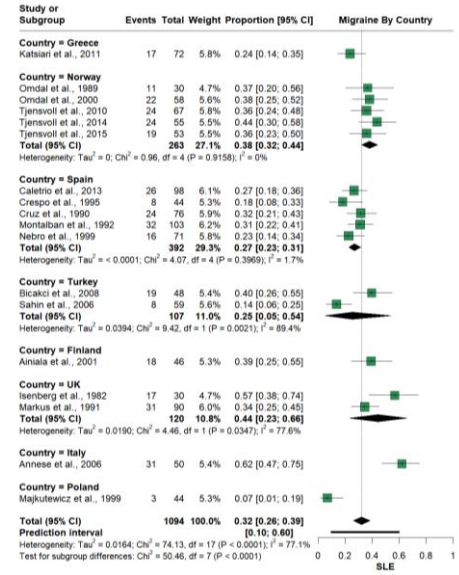


Figure 2: Subgroup Analysis Showing Prevalence By Country

Fig. 3

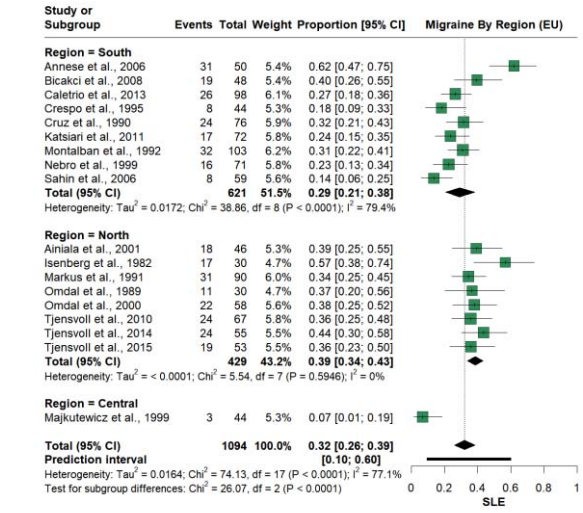


Figure 3: Subgroup Analysis Showing Prevalence By Europe Region

P475

Burden of restless legs syndrome in European migraineurs: A systematic review and meta-analysis

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[2]Continental Medical College, Lahore, Pakistan

Objective: This review aims to estimate the prevalence of restless legs syndrome (RLS) in European migraineurs.
Methods: We searched PubMed, Scopus, Embase, Web of Science and Google Scholar from inception to September 5, 2025 for studies reporting the prevalence of RLS in migraine patients in Europe. Statistical analyses were performed with R/RStudio

(v2025.05.1+513). Prevalences were pooled as proportions, stabilized using Freeman-Tukey double-arcsine transformations. Random-effects model was used. Pooled prevalence was reported with 95% confidence intervals (CI).

Results: Eleven studies met the eligibility criteria and were included, comprising 4029 migraineurs in total. Pooled prevalence of RLS in European migraine patients was calculated as 21% (95% CI 17% to 25%, I2 = 76.1%). Subgrouping by country demonstrated highest prevalence in Turkey (34%, 95% CI 24% to 47%) and lowest in Germany (17%, 95% CI 14% to 21%). Subgroup analysis by region revealed highest prevalence in East Europe (34%) and lowest prevalence in Western Europe (17%). Where reported, the prevalence of RLS was consistently higher in females compared to males.

Conclusion: This is the first systematic review and meta-analysis to quantify the burden of RLS in European migraineurs. Around one in five were found to be affected, with higher prevalence in women and marked regional variations. These findings show a significant clinical burden, and highlight the importance of routine screening and integrated management.

Fig. 1

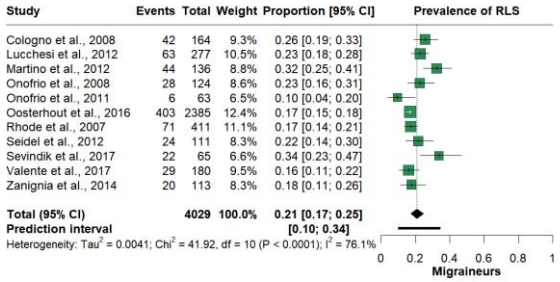


Figure 1: Forest Plot Showing Pooled Prevalence of RLS in Migraineurs

Fig. 2

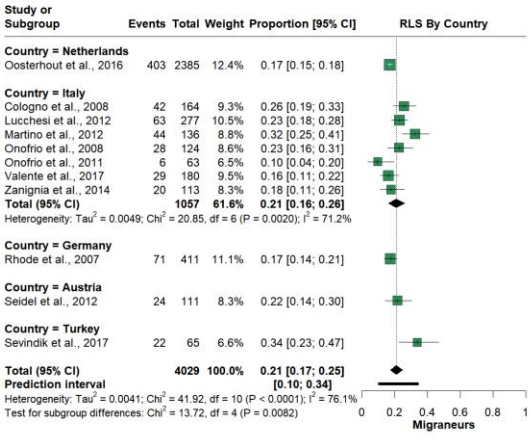


Figure 2: Subgroup Analysis By Country

Fig. 3

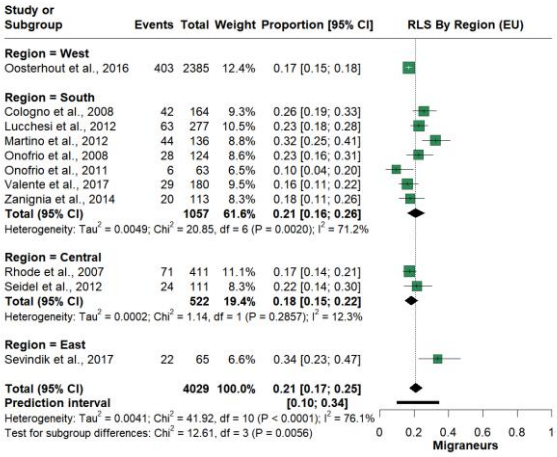


Figure 3: Subgroup Analysis By Region

P476

Burden of migraine in multiple sclerosis patients in Europe: A systematic review and meta-analysis

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[1]King Edward Medical University, Lahore, Pakistan

[2]Continental Medical College, Lahore, Pakistan

Objective: This review aims to estimate the prevalence of migraine in European multiple sclerosis (MS) patients.

Methods: PubMed, Scopus, Embase, Web of Science and Google Scholar were searched from inception to September 2025 for studies reporting the prevalence of migraine in multiple sclerosis patients in Europe. Statistical analyses were conducted with R/RStudio (v2025.05.1+513). Prevalences were pooled as proportions, stabilized with Freeman-Tukey double-arcsine transformations, and random-effects model was used for pooling. Prevalences were reported with 95% confidence intervals (CI).

Results: 28 studies were included (N = 8611). Pooled migraine prevalence in European MS patients was 25% (95% CI 20% to 30%). Subgroup analysis by country showed higher burden in Romania (47%) and lowest burden in Croatia (7%). West Europe demonstrated highest migraine prevalence (41%) and North Europe had lowest prevalence (14%). Prevalence of migraine in the studies was also noted as being higher in female patients compared to male patients.

Conclusion: This is the first meta-analysis to estimate migraine burden in European MS patients, reporting pooled as well as regional prevalences. Roughly one in four patients had migraine, with females having higher prevalence. These findings show considerable

migraine burden in this population, and signal need for increased clinical awareness and management.

Fig. 1

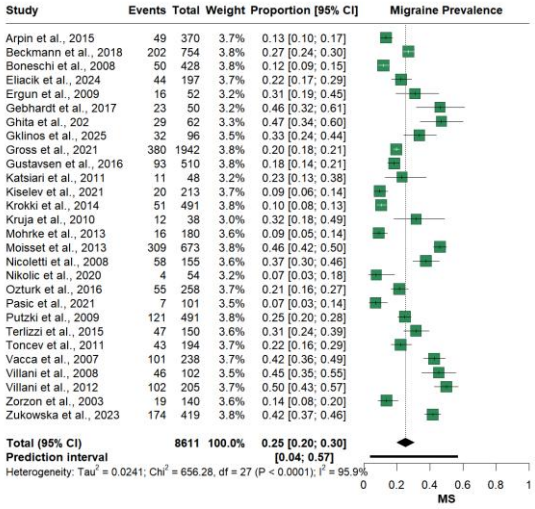


Figure 1: Forest Plot Showing Prevalence Of Migraine In Multiple Sclerosis Patients

Fig. 2

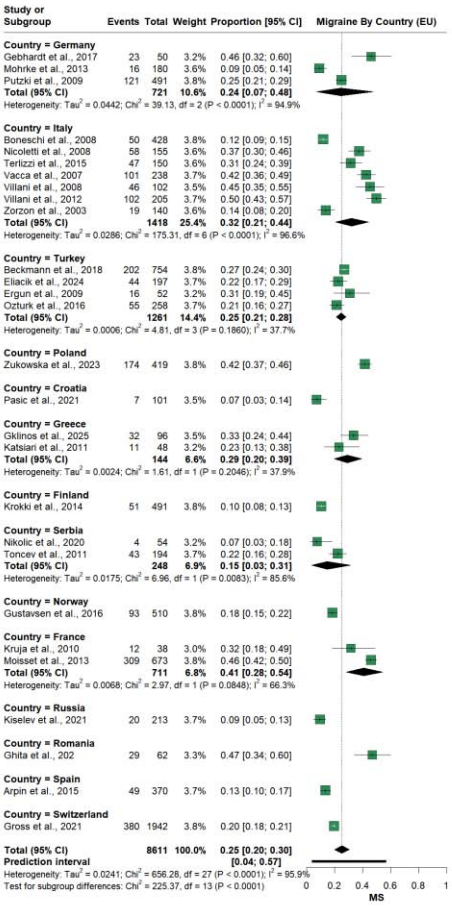


Figure 2: Subgroup Analysis By Country

Fig. 3

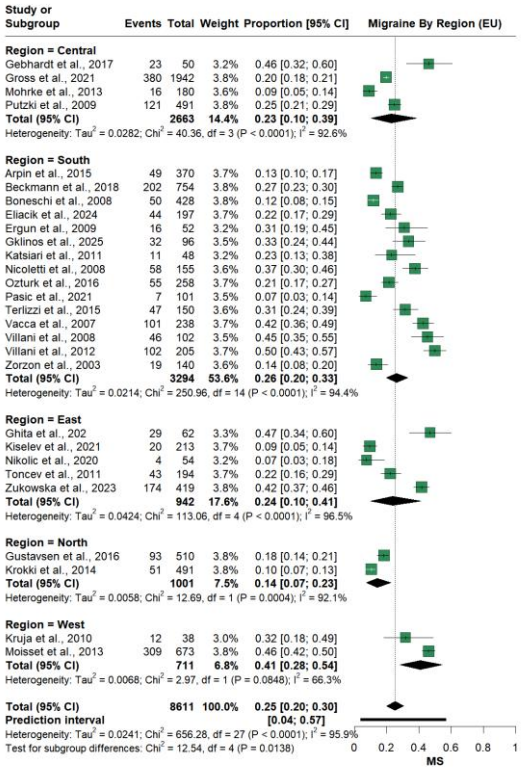


Figure 3: Subgroup Analysis By Region

P477

Three decades of migraine burden in Europe: Regional trends in disability-adjusted life years across Western, Central, and Eastern Europe

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[1]King Edward Medical University, Lahore, Pakistan

[2]Continental Medical College, Lahore, Pakistan

Objective: To quantify and compare three-decade trends in migraine-related disability-adjusted life years (DALYs) across Western, Central, and Eastern Europe using Global Burden of Disease (GBD) 2021 estimates.

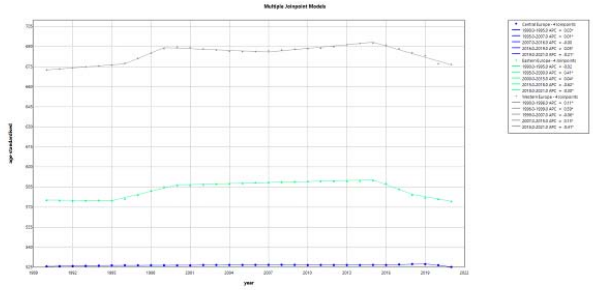
Methods: We extracted age-standardized DALYs for migraine from the Global Burden of Disease 2021 study for Western, Central, and Eastern Europe from 1990 to 2021. Trends were analyzed using Joinpoint regression to identify statistically significant changes in direction and magnitude, expressed as annual percentage change (APC) with 95% confidence intervals. Average annual percentage change (AAPC) was calculated to assess overall regional trends across the study period. Analyses were stratified by region.

Results: In Central Europe, DALYs rose modestly from 1990 to 2007 (APC up to 2.6%, p<0.001), remained stable until 2016, increased sharply between 2016 and 2019 (APC 5.3%, p=0.026), and then declined steeply after 2019 (APC - 21.2%, p<0.001), with no significant long-term trend (AAPC -0.24%, p=0.40). In Eastern

Europe, DALYs increased substantially from 1995 to 2015 (APC 41.0% to 4.3%, both p<0.001), followed by marked declines after 2015 (APC -61.6% and -30.4%, both p<0.001), yielding an overall stable longterm pattern (AAPC -0.55%, p=0.45). In Western Europe, DALYs rose sharply in the 1990s (APC upto 59.1%, p<0.001), decreased from 1999 to 2007 (APC -6.0%, p= 0.003), rose again between 2007 and 2015 (APC 13.3%, p<0.001), and then declined substantially after 2015 (APC -41.0%, p<0.001), with no significant overall change (AAPC 1.8%, p=0.23).

Conclusion: Migraine remains a stable yet substantial source of disability across Europe. These trends call for improved diagnosis and equitable access to effective treatment.

Fig. 1



P479

The role of unavoidable triggers in the chronification of migraine among teachers

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[2]Azerbaijan State Advanced Training Institute for Doctors named after A.Aliyev, Baku, Azerbaijan

Objective: Teachers and academic staff are one of the most common groups of people whose occupations have been observed in specialized neurological clinic. Their profession is accompanied by significant mental and emotional stress, long hours in front of the screen, lack of proper rest, and a low possibility of avoiding the already known migraine triggers. This research was conducted to assess the clinical features and work-related factors that lead to chronic migraine and medication overuse headache (MOH) in teachers.

Methods: We retrospectively reviewed the medical records of 502 patients who visited our headache clinic from January 1 to October 5, 2025. Out of these, 480 (95.6%) were diagnosed with migraine according to ICHD-3 criteria, and 440 (88%) were chronic migraine patients with medication overuse. A subgroup of 152 patients (30.3%) were teachers or lecturers. The study analyzed demographics, headache type, medication use, and trigger exposure.

Results: Majority of the teachers suffered from chronic migraine with medication overuse. The main triggers were found to be sleep deprivation, prolonged screen time, emotional stress, noise exposure, irregular meals, and physical inactivity. Most of them knew their triggers; however, they mentioned that they could not manage them because of too much work, preparing lessons, giving after-school tutoring, and domestic chores that went on late into the night.

Conclusion: Teachers are an occupational group at great risk for their episodic migraine to progress to chronic migraine and for them to develop a medication overuse headache. The fact that they are constantly exposed to certain professional stressors which they cannot avoid, makes it very difficult for them to control their triggers and as a result, they suffer from headaches more frequently. An educational program and changes in the work environment would not only have a positive effect on the proper management of migraine but would also improve the general health of this population.

P480

The long-term effectiveness and tolerability of rimegepant administered as needed in the acute treatment of migraine among chinese adults in a real-world study

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[2]Ruijin-Hainan hospital Shanghai Affiliated Jiao Tong University School of Medicine (Hainan Boao Research Hospotal), Boao, China

Objective: This analysis aimed to describe patterns in monthly migraine days (MMDs) and monthly tablet utilization, as well as tolerability in patients treated as needed (PRN) with rimegepant over 12 months (4 weeks as a month).

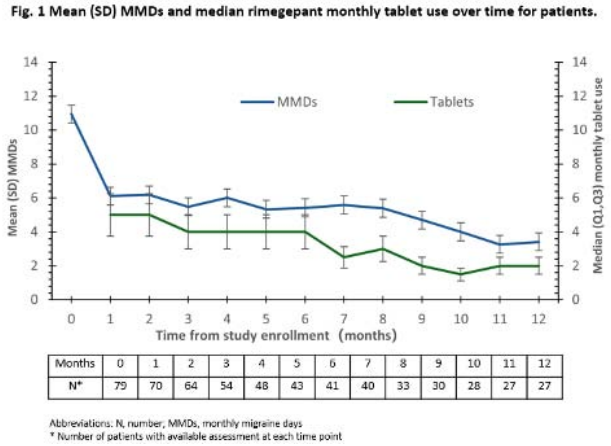
Methods: Eligible subjects were migraine adults who used rimegepant PRN for acute migraine treatment in a single-arm, prospective, real-world study (NCT05709106). Patients were eligible for inclusion in this analysis if, during follow-up months with non-missing data, at least 50% of those months satisfied the following criterion: the number of days on which rimegepant was used was equal to or greater than 50% of the MMDs. Those who treated with CGRP monoclonal antibodies or abotulinumtoxinA during the 12-month follow-up were excluded from this analysis. MMDs and monthly tablet utilization were calculated and described over 12 months.

Results: 79 patients were included in the analysis. Patients were predominantly female (n=55, 69.6%) with a mean (SD) age of 41.9 (11.4) years. The overall mean (SD) MMDs were 10.9 (8.1) at baseline and

decreased to 3.4 (4.0) by month 12 (**Figure 1**). Additionally, the median (Q1, Q3) number of rimegepant tablets administered per month declined from 5.0 (2.0, 9.0) at month 1 to 2.0 (0, 3.0) by month 12 (**Figure 1**). To exclude the effects of other analgesics, the usage of acute and preventive medications was also analyzed. Overall, the percentages of patients using any acute medications (from 91.1% at baseline to 29.6% at month 12) or preventive medications (from 20.3% at baseline to 3.7% at month 12) were both decreased from baseline over the 12 months, respectively. Treatment-emergent adverse events were reported in 20 (25.3%) patients.

Conclusion: Both MMDs and monthly tablet utilization showed a trend of reduction during one-year of follow-up for the acute treatment of migraine attacks with rimegepant on a PRN basis. Rimegepant also demonstrated a favorable safety profile and was well-tolerated.

Fig. 1



P481

Prevalence of migraine in fibromyalgia patients: A systematic review and meta-analysis

S. Arsalan Wasti[1], *M. Azaan Khan*[1], *F. Gul Awan*[1], *M. Azfar*[1], *M. Muddassar*[1], *J. Ajmal*[1]

[1]King Edward Medical University, Lahore, Pakistan

Objective: This review aims to estimate the prevalence of migraine in fibromyalgia patients.

Methods: PubMed, Scopus, Embase, Web of Science and grey literature were searched from inception to September 2025 for studies reporting prevalence of migraine in fibromyalgia patients. Analyses were conducted using R software, version 5.4.1. Prevalences were pooled as proportions, and stabilized through Freeman-Tukey double-arcsine transformations. Random-effects model was used for pooling. Prevalences were reported with 95% confidence intervals (CI).

Results: Twelve studies were included. A total of 55879 participants were analyzed. Pooled migraine prevalence in fibromyalgia patients was 36% (95% CI 24% to 49%). Subgroup analysis by country revealed marked variations, with country-wise prevalences ranging from 3% to 59%. Subgrouping by continent also revealed major differences in migraine burden (Asia: 15%, Europe: 41%, North America: 41%, Oceania: 59%, South America: 26%). One study reported data for migraine prevalence in both sexes and noted a two-fold higher burden of migraine in female fibromyalgia patients than in males.

Conclusion: This is the first meta-analysis to estimate migraine burden in fibromyalgia patients, demonstrating variations in migraine burden across regions and biologic sexes. Almost 2 in 5 fibromyalgia patients experienced migraine, highlighting significant burden and calling for adequate migraine care in this vulnerable population.

Fig. 1

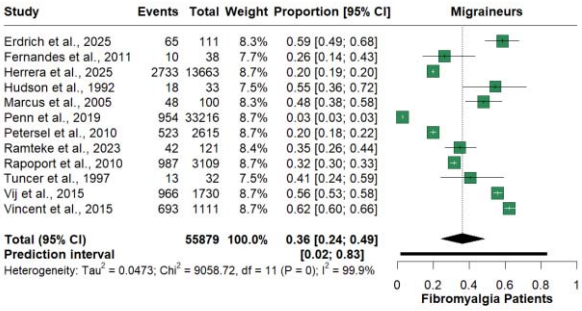


Figure 1: Pooled Migraine Prevalence In Fibromyalgia Patients

Fig. 2

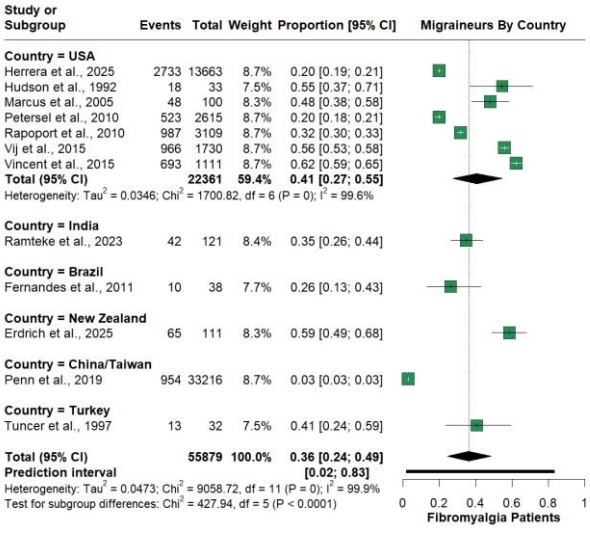


Figure 2: Migraine Prevalence In Fibromyalgia Patients By Country

Fig. 3

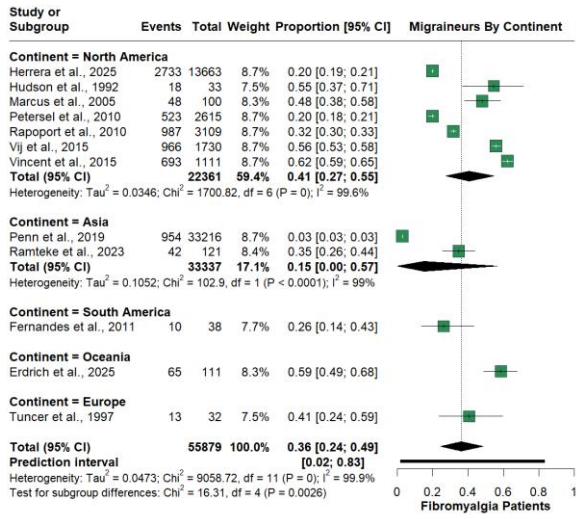


Figure 3: Migraine Prevalence In Fibromyalgia Patients By Continent

P482

Effectiveness of rimegepant in vestibular migraine: A prospective observational cohort study

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[2]The Second Affiliated Hospital Zhejiang University, The Department of Neurology, Hang Zhou, China

Objective: Vestibular migraine (VM) represents the second most common cause of episodic vertigo worldwide, yet therapeutic options remain scarce. This study aims to observe the clinical effectiveness of rimegepant in patients with VM.

Methods: Thirty-three individuals with VM were enrolled in a single-center, prospective, observational cohort study. All patient gave their informed consent to publish their details in an open access journal. Over a 4-week follow-up, mean frequencies of vertigo/dizziness and headache, as well as scores from the Dizziness Handicap Inventory (DHI), Generalized Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9), Headache Impact Test-6 (HIT-6), Vertigo Symptom Scale–Short Form (VSS-SF), and Activities-specific Balance Confidence Scale (ABC), were compared before and after rimegepant administration.

Results: At baseline, participants exhibited a high symptom burden, with elevated scores on the DHI, VSS-SF, GAD-7, PHQ-9, and HIT-6, and lower scores on the ABC. After rimegepant treatment, there was a substantial reduction in the monthly frequency of headache and vertigo/dizziness days (difference: headache: -5.88; vertigo/dizziness: -8.48). Notably, these improvements were already apparent at 2 weeks, indicating early onset of efficacy. Additionally, rimegepant treatment led to significant improvements in vestibular function (DHI: difference: -27.33; VSS-SF: difference: -6.21), psychological status (GAD-7: difference: -3.33; PHQ-9: difference: -3.33), and quality of life (HIT-6: difference: -11.27; ABC: difference: 19.98).

Conclusion: Rimegepant alleviates vestibular symptoms, reduces psychological distress, and improves quality of life in VM patients, with therapeutic effects emerging as early as 2 weeks.

Fig. 1

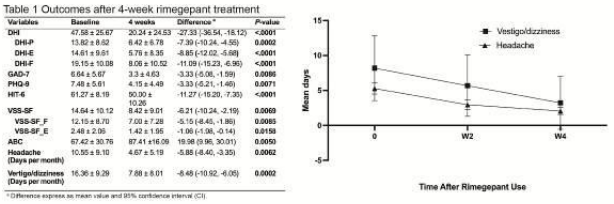


Table 1 Outcomes after 4-week rimegepant treatment

Variables	Baseline	4 weeks	Difference*	P-value
DHI	47.58 ± 25.67	20.24 ± 24.53	-27.33 (-36.54, -18.12)	<.0001
DHI-P	13.82 ± 8.62	6.42 ± 6.78	-7.39 (-10.24, -4.55)	0.0002
DHI-E	14.61 ± 9.61	5.79 ± 8.35	-8.85 (-12.02, -5.68)	<.0001
DHI-F	19.15 ± 10.08	8.06 ± 10.52	-11.09 (-15.23, -6.96)	<.0001
GAD-7	6.64 ± 5.67	3.3 ± 4.63	-3.33 (-5.08, -1.59)	0.0006
PHQ-9	7.48 ± 5.61	4.15 ± 4.49	-3.33 (-5.21, -1.46)	0.0071
HIT-6	61.27 ± 8.19	50.00 ± 10.26	-11.27 (-15.29, -7.35)	<.0001
VSS-SF	14.64 ± 10.12	8.42 ± 9.01	-6.21 (-10.24, -2.19)	0.0069
VSS-SF_F	12.15 ± 8.70	7.00 ± 7.28	-5.15 (-8.48, -1.86)	0.0085
VSS-SF_E	2.48 ± 2.06	1.42 ± 1.95	-1.06 (-1.98, -0.14)	0.0158
ABC	67.42 ± 30.78	87.41 ± 16.09	19.98 (9.96, 30.01)	0.0050
Headache (Days per month)	10.55 ± 5.10	4.67 ± 5.19	-5.88 (-8.40, -3.35)	0.0062
Vertigo/dizziness (Days per month)	16.36 ± 9.29	7.88 ± 8.01	-8.48 (-10.92, -6.05)	0.0002

* Difference express as mean value and 95% confidence interval (CI)

P483

What is the consistency of response to rimegepant at a group level in the acute treatment of migraine in UK adult patients? Protocol for a real-world, patient-centred study

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[1]Pfizer, Ltd., Tadworth, United Kingdom

[2]Pfizer R&D UK Ltd., Tadworth, United Kingdom

[3]Pfizer, Inc., New York, NY, United States

[4]Vitaccess Ltd, London, United Kingdom

[5]Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom

Objective: Rimegepant is the only small-molecule calcitonin gene-related peptide (CGRP) antagonist approved for acute migraine treatment and prevention of episodic migraine in adults. Safety and efficacy have been shown in clinical trials. Real-world effectiveness across multiple attacks over 4 weeks has been assessed in the US CONFIDENCE study (NCT06467370). The objective of CORRELATE-UK (NCT06898047) is to evaluate real-world effectiveness of rimegepant for acute treatment of migraine across multiple attacks [AJ1] over 12 weeks in a UK population.

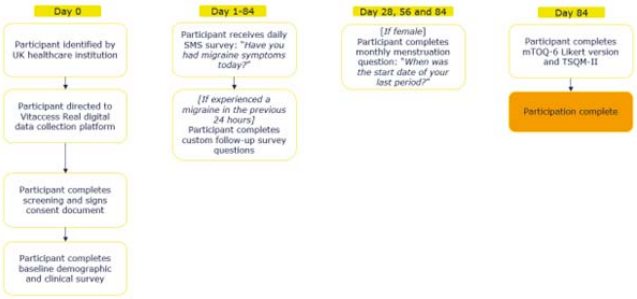
Methods: Figure 1 shows the study design. UK adults (n=250) with episodic/chronic migraine, newly prescribed rimegepant for acute treatment (preventives except rimegepant allowed, >4 attacks in 28 days pre-enrolment), will be recruited via 9 UK healthcare sites. Participants will enroll via the Vitaccess Real digital platform and complete a baseline demographic/clinical survey. For 12 weeks,

they will receive a daily SMS survey on migraine symptoms in the past 24 hours (96-hour response window). Rimegepant use and other follow-up data will be collected via custom surveys within the platform. At study end, participants will complete the 6-item Migraine Treatment Optimization Questionnaire (mTOQ-6; Likert) and the Treatment Satisfaction Questionnaire for Medication II (TSQM-II) via the platform. The primary endpoint is time to meaningful pain relief (MPR) after a single rimegepant dose, defined as participant-reported pain improvement that made a meaningful difference. Key secondary endpoints: time to improvement in non-pain symptoms and return to normal activities. Consistency of response across multiple attacks will be evaluated.

Results: Recruitment begins Autumn 2025. Results will be shared once available.

Conclusion: CORRELATE-UK will assess real-world effectiveness of rimegepant for acute migraine treatment across multiple attacks over 12 weeks in a UK population, including in those on preventive therapy and with chronic migraine.

Fig. 1



P484

Burden of migraine in rhinitis patients: A systematic review and meta-analysis

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Objective: This review aims to estimate the burden of migraine in rhinitis patients.

Methods: We searched PubMed, Scopus, Embase, Web of Science and Google Scholar from inception to September 2025 for studies reporting the prevalence of migraine in rhinitis patients. Analyses were performed in R/RStudio (v2025.05.1+513) and prevalences were pooled as proportions, stabilized with double-arcsine transformations.

Results: Twelve studies were included, totalling 1121835 participants. Pooled migraine prevalence in rhinitis patients was calculated as 21% (95% CI 11% to 34%). Subgroup analysis by continent showed non-significant between-subgroup differences (Asia: 19%, Europe: 22%, North America: 25%).

Conclusion: Approximately one in five rhinitis patients were estimated to experience migraine. Recognition of this overlap may improve diagnosis, reduce under-treatment, and guide strategies for integrated care.

Fig. 1

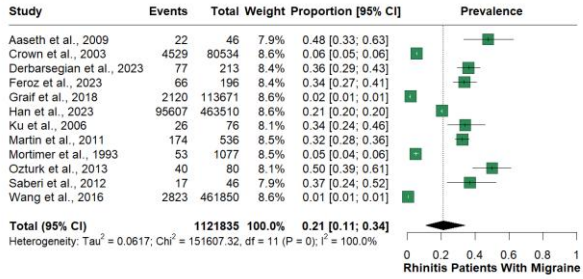


Figure 1: Forest Plot Showing Migraine Prevalence In Rhinitis Patients

Fig. 2

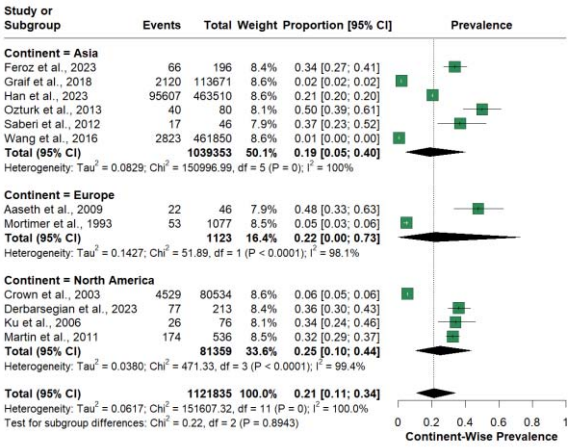


Figure 2: Subgroup Analysis By Continent

P486

Migraine epidemiology in Taiwan: Age-specific burden and impact of the COVID-19 pandemic

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Objective: This study evaluates migraine prevalence and local epidemiology in individuals aged ≥6 in Taiwan, addressing limited data in early age and COVID-19's impact on health-seeking behavior.

Methods: This cohort study used population-based claims data from the Taiwan National Health Insurance Research Database, covering 99.9% of the population. Individuals aged ≥6 years from 2018 to 2023 were identified as having migraine if they met

any of the following criteria: ≥2 outpatient visits or ≥1 inpatient visit with a migraine diagnosis; treatment with ergot alkaloids for headache; or use of migraine-specific medications, including triptans or CGRP monoclonal antibody (mAb). Chronic migraine (CM) was defined by ICD-10 code G43.7X, or CGRP mAb use, or high-dose onabotulinumtoxin A; others were classified as episodic migraine (EM). The COVID-19 period was defined as 2021–2022, with its impact assessed using a validation approach based on Meniere"s disease. Cardiovascular risk factors (hypertension, hyperlipidemia, diabetes, obesity, smoking) were identified using ATC codes.

Results: A total of 1,010,125 patients were identified as having migraine. Annual prevalence increased from 1,013.2 to 1,188.9 per 100,000 between 2018 and 2023. The overall prevalence during 2018–2023 was 4,223.9 per 100,000. Prevalence was 678.7 per 100,000 for ages 6–12 and 2,648.6 per 100,000 for ages 13–17. No apparent changes in health-seeking behavior were observed during the COVID-19 pandemic. Among all patients, 23.1% had at least one cardiovascular risk factor. EM accounted for 88.2% of all patients, with the highest prevalence in the 30–40 age group; CM accounted for 11.8% of all patients, peaking in the 40–50 age group.

Conclusion: Migraine prevalence in Taiwan has increased in recent years, especially after COVID-19, with a noticeable concern on individuals aged 6–18, while health-seeking behaviors remained unchanged during the pandemic.

P487

Migraine treatment outcomes with rimegepant in rimegepant-naive patients: A real-world, multi-center, prospective, observational study

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Objective: This analysis aimed to explore the real-world effectiveness and tolerability of rimegepant for acute migraine therapy in rimegepant-naive patients defined as those who had never used Rimegepant before joining the study.

Methods: A single arm, multicenter, prospective, observational registry (NCT06439628) aimed to recruit 3,000 adults who were prescribed rimegepant for acute treatment of migraine across 70 sites in China. Treatment history was collected at baseline. Patient-reported outcomes, including 1.Most severe pain after taking rimegepant, 2.Time to onset time of meaningful pain relief (MPR), 3. Time to onset for meaningful relief from associated symptoms (MRA), and 4. Patient satisfaction with pain relief and return to normal function (RNF), were collected via a remote digital platform (encouraged within 48 hours of treatment). Follow-up is planned for 12 months. This report focused on outcomes in rimegepant-naive subgroup at 3 months.

Results: A total of 2,141 participants were included in this subgroup analysis. The majority (81.4%) were female, with a mean (SD) age of 38.5 (10.7) years, and the mean (SD) monthly migraine days in the past three months was 7.0 (7.5). After taking rimegepant, the median (Q1, Q3) visual analog scale (VAS) score of most severe pain was 3.0 (2.0, 5.0). The median (Q1, Q3) times to MPR and MRA were 60 (30, 120) minutes and 30 (0, 60) minutes, respectively. Additionally, 85.8% of participants reported satisfaction (extremely/very/somewhat) with pain relief, and 86.1% reported satisfaction with RNF. A total of 6 (0.28%) adverse events (AEs) were reported during rimegepant treatment, with no serious AEs.

Conclusion: Subgroup analysis demonstrated that rimegepant is effective and well-tolerated for acute migraine therapy in rimegepant-naive patients.

P488

Changes in acute treatment effectiveness in migraine patients switching from standard of care to rimegepant: Findings from a real-world study

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Objective: This analysis aimed to explore acute treatment effectiveness changes among rimegepant-naive migraine patients switching from standard of care (SOC) to rimegepant.

Methods: A single-arm, multicenter, prospective, observational registry (NCT06439628) aimed to recruit 3,000 adults prescribed rimegepant for acute migraine treatment at 70 Chinese sites. Baseline data included treatment history, specifically analgesics and effectiveness for the most recent migraine attack (RMA) before enrollment. Patient-reported outcomes, including 1.worst pain after rimegepant, 2. Time to meaningful pain relief (MPR), 3. Time to meaningful relief from associated symptoms (MRA), and 4. Satisfaction with pain relief and return to normal function (RNF), were collected via a digital platform (encouraged within 48 hours of treatment). Follow-up is for 12 months. This report compares effectiveness

between SOC-treated RMAs and first recorded rimegepant-treated attacks at 3 months.

Results: A total of 1,696 participants were included. Most (81.4%) were female, and the mean (SD) monthly migraine days in the past three months was 7.5 (7.8). The most severe pain level after taking rimegepant was lower than that of SOC-treated RMAs *(p < 0.0001)*. Onset time of MPR and MRA after taking rimegepant were also shorter than those of SOC-treated RMAs *(p < 0.0001)*. Significantly more patients reported satisfaction (extremely/very/somewhat) with pain relief and RNF after taking rimegepant than those with SOC-treated RMAs *(p < 0.0001)* **(Table 1)**.

Conclusion: In this real-world study, migraineurs switching from SOC to rimegepant reported more effective pain relief, more rapid relief of pain and associated symptoms, and greater patient satisfaction with pain relief and RNF.

Fig. 1

Table 1. Comparison of treatment outcomes between RMAs treated with SOC ~~medications~~ and attacks treated with rimegepant (N=1,696)

Outcomes	SOC	Rimegepant	p value*
VAS score of the most severe pain after taking medicine, median (Q1, Q3)	6.0 (4.0, 8.0)	4.0 (2.0, 5.0)	< 0.0001
Onset time of MPR, median (Q1, Q3), mins	120.0 (60.0, 180.0)	60.0 (30.0, 120.0)	< 0.0001
Onset time of MRA, median (Q1, Q3), mins	65.5 (30.0, 150.0)	30.0 (0.0, 75.0)	< 0.0001
Satisfaction with pain relief, n (%)	1051(62.0%)	1440(84.9%)	< 0.0001
Satisfaction with RNF, n (%)	1070(63.1%)	1449 (85.4%)	< 0.0001

Abbreviations: n, number; RMAs, recent migraine attacks; SOC, standard of care; MPR, meaningful pain relief; MRA, meaningful relief from associated symptoms; RNF, return to normal function; min, minutes

* Statistical analysis was performed using Wilcoxon signed-rank test (for continuous variables like MPR onset time) or McNemar's test (for categorical variables like satisfaction rate) to compare outcomes between SOC-treated RMAs and rimegepant-treated attacks in the same participants.

P489

Efficacy of rimegepant in treating acute vertigo attacks in vestibular migraine: A retrospective open-label study

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Objective: To test the efficacy of Rimegepant (RIM) in treating acute vertigo attacks in patients with vestibular migraine (VM) or probable vestibular migraine (pVM).

Methods: This retrospective, single-centric, open-label investigation was conducted starting March 2025. Adults with VM or pVM were included. At the time of RIM prescription, patients did not receive any other acute therapy for vertigo. RIM is the only acute therapy for vertigo attacks.The intensity of attacks was assessed by a 10-score scale (with "1-3" rated mild , "4-6" moderate and "7-10" severe). RIM orally disintegrating tablet (ODT) was administered as a single 75 mg with the advice to take the drug at the onset of moderate to severe vertigo attack.Primary outcome was the percentage of attacks with reduction in vertigo from moderate or severe to absent or mild at 2 hours. Secondary outcomes were the percentage of attacks with reduction in headache and associated symptoms at 2 hours; and rates of serious adverse effects and discontinuation due to side effects.

Results: Of 55 total participants, 38 (69.1%) (mean [SD] age, 49.4 [14.2] years; 89.5% were women) with active illness treated 42 vertigo attacks (out of 47 total attacks). The median vertigo intensity scores was 7 (IQR: 7-8). At 2 hours, 32/42(76.2%) of attacks reported reduction in vertigo from moderate or severe to absent or mild at 2 hours. Among all attacks, 6/7(85.7%) reported reduction in tinnitus or ear pressure from moderate or severe to absent or mild at 2 hours, and 8/12(66.7%) reported such reduction in headache at 2 hours. 2/38(5.3%) discontinued RIM treatment due to worsening dizziness.

Conclusion: These findings suggest that RIM may be effective in reducing vertigo and associated symptoms in patients with VM or pVM. However, confirmation through large-scale, randomized controlled trials is warranted.

Fig. 1

Table 1. Baseline Physician-Reported Demographics and Clinical Characteristics of Patients

Variables	All RIM-used attacks	Ineffective	Effective
Age, n	42	10	32
Mean (SD), y	48.86 (14.50)	51.60 (13.40)	48.00 (14.92)
BMI score, Median [IQR]	23.63 [20.20, 24.44]	23.71 [22.48, 23.94]	23.27 [19.90, 24.74]
BMI < 25	30 (81.1%)	9 (100.0%)	21 (75.0%)
BMI 25-<30	7 (18.9%)	0 (0.0%)	7 (25.0%)
Ascens Sleep Score, n	42	10	32
Median [IQR]	3.50 [1.00, 7.00]	1.50 [1.00, 3.75]	5.00 [0.75, 7.25]
Migraine related variables			
Migraine-related headache days per month over the last 3 months, n	40	10	30
Median [IQR]	16.50 [6.00, 42.00]	12.00 [7.75, 51.00]	22.00 [6.00, 36.00]
With nausea or vomiting, n (%)	42	10	32
Yes	26 (61.9)	8 (80.0)	18 (56.3)
No	16 (38.1)	2 (20.0)	14 (43.8)
Patients with family history of dizziness or vertigo, n (%)	42	10	32
Yes	8 (19.0)	1 (10.0)	7 (21.9)
No	34 (81.0)	9 (90.0)	25 (78.1)

Abbreviations: IQR, the interquartile range; SD, standard deviation; BMI, body mass index;

P490

Efficacy, safety, and tolerability of atogepant in migraine patients from the UAE

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Objective: Atogepant is a novel oral calcitonin gene-related peptide receptor antagonist approved for migraine prevention, but evidence from the MENA region remains limited. We evaluated its efficacy and safety in chronic and episodic migraine patients in the United Arab Emirates.

Methods: This is a retrospective study of patients aged ≥18 years with chronic or episodic migraine who received atogepant for at least six months. Clinical

data were extracted from medical records at the American Center for Psychiatry and Neurology, Abu Dhabi. Baseline Monthly Migraine Days (MMD) were compared with a minimum follow-up documented MMD every two months. Safety was evaluated via descriptive analysis of reported adverse events.

Results: 86 patients were identified who were prescribed atogepant60 met the inclusion criteria and were analyzed. 23 (38%) had chronic migraine, whereas 37 (62%) were diagnosed with episodic migraine. The majority were female (85%) and Emirati nationals (70%). Out of 60, 6 patients completed 6 months, between 6-9-8 months 6 more patients completed treatment. By 12 months, 19 patients while the remaining 29 remained on treatment for over 12 months where 2 patients continued atogepant for 23 months. The baseline mean MMD for all patients was 12 (SD 8.1), which decreased to 4 (SD 5.2) at the most recent visit. Overall, 72% of patients achieved ≥50% reduction in MMD, 18% had less than 50% reduction, and 10% experienced no change. Paired sample t-test indicated a significant improvement, t (59) =9.39, ($p<0.001$). Regarding safety, 12 out of 60 (20%) reported adverse events, most commonly constipation (50%) and nausea (25%). Ten patients who reported AEs continued treatment, while two discontinued at the 6th (constipation and fatigue) and the 9th (constipation and nausea) visits due to the side effects.

Conclusion: Atogepant effectively reduced monthly migraine days in both chronic and episodic migraine patients and was generally safe and well-tolerated among patients in the UAE.

P491

Risk of hypertension with Atogepant use in migraine patients in the UAE

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Objective: Atogepant is an oral CGRP receptor antagonist used for migraine prevention. Previous studies have demonstrated potential risk of hypertension among some CGRP antagonist users (mAbs). However, it is not known if that risk would also apply for gepants users. This study evaluated the effect of atogepant on systolic and diastolic blood pressure in migraine patients in the UAE.

Methods: A retrospective study included adults ≥18 years with chronic or episodic migraine who received atogepant for at least 6 months. Data were extracted from medical records at the American Center for Psychiatry and Neurology, Abu Dhabi. We included only patients with recorded systolic and diastolic blood pressure at baseline and at least once every three months at their follow up vitits. We excluded patients with prior use of mAbs in the past 6 months prior to initiating treatment. Paired t-tests were used to assess changes from baseline.

Results: 86 patients were identified and 70 participants met the inclusion criteria; 82.9% were female, and 6% had a prior history of hypertension prior to initiating treatment.. Mean systolic blood pressure changed slightly from 121.7 ± 11.4 mmHg at baseline to 120.1 ± 12.2 mmHg at 6 months, while mean diastolic blood pressure changed from 79.0 ± 8.2 mmHg at baseline to 78.5 ± 7.8 mmHg at 6 months. Changes at three and twelve months were similarly minimal. Paired t-tests showed no statistically significant differences in systolic or diastolic blood pressure at any follow-up visit ($p > 0.05$).

Conclusion: Atogepant use in migraine patients was not associated with any significant changes in systolic or diastolic blood pressure, indicating no apparent risk of hypertension in this population.

P492

Autonomic nervous system function in exercise intolerant patients with post traumatic headache

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Objective: To investigate if exercise intolerance in patients with post traumatic headache (PTH) was characterized by abnormal autonomic nervous system (ANS) function.

Methods: Participants 18-60 years from the Trondheim Post Concussion Symptom (PCS) study with PTH and exercise intolerance, n =19, and controls matched on age and sex, n=24, were included. Participants with PTH had conducted orthostatic tilt test, deep breathing and Valsalva maneuver to measure function of the ANS, and Buffalo Concussion Treadmill Test to assess exercise intolerance. ANS function in controls was also tested with orthostatic tilt test, deep breathing and Valsalva maneuver.

Results: Participants with PTH and exercise intolerance did not exhibit statistically significant differences on measurements of the ANS compared to healthy controls. There were trends towards longer Valsalva recovery time for systolic blood pressure (1.8 vs 1.4 seconds, $p=0.065$) in the PTH group. ANS assessments revealed that one patient demonstrated findings characteristic of postural orthostatic tachycardia syndrome (POTS).

Conclusion: Although group differences in ANS measurements between participants with PTH and controls did not reach statistical significance, observable trends suggest possibly altered

sympathetic function (i.e. prolonged Valsalva recovery time). However, we found no trends towards parasympathetic dysfunction. Future studies with larger samples are needed to investigate if ANS function may be causally related to some symptoms in exercise intolerant PTH patients.

P493

Response and super-response to atogepant high-frequency episodic and chronic migraine at 24-week: Results from the GIANT II Study

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Objective: To evaluate the efficacy, safety, and tolerability of atogepant 60 mg over 24 weeks in patients with high-frequency episodic migraine (HFEM; 8–14 days/month) or chronic migraine (CM), with a focus on responder (≥50% reduction) and super-responder (≥75% reduction) rates.

Methods: GIANT II is a prospective, multicenter (n=16), real-world study within the Italian Migraine Registry (I-GRAINE). Consecutive adults with HFEM or CM who had failed ≥3 prior preventive treatments (AIFA criteria) received atogepant 60 mg/day for ≥24 months. Co-primary endpoints: responders and super-responder rates at weeks 21–24 vs baseline. Secondary endpoints: change in monthly migraine days (MMD for HFEM) or monthly headache days (MHD for CM), 100% response rate, acute medication intake (MAI), pain intensity (NRS), disability (HIT-6, MIDAS), interictal burden (MIBS-4), and treatment satisfaction (PGIC). Adverse events were collected.

Results: A total of 233 patients received ≥1 dose (safety population), 156 completed ≥24 weeks (effectiveness population). Overall, 39% had previously failed anti-CGRP mAbs. At week 24, 76.9% were responders, 45.5% super-responders, and 5.1% achieved 100% response (HFEM: 89.1%, 45.3%, 9.4%; CM: 68.5%, 45.3%, 2.2%). Mean changes from baseline (all $p<0.001$) were: MMD –10.0, MHD – 10.2, MAI – 12.1, NRS –3.1, HIT-6 –15.8, MIDAS –66.6, MIBS-4 -4.60. PGIC documented high satisfaction (much/very much improved: 88%). Among prior mAb non-responders, response rates were 70.7% (≥50%), 39.7% (≥75%), and 1.7% (100%), with consistent improvements across all endpoints. Adverse events occurred in 12.4% (mainly constipation and nausea); 2.1% discontinued.

Conclusion: Atogepant showed marked 6-month effectiveness in highly refractory patients, with three-quarters achieving response, nearly half super-response, and ~5% absolute response. Notably, most prior anti-CGRP mAb non-responders benefited (~71% responders; ~40% super-responders). The treatment was well tolerated and safe.

P494

Switching patterns of CGRP monoclonal antibodies in migraine: A service evaluation

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Objective: Monoclonal antibodies (mAbs) targeting calcitonin gene-related peptide have been used for migraine prevention for five years. We evaluated switching patterns in patients receiving mAbs.

Methods: Efficacy data of patients receiving mAbs at King"s College Hospital, London were collected from patient records as part of a service evaluation. Data were summarised as percentages or medians with interquartile ranges (IQR). Associations between categorical variables were assessed using Pearson Chi-Square tests. Response was defined as >30% improvement.

Results: In 223 patients (median age 48 years, IQR 35–57; 82% female), diagnoses included chronic migraine (62%), episodic migraine (29%), and new daily persistent headache with migraine phenotype (9%). Most (n=179, 80%) received one mAb; 36 (16%) received two, 8 (4%) received three.

The first used mAb was discontinued by 53 (23.8%): 21 (9.4%) for lack of response, 21 (9.4%) for loss of efficacy, and 11 (4.9%) for AEs. Cause of discontinuation was not associated with the type of mAb ($\chi^2 = 4.94$, df = 2, $P = 0.09$). Median treatment duration before losing efficacy was 123 weeks (IQR

92–165). Constipation (4, 36%) and skin reactions (3, 27%) were the most common AEs leading to discontinuation.
Efficacy data was unavailable for 4 out of 44 patients who received a second mAb due to short follow-up. Treatment was effective in 26 (65%), while 9 (22.5%) discontinued for lack of response, 3 (7.5%) for loss of efficacy, and 2 (5%) for AEs. A third mAb was used in 8 patients and was effective in 6 (75%), with 2 losing efficacy.
Of 13 patients who stopped the first mAb for non-response, 6 (46.2%) responded to the second. Among 19 who stopped due to loss of efficacy, 12 (63.2%) had ongoing benefit, and 2 (10.5%) lost efficacy.
Conclusion: Lack of response or loss of efficacy were the commonest causes for first mAb discontinuation. A notable proportion of initial non-responders benefited from switching to an alternative mAb.

P495

Does Fibromyalgia improve with CGRP targeting therapy?

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Objective: Previous data has shown that certain migraine co-morbidities, such as vertigo and mood disturbance, can improve with the use of CGRP monoclonal antibodies (CGRP mAbs), independent of headache improvement. Fibromyalgia has been reported as a common co-morbidity of migraine, however, there is a paucity of data exploring the effect of CGRP mAbs on symptoms.
Methods: A retrospective service evaluation was performed using clinic letters from the King"s College Hospital Tertiary headache service from January 2019-September 2025. Patients fulfilling International Classification of Headache Disorders-3 criteria for migraine who had received CGRP mAbs for at least 3 months, and who reported a diagnosis of fibromyalgia were included. Data on age, sex, specific CGRP mAb, patient-reported improvement in fibromyalgia symptoms and improvement in monthly headache days (MHD) were collected. A responder to CGRP mAb was defined as having at least 30% reduction in MHD from baseline at 3 months. Statistical analysis was performed using IBM SPSS Statistical Software (v 29).
Results: In total, 43 patients were identified, 38 (88%) women and 5 (12%) men. The median age was 47 years (IQR 36-53). The most commonly used CGRP monoclonal antibody was fremanezumab (63%), followed by erenumab (30%) and galcanezumab (7%). Improvement of fibromyalgia symptoms were reported by 12% (5/43), no improvement in 65% (28/43,) and worsening in 19% (8/43). There was no statistically significant difference in fibromyalgia symptom improvement between responders and non-responders (12% vs 25%, P = 0.20), and between fremanezumab, erenumab and galcanezumab use respectively (4% vs 23% vs 33%, P = 0.16).
Conclusion: Our study showed that a minority of patients with migraine and fibromyalgia will experience improvement in their fibromyalgia symptoms with CGRP mAbs. This may suggest the underlying biology of fibromyalgia in patients with migraine is largely driven by mechanisms other than CGRP.

P496

Reasons for discontinuing triptans among current users of rimegepant for the acute treatment of migraine in the CONFIDENCE study

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Objective: CONFIDENCE was a prospective observational study conducted via the Migraine Buddy® app to evaluate the real-world use of rimegepant for the acute treatment of migraine. Data from the CONFIDENCE study was used to better understand the reasons participants had previously discontinued ≥1 triptans.
Methods: The study enrolled US adults with 3–14 headache days in the prior 30 days and plans to use rimegepant in the subsequent 30 days. At enrolment, participants reported the number of triptans previously used and discontinued (lapsed), and the

reasons behind these lapses (all that applied from 9 items).

Results: Among the 416 participants in the CONFIDENCE study, 46 (11%) had no lapsed triptans, 132 (32%) had 1, 134 (32%) had 2, and 104 (25%) had ≥3. 103/370 (28%) participants with ≥1 lapsed triptan currently used another triptan. Among participants with responses, the most common reasons for prior triptan lapses were insufficient headache pain reduction (66%), side effects (50%), not working as well as it used to (28%), and not working quickly enough (28%). Insufficient pain reduction (59% of those with 1 lapsed triptan, 65% with 2, 77% with ≥3; linear by linear association p=0.004), not working as well as it used to (23%, 28%, 36%; p=0.033), and not working quickly enough (20%, 34%, 32%; p=0.034) were reasons generally reported by higher proportions of participants with higher numbers of lapsed triptans. Similar proportions of participants who had lapsed 1, 2, or ≥3 triptans reported side effects (45%, 54%, and 49%; p=0.481).

Conclusion: Insufficient pain reduction, side effects, not working as well as it used to, and not working quickly enough were common reasons for triptan lapse. Side effects were reported by ~50% of participants, irrespective of how many triptans had lapsed. The three other most common reasons were more frequently reported in participants with more lapsed triptans. NCT06467370

P497

Cycles in cluster headache – A prospective study with smart phone app

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Objective: Cluster headache (CH) is the most severe primary headache condition, leading to significant suffering and burden. CH is the prototype of a cyclic disorder, with circadian and circannual rhythmicity. Epidemiological data suggest a seasonal pattern in CH occurrence, with peaks around equinoxes, but different patterns have been described with a possible influence of latitude. Most epidemiologic studies on seasonal occurrence were retrospective. Studying cycles in CH such as circadian, circannual or multidien cycles provides further insight in the chronobiologic basis of the disorder. Aim of the study is to further characterize cycles in cluster headache in multinational cohorts distributed over the globe, using a smart phone app to prospectively register attacks.

Methods: MyClusters is a live app on the Apple and Google stores where users explicitly consent to sharing data for research. The App was launched on patients" initiative. All data is anonymized and aggregated in full compliance with General Data Protection Regulation (GDPR) regulations, ensuring both valuable research insights and absolute patient privacy.

Results: Currently as of 26/09/2025 there are 1241 users of the MyClusters app (Figure 1). 60% agreed to share their user data in anonymized form. This cohort includes 584 men (mean age 42.11±12.91) and 472 women (mean age 41.44+13.66). The mean disease duration is 9.9 years. 374 have episodic cluster headache and 647 chronic

Conclusion: We suggest that studying temporal dynamics with a smart phone app can yield important information on the chronobiology of the disease. Integrating patients" organizations in App and study design will ensure user friendliness and adherence.

P498

Development of the Sinus Headache Screener (SHS) for identification of non-rhinogenic facial pressure/pain

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Objective: Patients presenting with sinus headaches often have non-rhinogenic facial pain/pressure (NRFP). However, these patients are frequently misdiagnosed with sinusitis, leading to inappropriate antibiotic utilization and unnecessary surgical procedures. We introduce the Sinus Headache Screener (SHS), which was developed for the purpose of differentiating NRFP from sinusitis.

Methods: A question bank consisting of 89 items was developed through a qualitative interview process of 26 patients with midfacial pain or pressure. The question bank was then administered to a larger cohort of patients and a backward variable selection logistic model was utilized to identify the items that could best differentiate CRS from NRFP. The diagnosis of chronic rhinosinusitis (CRS) or NRFP was assigned based on imaging criteria. The predictive performance of the SHS was evaluated with the area under the receiver operating characteristic curve (AUROC).

Results: Of the 251 patients enrolled, 114 had CRS, and 137 had NRFP. Mean (SD) age was 50 (16), and 69.3% (n=174) were women. Eight items pertaining to symptom chronicity, triggers (weather changes, exercise), associated symptoms (motion sickness, loss of ability to smell, twitching on face, ear pain) and nasal mucus quality were selected and assigned a score. Using a total score of 1 or greater to identify

NRFP, the eight-item SHS had a sensitivity of 0.79 and specificity of 0.64, and positive/negative predictive values of 0.72/0.73. The AUROC was 0.822 (95% confidence interval 0.796, 0.902).
Conclusion: The SHS can serve as an effective screening tool for differentiating CRS from NRFP. Given the high incidence of NRFP in the general population, the SHS could significantly improve healthcare efficiency and cost.

P499

Cluster headache in the emergency department

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Objective: To analyse the treatment received and subsequent follow-up of patients diagnosed with cluster headache in the emergency department of a fourth level hospital.
Methods: We retrospectively reviewed 101 episodes with coding compatible with cluster headache, corresponding to 73 patients from July 2021 to May 2025.
Results: 71.2% were men compared to 28.8% women, with a mean age of 42.2 years (SD 12.97).
Most patients were not urgently evaluated by Neurology (87.1%) and a high percentage were not discharged to outpatient clinics (40.6%), while 9.9% were evaluated in outpatient clinics with an alternative diagnostic impression.
In relation to the treatment received in the emergency department, the most used was the combination of NSAIDs plus oxygen therapy in 21.8% of cases, followed by triptans plus oxygen therapy in 16.8% and isolated NSAIDs in 15.8%, followed by other more infrequent combinations. Anesthetic block was performed in 6.0%.
As for preventive treatment at discharge, no preventive treatment was initiated in 59.4%. In the remaining patients, the most used options were corticosteroids (12.9%), corticosteroids and verapamil (11.9%) and verapamil (6.9%).
The months with the most episodes were July, January and December with 13.9%, 11.9% and 10.9% of visits respectively, and those with the least were June and October with 4% and 5% respectively.
Conclusion: Most cases do not receive urgent care by Neurology, which results in worse therapeutic regimens, less use of preventive drugs at discharge and lack of subsequent follow-up.

P500

Validation of MIGRAGILE: A self-administered screening tool for the early detection of disabling migraine in primary care

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Objective: To develop and validate a self-administered screening tool (MIGRAGILE) for the early identification of disabling migraine, specifically high-frequency episodic migraine (HFEM) and chronic migraine (CM), in primary care.
Methods: MIGRAGILE was developed through a systematic literature review, application of ICHD-3 diagnostic criteria, and expert consensus using the Delphi method. Psychometric validation followed COSMIN guidelines, assessing sensitivity, specificity, area under the curve (AUC), test-retest reliability (intraclass correlation coefficient, ICC), and interrater reliability (Fleiss" Kappa). The tool was evaluated in a primary care population with headache, using neurologist-confirmed diagnosis as the gold standard.
Results: MIGRAGILE showed a sensitivity of 93.7%, specificity of 94.0%, and an AUC of 0.938. Test-retest reliability had an ICC of 0.89 (95% CI: 0.85–0.93), and interrater reliability was substantial (Fleiss" Kappa = 0.81). Compared to tools such as ID-Migraine™, CATI, and Structured Migraine Interview, MIGRAGILE demonstrated higher diagnostic performance and better suitability for digital self-administration.
Conclusion: MIGRAGILE is a valid, reliable, and clinically useful self-administered screening tool for early detection of disabling migraine in primary care. Its integration into nurse-led care models may improve diagnostic timeliness and therapeutic outcomes. Further research should explore its broader implementation.

P501

Trigeminal autonomic cephalalgias following unilateral dorsolateral medullary infarction: A case series

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Objective: Secondary trigeminal autonomic cephalalgias (TACs) have predominantly been associated with posterior fossa abnormalities, such as tumors and vascular malformations. However, TACs following brainstem ischemic lesions have rarely been reported. We aimed to determine the clinical characteristics and anatomical substrates for TACs after unilateral dorsolateral medullary infarction.

Methods: We identified four patients (3 men; mean age=58.2) who developed TACs after unilateral dorsolateral medullary infarction, fulfilling the diagnostic criteria of the International Classification of Headache Disorders (ICHD-3). All patients underwent detailed neurological examinations and neuroimaging including diffusion-weighted MRI and MRA. Headache characteristics and cranial autonomic symptoms were analyzed.

Results: All patients exhibited stabbing or electric shock-like pain in the ipsilateral periorbital, hemifacial, and temporal regions. Headaches developed weeks after the infarction with brief attacks lasting 1–2 minutes, occurring 1–5 times per day. Lacrimation (100%) and conjunctival injection (75%) were common autonomic features. Three patients (75%) met criteria for short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) and one with short-lasting unilateral neuralgiform headache with autonomic symptoms (SUNA). Notably, each patient exhibited at least one focal neurological deficit (e.g., nystagmus, sensory disturbance), which preceded or accompanied headache onset. Neuroimaging consistently revealed involvement of the trigeminal spinal tract and nucleus, as well as the adjacent spinothalamic tract.

Conclusion: In these cases, headache characteristics were more consistent with SUNCT or SUNA than with typical cluster headache. The presence of focal neurological signs in all patients highlights the importance of careful neurological examination in identifying secondary causes of TACs. All patients provided informed consent for publication in an open access journal.

P502

Trigeminal autonomic cephalalgia triggered by a viral upper respiratory tract infection

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Objective: The trigeminal autonomic cephalalgias (TACs) are a group of primary headache disorders characterized by unilateral pain and ipsilateral cranial autonomic symptoms. Secondary causes must always be excluded, especially in case of rare triggers.

Methods: A 32-year-old male, (consenting to have his data published), with previous history of migraine without aura, presents with pharyngeal discomfort, rhinorrhea, dry cough, and low fever, managed symptomatically. By the third day of illness, he develops severe, stabbing pain in the right maxilla irradiating to the ipsilateral occipitotemporal region along with ipsilateral ptosis, lacrimation and conjunctival injection. The episodes last 6-7 seconds individually, and repeat for 1-2 hours at a time, usually thrice daily at fixed hours, with a possible fourth episode during the night. After four days the episodes remitted, alongside resolution of the infectious symptoms. He had similar headaches since his teens, always associated with upper respiratory tract infections, but without autonomic features. He never experienced an episode without an infectious prodrome.

Results: Neurological examination was normal. Cranioencephalic MRI showed no abnormality correlating with the cephalalgia. There was only mild past response to paracetamol and no acute response to zolmitriptan. A presumptive diagnosis of secondary SUNCT was made. He is currently managed with a short term prophylactic course of prednisolone 60mg starting on the first day of a viral upper respiratory tract infection and has since experienced no further episodes.

Conclusion: This case highlights a unique presentation of upper respiratory tract infection as a rare TCA mimic/trigger. Secondary cephalalgias are uncommon, but there are cases described associated with tumors, rhinosinusitis. Management is challenging in the absence of definitive guidelines, and in this case patient preference for a short-acting treatment was taken into account.

P504

Factors contributing to inaccurate migraine diagnosis in a tertiary hospital setting in southern Thailand

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Objective: Migraine is a prevalent and disabling neurological disorder. Accurate and timely diagnosis is crucial for effective treatment. However, misdiagnosis or delayed diagnosis is common and leads to suboptimal care and worsened clinical outcomes. This study aims to identify demographic and clinical factors associated with the inappropriate initial diagnosis of migraine among patients attending the Neurology and Headache Clinics at Songkhla Hospital.

Methods: A prospective cross-sectional study was conducted from April 2024 to April 2025. Patients ≥18 years with a migraine diagnosis confirmed by two neurologists were enrolled and divided into two groups: those appropriately diagnosed at first consultation and those with prior misdiagnosis. Demographic data, clinical features, treatment history, and the initial diagnosing physician were recorded. Multivariable logistic regression was used to identify independent predictors of inappropriate diagnosis

Results: Among 90 patients (mean age 44.4 years; 85% female), 44% had an inappropriate diagnosis. Inappropriately diagnosed patients were more likely to be male (p=0.051), present with bilateral pain (38.5% vs. 19.6%), and report headache worsening with outdoor activities (p=0.019). They were also more likely to have seen non-neurologists initially (only 5.2% saw neurologists vs. 31.4% in the appropriate group, p<0.001). Multivariable analysis revealed that male sex (mOR 14.07, p=0.011), bilateral headache (mOR 3.86, p=0.021), symptom duration >5 months (mOR 3.96, p=0.030), and medication-overuse headache (mOR 3.21, p=0.043) were independently associated with misdiagnosis.
Conclusion: Recognizing factors associated with inaccurate migraine diagnosis can guide better screening, referral, and education for primary care providers. This may lead to earlier, more accurate diagnoses and improved patient outcomes.

Fig. 1

```
. melogit inapp_dx male dura5m twoside moh || firstdoc:, or nolog

Mixed-effects logistic regression               Number of obs     =         90
Group variable:         firstdoc                Number of groups  =          4

                                                Obs per group:
                                                              min =         14
                                                              avg =       22.5
                                                              max =         32

Integration method: mvaghermite                 Integration pts.  =          7

                                                Wald chi2(4)      =      13.82
Log likelihood = -47.113769                     Prob > chi2       =     0.0079
```

inapp_dx	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
male	14.07157	14.67211	2.54	0.011	1.823115	108.6103
dura5m	3.958161	2.510391	2.17	0.030	1.141917	13.71995
twoside	3.864744	2.2699	2.30	0.021	1.222307	12.21972
moh	3.214659	1.856176	2.02	0.043	1.036675	9.968439
_cons	.1336089	.1185589	-2.27	0.023	.0234701	.7605984
firstdoc						
var(_cons)	1.859061	1.763273			.2897009	11.92991

```
Note: Estimates are transformed only in the first equation.
Note: _cons estimates baseline odds (conditional on zero random effects).
LR test vs. logistic model: chibar2(01) = 11.83       Prob >= chibar2 = 0.0003
```

P505

Thunderclap headache as an isolated manifestation of vertebral artery dissection

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Objective: Headache red flags are crucial in emergency settings, allowing the identification of etiologies that require specific approaches. These include age over 50 years, explosive onset, positional headache, focal neurological deficits, headache waking the patient from sleep or headache with characteristics different from the patient"s usual pattern.
Methods: Patient consent to publish details in an open access journal.
Results: A 51-year-old man with no significant personal medical history was admitted in the Emergency Department with sudden onset, throbbing, left occipital headache, with maximum intensity of 8/10 from the start, unresponsive to paracetamol and only temporarily relieved by ibuprofen, for the last 15 days. The neurological exam was normal. Due to a new headache, sudden onset, and refractory nature investigation was carried out. A cerebral CT and an angio-CT revealed a fusiform aneurysm of the V4 segment of the left vertebral artery, with no evidence of hemorrhage. The case was discussed with Neurosurgery and Neuroradiology, and a decision of conservative treatment approach was made. A follow-up MRI with Angio-MRI revised the diagnosis to a pseudoaneurysm caused by dissection of the left vertebral artery. No focal signs or parenchymal vascular lesions were observed. There was no history of trauma, cervical manipulation or any predisposing activity/position. On the 9-month follow-up Angio-MRI, a significant reduction in the aneurysm size was observed. The headache progressively resolved and no new episodes occurred.
Conclusion: The initial diagnosis at the emergency department of a secondary headache due to an unruptured vascular malformation was revised during follow-up to acute headache attributed to vertebral artery dissection. We emphasize the importance of clinical and imaging re-evaluation of patients with explosive headaches, which enables definitive etiological diagnosis and, consequently, more appropriate preventive treatment.

P506

Intracranial hypertension without visual disturbance in seronegative viral meningitis

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Objective: Intracranial hypertension(IH) may be observed in patients with meningitis, but this is most often due to bacterial, fungal or tuberculous causes rather than viruses. IH secondary to viral infection (IHSVI) is a rare manifestation of viral meningitis. In known cases of IHSVI, specific viruses such as HIV, enterovirus, VZV and HHV-6 have commonly been detected in patients presenting with visual disturbance. We present a patient of IH with seronegative viral meningitis, but without visual disturbance.
Methods: Case
Results: A 20-year-old woman (BMI 21.2 kg/m²) was hospitalized with persistent headache, fever, and nausea for three weeks, with no visual disturbance. A neurological examination revealed bilateral papilledema, and cerebrospinal fluid (CSF) study

showed an opening pressure of 36cmH_2O, WBC 33/µL (with 98% lymphocytes), RBC 0, protein 25.5(15–45mg/dL), glucose 51(45–75 mg/dL).
CSF showed negative for CMV, HSV, VZV, enterovirus, VDRL, cryptococcal antigen, bacterial and fungal cultures. Her brain MRI revealed no other cause of elevated intracranial pressure or leptomeningeal enhancement.
She was initially started on IV mannitol six times daily and dexamethasone four times daily, which were tapered off when her symptoms disappeared and also started on acetazolamide 500 mg twice daily.
CSF study performed two weeks later showed an opening pressure of 19.5cmH_2O, WBC 3 cells/µL, RBC 0, protein 40.8mg/dL, and glucose 57mg/dL. She was discharged from the hospital and discontinued acetazolamide without experiencing any symptoms at her first outpatient follow-up.
Conclusion: This case shows that severe elevations in intracranial pressure can occur in seronegative viral meningitis without visual disturbance.

P507

Acute confusional migraine in adults – A case report

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Objective: Acute confusional migraine is characterized by transient impairment of higher cortical functions and behavioral changes, with or without altered consciousness. Episodes last around 6 hours, resolve fully within 24 hours, and are followed or accompanied by migraine. Its prevalence is low, and adult-onset is particularly rare. There are no recognized diagnostic criteria; diagnosis relies on clinical presentation, migraine history, and exclusion of other causes.
Methods: A 68-year-old man with hypertension and episodic migraine with visual aura presented to the emergency department with behavioral changes lasting 2 hours, preceded by a visual disturbance identical to his usual aura. During observation, he developed prosopagnosia toward relatives and severe hetero-aggressiveness. Diazepam, haloperidol, and chlorpromazine were administered, but agitation persisted. Brain CT with angiography and lab tests were unremarkable. Due to acute behavioral change and isolated fever (38.4°C), infectious encephalitis was suspected. Lumbar puncture was performed, and empiric antibiotics plus acyclovir were started but discontinued within hours after normal CSF and negative viral PCR. The patient remained afebrile; hyperthermia was attributed to neuroleptics.
Results: Brain MRI and EEG showed no significant findings. Symptoms resolved within 24 hours. After recovery, the patient reported that the episode had been preceded by his usual visual aura and migraine.
Conclusion: Although self-limiting, no abortive treatment is available; however, valproic acid and topiramate may be used to treat and prevent recurrences. The absence of formal criteria and the diagnosis being one of exclusion hinder clinical recognition.

P508

Diagnostic challenges of secondary headache due to arteriovenous fistula in a patient with neurofibromatosis type 1

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Objective: To highlight the diagnostic complexity of secondary headache due to rare vascular pathology in a patient with Neurofibromatosis Type 1 (NF1), initially misdiagnosed as migraine.
Methods: We present a rare clinical case of a patient with NF1 who developed a new-onset, migraine-like headache, ultimately diagnosed as a secondary headache due to an underlying craniovertebral arteriovenous fistula (AVF).
Results: A 52-year-old female with a longstanding history of NF1 presented with new-onset episodes of left-sided pulsatile hemicranial headaches, associated with photophobia and phonophobia but unresponsive to analgesics or triptans. Over the course of one year, headache frequency progressively increased, reaching 23 days per month. Migraine was preliminary diagnosed by family doctor. Three days prior to a scheduled neurologic consultation, she developed transient right-sided weakness and speech problems. Similar transient episodes subsequently occurred daily. Neurological examination was unremarkable, except for numerous cutaneous neurofibromas and café-au-lait spots (fig.1); a pulsatile mass was palpable in the left posterolateral cervical region. MRI and digital subtraction angiography (DSA) revealed a high-flow AVF in the left craniocervical junction, associated with marked vascular steal from the basilar circulation (fig.2). Endovascular embolization was performed using a balloon-assisted technique with Onyx and detachable coils, achieving complete AVF occlusion (fig 3). Post-procedure, the patient reported complete

resolution of headache and transient neurological symptoms.

Conclusion: New-onset headaches may mimic primary headache disorders but can signal serious secondary causes like AVF. Prompt imaging and referral are essential to prevent complications and ensure timely, effective treatment.

Fig. 1

Figure 1. Diverse Dermatological and Soft Tissue Lesions in the patient with NF1.
A.Neurofibroma deforming the distal phalanx of the left index finger.
B. Non-deforming flat neurofibroma of the dorsal surface of the right hand.
C. Multiple neurofibromas of different sizes, birthmarks and coffee and milk colored spots on the abdominal wall.
D. Large neurofibroma and coffee-colored spots in the left hamstring area.
E. Hemangioma of the right nasolabial fold. F. Xanthomatosis of the eyelids



Fig. 2

Figure 2. Total selective digital subtractive cerebral angiography.
A. Right-sided carotid AG series (direct projection): retrograde contrast of the basilar artery and its basin through the posterior cerebral artery.
C. Left-sided carotid AG series (lateral projection): contrasting AVM from the occipital artery.
D. Superselective AG series from the left occipital artery (lateral projection): intense contrast of AVM from the occipital artery with rapid contrast of ectatically dilated paravertebral vein on the left.
E. AG series from the right vertebral artery (direct projection): retrograde contrasting of the V4-segment of the left vertebral artery before the fistula and contrasting of the fistulous AVM, the basilar artery and the arteries of its basin are not contrasted (Steal-syndrome) is noted.
G. AG series from the left vertebral artery (direct projection): there is marked AV discharge through the fistula at the beginning of V4 segment into ectatically dilated paravertebral veins on the left side, there is no contrasting of arteries distal to the AVM
I. AG series from the left vertebral artery (lateral projection): there is marked AV discharge through the fistula at the beginning of V4-segment into ectatically dilated paravertebral veins on the left, there is no contrasting of arteries distal to AVM
K. AG series from the left subclavian artery (direct projection): in addition to direct AV fistula from the left vertebral artery, AV fistula from the left ascending cervical artery is detected.
L. AG series from the left subclavian artery (lateral projection): in addition to the direct AV fistula from the left vertebral artery, AV fistulas from the left ascending cervical artery are determined

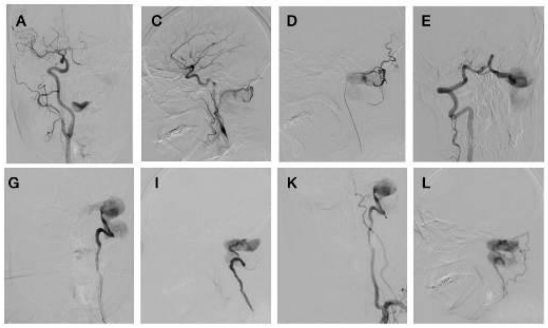
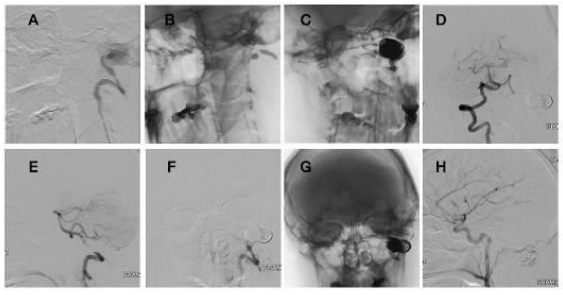


Fig. 3

Figure 3. Endovascular selective embolization to occlude the fistulous connections and exclude the AVM from cerebral circulation
A. One Eclips balloon catheter was guided from the right VA through the vertebrobasilar junction into the V4 segment of the left VA above the fistula but below the mouth of the posterior inferior cerebellar artery (PICA), the second one was guided from the left VA under the defect in the V4 segment of the left VA
B. Inflation of the Eclips balloon catheters was performed so that the fistula from the left VA was blocked. The distal tip of the "lower" balloon catheter is oriented into the fistula
C. Through the second lumen of the "lower" balloon catheter, detachable coils and liquid embolic system Onyx18.
D. Postoperative AV series from the right VA (direct projection) were introduced through the fistula into the ectatically dilated paravertebral vein on the left side: VA fistula turned off all vertebrobasilar bassin arteries contrasted, V4 segment of left PA up to the mouth of the PICA and PICA contrasted through the vertebrobasilar junction from the right VA
E. Postoperative AG-series from right VA (lateral projection): AV fistula is switched off all arteries of the vertebrobasilar bassin are contrasted, V4 segment of the left VA up to the mouth of the PICA and PICA are contrasted through the vertebrobasilar junction from the right VA
F. Postoperative AG-series from the left vertebral artery (straight projection): AV fistula from the left vertebral artery is disconnected together with the left vertebral artery at the level of its defect deconstructively
G. AV fistulae are disconnected also from the left ascending cervical artery
H. AV fistulae are disconnected also from the left occipital artery



P509

When the face twitches: An atypical neurological presentation of spontaneous intracranial hypotension

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Objective: Hemifacial spasm has been reported as a manifestation of spontaneous intracranial hypotension (SIH).

Downward traction of the VII cranial nerve and venous congestion near the nerve root may represent the underlying pathophysiological mechanisms.

Treatment with an epidural blood patch may lead to symptomatic improvement and enhance the response to botulinum toxin.

Methods: Case presentation with literature review.

Results: A 45-year-old man presented with right hemifacial spasm occurring multiple times per hour throughout the day and persistent during sleep. Further anamnesis revealed a new-onset, moderate-intensity occipital non-positional headache, triggered by Valsalva maneuvers and resolving spontaneously within a few minutes. He also experienced right-sided tinnitus and subjective memory impairment.

MRI revealed pachymeningeal enhancement, engorgement of the venous sinuses, pituitary enlargement, and brain sagging. There was no evidence of a dural arteriovenous fistula, neurovascular contact or parenchymal lesions.

He was initially treated with clonazepam without improvement, followed by botulinum toxin type A injections, which resulted in a partial reduction of the spasms.

Due to partial response, the patient underwent a lumbar epidural blood patch with 22 mL of autologous blood, which led to an improvement in the frequency of the spasms.

Conclusion: This case underscores the importance of integrating focal neurological deficits with headache syndromes, including rare manifestations of SIH.

Considering the long-term complications of venous congestion, an alternative treatment was proposed for both headache and hemifacial spasm.

P510

Headache due to pituitary gland adenoma and misdiagnosis

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Objective: Headaches are: primary and secondary. Secondary headaches can cause of different illnesses. Pituitary gland adenoma also cause of headache without any neurology deficits. But sometimes follows the sexual apathy, nervousness, mastopathy. The comprehensive anamneses are important for the diagnoses. Patients don"t pay attention this symptoms, but complains from headache without any causes. During anamnesis patients say about not only headache, also sometimes galactorrhea, if the tumor are very huge then visual impairment, sometimes amenorea, but if any impairment hormonproduction then we can detect bitemporal hemyanopsy, visual field defect, third nerve paresis nearby headache. There are very important: detailed anamnesis, brain MRI with contrast, hormone analyses.

Methods: The patient was complaining from headache, sometimes pain began from neck and irradiated to head. During to takke anamnesis it became known- her had disorder early menstrual cycle, sexual apathy, but never paid attention to this complain, focused only her headache. During several years her headache get severe and she began to felel every day. Therefore took care as a servical pathology till coming to our clinic.

MRI with contrast – Pituitary gland adenoma.

Blood analyses – prolactine-668mg/l, other analyses were normal.

Results: Severe and long-lasting headache without other complains (dysmenorrhea, depression ect.), without estimated hormonal status cause to misdiagnosis. Also the patients thinks other symptoms not belong to neurology and don't say this to doctor.

Deeply anamnes help me made Pituitary MRI and hormonal analyses and find origin of headache.

Conclusion: Headaches can be polyethiology, that"s why every detail of complain, headache without other neurology disorders, Pituitary MRI with contrast, there are red flags for diagnosis and help to avoid misdiagnosis and future complications.

Fig. 1

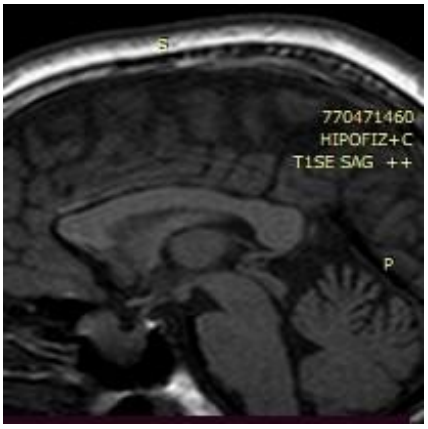


Fig. 2



P511

Cluster-like migraine? A case of seasonal headache with autonomic features responding to propranolol

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[1]Hospital Prof Dr Fernando Fonseca, Neurology, Lisbon, Portugal

Objective: Unilateral headaches with cranial autonomic features are the hallmark of trigeminal-autonomic cephalalgias (TACs), such as cluster headache. However, some patients present with overlapping symptoms that do not fit precisely into established diagnostic categories. Distinguishing between TACs and migraine variants is essential, as treatment approaches and expected outcomes differ significantly.

Methods: We describe a woman in her thirties with recurrent, strictly unilateral retro-orbital pain, described as stabbing and accompanied by conjunctival injection and rhinorrhea. The attacks followed a seasonal pattern, mostly in spring and autumn, and consistently worsened before menstruation. Each episode lasted several hours and occasionally extended into multiple days, which is far longer than typical TACs.

Results: Brain MRI was normal. Her general practitioner initiated prophylactic treatment with propranolol, leading to a marked reduction in both frequency and intensity of attacks, with sustained periods of remission. When treatment was paused, symptoms recurred with the same pattern. Reintroduction of propranolol again resulted in clear clinical improvement.

Conclusion: Although autonomic features initially suggested a TAC, the prolonged duration, hormonal sensitivity, and strong response to propranolol supported a migraine phenotype. The seasonal and menstrual pattern may reflect hypothalamic

involvement, given its role in both circadian and endocrine regulation.
This case highlights the diagnostic complexity of headache syndromes with overlapping features. Careful clinical characterization and monitoring treatment response are key. In selected cases, beta-blockers may be effective even when autonomic signs are present, if the overall course is more consistent with migraine.

P512

Development and validation of the predictive model for the differentiation between vestibular migraine and Ménière's disease

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Objective: Vestibular migraine (VM) and Meniere's disease (MD) present a significant diagnostic challenge due to their overlapping symptomatology, including recurrent vertigo, auditory disturbances, and headache. Accurately differentiating between VM and MD enables targeted interventions—addressing central neuromodulation versus peripheral endolymphatic management—thereby optimizing patient outcomes and refining clinical trial designs for disorder-specific therapies

Methods: Records of 110 VM and 110 MD patients were retrospectively analyzed. Logistic regression established a diagnostic equation. Sensitivity, specificity, accuracy, positive and negative predictive values were evaluated and displayed via ROC curve. Visualization tools (nomogram and applet) were developed. Additional VM/MD patients were recruited for validation using ROC and GiViTI calibration belt.

Results: Clinical and vestibular features differentiating VM from MD included attack frequency (X5), phonophobia (X13), electrocochleogram (ECochG, X18), head-shaking test (HST, X23), ocular VEMP (X27), and horizontal gain of vestibular autorotation test (VAT, X30). The regression equation was: P = 1/[1 + e-(-2.269× X5 - 2.395× X13 + 2.141× X18 + 3.949 × X23 + 2.798× X27 - 4.275× X30(1) - 5.811× X30(2) + 0.873)] (P, predictive value; e, natural logarithm). Nomographs and applets were used to visualize our result. After validation, the prediction model showed good discriminative power and calibrating power.

Conclusion: A diagnostic algorithm combining clinical features and auditory-vestibular regression equation is effective, feasible, and could improve VM and MD differential diagnosis.

Fig. 1

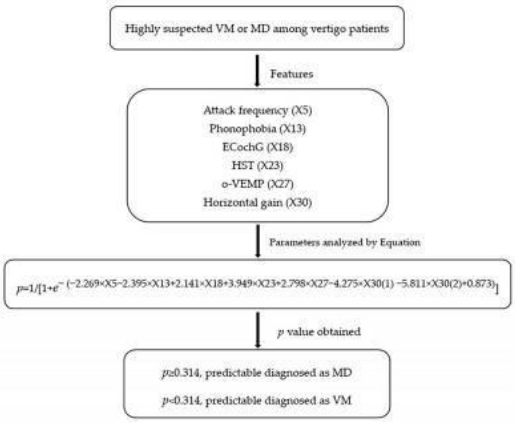


Figure 1. Differential diagnostic flow between VM and MD based on clinical and auditory-vestibular function features. EcochG, electrocochleogram; HST, head shake test; o-VEMP, Ocular Vestibular Evoked Myogenic Potential; VM, vestibular migraine; MD, Meniere's disease.

Fig. 2

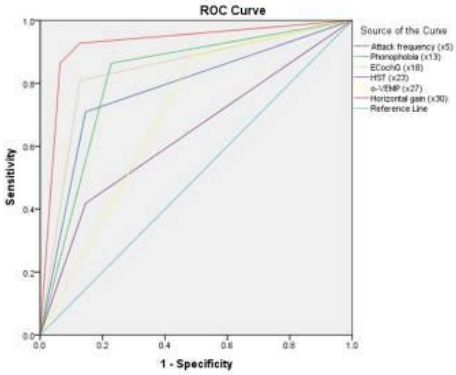


Figure 2. Receiver operating characteristic (ROC) curves of logistic model and specificity variables. EcochG, electrocochleogram; HST, head shake test; o-VEMP, Ocular Vestibular Evoked Myogenic Potential; VM, vestibular migraine; MD, Meniere's disease.

Fig. 3

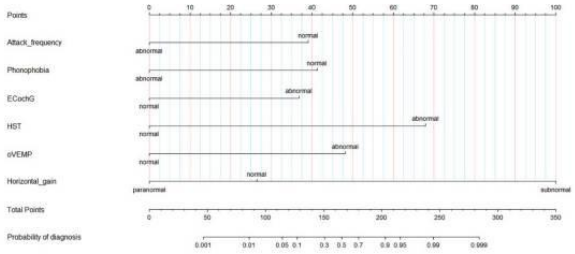


Figure 3. Diagnostic nomogram estimated by clinical and auditory-vestibular function features for patients with VM and MD. EcochG, electrocochleogram; HST, head shake test; o-VEMP, Ocular Vestibular Evoked Myogenic Potential; VM, vestibular migraine; MD, Meniere's disease.

P513

Dispelling mist that obscures positional vertigo in vestibular migraine

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Objective: A substantial subset of patients with Vestibular Migraine (VM) exhibit positional vertigo, a proportion of whom have superimposed Benign Paroxysmal Positional Vertigo (BPPV). Rapidly

identifying this BPPV component is diagnostically challenging but holds profound therapeutic implications. The difficulty stems from symptom overlap, yet the distinction is paramount as VM and BPPV arise from fundamentally distinct pathophysiologies—central sensory dysregulation versus peripheral canalithiasis. Accurate diagnosis is therefore the cornerstone of implementing targeted therapy, ensuring patients receive correct neuromodulatory or repositioning maneuvers

Methods: Retrospective data from 60 VM and 47 VM+BPPV patients were used to build a diagnostic model, and prospective data from 47 patients were applied for external validation. All had VM with positional vertigo, with or without BPPV. Clinical manifestations and vestibular function tests were analyzed via logistic regression.

Results: Univariate and multivariate analyses identified age, symptom duration, tinnitus, ear fullness, nausea, head-shaking nystagmus, Dix-Hallpike and roll test direction, and horizontal gain as differentiating factors. A nomogram and online calculator were created. The model achieved a C-index of 0.870 and showed good discrimination and calibration in internal and external validation.

Conclusion: This study offers a new perspective for diagnosing VM with positional vertigo by detecting the BPPV component and, for the first time, provides a prediction model integrating multiple predictors.While both disorders can manifest with positional triggers, their underlying mechanisms—peripheral end-organ dysfunction in BPPV versus central sensitization and integration failure in VM—demand divergent treatment pathways.Mastering this differentiation is essential to transcend empirical management and advance towards mechanism-based care, ultimately improving long-term patient outcomes and quality of life.

Fig. 1

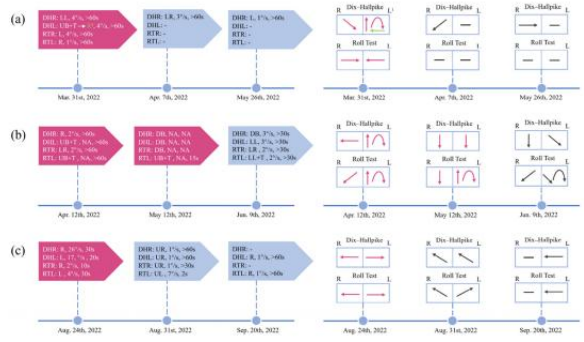


Fig. 2

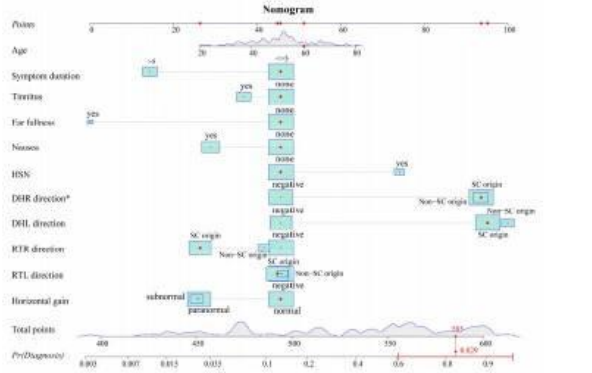


Figure 2. Nomogram. The nomogram predicts the diagnostic probability for the 100th patient of the dataset. Red dots represent the value of this predictor for this patient. The total score can be obtained by adding up the scores corresponding to these red dots. The predicted probability can be calculated from the total score. The probability of this patient is 0.829 from the graph and is greater than 0.471, indicating that the patient is more likely to have VM + BPPV. HSN: head shaking nystagmus; DHR: Dix–Hallpike right; DHL: Dix–Hallpike left; RTR: roll test right; RTL: roll test left; SC: semicircular canal; Pr: probability. * $p < 0.05$.

P514

Diagnostic value of the vestibular autorotation test in Ménière's disease, vestibular migraine and Ménière's disease with migraine

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Objective: Vestibular migraine (VM) and Menière's disease (MD) share multiple features in terms of clinical presentations and auditory-vestibular functions, and, therefore, more accurate diagnostic tools to distinguish between the two disorders are needed.

Methods: The study was of retrospective design and examined the data of 69 MD patients, 79 VM patients and 72 MD with migraine patients. Five vestibular autorotation test (VAT) parameters, i.e., horizontal gain/phase, vertical gain/phase and asymmetry were subjected to logistic regression. The receiver operating characteristic (ROC) curves were generated to determine the accuracy of the different parameters in the differential diagnosis of MD and VM.

Results: Our results showed that the horizontal gain of VAT significantly outperformed other parameters in distinguishing MD and VM. In addition, the sensitivity, specificity and accuracy of the horizontal gain were 95.7%, 50.6% and 71.6%, respectively, for the differentiation between VM and MD. In most MD patients, the horizontal gain decreased in the range of 3-4 Hz, while in most VM patients, horizontal gain increased in the range between 2-3 Hz. More MD with migraine patients had an increased horizontal gain when the frequency was less than 5.0 Hz and had a decreased horizontal gain when the frequency was greater than 5.0 Hz.

Conclusion: Our study suggested the VAT, especially the horizontal gain, as an indicator, may serve as a sensitive and objective indicator that helps distinguish between MD and VM. Moreover, VAT, due to its non-invasive and all-frequency nature, might be an important part of a test battery.

Fig. 1

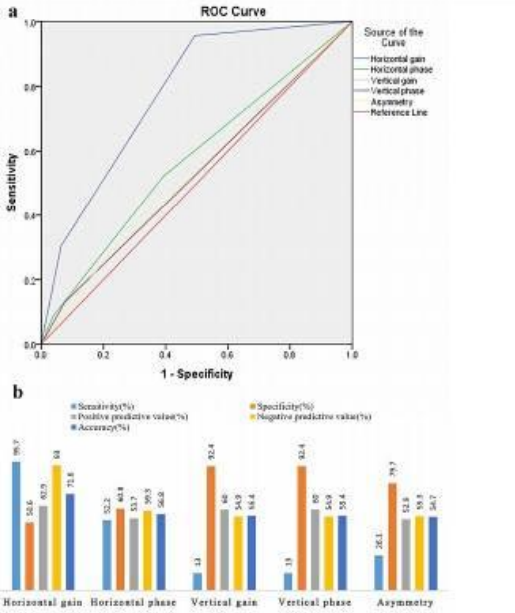


Figure 1. ROC curves of VAT in the study. (**a**) ROC curve analysis of different VAT parameters in the differential diagnosis of between MD and VM patients. Light blue line, horizontal gain; green line, horizontal phase; yellow line, vertical; purple line, vertical phase; red line, reference line. (**b**) The value of different VAT parameters in the differential diagnosis between MD and VM patients. MD, Menière's disease; VM, vestibular migraine; VAT, vestibular autorotation test.

Fig. 2

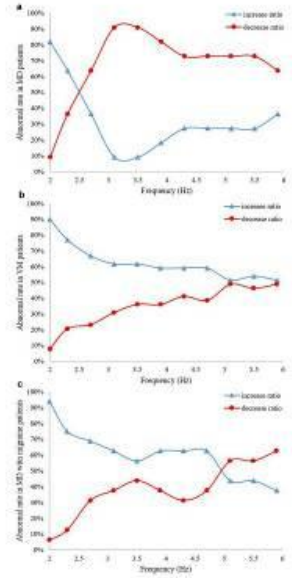


Figure 2. The proportion of the horizontal gain decrease in MD, VM and MD with migraine patients. (a,b) blue line, MD patients; light red line, VM patients; in most MD patients, the horizontal gain decreased in the range of 3–4 Hz, while in most of the VM patients, horizontal gain increased between the range of 2–3 Hz. MD, Menière's disease; VM, vestibular migraine. (**c**) Blue line, MD with migraine patient's horizontal gain increase ratio; light red line, MD with migraine patient's horizontal gain decrease ratio. More MD with migraine patients had an increased horizontal gain when the frequency was less than 5.0 Hz and had a decreased horizontal gain when the frequency was greater than 5.0 Hz.

P515

A novel liquid biopsy for patient triage

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Objective: Early brain tumour signs can be subtle and mistaken for conditions including migraine, fatigue and stress. Resulting diagnostic delays impact brain cancer patient quality of life and survival. Positive predictive value (PPV) of symptom-based suspected brain cancer referral guidelines, for the presence of "symptoms related to the central nervous system" is 2.9%, but such well-differentiated symptoms are rare. The PPV for symptoms such as headache is only 0.09%.

The Dxcover® Brain liquid biopsy is a rapid multiomic test that detects brain tumours in serum. Infrared spectroscopy produces a molecular signature, and an algorithm predicts presence or absence of cancer.

Objective: To introduce a rapid liquid biopsy to triage patients with non-specific symptoms of brain cancer.

Methods: EMBRACE is a prospective multicentre clinical validation study with 7 UK & European sites. Diagnostic performance (sensitivity & specificity) for the detection of malignant tumours was estimated across all patients, and for an intended-use population subgroup presenting with relatively non-specific and non-urgent symptoms including headache.

Results: Over 2500 patients participated, of which the intended use population was 1338. Among intended-use patients, 42% presented with headache as primary symptom, and test sensitivity was 86% (95%CI:80-90%) at 44% (95%CI:41-47%) specificity. Negative predictive value (NPV) is predicted to range from 99.0% to 99.8% in symptomatic populations with disease prevalence between 0.5% and 3%. Corresponding PPVs ranged from 0.8% to 4.5%.

Conclusion: Early and expeditious diagnosis is crucial to reduce the morbidity and mortality associated with brain cancer. This simple, non-invasive test would support clinical decision-making and facilitate patient triage to rapid imaging. Diagnosis when tumours are smaller is asssociated with reduced morbidity, reduced healthcare resource utilisation, and a mortality benefit (data under review).

P516

Red flags in headache attributed to infection: A diagnostic aid based on SNNOOP10 and ICHD-3 classification

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[2]University of Debrecen, Department of Neurology, Debrecen, Hungary

Objective: Infection-related headaches are common but often under-recognized, particularly when clinical features are subtle or atypical. Our aim was to develop a structured diagnostic aid that integrates the SNNOOP10 red flag system with the ICHD-3 classification to improve early detection of infectious causes of headache.
Methods: We performed a structured comparative analysis of the SNNOOP10 red flag symptoms and the corresponding infection-related categories in the International Classification of Headache Disorders, 3rd edition (ICHD-3). For each SNNOOP10 item, we identified the most relevant ICHD-3 diagnostic subtype and its potential infectious etiologies based on expert consensus and literature review. These relationships were summarized in a correlation table intended as a practical tool for use in emergency and inpatient neurology settings
Results: The analysis demonstrated a strong alignment between SNNOOP10 components and ICHD-3 infection-related categories. For instance, systemic fever was linked to meningitis or encephalitis, altered mental status to brain abscess or viral encephalitis, and immunosuppression to opportunistic infections such as cryptococcosis. The resulting table visually maps SNNOOP10 symptoms to relevant infectious mechanisms and ICHD-3 subtypes, supporting rapid and focused diagnostic reasoning.
Conclusion: An infection-adapted interpretation of SNNOOP10, when combined with ICHD-3 diagnostic criteria, may enhance early recognition of infection-associated headaches. This integrated framework offers a practical clinical support tool to aid urgent triage and improve diagnostic accuracy in settings where timely identification of CNS infections is critical.

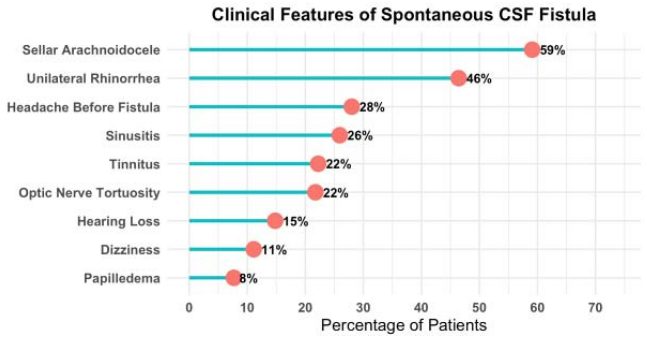
P517

Spontaneous anterior CSF leak as a pressure-release variant of idiopathic intracranial hypertension

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[1]National Institute of Neurology and Neurosurgery, Headache Clinic, Mexico City, Mexico

Objective: To describe clinical characteristics of patients with spontaneous CSF fistula presenting with headache and features resembling idiopathic intracranial hypertension (IIH) without secondary causes.
Methods: Retrospective review of patients diagnosed with spontaneous anterior CSF fistula (2016–2024) at a headache clinic in Mexico. Patients with history of trauma, neurosurgery, or skull base malformations were excluded. Demographic, clinical, opening pressure, treatment, and recurrence data were analyzed.
Results: Twenty-eight female patients were included. Mean BMI was 33.1 (SD 5.5). Mean age at symptom onset and diagnosis was 42.0 (SD 10.5) and 45.8 (SD 8.6) years, respectively. Tension-type headache phenotype predominated in 50% (95% CI 30–79), followed by migraine-like in 27% (95% CI 12–43). Median headache days per month was 4 (IQR 2.0–9.5). Mean opening pressure was 229 mmH_2O (SD 62.6) during active CSF leak and median 215 mmH_2O (IQR 198–285) at six months. Fistula location was identified in 12 patients, 5 at the sphenoid bone. Papilledema was present in 2 patients (8%). Rhinorrhea was present in 82% of patients, with 48% exhibiting unilateral discharge. Recurrence occurred in 17%, median time 36 months (IQR 0–36).Neuroimaging findings included arachnoidocele present in 40% and optic nerve tortuosity in 21% of patients.Acetazolamide was prescribed in 92%. No significant differences in BMI or opening pressure were found between patients with or without recurrence or papilledema. BMI and opening pressure showed no significant correlation (rho = 0.06, p = 0.81).
Conclusion: Spontaneous anterior CSF fistula may act as a compensatory mechanism for chronically elevated intracranial pressure, preventing overt signs and formal IIH thresholds. In mostly obese women with headache and mild to moderate CSF pressure elevation, spontaneous fistula may serve as a pressure-release variant of IIH.

Fig. 1



P518

Benign episodic unilateral mydriasis and headache: More than meets the eye

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[2]King's College London, Wolfson Sensory, Pain and Regeneration Centre, London, United Kingdom
[3]University Hospital Lewisham, Department of Neurology, London, United Kingdom

[4]King Abdullah University of Science and Technology, Thuwal, Saudi Arabia

Objective: Benign episodic unilateral mydriasis (BEUM) is a rare and incompletely understood entity that has previously been associated with migraine. Associations with other headache phenotypes have not been reported.
Methods: We present two cases of BEUM associated with differing headache phenotypes.
Results: A 47-year-old man presented to our service with approximately 30-40 episodes a day of unilateral right eye pupillary dilation, associated with blurring of right eye vision resolving in 2-3 minutes and 2-4/10 severity throbbing pain in the right occiput that lasted between 3-10 minutes. There were no migrainous features or cranial autonomic symptoms. There was no identifiable precipitating factor for these episodes. Examination performed interictally was unremarkable. Contrast-enhanced MRI and MRA brain imaging did not show any abnormality. Indomethacin and oral corticosteroids were not useful. Lamotrigine 100mg BD resulted in resolution of the pain, but with ongoing episodes of mydriasis.
A 36-year-old woman presented to our service with pupillary dilation of the right eye lasting 2-10 minutes at a time and occurring 3-4 times a week on average for about 1 year, before spontaneously remitting for 2.5 years. The episodes then recurred for 6 months at a reduced frequency, before spontaneously resolving again. There were no migrainous features or cranial autonomic symptoms. There was no identifiable precipitating factor. She also developed episodes of right-sided dull occipital headache lasting 3 hours to 3 days, associated with nausea and neck pain but no other symptoms. Apart from the onset of symptoms, these were not temporally correlated with mydriasis episodes. Contrast-enhanced MRI and MRA brain imaging showed incidental prominent optic nerve sheaths and intrasellar arachnoid herniation (without clinical signs of papilloedema) bilaterally, but no other relevant findings.
Conclusion: These two cases highlight the likely association of headache with BEUM, suggesting possible shared biological pathways.

P519

Migrainous infarction: A systematic review and critical reappraisal

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[2]Harvard Medical School, Boston, MA, United States

Objective: Migrainous infarction - ischemic stroke occurring during migraine with aura - is a rare stroke etiology, typically affecting young women. The mechanism by which aura might cause infarction remains uncertain, while emerging evidence suggests the reverse relation: cerebral ischemia may trigger spreading depolarization, perceived as migraine aura. We systematically reviewed reported cases to assess whether clinical or imaging data support migraine aura as a cause of infarction.
Methods: Following PRISMA guidelines, PubMed and Embase were searched without date or language restrictions for ischemic strokes attributed to migraine with aura. Two reviewers extracted clinical, neuroimaging, and etiological data, evaluating fulfillment of migrainous infarction criteria and evidence supporting aura-induced ischemia.
Results: Among 2,762 screened records, 156 cases (102 women, mean age 35.5 years) published between 1883 and 2024 in nine languages were identified. One hundred twenty-three patients had prior migraine with aura, but in 85 cases the presenting symptoms differed from previous auras. Neuroimaging confirmed ischemic stroke in 128 patients, yet none showed patterns suggestive of spreading depolarization–induced infarction, such as lesions spanning adjacent vascular territories. Only 33 cases underwent a basic etiologic work-up; none received a guideline-recommended evaluation including echocardiography, ≥48-h cardiac monitoring, vascular imaging, and antiphospholipid screening.
Conclusion: We did not identify cases clearly demonstrating cerebral infarction caused by migraine aura. Co-occurring migraine with aura and cerebral infarction may be better explained by ischemia-induced spreading depolarization. A diagnosis of migrainous infarction may lead to insufficient diagnostic evaluation to rule out alternative stroke etiologies.

P520

Clinical characteristics and treatment outcomes in resistant and refractory migraine: Application of the European Headache Federation (EHF) 2020 criteria in a UK tertiary headache cohort

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Objective: To characterise resistant and refractory migraine patients according to EHF 2020 criteria in a tertiary UK headache service and to compare demographics, phenotype, and treatment outcomes
Methods: Consecutive migraine patients referred to Leeds Headache Service between 2019 and 2024 were included. Demographics, disease duration, baseline headache/migraine frequency, and treatment outcomes (oral, BTX-A, and CGRPmab) Classification as resistant(rM)or refractory(RM) according to

EHF2020 criteria.Data was analysed using 'base r' and the 'mgcv' packages. A logistic regression model was formulated to ascertain predictors of refractoriness.
Results: A total of 173 consecutive migraine patients were included. 28% classified as RM, 83.7% were female,median age 46 years (IQR19),median monthly migraine frequency 20 (p=0.06), mean BMI of 29.0 and complex psychiatric in 28%. rM patients with median age 43 years (IQR 12.5); 82.2% female, and 17.5 migraine days/month. Migraine Aura present in 53%, with >1 aura subtype more common in resistant patients. (p=0.02, OR 0.16) Higher BMI +depression showed a trend to respond less to first line antiCGRP. We found age as significant at predicting response to AntiCGRP mab at 12mo (p=0.02).BTX-A was trialled in 85.7% of RM patients. rM patients on Erenumab showed a trend of greater efficacy over the CGRP-ligand mabs (p=0.17). Galcanezumab looked to be significantly less effective compared with Erenumab (p=0.02). Galcanezumab appeared 14.4% less likely to result in response at 12 months compared with Erenumab in our cohort. Sex, disease duration, depression, anxiety or presence of aura were not independently predictive of RM in our cohort.
Conclusion: EHF 2020 Criteria for resistant and refractory migraine was applicable in our cohort. RM accounted more than one-quarter of our patients with a high proportion of migraine aura, depression, high BMI. Older rM patients seem to respond better to Erenumab compared to ligand antiCGRP.

P521

Headache characteristics in patients with epilepsy – An observational study

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Objective: Headache and epilepsy are two closely related disorders, with the relation between the two disorders still a matter of debate. Our aim was to assess the clinical characteristics of headache in patients with epilepsy and to compare the seizure characteristics in patients with and without headache.
Methods: 125 consecutive patients with epilepsy (according to the ILAE classification of epilepsies 2017) were recruited between May 2023 to December 2024 and were subjected to a semi-structured interview. Data related to seizure characteristics and headache characteristics was collected. Internation classification of headache disorders – III (ICHD-3) was used to classify the headache phenotypes
Results: Headache was reported by 92% patients. Inter-ictal headache (78%) is the most common type of headache followed by post-ictal headache. Migraine (72%) was the most common phenotype reported in the inter-ictal group. There was a significant association between the seizure type and headache in those with overall headache and post-ictal headache. Mean age of onset of seizures was significantly lower in patients with post-ictal headache (p=0.04). QOLIE-10 score significantly higher in those who reported post-ictal headache (p= 0.03).
Conclusion: In epilepsy patients, Inter-ictal headache is more common with migraine being the most common phenotype. Post-ictal headache is the commonest among the peri-ictal headaches, occurs in younger onset epilepsy patients and its presence affects quality of life in epilepsy patients

P523

The role of a double-blind, placebo-controlled intramuscular indomethacin test (IndoTest) for the diagnosis of indomethacin-sensitive headache in an outpatient setting: A prospective cohort study

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Objective: Accurate diagnosis of indomethacin-sensitive headache is vital and can save patients from a frustrating journey of trying unhelpful treatments. The simplest way is an oral indomethacin trial; however, for many patients with comorbidities, this can be a relative contraindication and therefore not done. In these cases, an observed double-blind, placebo-controlled intramuscular (IM) indomethacin test (IndoTest) is recommended.
Methods: We collected a prospective cohort (2024-2025) of adults who underwent an outpatient IndoTest at King"s College Hospital London as part of a service evaluation. Reasons for referral, headache phenotype with test response, and final diagnosis, alongside patient characteristics were recorded.
Results: Thirty patients were screened and contacted; two did not attend, and six did not proceed with the IndoTest due to medical issues present upon review of day one of the IndoTest. The average age was 50 years old (range 31-69), 77 % women. The reason for the referral was possible hemicrania continua (80%), paroxysmal hemicrania (17%) and primary cough headache (3%). The majority of patients had a relative contraindication to the oral test, and 11 patients had

tried the oral trial already, 45% reaching the maximum daily dose of 225mg.
There were 6 patients (27%) who had a positive IndoTest, 5 hemicrania continua and 1 primary stabbing headache. Two had tried indomethacin orally, one reached the maximum dose with an unclear response and caused low mood. The rest had relative contraindications to an oral test. Following the IndoTest, melatonin (n = 3), greater occipital nerve injections (n = 3), and non-invasive vagal nerve stimulator (n = 3) were initiated.
Conclusion: The double-blind, placebo-controlled IndoTest is a useful tool, especially for those who are not able to tolerate the oral test. In the absence of this, patients may be incorrectly managed.

P524

Phenotypic features of menstrually-related migraine without aura

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Objective: Menstrually-related migraine (MRM) is often reported as a severe subtype of migraine. However, International Classification of Headache Disorders (ICHD)-3 does not provide specific criteria for MRM based on clinical phenotype. Aim of this study was to characterize clinical phenotype in women experiencing MRM.
Methods: A semi-structured interview (SSI) was used to characterize the clinical phenotype in women screened for a separate study (ClinicalTrials.gov:NCT06470958). These women were required to report at hospital during ongoing migraine attacks without aura in relation to their menstrual period. Women who arrived at hospital during ongoing attacks were also clinically phenotyped during these attacks.
Results: A total of 32 women with MRM were interviewed, whereof 18 completed a questionnaire during ongoing attacks. Mean age was 30.7 years (SD 5.4). Mean disease duration was 11.3 years (SD: 6.6). In total group, 59.4 reported unilateral pain, 84.4% throbbing quality, 100% moderate/severe pain, 96.9% experienced aggravation by routine physical activity, 90.6% reported nausea, 93.8% photophobia and 78.1% phonophobia. In the subgroup of 18 women phenotyped during ongoing attacks, unilateral pain was reported by 39.0% (compared to 66.7% in the SSI), throbbing quality 67.0% (SSI: 83.3%), moderate/severe pain 88.9% (SSI: 100%), aggravation by routine physical activity 100% (SSI: 94.4%), nausea 44.0% (SSI: 100%), photophobia 83.0% (SSI: 88.9%) and phonophobia 67.0% (SSI: 61.1%).
Conclusion: This study shows that clinical phenotype of migraine attacks during the menstrual period differs from attacks outside the menstrual period. Importantly, less than 50% of the patients experienced unilateral pain and nausea during MRM attacks. These findings highlights the need for a comprehensive characterization of MRM phenotype in a large-scale MRM population to improve diagnosis of this subtype of migraine in the ICHD.

P525

Underestimated headache frequency in healthy control volunteers

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Objective: Reliable identification of "healthy controls" (HC) is important in migraine research. Volunteers who consider themselves "headache-free" may underestimate headache (HA) frequency and have unrecognised migraine, complicating control selection. We explored discrepancies between self-perceived and objective HA frequency and characterised migraine-related features and history.
Methods: Pre-screening data from 56 volunteers (aged 18–52) registering as HC for our migraine studies were analysed. HC was defined as <4 HA/year and no migraine characteristics per ICHD-3. Participants reported HA occurrence via an open-ended question, a categorical scale (frequently, sometimes, rarely, very rarely, never) and a quantitative scale (daily, <3/week, <3/month, <3/year, <1/year, never had). Associated symptoms per ICHD-3: photophobia, phonophobia, motion sensitivity, nausea, vomiting,) and other medical or family history were recorded. Verbal descriptions were categorised, and descriptive analyses explored mismatches between perceived and reported frequency.
Results: Although all participants self-identified as headache-free, 31/56 did not meet preliminary HC criteria. Self-perception often underestimated frequency: 15/31 reported ≥2–3 HA/month, of which 11/15 selected "rare" or "very rare"; 27/31 reported migraine characteristics, and 19/27 had ≥2 features. Most frequent qualitative descriptions were "occasional HA", "due to dehydration", or "sleep deprivation".
Conclusion: Discrepancies between self-perceived and reported phenotype were common: 55% of volunteers identifying as "headache-free" did not meet HC criteria. Many reported migraine-like features per ICHD-3, suggesting possible undiagnosed migraine. These findings open the discussion of how HC should

be defined in migraine studies and highlight the need for structured screening to ensure valid HC selection.

P526

Challenging the criteria: A case of unclassifiable trigeminal autonomic-like headache

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Objective: To discuss the diagnostic challenges of headaches with prominent autonomic features that don't meet criteria for any defined trigeminal autonomic cephalalgia.
Methods: Clinical case report.
Results: A 52-year-old woman with a history of right-sided hemicranial headache associated with the menstrual cycle, resolved after surgical menopause. No regular medication or relevant family history. Over the past two years, she developed recurrent episodes of alternating nasal congestion, more intense on the right side, usually preceded two days earlier by hypersalivation and accompanied by ipsilateral periorbital pain (VAS 8/10). The episodes last about three days, without a clear circadian or seasonal pattern. Initially, the episodes occurred monthly, but they progressed to a weekly frequency. Symptoms were associated with photophobia, osmophobia, restlessness, and no response to rest. During right-sided attacks, she reported ipsilateral upper limb paresthesias. Symptoms worsened in the supine position due to bilateral disabling nasal congestion. Attacks are generally triggered by strong odours and not by innocuous stimuli. She denied interictal continuous pain, ptosis, eyelid edema, conjunctival injection, tearing, rhinorrhea, altered facial sweating, nausea, vomiting, fever, weight loss, jaw claudication, ocular pain, motor deficits, trauma or analgesic overuse. Neurological examination and fundoscopy were normal. Blood tests, MRI and MRA were unremarkable. Frovatriptan provided fast relief, although some residual pain persists for up to 1 day. Indomethacin was tried but rapidly dismissed due to side effects. Verapamil, titrated up to 80mg bid, led to partial symptom relief.
Conclusion: Despite the atypical pain duration, the presence of prominent autonomic signs and the partial response to Verapamil favours a diagnosis within the trigeminal autonomic cephalalgia spectrum, highlighting the diagnostic complexity of these entities.
Disclosure: the patient gave her informed consent to publish her details.

P527

CSF hypotension headache and Postural Orthostatic Tachycardia Syndrome (POTS)

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Objective: Can orthostatic headache following spinal anaesthesia be explained solely by CSF hypotension, or might it reflect overlap with autonomic disorders such as POTS?
Methods: Clinical observation of a 65-year-old male with post-spinal anaesthesia orthostatic headache
Results: A 65-year-old male developed headache 2 days after spinal anaesthesia. The headache was 6/10 in the pain scale, had photophobia and phonophobia, worsened with orthostatism and was partially relieved by oral painkillers. At that time he was treated only with oral analgesics. Two months later the headache got worse, (8/10 in the pain scale) and with inability to tolerate standing. A Neuraxis MRI did not document signs of CSF hypotension (Bern Score = 0), intracranial bleeding or cerebral venous thrombosis. A lumbar puncture in the left lateral decubitus position revealed opening pressure of 5cmCSF. The CSF analysis was normal. After treatment with painkillers, caffeine and two epidural blood patches there was a modest improvement of the headache. An occipital nerve block was successful in reducing the headache to 2/10. Nevertheless, the patient began to complain of unspecific symptoms upon assuming the upright position. These symptoms included light-headedness, malaise, and palpitation. A heart rate increase of 29bpm was noted in orthostatic position, without orthostatic hypotension. A tilt table test confirmed the diagnosis of POTS. The patient began propranolol that resolved his complaints
Conclusion: This case shows the clinical overlap between CSF hypotension manifestations and POTS. Orthostatic headache, although typical of CSF hypotension, can occur in POTS due to autonomic mechanisms still to be ascertained. The persistence of symptoms with orthostatism should motivate the exclusion of complications and additional investigation of other etiologies that are associated with orthostatic headaches. The association between these two conditions requires further investigation as a causality is yet to be established with certainty

P528

Tension headache treatment using local mechanical vibration targeting temporalis and occipitalis muscles – A non-invasive method

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Objective: Tension headaches are the most common type of headache and thought to be caused by stress

in daily life. So, this study uses a non-invasive vibration technique to target the precranial muscles' myofascial trigger points, which can reduce pain

Methods: A randomized control trial was conducted. The study included thirty young active university students (Aged from 19-24 years) equally distributed into two groups; an experimental group that took a local mechanical vibration therapy through innovative tension headache band and a control group that had a placebo treatment for the tension headache. The tension headache band with four local Vibrating Mini Motor Disc (SKU 850917; New York, USA) rotates 12000 rotations per minute with frequency of 150 Hz was used. The pain level was detected in the baseline, immediately, and after 2 hours of vibration intervention using numerical pain rating scale.

Results: Mann-Whitney U-test showed statistically significant reduction of pain level immediate and after 2 hours of vibration intervention in comparison to the control group. Friedman test showed statically significant reduction among the three conditions of intervention in the experimental group only. There was no statically significant differences between male and female in both groups

Conclusion: Patients with tension headaches who received vibration therapy employing 150 Hz frequency ranges experienced improvements in their NPRS and disability. Mechanical Vibration therapy may therefore be a useful strategy for relieving tension headache discomfort.

All patient gave their informed consent to publish their details in an open access journal.

P531

DaxibotulinumtoxinA efficacy, safety & effect duration in migraine prevention

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Objective: DaxibotulinumtoxinA efficacy, safety & effect duration in Chronic Migraine (CM)**.**

Background: OnabotulinumtoxinA CM effect duration is 8-12 wks. DaxibotulinumtoxinA (daxibot, DAXXI), a longer acting toxin w/facial esthetic, cervical dystonia, & upper limb spasticity efficacy, was studied for CM efficacy, safety & effect duration.

Methods: Open, prospective, 2-cntr CM study w/1 daxibot subq cycle & 2 protocols, PREEMPT & EEG paradigms.

Primary outcome: monthly migraine d (MMD) reduction baseline (bl) vs wks9-12.

Secondary outcomes: Time to retreatment qualification, ≥50%MMD reduction, Acute Medication Reduction wks9–12, MIDAS wk12, PGIC, safety.

Results: Each endpoint had numerical but not statistically significant change in favor of daxibot from bl, likely due to small sample size (N=31). Standard protocol reduced MMDs -1.35 d, EEG -0.8 d, pooled -1.45 d. Pooled mean time to retreatment qualification 192 days or ~27 weeks; only 3 (10%) met retreatment criteria. AEs mostly mild, c/w previous botulinum trials. No SAEs related to daxibot & no AE/efficacy discontinuations.

Conclusion: Daxibot appears safe & effective in CM prevention w/2 injection protocols. Prolonged benefit duration noted; placebo-controlled studies indicated. Injecting daxibot q12 wks may prevent wearing off seen w/other migraine botulinum toxins, & could result in better standard of care.

P532

High lung doses of Aerosolized Acetylsalicylic Acid (ASA) feasible with new customized mesh nebulizer device: The ASCOT™ inhaler

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Objective: To assess the optimum drug concentration and device parameters for high alveolar deposition and acceptable treatment time of ASA. Commercially available mesh nebulizers generate inappropriate particle sizes for deep lung delivery of ASA, or even produce no aerosol at all, calling for a customized high-performance nebulizer. Dose requirements (up to 1,000 mg ASA) and human factor aspects are a challenge for migraine treatments. Nebulizer design must consider these requirements.

Methods: Initial bench tests indicated individual mesh and electronic parameters for different ASA concentrations. Particle size by laser diffraction, total output rate (TOR) were used as criteria for optimization of hard- and software parameters. Drug stability post nebulization and Delivered Dose ex mouthpiece (DD) was confirmed externally (Actarmo Medical, Munich). Following the optimization cycles, in-vitro aerosol characterization studies were done. Data were used to calculate lung dose and treatment time using the ICRP model.

Results: Particle size for LASAG (µm) were at 4.6 ± 0.45 (1g/5ml), and 4.0 ± 0.25 (2g/5ml). TOR (ml/min) was at 1.25 ± 0.45 (1g/5ml), and 0.9 ± 0.25 (2g/5ml), corresponding to a TOR of 2.25 ± 0.65 with NaCL. Given a 1:1 ratio of inhalation/exhalation (4 sec/4sec), treatment times were estimated to be between 10-12 minutes for one vial (500 mg ASA). DD (mg ASA) was

at 400 ± 25. The optimized setup was used in a PK-study with 16 healthy subjects, confirming the expected high deep lung deposition. Bioavailability of ASA was at 62% of the previously measured DD.
Conclusion: The PK-study indicates that the ASCOT™ Inhaler delivers therapeutically relevant doses of ASA to the lung in healthy subjects. Measured bioavailability confirmed bench tests and model calculations. Results will be included in further device optimizations.

P533

Sex differences in sildenafil-induced migraine attacks: Results from a double-blind, placebo-controlled provocation study

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Objective: Sildenafil, a phosphodiesterase 5 inhibitor, can provoke migraine attacks in susceptible individuals and is used in experimental human provocation models to explore migraine mechanisms. The drug"s effects have been studied predominantly in women with migraine and potential sex-specific differences in migraine susceptibility remain largely unexamined. This study aimed to evaluate the sildenafil´s effects in a cohort of men with migraine without aura and to compare the migraine-inducing effects of sildenafil between women and men with migraine without aura, to explore whether sex modifies the response to pharmacological provocation.
Methods: In the male cohort, 12 men with migraine without aura completed a randomized, double-blind, placebo-controlled, cross-over provocation study. Each participant received a single oral dose of sildenafil 100 mg or placebo on two separate days, with 12-hour post-dose monitoring (Figure 1). In the female cohort, 15 women with migraine without aura participated in a an open-label, single-arm provocation study with a single oral dose of sildenafil 100 mg, followed by 12-hour monitoring (Figure 2).
Results: In the female study, 11 out of 15 participants (73%) experienced a migraine-like attack following sildenafil. In the male study, only 3 migraine attacks were reported across 10 participants. Despite data from the male cohort remain blinded with respect to individual-level response patterns, these findings suggest a lower rate of sildenafil-induced migraine in men compared to women. The last two male participants will be recruited and tested before the conference.
Conclusion: Preliminary data indicate a potential sex difference in response to sildenafil as a migraine-provoking agent. These findings could reflect biological differences in migraine pathophysiology and support the importance of considering sex as a factor in provocation model design. Final data from the male cohort will be presented at the conference.

Fig. 1

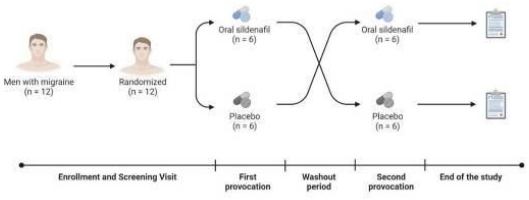
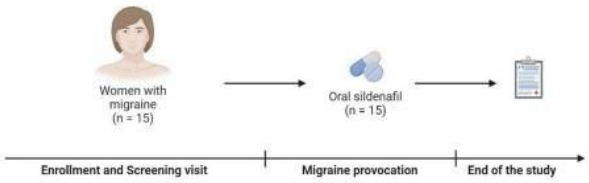


Fig. 2



P534

The efficacy of gepants in the prophylactic management of migraine: A systematic review

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Objective: To evaluate the efficacy of Gepants in the prophylactic management of migraine, focusing on the reduction of attack frequency in adult patients.
Methods: This systematic review was conducted in accordance with Cochrane and PRISMA guidelines, with protocol registered in PROSPERO (CRD420251017211). PubMed and BVS were searched through March 2025 for randomized controlled trials (RCTs) evaluating rimegepant or atogepant for migraine prevention. Included studies enrolled adults with migraine onset before age 50 and 4–14 migraine days per month.
Results: Six RCTs were analyzed. The primary outcome was the reduction in monthly migraine days compared to placebo. Rimegepant 75 mg taken every other day reduced migraine days by 0.8 (95% CI: -1.5 to -0.2; p = 0.0099). Atogepant showed reductions of 1.2 days with 10 mg QD, 0.9 to 1.4 days with 30 mg QD, 0.7 to 2.4 days with 60 mg QD, 1.4 to 2.4 days with 30 mg BID, and 1.3 days with 60 mg BID.

Conclusion: Gepants represent a safe and effective oral option for migraine prevention, with significant reductions in attack frequency and improved patient-reported outcomes. Their favorable safety profile and ease of use make them a valuable alternative to existing therapies. Further long-term, head-to-head studies are needed to confirm their sustained efficacy and comparative effectiveness.

P535

Is there an association between the effectiveness of anti-CGRP monoclonal antibodies in migraine and injection site reactions?

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Objective: Monoclonal antibodies (mAbs) that target the calcitonin gene-related peptide (CGRP) pathway are an effective prophylactic treatment for migraine. However, their subcutaneous administration can cause local injection site reactions (ISRs), such as erythema, induration or pain. It has been hypothesized that these reactions could alter the absorption and, consequently, the clinical effectiveness of these protein-based drugs. This study aimed to determine the frequency of ISRs and to investigate whether their presence is associated with treatment efficacy.

Methods: We conducted a retrospective, observational study of 334 patients treated with subcutaneous anti-CGRP mAbs at our center between 2021 and 2024. The cohort included patients receiving erenumab (24.8%), galcanezumab (27.8%) and fremanezumab (47.4%). Clinical effectiveness was assessed by comparing changes in the number of migraine and headache days, medication overuse status, and scores on the MIDAS and HIT-6 questionnaires between patients who experienced ISRs.

Results: Injection site reactions were reported in 29.5% of the 334 patients. The most common injection site was the abdomen (47.3%), followed by multiple sites (29.3%), the leg (18.5%), and the arm (5%). Despite the high incidence of local reactions, no statistically significant differences were found in any of the measured efficacy outcomes when comparing patients with and without ISRs.

Conclusion: Local reactions at the injection site are a common occurrence, affecting nearly one-third of patients on subcutaneous anti-CGRP mAb therapy for migraine. However, our findings suggest that the presence of these reactions does not compromise the clinical efficacy of the treatment. While ISRs may cause patient discomfort, they do not appear to influence therapeutic outcomes.

Fig. 1



P536

Efficacy of pharmacological and non-pharmacological interventions in the prophylaxis cluster headache: A systematic review

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Objective: This systematic review evaluates the efficacy and safety of prophylactic treatments for cluster headache (CH). The main question is which preventive therapies effectively reduce attack frequency, intensity, and duration, and their safety profiles. Objectives include assessing pharmacological treatments like galcanezumab, verapamil, lithium, and non-pharmacological options such as non-invasive vagus nerve stimulation (nVNS).

Methods: Following Cochrane and PRISMA guidelines, the protocol was registered in PROSPERO (CRD420251012089) and published on Zenodo (DOI: 10.5281/zenodo.15105877). Included were English-language RCTs and observational studies on adults with frequent or refractory CH undergoing prophylaxis. Exclusions were studies with ineligible designs, pediatric subjects, or lacking relevant outcomes. Searches were conducted in PubMed, Embase, and Cochrane Central from February 2025 onward, plus backward snowballing. Two reviewers independently extracted data and assessed bias using Cochrane"s RoB-I tool.

Results: From 1,029 articles, 16 met criteria, including RCTs and observational studies with adults experiencing frequent or refractory CH. Galcanezumab showed significant reductions in attack frequency, with ~79% achieving ≥50% reduction by week three. Verapamil and lithium also reduced attacks, differing in onset and side effects. nVNS effectively lowered attack frequency and intensity and

reduced abortive medication use. Most studies had moderate risk of bias. Quality of life improved notably with nVNS.
Conclusion: Both pharmacological and non-pharmacological prophylaxis effectively manage CH. Galcanezumab and nVNS have the strongest evidence for reducing attack frequency and severity. More long-term, large-scale studies are needed to confirm findings and tailor treatments.

P537

Comparative effectiveness: Amitriptyline and toxin botulinum in tension type headache

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Objective: The study aimed to compare the efficacy of two antidepressant drugs in the treatment of tension headache: amitriptyline and botulinum toxin, based on recent evidence, especially between 2010 and 2025.
Methods: Data was searched in the available literature, covering evidence on both the intensity of TTE attacks and their reduction.
Results: Amitriptyline is effective in reducing the frequency, duration and intensity of TTC crises. On the other hand, botulinum toxin proved to be an effective alternative for patients who do not respond to or tolerate tricyclic antidepressants.
Conclusion: Amitriptyline remains the first-line drug in the treatment of most people. However, botulinum toxin is an important alternative for cases that do not respond to the conventional approach

P538

Performance analysis of galcanezumab in the prophylaxis of cluster headache: A systematic review of clinical trials

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Objective: To assess the quality, safety and effectiveness of Galcanezumab as a preventive and abortive therapy for Cluster Headache.
Methods: Searches for clinical trials were conducted in the PubMed® database. Six randomized studies, published between 2019 and 2022, which analyzed the impact of the monoclonal antibody Galcanezumab in cluster headache were included. Effectiveness was the primary outcome, the secondary outcomes were safety and side effects.
Results: Galcanezumab has shown effectiveness in preventing cluster headache, with 63,4% to 81% of patients reporting significant improvement in the frequentness of episodes. The safety of the treatment was considered to be acceptable, with 43% to 72.6% of patients showing adverse effects, the most frequent being nasopharyngitis (6%to 22%) and injection-site pain (0% to 8%). Severe side effects were rare, with a discontinuation due to side effects rate varying between 2% to 3,1%.
Conclusion: The use of immunotherapy represents great advance in the studies on treating cluster headaches. In the long term, however, additional studies, with a larger number of subjects, will be necessary to consolidate the findings and rectify the biases of the therapeutic approach.

P539

Botulinum toxin as a preventive therapy for tension type headache: A systematic review

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Objective: To evaluate the efficacy and safety of botulinum toxin use in the prevention of tension-type headache, considering its mechanisms of action, clinical outcomes, and potential adverse effects.
Methods: This study is a Systematic Review following the PRISMA methodology, analyzing five selected articles from the PubMed, Scielo, Cochrane, and LILACS databases. The descriptors used were "Botulinum Toxins Type A," "Toxina botulínica tipo A," "botox," "Tension-Type Headache," and "Therapeutic Uses." Inclusion and exclusion criteria were applied, along with bias risk assessment.
Results: A total of articles were identified, but only five met the eligibility criteria. The results varied: some studies showed a reduction in pain frequency and intensity, while others found no significant differences compared to placebo. One study

highlighted anti-inflammatory effects in the occipital region, and another suggested that onabotulinumtoxinA could be an effective option for primary trochlear headache.
Conclusion: despite advances, methodological inconsistencies remain, and greater standardization is needed to strengthen evidence regarding its effectiveness.

P540

Reporting of lack of efficacy of anti-CGRP monoclonal antibodies in migraine patients treated with other concomitant monoclonal antibodies: A VigiBase disproportionality analysis

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Objective: Monoclonal antibodies (mAbs) targeting the calcitonin gene-related peptide (CGRP) pathway are effective preventive treatments for migraine. The impact of concurrent use of other mAbs for different indications on the efficacy of anti-CGRP mAbs remains unclear. This study evaluated reports of lack of efficacy of anti-CGRP mAbs in patients concomitantly treated with other mAbs using VigiBase, the global pharmacovigilance database.
Methods: Reports listing erenumab, galcanezumab, fremanezumab, or eptinezumab as suspected or interacting drugs and collected in VigiBase up to March 9th, 2025 were included and classified as cases (reporting lack of efficacy) or non-cases (reporting other adverse drug reactions). Disproportionality analysis was performed and adjusted reporting odds ratios (aRORs) with 95% confidence intervals (CIs) estimated via multivariable logistic regression. A signal of disproportionate reporting was defined as aROR with 95% CI lower bound >1.
Results: The study included 20866 cases and 76538 non-cases. Non-health professionals were the most frequent reporters, more so among cases (68.1% vs 58.7%, P<0.0001). Female patients were less represented in cases than non-cases (65.2% vs 76.4%, P<0.0001), as were young adults (16.2% vs 22.8%, P<0.0001). Co-reporting of other mAbs for non-migraine indications was uncommon (0.6% cases vs 1.1% non-cases) and not associated with increased odds of reporting lack of efficacy of anti-CGRP mAb treatment (aROR 0.601; 95% CI lower bound <1).
Conclusion: The concomitant use of other mAbs in patients receiving anti-CGRP mAbs for migraine is not associated with increased reporting of lack of efficacy in VigiBase. These findings offer preliminary reassurance regarding the real-world effectiveness of anti-CGRP mAbs when administered in combinations with mAbs for other indications.

P541

Pharmacokinetics and safety of Lu AG09222, an anti-PACAP monoclonal antibody in development for migraine prevention

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Objective: To investigate the pharmacokinetics (PK) and safety of Lu AG09222 using data from three phase 1 clinical trials. Lu AG09222 is a humanised monoclonal antibody targeting pituitary adenylate cyclase-activating polypeptide (PACAP) that is in development for migraine prevention.
Methods: Data were included from a (1) first-in-human single ascending dose trial in healthy participants, including a cohort with co-administered sumatriptan (Lu AG09222 n=68; placebo n=28); (2) single-dose trial in healthy Caucasian, Chinese, and Japanese participants (Lu AG09222 n=40; placebo n=12); and (3) multiple-dose trial in participants with symptomatic allergic rhinitis (Lu AG09222 n=20; placebo n=10). Assessments included intravenous (IV) doses ranging from 1 mg to 750 mg and subcutaneous (SC) doses of 100 mg and 600 mg.
Results: Overall, 128 and 50 participants received Lu AG09222 and placebo, respectively. Half-life was ~15 days (IV) and ~15–17 days (SC). Bioavailability after SC administration was ~80%. Maximum serum concentration and area under the curve increased in a dose-proportionate manner in participants receiving single IV doses from 1 mg to 750 mg. After multiple SC doses, exposure increased proportionally between 100 mg and 600 mg. There were no PK differences by sex, and PK was comparable in Caucasian, Japanese, and Chinese cohorts. Co-administration with sumatriptan did not result in PK interactions. Most treatment emergent adverse events (TEAEs) were mild; the most common TEAEs were injection site reactions (SC) and headache (both IV and SC). One

serious AE, perniosis of moderate severity, occurred in a participant 112 days after receiving a single IV dose of 750 mg Lu AG09222 co-administered with sumatriptan.

Conclusion: Lu AG09222 exhibited a consistent PK profile across dosing regimens, route of administration and race/ethnicity. Across these trials, no safety concerns were identified, and Lu AG09222 was generally well-tolerated.

P542

Discontinuation of anti-calcitonin Gene-Related Peptide (CGRP) monoclonal Antibodies (mAbs) in migraine patients after 12 months of good response: Are there any predictors of restarting mAbs need? Real-world cohort of 103 patients

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Objective: To assess whether specific demographic or clinical factors in migraine patients with good response to mAbs for at least 12 months are associated with the likelihood of retreatment after discontinuation of antiCGRP mAbs.

Methods: Retrospective observational cohort study at a tertiary Headache Unit. We included consecutive patients with high-frequency episodic migraine (HFEM) or chronic migraine (CM) treated with anti-CGRP mAbs for ≥12 months, who discontinued due to a sustained good response, defined as ≥50% reduction in baseline monthly headache days (MHD) or ≤4 MHD. Data collected included age, sex, MHD at discontinuation, treatment duration, use of concomitant botulinum toxin, and presence other chronic pain conditions. Follow-up included MHD and HIT-6 scores every 3 months. Patients provided informed consent; study approved by local Ethics Committee (HCB/2021/1327). Variables associated with mAbs reinitiation were analyzed using multivariate logistic regression (SPSS v20).

Results: We included 103 patients (mean age 49.0±13.7 years; 86.4% female); 60 had HFEM and 43 CM. They received fremanezumab (n=77) or galcanezumab (n=26) for a median of 25.9 months (IQR 15.6–39.7). Concomitant botulinum toxin was used in 40.8%. mAbs was reinitiated in 46 patients (44.7%) after a median of 91 days (IQR 67.3–126.2). No clinical or demographic variable was significantly associated with reinitiation.

Conclusion: In this real-world cohort, nearly half of the patients who discontinued anti-CGRP monoclonal antibodies after a sustained good response eventually required resuming treatment. No clinical or demographic predictors were identified, supporting individualized decisions and close follow-up.

P543

Population pharmacokinetics and pharmacodynamics of Lu AG09222, an anti-PACAP monoclonal antibody in development for migraine prevention

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Objective: To characterise the population pharmacokinetics (popPK) of Lu AG09222, a humanised anti-pituitary adenylate cyclase-activating polypeptide (PACAP) monoclonal antibody in development for migraine prevention, and to explore its pharmacokinetics (PK) and pharmacodynamics (PD) in terms of PACAP binding (target engagement).

Methods: Data were pooled from five clinical trials: four phase 1 trials in healthy individuals and one phase 2 trial in participants with migraine. These included both intravenous (IV) and subcutaneous (SC) routes of administration, with single and multiple dosing regimens. Concentrations of Lu AG09222:PACAP complexes in serum (reflecting target engagement) were used as input variables for popPK and PK/PD analyses, which were performed using nonlinear mixed-effects modelling. The interaction between Lu AG09222 and PACAP was characterised through the full target-mediated drug disposition (TMDD) model. Serum disposition of unbound Lu AG09222 was described using a two-compartment model with first-order absorption (for SC administration) and elimination.

Results: Dose- and time-dependent increases in Lu AG09222:PACAP-complex concentrations were observed, reaching approximately 50 picomolar at the highest tested dose of 750 mg IV. A clear relationship between the PK profile of Lu AG09222 and its PD effect on PACAP binding was noted for both IV and SC administration. TMDD-based model simulations showed that doses above 100 mg resulted in sustained PACAP inhibition exceeding 90% for several weeks, with modelling indicating up to 8 weeks at higher doses for both IV and SC administration.

Conclusion: Both popPK analysis and TMDD-based model simulations of Lu AG09222 demonstrated prolonged, high-level PACAP inhibition after IV and SC administration. These results support the potential of Lu AG09222 for sustained PACAP binding and inhibition in migraine prevention.

P544

Rapid delta-band functional connectivity changes in HD-EEG after one month of atogepant in migraine patients

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Objective: Atogepant is a novel oral CGRP receptor antagonist approved for migraine prevention.While its peripheral mechanisms are well characterized, little is known about its potential effects on central functional brain networks.Our study aims to investigate changes in resting-state 23 functional connectivity(FC) using high-density EEG (HD-EEG) after one month of atogepant in patients with migraine, and to assess the relationship between these changes and clinical response.

Methods: 12 patients with high-frequency episodic migraine (HFEM;n=7) or chronic migraine (CM;n=5) underwent HD-EEG recordings at two time points:before starting Atogepant (T0) and after one month of therapy(T1).15 healthy controls(HC) were also enrolled.Clinical evaluations included: monthly migraine days, monthly symptomatic drugs intake, modified Migraine Disability Assessment, the headache impact test(HIT-6), the Migraine-Specific Quality of Life Questionnaire, the 12-item Allodynia Symptom Checklist, and the Migraine Interictal Burden Scale.EG-based FC was analyzed in source space using the weighted Phase Lag Index (wPLI) across δ,θ,α,β,low-γ, and high-γ bands.

Results: Compared to HCs, HFEM+CM patients exhibited increased δ band FC in temporo-parietal,orbitofrontal,insular,and limbic regions.At T1 a significant reduction in this aberrant FC was observed,particularly in bilateral temporo-parietal,cingulate,insular, and prefrontal cortices.Baseline δ-band FC correlated with greater clinical disability,while therapy-induced FC changes(ΔmNC) were associated with improvements in mMIDAS,HIT-6, and ASC-12 scores,highlighting the clinical relevance of δ band network modulation

Conclusion: Our study provides preliminary evidence that one-month therapy with atogepant modulates δ band FC in HFEM+CM patients.These changes in central brain networks are associated with clinical improvement and may serve as a neurophysiological marker of CGRP receptor antagonist efficacy.Larger-scale studies are needed to confirm and extend our findings.

Fig. 1

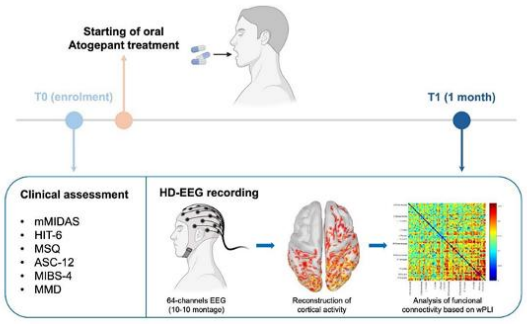


Fig. 2

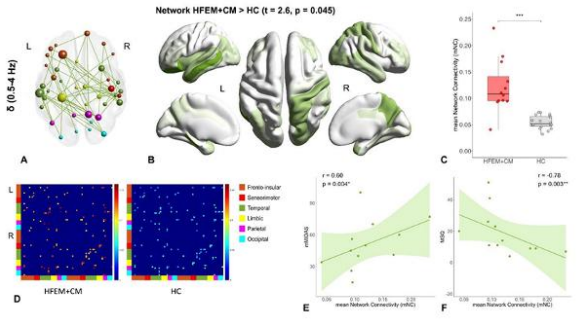
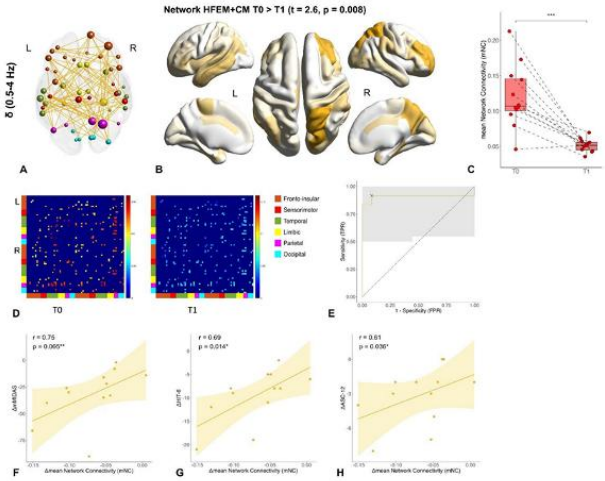


Fig. 3



P545

Failure of CGRP inhibition as a treatment for complex regional pain syndrome

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Objective: Calcitonin gene-related peptide (CGRP) is a potent vasodilator and pain modulator involved in migraine pathophysiology and possibly in complex regional pain syndrome (CRPS). Both conditions have

been associated with elevated CGRP levels, raising interest in targeting this peptide therapeutically.
Methods: We report a 51-year-old woman with chronic, treatment-resistant migraine and a 2-year history of CRPS following Achilles tendon rupture.
The patient gave their informed consent to publish their details in an open access journal.
Results: Preventive migraine therapies, including oral drugs and botulinum toxin, were ineffective. She was started on galcanezumab (anti-CGRP monoclonal antibody), resulting in a rapid and sustained reduction in migraine frequency (from 16 to 4 days/month) and severity, with significant improvement in quality of life. Rimegepant (a CGRP receptor antagonist) was also effective for acute attacks. However, despite this response, CRPS-related pain and autonomic symptoms remained unchanged, with scales of pain dimension (PGIC and PNVRS) revealing severe pain persistence and lack of perceived change in CPRS-related symptoms despite six months of anti-CGRP therapy.
Conclusion: This case highlights a clinical dissociation between two CGRP-associated conditions. Despite a marked improvement in migraine with anti-CGRP therapies, chronic CRPS did not respond to the same treatment. This may suggest that, in the chronic phase of CRPS, the pathophysiological mechanisms may not predominantly depend on CGRP, reflecting differences in pain pathophysiology in the chronic stage. While migraine predominantly involves CGRP-mediated trigeminovascular pathways, CRPS may involve more complex and multifactorial mechanisms, including central sensitization, neurogenic inflammation, and autonomic dysfunction. This example underscores the importance of a differentiated approach to chronic pain conditions, even in the presence of shared biomarkers.

P547

Migraine prevention with Fremanezumab: Efficacy assessment

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Objective: To analyze Fremanezumab (FRM's) efficacy in migraine prevention.
Methods: This study examines FRM's efficacy based on a literature search in Scielo and PubMed.The descriptors "Migraine,""Fremanezumab,""Efficacy" and "Prevention" were used,including their Portuguese and English equivalents.Articles published in the past five years on FRM's therapeutic potential were included.FRM,a humanized IgG2a/kappa monoclonal antibody,blocks CGRP,reducing migraine frequency by modulating the trigeminal system.It reaches peak concentration in 5-7 days,with 55%-66% bioavailability and a 30-day half-life,allowing gradual elimination without dose adjustments for elderly or those with mild to moderate hepatic or renal insufficiency.
Results: According to Silberstein et al. (2017),chronic migraine patients treated with FRM had a significant reduction in headache days:4.3 days with quarterly doses,4.6 days with monthly doses,versus 2.5 days in the placebo group.Additionally, 40% of patients had at least a 50% reduction in attack frequency. Similarly,Friedman and Cohen(2020) highlight FRM as a specific option for migraine prevention,even in difficult-to-treat cases.
Conclusion: FRM demonstrares sustained long-term efficacy and significant clinical benefits, including in patients with comorbidities like depression and medication overuse. Its innovative mechanisms and favorable pharmacokinetics make it a promising option for migraine prevention.

P548

Safety and effectiveness of rimegepant for acute treatment of migraine in adults unsuitable for triptan use: Results from a 12-week open-label extension phase

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Objective: To evaluate safety and attack-to-attack reliability of rimegepant (RIM) for acute treatment of migraine over 12 weeks in adults unsuitable for triptans, and to explore changes in monthly migraine days (MMDs).
Methods: This was a 12-week open-label (OL) extension of a randomized double-blind (DB) placebo-controlled trial in adults unsuitable for triptans due to history of intolerance or lack of efficacy to ≥2 triptans, or contraindication (NCT05509400). Participants

treated migraine attacks of moderate or severe pain intensity with RIM 75 mg orally disintegrating table (ODT) as needed (PRN), up to once per day. Safety was assessed by adverse events (AEs). Efficacy endpoints included: (1) reliability of RIM effect, (2) mean change from historical baseline (HBL) in MMDs, and (3) percentage of participants with ≥50% reduction from HBL in MMDs. Reliability was defined as response rates for ≥4 of the first 5 evaluable qualifying migraine attacks (EQMAs) ≥23 hours apart during the OL phase being no more than 7% less than the single EQMA rate for RIM participants in the DB phase. Response was defined as migraine symptoms "moderately or very much better" at 24 h post-dose.

Results: 552 participants took OL RIM and 94.0% completed the OL phase. Mean time on treatment was 9.4 weeks and mean exposure was 4.9 ODTs per month. Severe AEs (0.5%), serious AEs (0.4%), and AEs leading to RIM discontinuation (0.9%) were infrequent. Reliability of RIM effect was met: response was 64.2% for the DB EQMA and 65.1%–71.1% across the first 5 OL EQMAs (**Table 1**). Mean (SD) change in MMDs was −2.8 (3.3) days (**Figure 1**), and 38.9% of participants achieved ≥50% reduction (**Figure 2**).

Conclusion: In triptan-unsuitable adults, RIM 75 mg ODT PRN for up to 12 weeks demonstrated favorable safety, stable population-level effects across repeated attacks, and fewer MMDs.

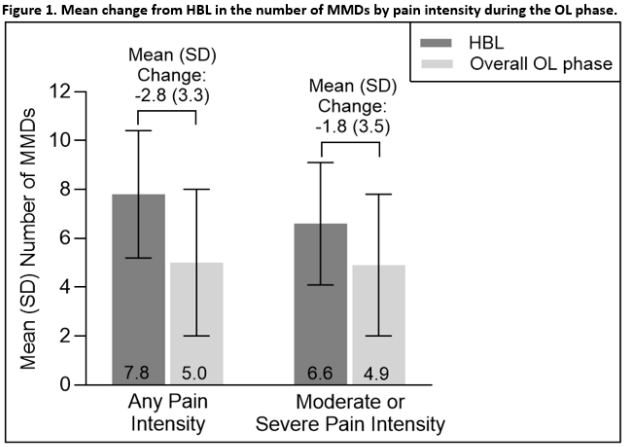
Fig. 1

Table 1. Reliability of rimegepant effect

EQMA	Percentage	Percentage Difference (DB phase – OL phase)
DB phase EQMA		
n/N[a]	156/243	
% (95% CI)	64.2 (58.2, 70.2)	-
OL phase first EQMA		
n/N[b]	345/530	
% (95% CI)	65.1 (61.0, 69.2)	-0.9*
OL phase second EQMA		
n/N[b]	342/511	
% (95% CI)	66.9 (62.8, 71.0)	-2.7*
OL phase third EQMA		
n/N[b]	340/492	
% (95% CI)	69.1 (65.0, 73.2)	-4.9*
OL phase fourth EQMA		
n/N[b]	317/448	
% (95% CI)	70.8 (66.5, 75.0)	-6.6*
OL phase fifth EQMA		
n/N[b]	248/349	
% (95% CI)	71.1 (66.3, 75.8)	-6.9*

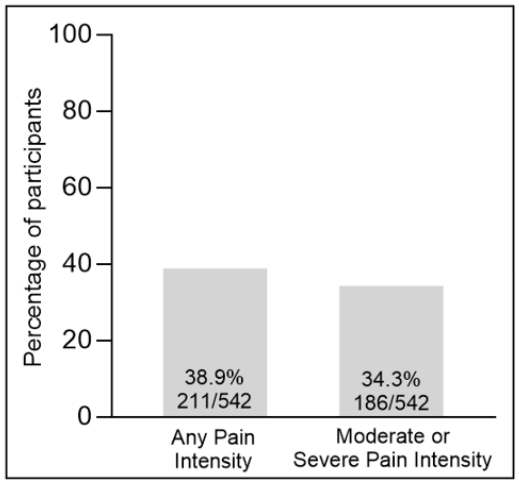
EQMA was a migraine attack of moderate or severe pain intensity that was first treated with rimegepant (not non-study medication such as ibuprofen) and had non-missing quality of life data 24 h post dose.
[a] Evaluable participants who took rimegepant during the DB phase
[b] Evaluable participants who took OL rimegepant.
*Difference between phases is ≤ pre-specified threshold of +7%.
Abbreviations: DB, double-blind; EQMA, evaluable qualifying migraine attack; n, number of participants with response; N, number of participants evaluated; OL, open-label.

Fig. 2



Analyzed in participants who took OL rimegepant and were in the OL phase for ≥14 days (N=542). Abbreviations: HBL, historical baseline; MMDs, monthly migraine days; OL, open-label; SD, standard deviation.

Fig. 3



Analyzed in participants who took OL rimegepant and were in the OL phase for ≥14 days (N=542). Abbreviations: HBL, historical baseline; MMDs, monthly migraine days; OL, open-label.

P549

Efficacy, safety, and tolerability of atogepant for the acute treatment of migraine: Results from the ECLIPSE trial

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Objective: Evaluate the efficacy, safety, and tolerability of atogepant 60 mg compared with placebo for the acute treatment of a single migraine attack.
Methods: ECLIPSE was a randomized, double-blind (DB), placebo-controlled study to evaluate the efficacy, safety, and tolerability of atogepant for the acute treatment of migraine. Subjects were randomized to 4 DB treatment sequences to treat 4 qualifying migraine attacks with moderate or severe headache with atogepant or placebo. The first attack (1:1 placebo to atogepant allocation) was the single attack used for the primary and 16 secondary efficacy endpoints. The primary endpoint was pain freedom at 2 hours postdose (2h). Two of the key secondary endpoints were absence of the most bothersome symptom (MBS) and pain relief at 2h. The multiple-attack design was to evaluate consistency of effect. After treating 4 qualifying DB migraine attacks within 16 weeks, subjects entered an open-label (OL) period up to week 24. Efficacy was assessed after all main study subjects completed the DB period; safety was assessed for DB and available OL data.
Results: Atogepant (N=602) was superior (*P*<.0001) to placebo (N=612) when percent responders were compared for pain freedom (atogepant=24.3%; placebo=13.1%; OR:2.36[1.76,3.15]), MBS freedom (atogepant=43.7%; placebo=32.7%; OR:1.77[1.41,2.24]), and pain relief (atogepant=72.1%; placebo=54.4%; OR:2.35[1.85,2.98]) at 2h. There were no treatment-emergent adverse events (AEs) with incidence ≥2%, and one serious AE (SAE) occurred after placebo treatment for the first attack. No SAEs were considered related to atogepant or occurred in >1 subject in the DB period. No new safety signals were identified.
Conclusion: Atogepant was efficacious, safe, and well tolerated for the acute treatment of migraine.

P551
Preclinical platforms for headache therapeutics: PACAP-38 and Capsaicin Vasodilation models in rodents
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Objective: Migraine is a complex neurovascular disorder involving vasodilation, neuroimmune activation, and nociceptive signaling. PACAP-38 and capsaicin are key mediators implicated in migraine pathophysiology through distinct mechanisms; PACAP-38 via signaling through its receptors and mast cell activation, and capsaicin via TRPV1 receptor-mediated neurogenic inflammation. This study aimed to establish and validate two complementary in vivo models of dermal vasodilation in anesthetized rats to support mechanistic profiling and therapeutic screening of headache-relevant targets.
Methods: In the PACAP model, male Sprague-Dawley rats received intravenous DPBS 24 hours prior to intradermal PACAP-38 (1 nmol or 10 pmol/site) or PBS vehicle. In the capsaicin model, male Wistar rats received topical capsaicin (1 mg/site) or ethanol:acetone vehicle applied on the ears (1 - 2 mg/site), abdomen, or back. Vasodilation was monitored using laser speckle contrast imaging (Moor FLPI2) at baseline and at intervals up to 60 minutes (PACAP) or 30 minutes (capsaicin).
Results: PACAP-38 at 1 nmol/site administered at the lower abdomen level induced a robust increase in dermal blood flow (~50%), sustained over 60 minutes. No effect was observed at the lower dose (10 pmol/site) or when administered at the dorsal lower back level, indicating a dose- and site-dependent response. The capsaicin effect in the ear was dose-dependent, with the 2 mg/site dose producing a peak increase of ~83% at 15–17.5 minutes, compared to ~48% with the 1 mg/site dose. In the abdomen, capsaicin elicited a peak increase of ~43–48% between 10 and 20 minutes, with consistent significance across time points. In the back, the response was moderate (~37–41%), peaking around 15–20 minutes. Responses were consistent across anatomical sites and time points, validating the model"s robustness for mechanistic profiling.
Conclusion: These models offer a translational platform for dissecting migraine-relevant mechanisms and validating therapeutic hypotheses.

P552
Candesartan exerts an antinociceptive effect in trigeminal pain model and reduces serotonin content in the brainstem
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Objective: Candesartan, an AT1 angiotensin receptor antagonist, primarily a cardiovascular drug, has also

been used for migraine prophylaxis. While its clinical benefit in migraine prevention has been proven, the mechanism of this effect is still unknown. Considering that some migraine prophylactics target serotonergic and/or noradrenergic transmission and that the projections from serotonergic/noradrenergic brainstem nuclei can modulate trigeminal nociception, we tested the effect of candesartan in a trigeminal pain model and its propensity to affect the content of these monoamines in the brainstem.

Methods: The antinociceptive effect of candesartan was investigated in the orofacial formalin test (OFT) in mice, after acute and five-day repeated oral administration. Its effect on motor ability was assessed by rotarod test. Serotonin and noradrenaline concentrations in brainstem homogenates were determined by HPLC with electrochemical detection.

Results: Candesartan significantly and dose-dependently reduced the duration nociceptive behavior in the first and second phase of the OFT, after both acute (0.5-7 mg/kg) and prolonged administration (0.5-4 mg/kg; Fig 1). The highest acutely administered dose (7 mg/kg) did not affect rotarod performance (Fig 2). Repeated administration of candesartan (4 mg/kg/day) significantly reduced serotonin concentrations in the brainstem, while the concentrations of noradrenaline remained unaffected (Fig 3).

Conclusion: Candesartan has an antinociceptive effect in the trigeminal pain model after single and repeated prophylactic administration. Its effect after repeated administration may be related to the reduction of serotonin levels in the brainstem. These results could contribute to understanding the mechanism of action of candesartan in migraine prophylaxis.

Fig. 1

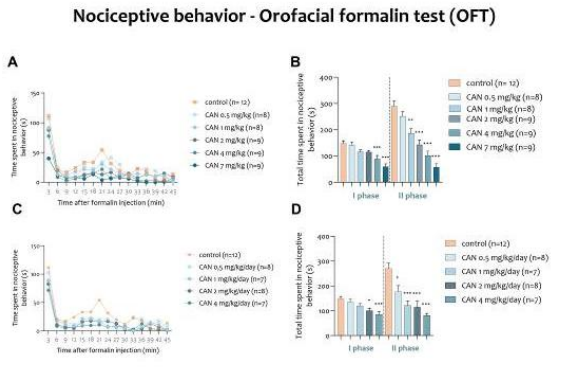


Fig 1. Candesartan (CAN) exerted antinociceptive effects after both acute and repeated administration. Time course of nociceptive behavior (face rubbing) in 3-min bins is represented on graphs on the left side (panels A and C) and the total time spent in nociceptive behavior in phase I (0–9 min post-formalin) and phase II (9–45 min post-formalin) is represented on graphs on the right side (panels B and D). Standard error bars are omitted from the time course graphs in the interest of clarity. The columns represent mean group values (with standard error bars). CAN was administered orally, 45 min before (panels A and B), or repeatedly over 5 days before formalin injection (panels C and D). Statistical significance (*P < 0.05, **P < 0.01, ***P < 0.001; one-way ANOVA followed by Tukey post-hoc test) was determined in comparison with the control group.

Fig. 2

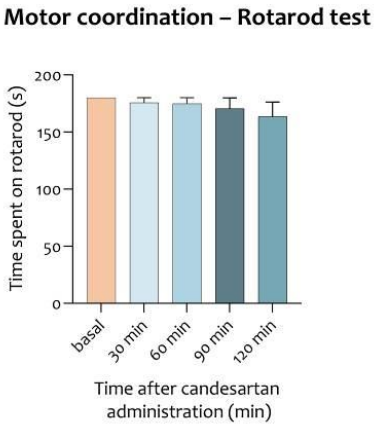


Fig 2. Candesartan did not affect rotarod performance of experimental animals. Candesartan was orally administered in the highest acute dose that was examined in OFT (7 mg/kg, n=7), and rotarod performance was evaluated in four time points (30, 60, 90, and 120 min following drug application). Columns represent mean group values (with standard error bars) of the time spent on the rotating rod. Statistical significance was determined with the Mann-Whitney U test in comparison with the basal values.

Fig. 3

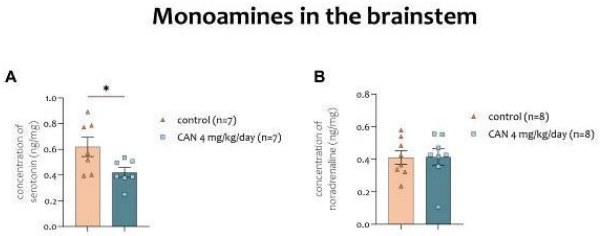


Fig 3. Repeated administration of candesartan significantly reduced serotonin concentration in the brainstem (A), while the concentration of noradrenaline remained unaffected (B). Candesartan was orally administered at a dose of 4 mg/kg/day for five consecutive days. Serotonin and noradrenaline concentrations in brainstem homogenates were determined by HPLC with electrochemical detection. Columns represent mean group values (with standard error bars). Statistical comparisons with the control group were performed using the Student t-test (*P<0.05).

P553

Time course of rimegepant effect for acute treatment of migraine in adults unsuitable for triptans: Exploratory endpoints from a phase 4 randomized double-blind placebo-controlled study

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Objective: To assess the time-course of rimegepant-mediated improvements in migraine symptoms

following acute treatment in adults unsuitable for triptans.

Methods: Exploratory endpoints from a trial of rimegepant in adults unsuitable for triptans due to history of intolerance or lack of efficacy to ≥2 triptans, or contraindication (NCT05509400) are reported. Participants randomized to single-dose rimegepant 75 mg orally disintegrating tablet or placebo treated 1 migraine attack of moderate or severe pain intensity. The percentage of participants with migraine pain relief, migraine pain freedom, return to normal function, and most bothersome symptom (MBS; nausea, photophobia, or phonophobia) freedom was assessed from 15 minutes to 48 hours post-dose. Treatment comparisons used crude risk estimation (nominal P values).

Results: Participants (rimegepant=286, placebo=284) were mostly female (89.3%) and had documented failure to ≥2 triptans with ≥1 reason due to prior intolerance (30.5%) or lack of efficacy (84.9%); 9.1% had a contraindication. Improvements of ≥5% for rimegepant over placebo with nominal P≤0.05 (difference [95% CI]) were first observed at 1 hour for pain relief (8.6% [1.3%, 15.8%]; P=0.0201), 1.5 hours for pain freedom (6.2% [1.5%, 11.0%]; P=0.0103) and return to normal function (7.1% [1.1%, 13.1%]; P=0.0210), and 2 hours for MBS freedom (12.5% [5.4%, 19.5%]; P=0.0005). Improvements of ≥5% over placebo were maintained at all subsequent time points. Differences (95% CI) at 48 hours were 31.2% (23.5%, 39.0%; P<0.0001) for pain relief, 33.4% (25.9%, 40.9%; P<0.0001) for pain freedom, 34.1% (25.8%, 42.5%; P<0.0001) for return to normal function, and 23.2% (15.5%, 31.0%; P<0.0001) for MBS freedom.

Conclusion: Improvements in migraine symptoms occurred within 1–2 hours of treatment with rimegepant and were sustained over 48 hours in adults unsuitable for triptans.

P554

Dual inhibition of FAAH and TRPV1 receptors counteracts nitroglycerin-induced migraine-like symptoms only in male rats

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Objective: Anandamide (AEA), an endogenous cannabinoid, plays a key role in migraine pain via CB receptors and TRPV1. Inhibiting AEA degradation through FAAH and blocking TRPV1 both show anti-nociceptive effects. Recent findings suggest dual FAAH/TRPV1 inhibition may enhance analgesia. This study explored the interaction between the endocannabinoid system (ECS) and TRPV1 in a nitroglycerin (NTG)-induced migraine model using a dual FAAH inhibitor and TRPV1 antagonist (arachidonoyl serotonin, AA-5-HT) as a pharmacological probe.

Methods: Adult male and female Sprague-Dawley rats received NTG (10 mg/kg, i.p.) or vehicle 4 hours before behavioral testing. Fifteen minutes before testing, animals were treated with AA-5-HT (5 mg/kg, i.p.), a dual FAAH/TRPV1 blocker, or vehicle. Behavioral tests included the elevated plus maze (EPM) test, immediately followed by the orofacial formalin test. Subsequently, rats were euthanized for the assessment of serum CGRP levels in both sexes.

Results: In the EPM test, NTG induced anxiety-like behavior, detected as a reduction in the time spent and the distance traveled in the maze open arms, only in male rats. This behavior was not influenced by AA-5-HT administration. NTG administration induced an increase in nocifensive behavior during the second phase of the orofacial formalin test and in CGRP serum levels in both sexes. However, only in males, the administration of AA-5-HT counteracted NTG-induced increase in nocifensive behavior and serum CGRP levels.

Conclusion: The dual inhibition of AEA degradation and TRPV1 activity induces sex-specific effects in the NTG-induced migraine model, with anti-hyperalgesic effects observed exclusively in males. These results suggest a sex-specific role of the endocannabinoid system in migraine.

P555

Calcitonin gene-related peptide induces headache exacerbations in people with idiopathic intracranial hypertension

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Objective: Calcitonin gene-related peptide (CGRP), known for its role in migraine pathogenesis, may also underlie headache generation in idiopathic intracranial hypertension (IIH), which commonly presents with migraine-like features.

Methods: A randomized, double-blind, placebo-controlled, two-way crossover trial was conducted. Seventeen adults with IIH and no prior migraine were randomly assigned to receive a 20-min continuous intravenous infusion of CGRP (1.5 µg/min) or placebo (isotonic saline) on two separate experimental days.

Primary outcome was the difference in incidence of typical IIH headache exacerbations with migraine features between CGRP and placebo during a 12-h observational period post-infusion. Secondary outcomes were the differences in area under the curve (AUC) for headache intensity, intracranial pressure (ICP) and cerebrovascular haemodynamics.

Results: Twelve (71%) participants developed IIH headache attacks with migraine-like features after CGRP infusion, compared with three (18%) after placebo (P=0.0077). The AUC for headache intensity was higher following CGRP infusion (P=0.0157). Although the AUC of mean ICP remained unchanged, ICP amplitude increased significantly after CGRP (P=0.0052). Cerebrovascular haemodynamics were significantly altered after CGRP (increased: heart rate (P<0.0001), tissue oxygenation index (P=0.0413), oxygenated haemoglobin (P<0.0001) and decreased: mean arterial pressure (P=0.0099), middle cerebral artery blood velocity (P=0.0055)).

Conclusion: These findings suggest that CGRP is a potent inducer of migraine-like headaches in IIH and may represent a promising therapeutic target.

P556

Bridging the gap: Unraveling molecular mechanisms, regional activity patterns and connectivity pathways in headache disorders

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Objective: Chronic headache disorders severely affect psychosocial functioning and are often poorly managed. Understanding their molecular, regional, and connectivity mechanisms is key to improving and developing more effective treatments. Despite available fundamental and clinical data, combined reports remain scare. This study pioneers in bridging the gap between diverse fields of expertise by providing a comprehensive overview of the molecular mechanisms, regional activity patterns, and connectivity pathways involved in migraine, cluster headache (CH), paroxysmal hemicrania (PH), hemicrania continua (HC), and occipital neuralgia (ON), all interpreted from a clinical perspective.

Methods: Literature on molecular mechanisms, regional activity and connectivity pathways for migraine, CH, PH, HC and ON has been collected from the PubMed, MEDLINE and EMBASE databases.

Results: In total, 120 and 97 articles are included in the analysis of the molecular mechanism and regional activity patterns/connectivity pathways respectively. Molecular data identify the trigeminal nucleus caudalis (TNC) as a key site in headache pathology, rich in neuropeptides like VIP, glutamate, substance P, and serotonin (Figure 1). Sensitization of higher cortical brain areas, neuroinflammation within the trigeminal system and vasodilatation of cranial vessels seem to contribute to headache pain. Headache disorders are associated with atypical regional activity patterns and connectivity pathways in pain processing areas, as well as the default mode network, salience network, and sensorimotor network. These abnormalities help explain both general headache symptoms and disorder-specific features, such as cortical spreading depression in migraine, rhythmic attacks in CH, and autonomic symptoms in CH, PH, and HC.

Conclusion: The current article fosters a deeper understanding of the molecular mechanisms, neuronal pathways and clinical symptoms involved in headache pathology across different fields of expertise.

Fig. 1

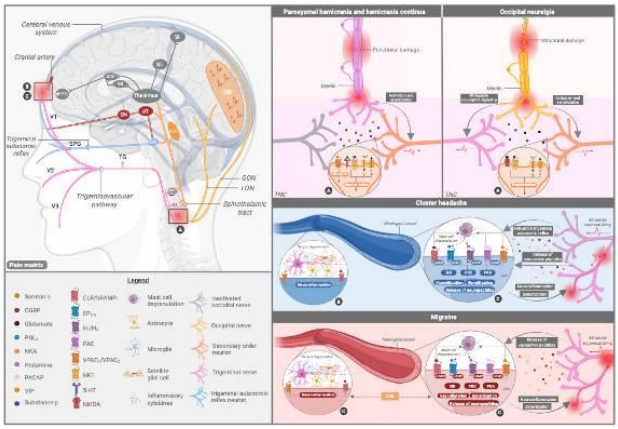


Fig. 2

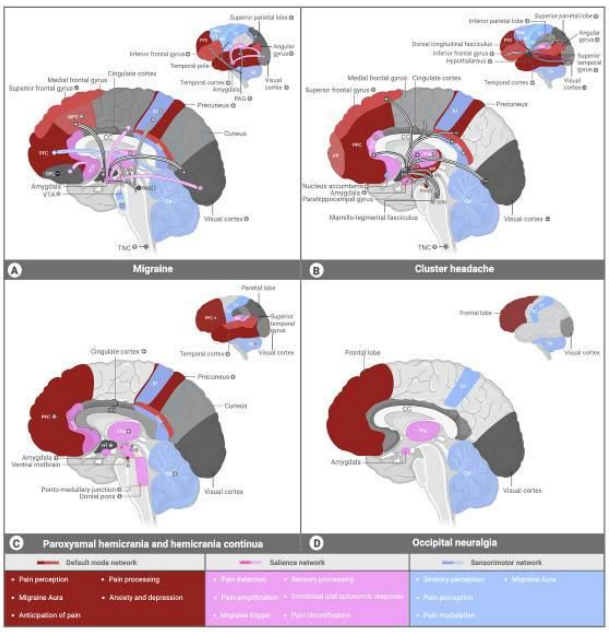
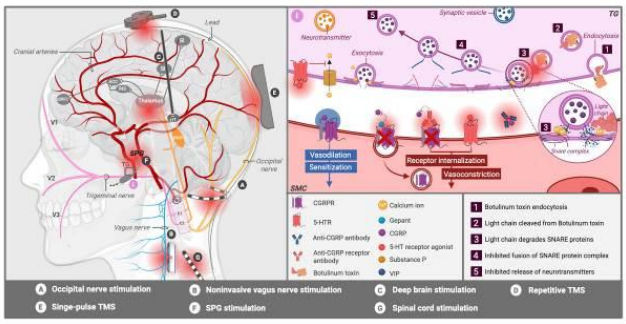


Fig. 3



P557

Eye movement patterns reflect vertigo sensations in vestibular migraine

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Objective: Vertigo in vestibular migraine (VM) is often difficult to describe yet may provide mechanistic clues. We examined the relationship between subjective vertigo sensations and eye movement patterns to explore oculo-perceptual dynamics in VM.
Methods: Fifteen participants with VM (diagnosed per Bárány Society and ICHD-3 criteria) and ten healthy participants (HP) underwent neuro-otological testing, including 3D video-oculography (VOG) in primary gaze, with and without visual fixation (20 seconds per condition). Participants reported any subjective sensations during testing. Three VM patient and one HP also received intravenous nitroglycerin (0.5 µg/kg) as part of the NITROVest study (IRAS 312478).
Results: All VM participants described sensations of spinning, sliding, oscillation, or unsteadiness. Gaze remained stable with fixation in all participants; however, ocular drifts emerged without fixation. In VM patients, spontaneous nystagmus and eye drifts were directionally congruent with their reported vertigo axis—horizontal or vertical. The three VM cases triggered with NTG experienced an increase of those symptoms and eye movements following infusion, whereas no changes occurred in the HP.
Conclusion: Eye movement abnormalities in VM, though subtle, showed directional alignment with subjective vertigo experiences, indicating oculo-perceptual congruence. These findings support the concept that central vestibular dysregulation in VM may enhance internal eye motion signals, contributing to vertiginous sensations. Understanding this perceptual-motor linkage may aid in deciphering VM pathophysiology and support future efforts in biomarker development.

P558

Preserved reaction time but increased cognitive errors after nitroglycerin in vestibular migraine: A brain fog phenotype?

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Objective: Patients with migraine often report "brain fog", a subjective cognitive dysfunction that lacks objective characterization. Nitroglycerin (NTG) infusion, a validated human migraine model, may reveal subtle cognitive changes during interictal or early migraine states. We used a sustained attention to response task (SART) to assess error rate and reaction time before and after NTG administration in vestibular migraine patients.
Methods: Seven participants with vestibular migraine completed a computerized SART task before and after i.v. NTG (0.5 mcg/Kg) as part of the NitroVest study at King"s College London. Outcome measures included number of mistakes and mean reaction time (latency). Data were tested for normality (Shapiro-Wilk) and compared using paired *t*-tests. Due to missing data, two participants were excluded from the cognitive performance analyses, resulting in a final sample size of $n = 5$.
Results: SART latency was preserved after NTG: mean latency before = 293 ms (SD = 62), after NTG = 291 ms (SD = 54), $t(4) = 1.35$, $P = 0.25$. However, participants made significantly more mistakes after NTG: mean mistakes before = 6.2 (SD = 4.4), after NTG = 8.3 (SD = 3.1), $t(4) = -2.98$, $P = 0.041$, 95% CI [-6.95, -0.25].
Conclusion: Despite preserved response speed, migraine patients made more cognitive errors after

NTG, consistent with a "brain fog" phenotype characterized by inefficient attention rather than global slowing. This dissociation between speed and accuracy may reflect early cognitive changes in the migraine cascade. NTG-induced paradigms may help quantify subjective brain fog and define its neural mechanisms

P559

Hyperprolactinemia and migraine-like headache: A case report and literature review

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[3]Hospital CUF, Porto, Portugal

Objective: Prolactin (PRL), a pituitary hormone, has been increasingly implicated in migraine pathophysiology. Clinical and experimental studies suggest that hyperprolactinemia may contribute to headache—particularly in women—through sensitization of trigeminal nociceptors and interaction with CGRP pathways. Headache may be independent of tumor mass effect and respond to dopamine agonists.
Methods: We present a case of migraine-like headache in a young woman with hyperprolactinemia due to a prolactinoma, highlighting pathophysiology and treatment.The patient provided informed consent for journal publication.
Results: A 23-year-old female pharmacist initially presented to gynecology with headaches as the primary complaint. Routine labs revealed elevated prolactin. Brain MRI showed an indeterminate pituitary lesion. She was treated with bromocriptine for three months, achieving complete headache resolution. Symptoms recurred several months after discontinuation, prompting endocrinology follow-up. Repeat MRI showed a pituitary microadenoma, and cabergoline was reinitiated, with significant headache improvement. Three months before reassessment, the cabergoline dose was halved per endocrinologist recommendation. Headaches then recurred—mainly during periovulatory and perimenstrual phases. Prolactin levels slightly increased. Headaches were severe, holocranial, migrainous with nausea, and resistant to analgesics. Neurological exam was unremarkable. Eletriptan was prescribed for acute attacks. Endocrinology follow-up was advised.
Conclusion: This case supports the role of PRL in migraine-like headaches via neuromodulatory effects, independent of tumor mass. PRL receptors in trigeminal pathways suggest a sensitization mechanism. Dopamine agonists may relieve symptoms, even without tumor shrinkage, indicating a hormonal component. Pituitary hormones like PRL and hypothalamic peptides such as oxytocin may underlie sex differences in migraine.Endocrine evaluation is advised in refractory or atypical headache cases.

P562

Clinical and brain metabolic features distinguishing outcome groups in chronic migraine with medication overuse: An FDG PET study

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Objective: To investigate clinical and metabolic correlates of outcome in chronic migraine with medication overuse (CM-MO) using ^18F-FDG PET.
Methods: Twenty-seven CM-MO patients and 17 healthy controls underwent baseline clinical evaluation of headache profiles, mood, sleep quality, and dependence on painkillers (Severity of Dependence Scale [SDS], Modified Leeds Dependence Questionnaire and Yale–Brown Obsessive Compulsive Scale), along with ^18F-FDG PET imaging. At 1-year follow-up, patients were classified as good (n=14) or poor outcome (n=13) based on headache frequency and analgesic use. Poor outcome was defined as continued frequent painkiller use (≥10–15 days/month, depending on drug type) and ≤50% reduction in monthly headache days. Group differences in FDG uptake and covariance patterns were assessed, and their associations with clinical measures were evaluated.
Results: Poor-outcome patients were older, had longer chronic migraine history, and higher SDS scores than good-outcome patients (9.5 ± 2.5 vs. 7.4 ± 2.6, p= 0.043), despite similar baseline headache freuqency and painkiller use frequency, mood, and sleep. No metabolic differences were found between all CM-MO patients and controls. Stratified analyses showed hypermetabolism in the right inferior temporal gyrus in good-outcome patients, and in the nucleus accumbens, thalamus, orbitofrontal/subcallosal cortex, and cerebellum in poor-outcome patients. Poor-outcome patients exhibited stronger cerebellar-putamen and cerebellar–occipital covariance. Among patients with CM-MO, bilateral cerebellar activity (right: r=0.469, p=0.018; left: r=0.459, p=0.021) and cerebellar–putamen covariance (right: r= 0.576, p= 0.003; left: r=0.664, p<0.001) were correlated with SDS scores.
Conclusion: Distinct clinical and metabolic profiles differentiate outcome groups in CM-MO, with

cerebellar circuits emerging as a hub linking dependence and refractory headache.

Fig. 1

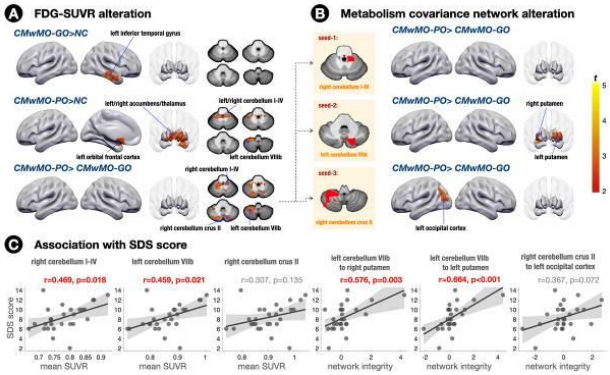


Fig. 2

Table 1. Clinical features of chronic migraine with medication overuse by outcome group

Variable	CM with MO (n=27)	Poor outcome (n=13)	Good outcome (n=14)	p-value
Age	42.3 ± 9.0	45.9 ± 9.6	39.0 ± 7.3	0.046
Sex (F/M)	20/7	9/4	11/3	0.580
Duration of CM	137.3 ± 87.9	182.6±85.2	95.1±69.2	0.007
Headache days per month	21.6 ± 6.1	23.5 ± 6.5	19.7 ± 5.3	0.105
Painkiller days per month	20.7 ± 6.3	22.8 ± 6.3	18.7 ± 5.8	0.090
HADS-A	8.3 ± 4.3	7.6 ± 4.4	8.9 ± 9.3	0.467
HADS-D	6.2 ± 3.6	7.1 ± 4.2	5.3 ± 2.9	0.204
LDQ score	14.8 ± 6.4	17.1 ± 6.8	12.6 ± 5.4	0.071
SDS score	8.4 ± 2.7	9.5 ± 2.5	7.4 ± 2.6	0.043
BOCS score	17.9 ± 6.7	19.2 ± 8.3	16.6 ± 4.8	0.327
PSQI score	10.3 ± 3.2	10.8 ± 3.1	9.8 ± 3.3	0.437

HADS – Hospital Anxiety and Depression Scale; LDQ –Modified Leeds Dependence Questionnaire; SDS – Severity of Dependence Scale; Y-BOCS – Yale–Brown Obsessive Compulsive Scale; PSQI – Pittsburgh Sleep Quality Index

P563

Beyond symptom: Exploring the analgesic properties of vomiting in migraine patients

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Objective: To characterize the prevalence, temporal kinetics, and extent of vomiting-induced migraine pain relief (VIMPR).

Methods: We conducted an explorative, cross-sectional, questionnaire-based study on migraine patients referring to our headache center. We assessed vomiting frequency, number of episodes, pain intensity on numerical rating scales (0-10) for attacks with and without vomiting, temporal relationship between vomiting and VIMPR, pain recurrence patterns, as well as vomiting induction behaviors.

Results: Among 106 migraine patients, 82 (77.4%) reported vomiting during attacks. Attacks with vomiting were significantly more painful than those without (median 9.0 vs 7.0, p<0.001). VIMPR occurred in 45 patients (54.9%), with 12 (14.6%) experiencing complete attack cessation while 33 (40.2%) only temporary reduction. Onset of pain relief occurred within seconds in 28.9% of patients, within minutes in 40.0%, and within hours in 31.1%. Among patients with pain recurrence, 57.6% experienced reduced intensity compared to pre-vomiting levels. Voluntary vomiting induction was reported by 22 patients (26.8%), and was more common among those familiar with VIMPR (40.0% vs 10.8%, p=0.007).

Conclusion: Vomiting provides therapeutic benefit in more than half of migraine patients. The rapid onset of VIMPR suggests activation of endogenous antinociceptive mechanisms rather than coincidental attack resolution. The learned behavior of voluntary vomiting induction further supports the genuine neurobiological basis of VIMPR. Overall, findings highlight vomiting as a potential activator of migraine pain–terminating circuits, and underscore the need for further studies to elucidate the underlying neurological mechanisms.

Fig. 1

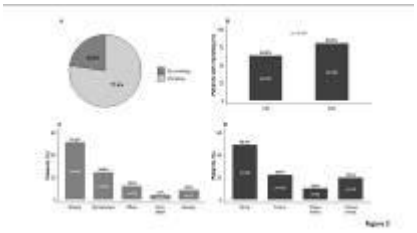


Fig. 2

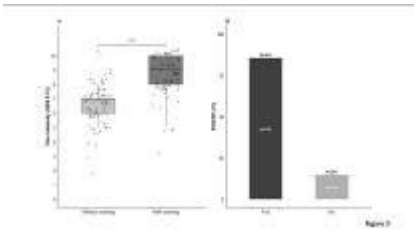
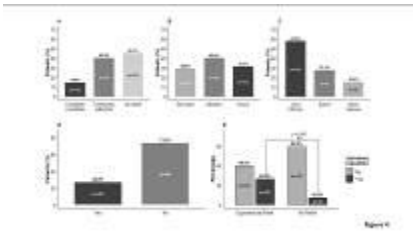


Fig. 3



P564

Arterial spin labeling evaluation of cerebral perfusion during spontaneous attacks of migraine without aura – A 3-Tesla MRI Study

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Objective: Migraine is a complex disorder that involves both peripheral and central components of the trigeminovascular pain pathway. However, the interaction between these peripheral and central structures of this system is unknown. During migraine attacks, dilation of meningeal and cerebral arteries on the pain side has been suggested to reflect peripheral activation of the trigeminovascular system. A key question is whether changes in cerebral blood flow (CBF) may reflect increased neuronal activation on pain side during migraine attacks, potentially serving as a surrogate marker for underlying central mechanisms.

Methods: Migraine patients without aura were MRI scanned during spontaneous attacks and on a separate, attack-free day, using arterial spin labeling at 3T.

Results: Twenty-one patients were scanned during a migraine attack, and 17 of them were also scanned on an attack-free day. Among these, 13 patients were scanned during unilateral attacks. The CBF increased on pain side during these unilateral attacks, compared to attack-free days (7%, p= 0.038). This increase in CBF was positively correlated with pain intensity (p=0.038). The CBF remained unchanged between attack day and attack-free day in patients with bilateral attacks (p=0.154).

Conclusion: The CBF was increased on pain side during spontaneous attacks of migraine without aura. This increase was positively correlated with pain intensity. Our findings suggest lateralized changes in neuronal activity during migraine attacks, supporting the previously observed lateralized vasodilation towards the pain side. Further studies are needed to clarify the sequential activation of peripheral and central mechanisms during migraine attacks.

P565

The association between vertigo and neck discomfort in chronic migraine

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Objective: A position paper of the Barany society on cervicogenic dizziness concluded more research was necessary prior to the establishment of this a separate entity. However, ENT and Neuro-otology doctors often diagnose cervicogenic dizziness. We hypothesised whether neck pain and vertigo could be plausibly related to shared migraine mechanisms.

Methods: Chronic migraine patients seen within the Tertiary Neurology Service at King"s College Hospital between 2015 and 2020 were identified (*n*=589). Extended phenotypic data was extracted from the first clinic consultation letter, and tabulated (IBM SPSS *v* 31). All migraine symptoms were coded as dichotomous variables (present or absent), and descriptive statistics were used to summarise the patient demographics: age, sex, presence of aura, monthly headache days. The presence neck discomfort was analysed using a binomial logistic regression model with logit link function, and predictors of vertigo, age, aura, gender, monthly headache days and allodynia. Significance was assessed at $P<0.005$.

Results: Patients were aged 16-92 years (median 47, IQR 37-57), and 83% were female. Half the patients had aura. The median number of monthly headache days was 30 (IQR 22-30). Of the patient group, 264 reported vertigo with attacks (44.8%) and 240 (40.7%) reported neck discomfort. The percentage agreement of reporting of vertigo and neck discomfort was 52.8%. The presence of vertigo was significantly associated with neck discomfort (OR 1.85, 95% CI 1.28-2.68, P=0.001). There were no other variables of significance in the model.

Conclusion: We demonstrate in a large cohort of chronic migraine patients that vertigo and neck discomfort commonly co-exist. One explanation would be shared thalamic sensitisation mechanisms. could the data offer a plausible explanation for what has been termed cervicogenic dizziness and warrants further exploration.

P566

Altered functional connectivity between the middle cingulate cortex and occipital cortex in migraine: A REFORM study

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Objective: Functional magnetic resonance imaging (fMRI) has advanced our understanding of migraine neurobiology. However, prior evidence is limited by small samples and suboptimal statistical thresholds. To address these limitations, we compared resting-state functional connectivity (rs-FC) between a large sample of people with migraine and matched healthy controls (HCs), as well as across migraine subtypes.

Methods: Adults with migraine and age- and sex-matched HCs underwent 3T rs-fMRI. We analysed rs-FC using multivoxel pattern analysis and seed-based approaches, applying general linear models and ANCOVA tests with Bonferroni-adjusted clusterwise family-wise error correction ($p \leq 0.001$). rs-FC, measured as Z scores, were compared across migraine subtypes using Bonferroni-adjusted general linear models ($p < 0.05$).

Results: We included rs-fMRI data from 264 migraine participants and 151 HCs. The multivoxel pattern analysis revealed significant rs-FC differences in the bilateral middle cingulate cortex between migraine participants and HCs (p <0.001). The seed-based analysis showed increased rs-FC between the middle cingulate cortex and both the right lateral occipital cortex and bilateral occipital pole in migraine participants compared to HCs (both p <0.001). Furthermore, increased rs-FC was identified between the limbic lobe and the right occipital pole (p=0.0014) and precuneus (p<0.001). The cingulate-occipital rs-FC was consistently increased across migraine subtypes (p <0.001). Ictal participants who were scanned during attacks exhibited an increased hypothalamic rs-FC with the bilateral precuneus, compared with HCs (p <0.001).

Conclusion: The rs-FC alterations between the middle cingulate and occipital regions may represent a migraine-specific trait, supporting a link between nociceptive and visual processing. These findings offer novel insights into migraine pathophysiology and suggest altered cingulate-occipital rs-FC as a potential biomarker.

P567

Tear fluid calcitonin gene-related peptide is elevated in headache during high altitude exposure

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Objective: High-altitude headache (HAH) is a common neurological condition associated with rapid ascent to high altitude. The pathophysiological mechanisms underlying HAH remain incompletely understood. Calcitonin gene-related peptide (CGRP) may play a role in the pathophysiology due to shared clinical presentation of migraine and HAH. In this study tear fluid CGRP was investigated in healthy subjects during a high altitude stay at 4554m.

Methods: This study is a prospective field study during a high-altitude trekking expedition in the Alps over 4 days beginning at Varallo (450m) to the Margherita hut (4554m). Headache and accompanying symptoms were raised using a structured questionnaire daily and tear fluid samples were collected from both eyes at study day 1 (baseline, 450 m), at study day 3 (3647 m) and at study day 4 (4554 m). Tear fluid CGRP concentrations were quantified using a commercially available ELISA kit.

Results: 13 participants were included in the analysis. At 4554m, 11 participants (84.6%) reported headache and eight participants (61.5%) reported HAH. Participants fulfilling the ICHD-3 criteria for HAH, increase of tear fluid CGRP was significantly higher compared to participants without HAH (HAH: +1.49 ± 1.74 ng/ml, no HAH: -0.42 ± 0.64 ng/ml; $p = 0.011$). Further, the increase of tear fluid CGRP levels was significantly higher in participants with a moderate-to-severe headache (+1.86 ± 1.86 ng/ml) compared to participants with mild headache (- 0.19 ± 0.75 ng/ml; $p = 0.008$).

Conclusion: CGRP might play a role in the pathophysiology of high-altitude headache and might not only be a key mediator of primary, but also secondary headache. Further studies with a larger number of participants are needed to improve our knowledge of high-altitude headache.

P568

Targeted steroid phenotyping from newly diagnosed and treatment naïve patients with idiopathic intracranial hypertension with a translational perspective

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Objective: Idiopathic intracranial hypertension (IIH) is a complex neurometabolic disorder, most commonly affecting obese women of reproductive age. Emerging evidence suggests that steroid hormones may contribute to IIH pathophysiology, however the literature lacks a comprehensive characterization of steroid profiles in treatment naïve, newly diagnosed patients with IIH and at clinical remission.
Methods: We performed targeted steroid profiling in treatment-naïve IIH patients (n=56) and compared to matched controls (n=35). Furthermore, we compared them at disease baseline and at remission (n=10). We quantified the level of 13 key steroid hormones, including progestins, androgens and corticosteroids in cerebrospinal fluid (CSF) and serum. We also assessed the capacity of progesterone to elicit a calcium response in choroid plexus (CP) from transgenic mice as a surrogate marker for CSF production.
Results: We found that 7 steroids in the CSF and 3 steroids in the serum were differential. In CSF we found a 27% increase of pregnenolone ($P<0.001$), 46% increase of progesterone ($P<0.05$) and a 31% increase of 17-OH pregnenolone ($P<0.001$) in IIH compared to controls. At disease remission we found that CSF pregnenolone was 43% lower ($P<0.005$) and CSF testosterone was 37% lower ($P<0.005$) compared to baseline. Progesterone increased calcium activity in CP from transgenic mice.
Conclusion: Androgens and progestins were elevated in treatment naïve and newly diagnosed IIH patients, which indicate a link between endocrine dysfunction and CSF dynamics in IIH. Furthermore, in a translational study we showed that progesterone increased calcium activity in CP the main site of CSF secretion. This implies that progesterone increase CSF secretion and therefore contribute to the elevated intracranial pressure in IIH.

P569

TMS-EEG indicates altered cortical excitability in visual snow syndrome

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Objective: Visual snow syndrome (VSS) involves dysfunctional central visual processing, with altered glutamatergic and GABAergic neurotransmission in V1 and V5. Up to 80% of patients have comorbid migraine, which exacerbates VSS symptoms, suggesting shared pathophysiology. Transcranial magnetic stimulation (TMS) with electroencephalography (EEG) assesses excitation/inhibition (E/I) balance. Time-frequency decomposition of TMS-EEG signal results in TMS-related spectral perturbations (TRSP), with early alpha TRSP reflecting GABAA receptor-mediated inhibition and late alpha/beta TRSP modulated by GABAA and GABAB receptors. Our aim was to investigate TMS-EEG biometrics as markers of impaired cortical E/I balance in VSS.
Methods: TRSP were recorded from left M1, V1 and V5 in 15 participants with visual snow syndrome (VSS with concomitant migraine; mean age=35.2), 15 episodic migraineurs (MO; mean age=34.5) and 15 healthy controls (HV; mean age=26.6). Group differences were calculated using multiple independent t-tests with cluster-based permutation analysis to correct for multiple comparisons.
Results: VSS exhibited significantly reduced suppression of late alpha and beta TRSP over M1 (260–520 ms; 210–400 ms) and reduced late alpha (520–800 ms) compared with HV ($P = 0.047$; $P = 0.04$; $P = 0.009$). MO also showed reduced late alpha (500–800 ms) compared with HV ($P = 0.019$). In addition, VSS demonstrated lower gamma TRSP suppression (190–320 ms) over V1 and reduced late alpha (500–800 ms) over V5 compared with HV ($P = 0.041$). Finally, VSS showed lower late alpha (500–760 ms) over V5 compared with MO ($P = 0.009$).
Conclusion: Increased alpha/beta suppression over M1 and reduced gamma TRSP over V1, together with lower late alpha over M1 and V5, suggest impaired GABA receptor–mediated inhibition. The difference in late alpha TRSP over V5 with respect to both HV and MO demonstrates a distinct neurophysiological profile in VSS, indicating region-specific E/I imbalance.

P570

Neuronal and vascular network activity in familial hemiplegic migraine type 2 mutant mice

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Objective: Mice of a novel knock-in (KI) familial hemiplegic migraine type 2 (FHM2) model display regular, spontaneous events of spreading depolarization (SD). The FHM2 mutant mice carry the human pathogenic T345A missense mutation in the a2 subunit of Na+/K+ ATPase (Jansen et al. Neurobiol Dis 2024;202:106714) and provide a unique opportunity to study mechanisms and consequences of spontaneously occurring SD *in vivo.*
Methods: In the present work, we explored brain activity features that may contribute to the initiation of spontaneous SD, focusing on neuronal and vascular network changes, and shifts in sleep state.
Results: Non-invasive on-the-skull recordings revealed a consistent daily-to-bidaily occurrence of SD, similar to what had been reported with invasive recording. With respect to sleep features, homozygous FHM2 mutant mice exhibited reduced REM sleep and prolonged periods of active wakefulness compared to heterozygous and wild-type littermates. The majority of SD events started during NREM sleep. EEG recordings show altered brain activity with a reduction in spectral power and slowing of the theta peak frequency. To assess possible vascular reactivity and functional neurovascular network changes underlying the SD phenotype, we applied functional ultrasound imaging (fUSi). Stimulus-evoked fUSi responses to visual and whisker stimulation uncovered genotype-dependent alterations in cerebral hemodynamics. Resting-state fUSi experiments are ongoing and will allow us to assess functional connectivity features of the FHM2 mouse model across brain regions, including the hippocampus and visual cortex.
Conclusion: Our findings highlight distinct hippocampal and cortical neurophysiological and vascular changes in FHM2 mutant mice, including sleep-related trigger mechanisms of SD. Together this offers insight into the mechanisms leading to spontaneous initiation of SD in this genetic context and contribute to a better understanding of migraine auro pathophysiology.

P571
Auditory processing deficits in migraine: CGRP drives excitotoxic cochlear injury via ZBP1-Mediated PANoptosis
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Objective: While sensory processing abnormalities—affecting visual, somatosensory, and proprioceptive systems—are well-documented in migraine, the auditory domain remains largely unexplored, particularly regarding peripheral mechanisms. This study aims to elucidate how migraine induces peripheral auditory damage and the role of CGRP in the inner ear, which may contribute to the precise subtyping of migraine and inform targeted auditory-protective therapies
Methods: A mouse model of chronic migraine was established with injections of NTG. The expression of CGRP in the cochlea was measured. Auditory brainstem response (ABR) was used to evaluate hearing function. The target differentially expressed pathway was validated and manipulated in both HEI-OC1 cells and the inner ear.
Results: Mice developed hind paw mechanical and hot plate hyperalgesia after NTG injections. The CGRP and its receptor expression was upregulated,especially in outer hair cells(OHCs).The migraine mouse model exhibited higher ABR thresholds, longer wave I latency and hair cell injury, all of which could be reversed by Rimegepant.We found that ZBP1 and its related PANoptosis and inflammation pathway were significantly upregulated in the cochlea.Blockade of ZBP1 and its downstream signaling could rescue migraine-related hair cell injury both in vivo and in vitro.
Conclusion: We extend the pathophysiology relevance of migraine and auditory dysfunction, demonstrate that migraine causes functional and structural damage to the OHCs(the cochlear amplifiers)-rather than to spiral ganglion neurons,challenging the previous common presumed injury site. We identified CGRP-mediated excitotoxicity as the direct driver of this damage, beyond classic vascular permeability mechanisms.These findings refine the mechanistic model of migraine-related auditory dysfunction and provide a phenotypic basis for further subtyping of cochlear migraine, paving the way for mechanism-driven auditory protection strategies.

Fig. 1

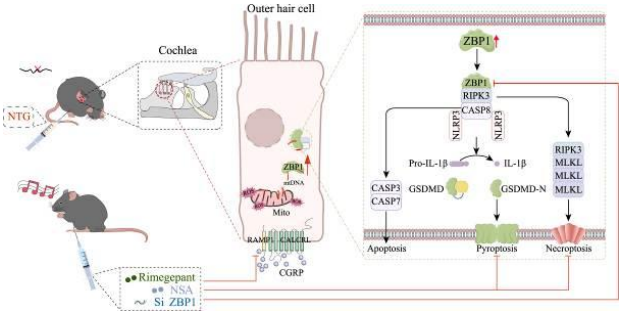


Fig. 2

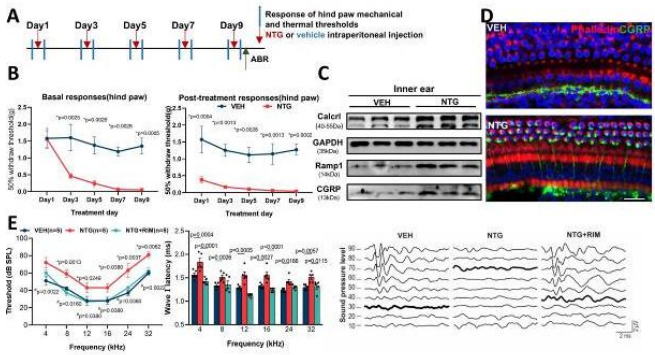


Fig.1 The nitroglycerin-induced chronic migraine mouse model exhibited increased expression level of CGRP in cochlea and auditory dysfunction, which could be rescued by Rimegepant.

Fig. 3

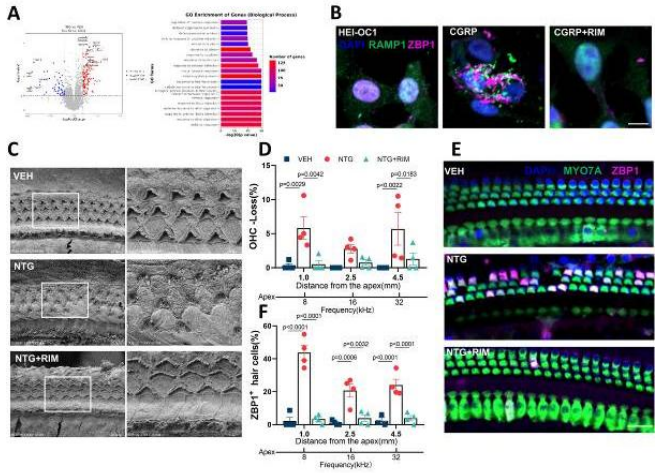


Fig.2 ZBP1 was activated in the cochlea of migraine mouse model group and CGRP stimulated HEI-OC1 cells, inducing hair cell injury.

P572

Sleep macro- and microstructure in migraine and cluster headache: A systematic review of objective assessments

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Objective: Sleep disturbances are commonly reported in primary headache, yet the neurophysiological basis remains poorly defined. While subjective reports of sleep disruption are well established, there is no consensus on the objective alterations in sleep architecture which may occur in headache.

Methods: We conducted a systematic review across 4 databases (Embase, Medline, PubMed and APA PsycInfo) to identify studies assessing objective sleep parameters via polysomnography or actigraphy in individuals with migraine or cluster headache, including relevant preclinical models. Sleep macrostructure and microstructure were evaluated across different ages and headache attack phases.

Results: Thirty-one studies met the inclusion criteria, with significant heterogeneity resulting in varied findings. Among paediatric migraine, evidence indicates a significant reduction in total sleep time and rapid eye movement (REM) sleep, in addition to elevated wake after sleep onset. In adult migraine, findings were more variable, though several studies indicate an increase in sleep fragmentation, although such measures are under-reported. Though limited, microstructural analysis including cyclic alternating pattern and sleep spindles revealed alterations compared to controls, though a consistent pattern of changes is not yet apparent across studies. Notably, a small number of studies report reduced arousability the night preceding headache headache onset, compared to headache-free periods, suggesting headache-phase specific changes in sleep architecture.

Conclusion: Objective evidence supports disrupted sleep architecture in headache disorders, particularly in relation to fragmentation and microstructure. These changes may reflect shared pathophysiological mechanisms involving brainstem and hypothalamic arousal networks. Greater methodological consistency, patient stratification and detailed reporting of headache phase are essential to establish whether a reproducible sleep phenotype exists in migraine and cluster headache.

P573

Increased susceptibility to cortical spreading depolarization in mouse models of migraine and depression

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Objective: Migraine often coexists with depression, increasing the overall disease burden. Cortical spreading depolarization (CSD), the physiological correlate of migraine aura, can be measured in preclinical mouse models. This study aims to assess CSD susceptibility in mouse models of migraine, depression, and, a novel combined model of both conditions, in order to better understand their relationship.

Methods: C57BL/6J 8-week-old female and male mice were randomly assigned to four groups: (1) Control, (2) Migraine, (3) Depression, and (4) Migraine+Depression. The Migraine group received 5 nitroglycerin injections (10 mg/kg) administered every other day for 9 days. The Depression group underwent a 21-day chronic unpredictable mild stress

protocol. The Migraine+Depression group was exposed to both protocols. KCl-induced CSDs were recorded in anesthetised mice 24h after completion of the protocols. The number of CSDs were quantified, and data were analysed using Poisson models in R, with results expressed as incidence rate ratios (IRRs), representing the relative change in CSD counts between groups.

Results: Poisson models revealed that female mice in the Migraine (IRR=1.45; p=0.001), Depression (IRR=1.75; p<0.001), and Migraine+Depression groups (IRR=1.90; p<0.001) showed significantly higher CSDs counts compared with Controls. By contrast, no significant differences were detected among male groups.

Conclusion: These findings suggest that depression alone and the combination of migraine and depression markedly increase CSD susceptibility in females mice, to a level comparable with that observed in the migraine model. In contrast, no significant effects were detected in males, underscoring a sex-specific influence on CSD susceptibility. Taken together, these results provide experimental evidence for a comorbid interaction between migraine and depression, particularly in females.

P576

Sensory certainty and placebo effect in migraine: The role of interoceptive awareness

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Objective: The Bayesian Brain Hypothesis (BBH) proposes that pain perception results from the interaction between certainty in priors (e.g. conditioning) and sensory signals [1]. Migraine may emerge from an increased reliance on prior experiences, contributing to its chronification. We aimed to assess the certainty of sensory signals, the placebo effect, and their associations with clinical characteristics using the Focused Analgesia Selection Test (FAST) and an experimental placebo paradigm.

Methods: This abstract reports preliminary data from an ongoing study including episodic migraine patients (MG) and healthy controls (H). Participants attended two sessions: (1) clinical assessment and (2) completion of the FAST and a conditioning + verbal suggestion paradigm. Primary outcomes included FASTR2, FASTICC, expectations (E1–E3), conditioning strength (CondSTR), placebo effect (PlacEff), years with symptoms (YS), and the Multidimensional Assessment of Interoceptive Awareness (MAIA).

Results: To date, 27 MG and 19 H have been enrolled. PlacEff did not differ between groups (p = 0.403). In MG, ICC correlated negatively with PlacEff (FASTR2: rs = –0.447, p = 0.019; FASTICC: rs = –0.375, p = 0.054), suggesting that greater sensory certainty is associated with a lower placebo effect. In H, higher MAIA "Not Distracting" scores showed a trend towards moderating the FASTICC–PlacEff relationship (p = 0.056), which was not observed in MG (p = 0.175).

Conclusion: These preliminary results suggest that migraine patients with greater sensory certainty (higher FAST outcomes) may exhibit lower placebo effects. The MAIA findings indicate that higher interoceptive awareness in healthy individuals may help preserve flexibility between sensory input and expectation—a mechanism that seems less effective in migraine and may relate to its persistence.

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P577

Neuroimmune dysregulation and comorbidity mechanisms of major depressive disorder and migraine

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Objective: Although major depressive disorder (MDD) and migraines often present together, their comorbidity mechanisms are complex. This study aims to identify potential biomarkers and common mechanisms of MDD-migraine through neuroimmune microenvironment and transcriptome data, which is crucial for understanding its pathogenesis and developing diagnostic and treatment strategies.

Methods: We constructed a dynamic atlas of neural-peripheral immune cells in patients experiencing MDD-migraine comorbidity. Differentially expressed genes (DEGs) were identified and performed functional enrichment and metabolic analyses of cell types involved in MDD and migraine. Multiple classification models were built by combining single-nucleus RNA sequencing and transcriptome data from patients with MDD to screen hub genes. In addition, cluster, cell communication, and trajectory analyses of major cell types in migraines were performed. Finally, common pathways in MDD-migraine comorbidity were identified.

Results: We identified 60,982 and 22, 523 cells in patients with MDD and migraines, respectively. The proportions of oligodendrocytes and excitatory neurons were increased in the MDD group, while that of T cells was significantly increased in the migraine group. DEGs in the MDD and migraine cell types were associated with Rap1 signaling. Metabolic reprogramming was found to involved in the pathological processes of MDD and migraines. Six hub genes were screened using the optimal model: AHI1, NRCAM, PTMA, RABGAP1L, RPL15, and RPL41. T cells were the major cell subpopulation in migraines, and CD8+ T cells were the starting point of differentiation. Finally, eight common pathways were identified between MDD and migraine.
Conclusion: This study provides new insights into the pathogenesis of MDD-migraine comorbidity suggesting that the identified key genes and signaling pathways may provide potential targets for the early diagnosis and treatment of the disease.

P578

Distinct inflammatory profiles across migraine clinical states: A systematic review and meta-analysis

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Objective: Although several meta-analyses have emphasised the role of inflammation in migraine, none have accounted for the diversity of its clinical manifestations. This review and meta-analysis provides a comprehensive and reliable assessment of cytokine levels in migraine.
Methods: Original studies on cytokine levels in migraine were included through a systematic search on PubMed, Embase and Cochrane on July 4–5, 2024. Non-inclusion criteria covered studies on hemiplegic migraine, controls with tension-type headache, and unclear cytokine identification. Studies involving less than 10 participants *per* group or lacking accessible numeral data were not included.
Results: Fifty-seven studies were included in the narrative review and/or meta-analysis. In episodic migraine patients *versus* controls, blood levels of interleukin-6 (IL-6, Standardized Mean Difference [SMD] 0.37 [95% CI, 0.10; 0.63], P=0.008, I^2=71.8%, nine articles), transforming growth factor β (TGF- β, SMD 0.64 [95% CI, 0.44; 0.84], P=0.000, I^2=0.0%, two articles) and C-X-C motif ligand 8 (CXCL-8, narrative review, three articles) were elevated. Levels of IL-6 (narrative review, three articles; SMD 1.40 [95% CI, 0.95; 1.86], P=0.000, I^2=0.0%, two articles) and adiponectin (ADP, SMD 0.59 [95% CI, 0.19; 0.99], P=0.003, I^2=36.0%, three articles) were elevated in chronic *versus* episodic migraine. Levels of interleukin-1β (IL-1β, SMD 0.43 [95% CI, 0.10; 0.75], P=0.010, I^2=0.0%, two articles), interleukin-10 (IL-10, narrative review, two studies) and salivary levels of IL-6 (narrative review, two articles) were elevated in ictal *versus* interictal migraine.
Conclusion: This study highlights the association of distinct cytokine profiles with migraine disease (IL-6, TGF-β, CXCL-8), migraine attacks (IL-1β, IL-6, IL-10) and migraine chronification (IL-6, ADP). Differences in inflammatory profiles across migraine clinical states have significant implications for understanding disease mechanisms, progression, and potential therapeutic interventions.

P579

Pituitary adenylate cyclase-activating polypeptide-38 (PACAP-38)-mediated mast cell degranulation: Targeting immune interactions

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Objective: PACAP-38 is involved in vasodilation, nociceptive signalling, and immune interactions. Previous studies suggest that PACAP-38 influences mast cell activity, particularly in meningeal tissues, where mast cell-derived mediators contribute to inflammatory processes. This study aimed to establish an in vitro PACAP-mediated mast cell degranulation (MCD) model to investigate the effects of PACAP-38 on histamine release and assess the inhibitory potential of a PACAP-targeting antibody.
Methods: Rat peritoneal mast cells were incubated with increasing concentrations of PACAP-38 (0.005 to 30 µM) for a two-hour stimulation period. Histamine release was quantified using an enzyme immunoassay, with Compound 48/80 (a selective mast cell activator) serving as a positive control. To evaluate inhibition, mast cells were pre-treated with either an anti-PACAP antibody or control human IgG (hIgG) at concentrations of 0.01–30 µM prior to PACAP-38 exposure. Cromoglycate, a mast cell stabilizer, was included as a reference inhibitor.
Results: PACAP-38 induced a robust concentration-dependent histamine release, confirming its role in mast cell activation. Anti-PACAP significantly inhibited PACAP-38-mediated histamine release, with up to 151% relative inhibition. Cromoglycate efficiently inhibited histamine release induced by PACAP-38, and hIgG exhibited no inhibitory effect, verifying its function as a negative control.

Conclusion: Our findings provide further evidence that PACAP-38 plays a role in MCD and immune interactions. The MCD model offers a platform to assess molecular modulators of mast cell responses. The observed inhibition of histamine release by anti-PACAP suggests opportunities for further investigation, particularly in understanding the broader implications of PACAP-driven immune processes. Future studies will be necessary to define how PACAP-targeted approaches may contribute to the regulation of inflammatory pathways and potentially MCD in the context of pain pathophysiology.

P580

When headaches speak first: Trigeminal autonomic cephalalgia as an early clue to autoimmune encephalitis – A case report

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Objective: Trigeminal autonomic cephalalgia (TAC) syndromes, although rare in the spectrum of headache disorders, are of great importance to recognize, because they can be debilitating and may be linked to potentially serious underlying causes. We present a patient with a TAC-like headache, where the diagnostic workup revealed a new secondary cause for TAC syndromes.
Methods: A 62-year-old male patient has been referred with a complaint of experiencing a new-onset headache located in the left orbitofrontal region. Each episode lasted 15 minutes and was repeated 3 to 4 times a day with mild continuous pain between episodes. Severe pain was associated with psychomotor agitation and ipsilateral cranial autonomic symptoms. Brain and vascular imaging showed mild pachymeningeal enhancement. Cerebrospinal fluid pressure and analysis were normal except for a high protein level. Further investigation for a secondary cause revealed a positive result for serum anti-N-methyl D-aspartate (NMDA) receptor antibody. The headaches were resolved after 5 days of intravenous methylprednisolone followed by oral prednisolone.
Results: There are various etiologies for secondary TACs. Most of them are structural lesions, especially in the sella turcica region, and vascular disorders such as dissection or aneurysm. To our knowledge, this is the first case of TAC associated with autoimmune encephalitis antibodies that responded significantly to corticosteroids.
Conclusion: This patient, along with cases of Neuromyelitis Optica-Spectrum Disorder (NMO-SD) with TAC presentation, highlights the role of autoimmunity in TAC syndromes.

P581

The role of microglia in migraine pathophysiology: Emerging mechanisms and translational potential

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Objective: To review current findings on microglial involvement in migraine pathophysiology, with an emphasis on molecular signaling pathways, sex-specific responses, and therapeutic implications.
Methods: We conducted a literature review of preclinical and clinical studies (2018–2025) investigating microglial function in migraine models, focusing on inflammatory mediators, neuron–glia interactions, and genetic or pharmacological manipulation of microglial activity.
Results: Experimental studies demonstrate that microglial activation in key migraine-related brain regions (e.g., trigeminal nucleus caudalis, thalamus, cortex) precedes or accompanies headache-like behavior in animal models. Activated microglia release pro-inflammatory cytokines (IL-1β, TNF-α) and promote neuronal sensitization via purinergic (P2X4, P2X7), TLR4, and cGAS-STING pathways. Notably, sex-dependent differences in microglial responses have been observed, potentially contributing to the female predominance in migraine prevalence. Emerging data also suggest that CGRP and microglial signaling may intersect to exacerbate pain pathways.
Conclusion: Microglia are not passive bystanders but active modulators of migraine pathophysiology. Targeting microglial signaling offers a novel therapeutic avenue and may help refine current treatments by accounting for neuroimmune mechanisms. Further studies are needed to delineate the temporal dynamics and regional specificity of microglial responses in migraine.

P582

Migraine as a differential diagnosis for cadasil in young individuals

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Objective: To identify migraine as an initial symptom of CADASIL.
Methods: Assess migraine in patients with CADASIL.
Results: The proportion of migraine in patients with CADASIL is five times higher than in the general population. The first symptoms usually occur before the age of 20, with the average age of onset being 30 years. In women, symptoms appear earlier than in men. Migraine often precedes other symptoms by many years and MRI scans may still appear normal, leading to delays and diagnostic errors. The relationship between migraine and CADASIL may be explained by the identification of genetic abnormalities occurring on chromosome 19, the same chromosome involved in familial hemiplegic migraine. A characteristic feature of migraine in CADASIL is the presence of aura symptoms, with visual symptoms being the most prevalent, followed by sensory, aphasic, motor symptoms. Some individuals present with atypical aura. A possible mechanism for the increased prevalence of aura in CADASIL patients is an increased susceptibility to cortical spreading depression. The triggering factors of migraine with aura are similar to those in the general population.
Conclusion: Migraine, especially when accompanied by aura symptoms, may be an initial symptom of CADASIL and should be considered as a differential diagnosis, particularly in younger individuals

P583
Pathophysiological mechanisms in infectious headache
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Objective: Headache is a frequent manifestation of both systemic and central nervous system (CNS) infections, yet its underlying pathophysiology remains underrecognized and poorly characterized in clinical neurology. This abstract aims to summarize key mechanistic pathways linking infection and headache, emphasizing their diagnostic and therapeutic relevance.
Methods: We conducted a targeted literature review using PubMed and Scopus databases to identify recent studies addressing the mechanisms of infection-associated headache. Articles discussing intracranial and systemic infectious processes, meningeal nociception, cytokine-mediated inflammation, and post-infectious neuroimmune changes were included. Conceptual synthesis was aligned with the ICHD-3 framework to ensure clinical relevance.
Results: Infectious headache develops through overlapping mechanisms, including meningeal irritation, activation of the trigeminovascular system, intracranial pressure changes, and systemic inflammation. Post-infectious cases may reflect sustained neuroimmune activation even after pathogen clearance.
Conclusion: Infectious headache is not a uniform entity but results from distinct and overlapping pathophysiological mechanisms. Recognizing these pathways may improve classification, enhance clinical suspicion in atypical cases, and support the development of mechanism-based treatment strategies. Integrating immune and structural insights into routine diagnostic frameworks may refine the management of infection-related headaches in both acute and post-infectious settings.

P584
Altered cytokine receptor expression in cluster headache patients
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Objective: To investigate cytokine receptor expression in cluster headache (CH).
Methods: RNA was purified from collected blood samples from 16x CH participants and 16x control participants. RNA was also purified from fibroblast cultures from 11x CH participants and 9x control participants. RNA was converted to cDNA to perform RTqPCR on a QuantStudio 5 instrument using SYBR green. Primers for 7x cytokine receptor genes (CCR3 and CCR5 (cytokines: CCL8, CCL11, CCL13), CXCR3 (cytokines: CXCL10, CXCL11), MET (cytokine: HGF), TNFRSF10c (cytokine: TNFSF10), TNFRSF25 (cytokine: TNFSF12) and OSMR (cytokine: OSM)) were obtained from Invitrogen. RNA expression was normalized to housekeeping gene TBP. Group averages were analysed using welch t-test in R-studios.
Results: In blood samples, a significant increase was seen in RNA expression of TNFRSF10c (P<0.05) and TNFRSF25 (P<0.05) in CH group vs healthy controls, no difference was seen in RNA expression of CCR3, CCR5, CXCR3, or MET genes. In fibroblast culture supernatant, RNA expression was significantly increased in CXCR3 ($P>0.05$) and TNFRSF10c (P<0,05) and significantly decreased in OSM (P<0.01) in CH group vs healthy controls. No difference was seen in expression of MET or TNFRSF25 genes.

Conclusion: There is altered expression of receptors for cytokines in both blood and fibroblast samples from participants with cluster headache. This is in line with the previous distinct alterations in cytokine expression seen in Swedish1 and Danish2 patients with cluster headache.

1 Ran, C., Olofsgård, F.J., Wellfelt, K., Steinberg, A. and Belin, A.C., 2024. Elevated cytokine levels in the central nervous system of cluster headache patients in bout and in remission. *The Journal of Headache and Pain*, *25*(1), p.121.

2 Lund, N.L.T., Westgate, C.S.J., Søborg, M.L.K., Snoer, A.H., Jensen, R.H., Hansen, T.F. and Petersen, A.S., 2025. Distinct Alterations of Inflammatory Biomarkers in Cluster Headache: A Case Control Study. *Annals of Neurology*.

P585

Isolated trigeminal sensory neuropathy in a patient with mixed connective tissue disease: A diagnostic challenge

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Objective: Trigeminal neuropathy is a rare condition with a broad differential diagnosis, including autoimmune, infectious, structural and neoplastic causes. Diagnostic evaluation may be complex, particularly in patients with systemic inflammatory conditions.

Methods: We present the case of a 46-year-old Caucasian male from Greece, residing in Portugal, with mixed connective tissue disease (Raynaud"s phenomenon, sacroiliitis, pulmonary hypertension), a clipped left occipital artery aneurysm, atrial flutter and resected dorsal melanoma. He developed progressive numbness on the left side of the face from June 2024, starting centrally and spreading centrifugally. He denied sicca symptoms. Chronic medication included gabapentin 100mg three times daily, prednisolone 10mg, hydroxychloroquine 400mg, aspirin 150mg, pentoxifylline 400mg, nifedipine 20mg, furosemide, tadalafil and ambrisentan. He was not on anticoagulants and had no known drug allergies.

Results: Neurological examination revealed isolated tactile hypoesthesia of the left hemiface.Brain MRI was unremarkable.Electromyography showed a severe sensory lesion of the left trigeminal nerve and abnormal blink reflex, without motor involvement. CSF was normal, with negative microbiology, no oligoclonal bands/neoplastic cells. Immunological studies showed high-titre ANA (1:1280) and strong anti-RNP, anti-SSA(Ro), and anti-Ro52 positivity in serum and CSF. Antineuronal antibodies were negative.

A diagnosis of isolated trigeminal sensory neuropathy was made, likely autoimmune.The patient was referred to rheumatology to escalate immunosuppression.

Conclusion: This case highlights the importance of considering autoimmune mechanisms in isolated trigeminal neuropathies, especially in patients with systemic connective tissue disease. EMG may assist in detecting trigeminal dysfunction, and intrathecal autoantibodies, even without structural lesions, support an immune-mediated process and underscore the value of CSF analysis in atypical neurological presentations.

P586

Migraine and allergy – Two faces of the same hypersensitivity?

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Objective: The link between migraines and allergies is unclear, with experts divided on the relationship. New tests like the ALEX² test can measure IgE levels for over 295 allergens, but some migraine patients with allergy histories still get negative results. This suggests there may be other types of allergies not related to IgE. The ALEX² study investigates the prevalence of allergies in migraine patients with known allergies.

Methods: Analysis of a group of 47 patients (36 women, 11 men; mean age 35.6 ± 9.4 years) diagnosed with migraine (ICHD-3 criteria) and a history of allergies (seasonal symptoms, urticaria, asthma, allergic rhinitis). • All patients underwent the ALEX² test (MacroArray Diagnostics, Austria). Assessed: ALEX² test result (positive vs. negative); Type of allergic symptoms from the history; Impact of migraine on quality of life (MIDAS); Serum total IgE concentration

Results: In a study of 47 patients with allergies and migraines, the ALEX² test revealed that 28 patients (59.6%) had no allergies. Among those testing negative for allergies: - 60.7% reported seasonal symptoms like sneezing and nasal itching. - 28.5% experienced skin symptoms such as hives. - 10.8% had allergic asthma. - 21.4% had elevated total IgE levels (greater than 100 IU/ml). There was no significant difference in migraine frequency or mean MIDAS scores between patients with positive and negative ALEX² results. Antihistamine treatment did not notably affect migraine outcomes.

Conclusion: Many patients with allergies and migraines do not show sensitization on the ALEX² test. This suggests that allergy-like symptoms may stem from non-IgE-mediated mechanisms, such as hypersensitivity or autonomic hyperresponsiveness. Additionally, the lack of correlation between ALEX² scores and migraine severity implies that other factors, like neurogenic inflammation, may be more influential. More research is needed to understand the role of non-IgE-mediated hypersensitivity in these patients.

P587

Foreign body granuloma: An endovascular cerebral aneurysm treatment complication

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Objective: Foreign body granuloma (FBG) is a rare complication after endovascular treatment of unruptured intracranial aneurysms (UIAs), thought to result from embolization of hydrophilic polymer coatings and subsequent granulomatous inflammation. Presentation and imaging can mimic infection, vasculitis, or embolic stroke

Methods: Retrospective case series of three women who developed new neurological symptoms after endovascular UIA treatment. We reviewed clinical course, MRI features, devices used, management, and outcomes.

Results: Ages were 53–72 years. Symptom onset ranged from hours to weeks post-procedure and included headache, transient focal deficits, hemiparesis, and encephalopathy. MRI showed multiple enhancing parenchymal lesions with or without leptomeningeal enhancement with edema and SWI microbleeds, without diffusion restriction or infectious/vasculitic markers. Patients received high-dose corticosteroids with taper and showed marked clinical and radiological improvement. All three cases involved the use of PHENOM PLUS catheter

Conclusion: FBG should be considered when unexplained neurological symptoms and enhancing brain lesions arise after endovascular UIA therapy. Early recognition enables corticosteroid treatment, which was associated with improvement in our steroid-treated patients; delayed recognition may preclude immunotherapy. The repeated presence of the PHENOM PLUS catheter across all cases raises concern for a potential role in this complication. Systematic reporting and device-level investigations are needed to define incidence, risk factors, and optimal management.

Fig. 1

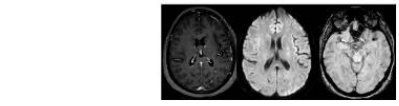


Figure 1: Case 1, 2 January 2025 (A) Post-contrast T1-weighted MRI demonstrates multiple parenchymal and leptomeningeal enhancing foci are demonstrated in the left hemisphere, predominantly within watershed regions and in the left occipital lobe (B) Diffusion-weighted imaging reveals peripherally enhancing lesion measuring approximately 5 mm in the left parieto-occipital region demonstrates diffusion restriction. In addition, a few small foci of diffusion restriction were noted in the right occipital lobe (C) Susceptibility-weighted imaging shows scattered small hemorrhagic foci in the left hemisphere. The imaging appearance is most suspicious for an inflammatory/vasculitic process such as a cerebral foreign body reaction

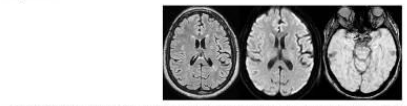


Figure 2: Case 1, 4 April 2025 (A) Post-contrast Fluid attenuated-weighted MRI shows marked improvement with a decrease in both the number and size of enhancing lesions, no significant change is observed in the number of lesions (B) Diffusion-weighted imaging demonstrates improvement in diffusion restriction lesions (C) No interval change in the Susceptibility-weighted imaging detected lesions.

Fig. 2

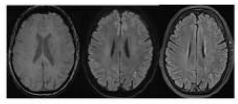


Figure 3: Case 2, 24. December 2024 (A) Susceptibility-weighted imaging showed multiple susceptibility foci consistent primarily with microhemorrhages, predominantly in the right hemisphere (B) Diffusion-weighted imaging demonstrated multiple diffusion-restricting foci in the right hemisphere, involving both cortex and white matter in the frontal, parietal, and occipital lobes, as well as the right lentiform nucleus. A few small foci of mild restriction are also demonstrated in the left hemisphere, most prominent cortically in the left lateral parietal region (C) Multiple areas of increased T2/FLAIR signal are noted in the periventricular, deep, and subcortical white matter, likely representing chronic microangiopathic changes.

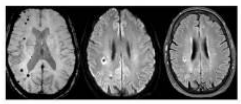


Figure 4: Case 2, 17 March 2025 (A) Susceptibility-weighted imaging showed multiple susceptibility foci are demonstrated in the right hemisphere. Many appear more prominent at present. (B) Diffusion-weighted imaging demonstrated no acute lesions (C) No pathological enhancement on FLAIR post contrast.

Fig. 3

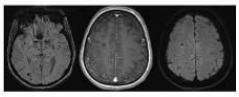


Figure 5: Case 3, 25 March 2025 (A) Susceptibility-weighted imaging showed multiple abnormal signal foci within the right carotid territory. (B) Post-contrast T1-weighted images demonstrated many of these foci were associated with areas of enhancement, including leptomeningeal enhancement in the posterior hemisphere. Most of the enhancing foci were located in anterior and posterior watershed regions (C) No diffusion-restricting lesions were demonstrated

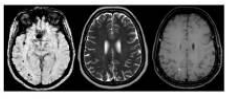


Figure 6: Case 3, 30 June 2025 (A) Susceptibility-weighted imaging showed multiple susceptibility foci in both hemispheres, predominantly on the right, involving cortical, subcortical, and deep white matter regions, similar to the previous study (B) T2WI demonstrated several hyperintense foci are demonstrated in the right fronto-parietal subcortical white matter, without diffusion restriction (C) Some of these foci show enhancement on Black Blood sequence.

P588

The rRole of inflammatory mediators (IL-1β, TNF-α, CGRP, Substance P) in migraine pathophysiology: A meta-analysis

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Objective: Headache disorders, like migraines, are linked to neuroinflammation, but the underlying inflammatory pathways are not fully understood. This meta-analysis evaluates the role of key inflammatory mediators, such as cytokines and neuropeptides, in migraine pathophysiology, and explores sex/age-

related differences in inflammatory responses across studies.

Methods: We performed a meta-analysis of 12 studies published between 2005 and 2023, including data on inflammatory markers (IL-1β, IL-6, TNF-α, CGRP, Substance P) in patients with migraine. Studies included blood and cerebrospinal fluid (CSF) samples, as well as neuroimaging data (fMRI, PET). A subgroup analysis was conducted based on sex, age, and migraine type (episodic vs. chronic).

Results: The analysis included 1,200 participants (600 migraine patients, 600 healthy controls). Elevated levels of IL-1β, TNF-α, and CGRP were found in migraine patients compared to controls ($p < 0.05$). Female patients had significantly higher IL-6 and Substance P levels than males. Chronic migraine patients showed increased central inflammation, with evidence of microglial activation on neuroimaging. Older patients exhibited higher levels of IL-1β and TNF-α, indicating a persistent inflammatory state.

Conclusion: This study confirms the role of neuroinflammation in migraine and headache disorders. Both peripheral and central inflammatory markers were elevated in migraine patients, with significant differences between sexes and age groups. These findings support the need for personalized treatment strategies targeting inflammatory pathways, particularly in chronic migraine patients.

P590

A new anatomical and functional perspective of the scapula as a mechanical hub in human movement: Insights from scapular dyskinesis in Tension-Type Headache (TTH)

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Objective: The scapula plays a pivotal role as a biomechanical hub in human movement, facilitating force transmission between the spine, upper limb, and thoracic cage. Emerging evidence suggests that altered scapular dynamics—termed *scapular dyskinesis*—may contribute to musculoskeletal dysfunctions beyond the shoulder complex, including tension-type headache (TTH), the most prevalent form of primary headache.

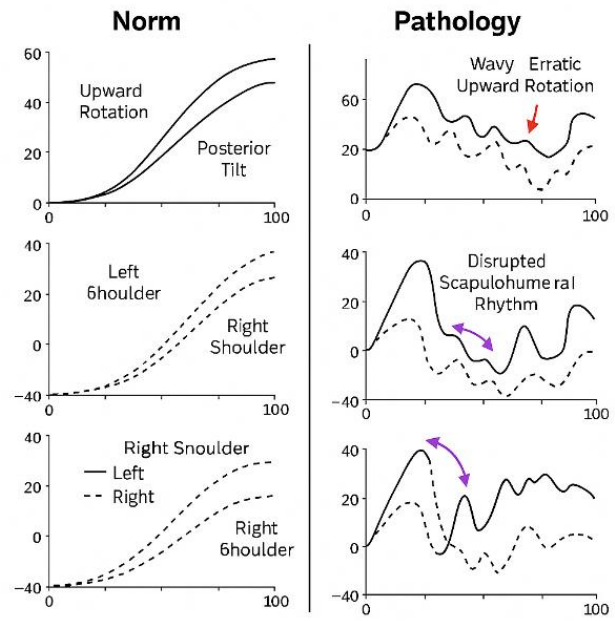
To investigate the patterns of scapular motion in individuals with TTH and explore the functional implications of scapular dyskinesis in the context of postural imbalance and cervicoscapular dysfunction.

Methods: Using the ShowMotion™ 3D kinematic analysis system, we assessed scapular motion in a series of patients diagnosed with TTH. Each case included pre- and post-treatment comparisons of upward rotation and posterior tilt during shoulder elevation. Visual patterns were analyzed for symmetry, smoothness, timing, and range of motion. All patients reported associated postural alterations and chronic headache symptoms.

Results: Using the ShowMotion™ 3D kinematic analysis system, we assessed scapular motion in a series of patients diagnosed with TTH. Each case included pre- and post-treatment comparisons of upward rotation and posterior tilt during shoulder elevation. Visual patterns were analyzed for symmetry, smoothness, timing, and range of motion (figure). All patients reported associated postural alterations and chronic headache symptoms.

Conclusion: This study supports a novel integrative view of the scapula as a dynamic mechanical hub whose dysfunction may contribute to tension-type headache through disrupted postural and neuromuscular control.

Fig. 1



P591

CGRP, VIP and PACAP plasmatic levels in migraine patients before and after anti-CGRP(R) monoclonal antibodies prophylaxis

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Objective: CGRP, VIP, and PACAP are key mediators in migraine pathophysiology. Anti-CGRP(R) mAbs have recently emerged as the first targeted, effective prophylactic therapy. This study aimed to evaluate plasma levels of these neuropeptides pre- and post-

anti-CGRP(R) mAb treatment, assessing changes and potential predictors of response.

Methods: From Feb 2022 to Feb 2023, we enrolled 56 migraineurs who began prophylaxis with erenumab (n=26), galcanezumab (n=16), or fremanezumab (n=14). Responders were defined as those achieving ≥50% MMDs reduction at 6 months. Blood was collected at T0, T1 (3 mo), T2 (6 mo), and T3 (12 mo). CGRP, VIP, and PACAP plasma levels were assessed via RIA and ELISA.

Results: Overall, 80.3% (45/56) responded to anti-CGRP(R) mAbs, with a significant reduction in all clinical variables (MIDAS, HIT-6, ASC, MMDs) from T0 to T3 (Fig.1). In the erenumab group, CGRP levels showed no significant change, though responders exhibited a decreasing trend from T0 to T2 compared to non-responders. Galcanezumab induced a significant CGRP reduction by T1 ($p < 0.01$). Fremanezumab led to a rapid CGRP rise >3000 pg/ml, likely assay interference. VIP and PACAP levels remained stable in plasma from T0 to T3, with no significant differences between responders and non-responders (Fig.2).

Conclusion: Anti-CGRP(R) mAbs are very effective migraine prophylactic agents. Galcanezumab significantly reduced plasma CGRP by 3 months, with near-undetectable levels at 6 months, consistent with its CGRP-binding mechanism and prior studies. In contrast, erenumab did not affect significantly CGRP plasmatic levels, potentially due to its different binding site on the CGRP receptor. VIP and PACAP levels remained unaffected by treatment. Further studies are needed to clarify their interplay with CGRP in migraine pathogenesis.

Fig. 1

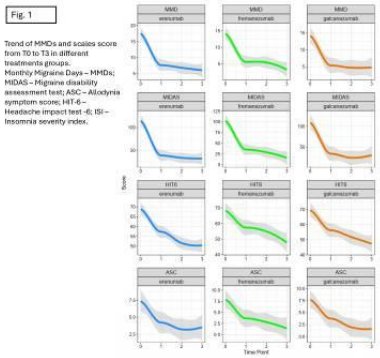
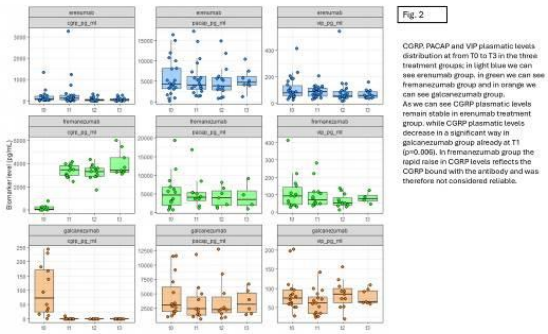


Fig. 2



P592

Short-term longitudinal white matter structural changes in patients with migraine with 12-week positive response to fremanezumab

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Objective: To evaluate the longitudinal progression of white matter structure in patients with migraine with positive and no response to fremanezumab 12 weeks after the first administration.

Methods: Diffusion-weighted MRI (DWI) data were acquired 1-2 weeks before the first use of fremanezumab, and 12 weeks later. The images were assessed in 75 patients with chronic migraine (CM) or high frequency episodic migraine (HFEM). A reduction of at least 50% in the monthly migraine frequency was defined as positive response to treatment. After DWI denoising and artifacts correction, white matter structure was assessed using Diffusion Tensor Imaging (DTI) parameters, including free water correction (FW-DTI), and advanced diffusion descriptors obtained with novel techniques, AMURA and MISFIT, in the regions from the JHU ICBM-DTI-81 Atlas with volume higher than 2000 mm^3 (28 regions). The longitudinal progression for each group defined according to response to treatment was analyzed with Generalized Linear Mixed Models, correcting the models by age and medication overuse headache. A p

Results: The clinical characteristics of the sample are shown in Table 1. Positive response to fremanezumab

was observed in 43 patients (57.3%). Statistically significant longitudinal changes were only observed in responders, as detailed in Table 2. Most changes were found for patients with HFEM in the external and internal capsules, and the superior corona radiata of the left hemisphere. DTI diffusivity measures showed longitudinal decrease, and AMURA and MISFIT descriptors time-dependent increase. Representative examples are shown in Figure 1, including the complete list of diffusion descriptors. For the whole group of patients and baseline CM, longitudinal changes were only identified with FW-DTI and MISFIT, with the same trend as for patients with HFEM.

Conclusion: Fremanezumab causes short-term localized white matter longitudinal changes in patients with migraine with positive response.

Fig. 1

Table 1. Clinical characteristics of responders and non-responders to fremanezumab.

	Responders (N = 43)	Non-responders (N = 32)
Time between MRI acquisitions (weeks)	12.9 ± 2.0	12.6 ± 2.2
Age (years)	45.5 ± 11.3	42.3 ± 13.7
Sex F/M	38/5 (88/12%)	26/6 (81/19%)
CM/HFEM at baseline	28/15 (65/35%)	25/7 (78/22%)
Aura	7 (16%)	1 (3%)
Previous number of preventive treatments	4.0 ± 0.9	3.6 ± 1.0
Medication overuse headache (baseline)	36 (84%)	27 (84%)
Medication overuse headache (week 12)	11 (26%)	23 (72%)
Total duration of migraine (years)	32.2 ± 10.9	21.5 ± 12.4
Time from onset of CM/HFEM (months)	67 [34-128]	54 [30-103]
Headache frequency (days/month; baseline)	17 [13-25]	21 [15-25]
Headache frequency (days/month; week 12)	6 [4-9]	17 [13-25]
Migraine frequency (days/month; baseline)	12 [10-16]	15 [11-18]
Migraine frequency (days/month; week 12)	3 [2-5]	13 [9-17]

Values are expressed as mean ± SD, median [interquartile range], or frequency.

Fig. 2

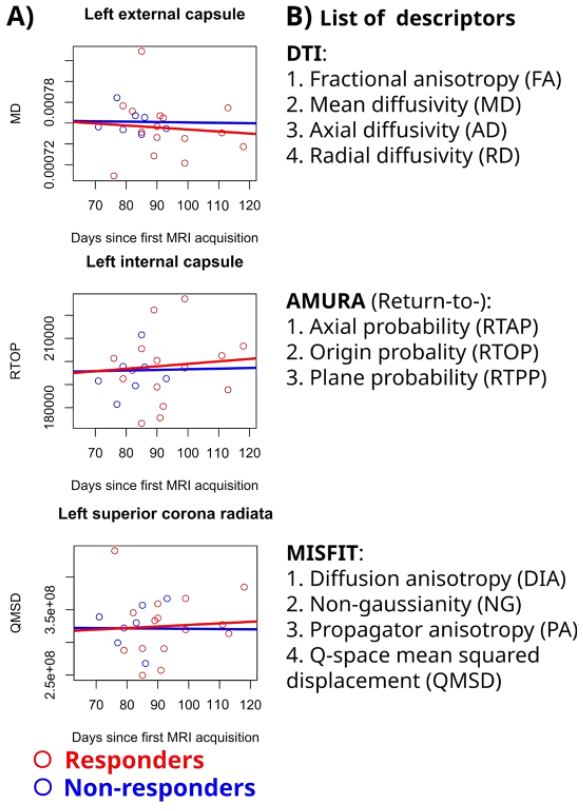
Table 2. Time-dependent diffusion changes in the responders compared to the non-responders.

	Coef. Responders	p-value*	Coef. Non-responders	p-value
All patients				
NG R sagital stratum	7.9 [4.0, 11.7]•10^5	0.007	0.1•10^5	0.98
Patients with CM at baseline				
AD-FW R cerebral peduncle	-3.5 [-5.5, -1.4]•10^7	0.024	-0.0•10^7	1
AD-FW R internal capsule	-5.6 [-9.3, -1.8]•10^7	0.046	0.9•10^7	0.65
AD-FW R thalamic radiation	-6.7 [-10.4, -3.1]•10^7	0.024	1.5•10^7	0.50
AD-FW R sagittal stratum	-5.9 [-9.3, -2.4]•10^7	0.024	1.0•10^7	0.59
NG R sagittal stratum	9.2 [4.2, 14.0]•10^5	0.029	-0.2•10^5	0.92
Patients with HFEM at baseline				
AD L cerebral peduncle	-4.0 [-6.4, -1.4]•10^7	0.045	-1.5•10^7	0.35
AD L internal capsule	-2.6 [-3.7, -1.4]•10^7	0.002	0.4•10^7	0.55
AD L superior corona radiata	-2.4 [-3.9, -0.9]•10^7	0.028	-0.5•10^7	0.39
AD L external capsule	-2.2 [-3.6, -0.5]•10^7	0.045	0.2•10^7	0.60
MD L internal capsule	-2.1 [-3.2, -1.1]•10^7	0.005	-0.2•10^7	0.74
MD L superior corona radiata	-1.8 [-2.9, -0.8]•10^7	0.023	-0.1•10^7	0.88
MD L external capsule	-2.2 [-3.4, -1.1]•10^7	0.005	-0.1•10^7	0.88
RD L internal capsule	-1.8 [-3.0, -0.7]•10^7	0.036	-0.5•10^7	0.42
RD L external capsule	-2.1 [-3.1, -1.1]•10^7	0.036	-0.2•10^7	0.69
RD L cingulum	-1.8 [-3.1, -0.6]•10^7	0.036	0.1•10^7	0.89
QMSD splenium of corpus callosum	7.3 [1.9, 12.9]•10^{-5}	0.032	2.5•10^{-5}	0.56
QMSD R cerebral peduncle	13.5 [6.7, 20.1]•10^{-5}	0.002	-2.8•10^{-5}	0.34
QMSD L cerebral peduncle	10.0 [3.6, 16.4]•10^{-5}	0.016	-2.3•10^{-5}	0.26
QMSD L internal capsule	5.2 [2.6, 7.8]•10^{-5}	0.002	0.3•10^{-5}	0.78
QMSD R superior corona radiata	1.8 [0.5, 3.1]•10^{-5}	0.027	-0.7•10^{-5}	0.43
QMSD L superior corona radiata	2.2 [1.0, 3.5]•10^{-5}	0.005	-0.2•10^{-5}	0.75
QMSD R posterior corona radiata	1.7 [0.6, 2.9]•10^{-5}	0.023	0.7•10^{-5}	0.45
QMSD L external capsule	2.2 [1.1, 3.4]•10^{-5}	0.002	0.3•10^{-5}	0.49
QMSD R cingulum	3.3 [0.8, 6.0]•10^{-5}	0.036	-0.1•10^{-5}	0.93
QMSD L cingulum	5.3 [1.7, 9.2]•10^{-5}	0.023	-0.7•10^{-5}	0.71
RTOP L internal capsule	1.3 [0.6, 2.0]•10^2	0.038	0.7•10^2	0.81
RTOP L superior corona radiata	0.7 [0.3, 1.2]•10^2	0.043	-0.5•10^2	0.77
RTOP L external capsule	0.8 [0.4, 1.2]•10^2	0.038	0.8•10^2	0.58

-FW = free-water corrected; L = left; R = right. *Adjusted p-value after Benjamini-Hochberg correction for multiple comparisons. Each coefficient shows the change of the value of the parameter per day, and the 95% confidence interval. At the right, the corresponding coefficient for the non-responders is shown. Internal capsule refers to the retrolenticular part of the internal capsule (all cases), and thalamic radiation to the posterior thalamic radiation.

Fig. 3

Figure 1. Longitudinal changes and list of employed diffusion descriptors. A) Scatter plots of three variables showing statistically significant longitudinal progression only in HFEM responders to fremanezumab. B) List of diffusion descriptors according to the employed diffusion technique.



P593

Optic nerve sheath diameter as a diagnostic marker in idiopathic intracranial hypertension: A prospective case-control study

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Objective: This study investigates the diagnostic value of optic nerve sheath diameter (ONSD) measured by transorbital ultrasound in patients with Idiopathic Intracranial Hypertension (IIH). The primary objective is to determine whether ONSD differs significantly between IIH patients and controls. A secondary aim is to assess whether ONSD decreases following a therapeutic lumbar puncture in IIH patients.

Methods: We prospectively enrolled patients with a diagnosis of IIH and healthy controls. All participants underwent bilateral ONSD measurement using transorbital ultrasound. For IIH patients, assessments were performed immediately before and within 24 hours after a therapeutic lumbar puncture. ONSD was calculated as the average of three consecutive measurements for each eye. Demographic and clinical data, including BMI, presence of papilledema, and CSF opening pressure, were recorded.

Results: As of the current analysis, 7 IIH patients (mean age 35.0 ± 12.6 years; 100% female) and 7 controls subject were included. Baseline mean right ONSD was significantly larger in the IIH group (6.29 ± 0.61 mm) compared to the controls (4.75 ± 0.52 mm). Similar differences were observed in left ONSD (6.30 ± 0.36 mm in IIH vs 4.56 ± 0.60 mm in controls). All IIH patients had elevated CSF opening pressure (mean 29.8 ± 2.1 cmH_2O). Post-lumbar puncture ONSD data collection is ongoing and will be presented.

Conclusion: Preliminary results suggest that optic nerve sheath diameter measured via transorbital ultrasound is increased in patients with IIH compared to controls. This non-invasive tool may serve as a useful adjunct in the diagnosis and monitoring of IIH. Further data are being collected to evaluate dynamic changes in ONSD following lumbar puncture

P594

Multimodal assessment in migraine with aura mimicking stroke: Diagnostic challenges and the role of demographic, clinical, and biochemical markers

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Objective: Migraine with aura (MA) is a frequent stroke mimic (SM). Increasing awareness of the clinical and radiological characteristics may improve diagnosis and reduce unnecessary treatments. Our main goal was to describe the clinical, analytical and neuroimaging characteristics of MA as SM. As secondary goals, we evaluated factors associated with CT perfusion (CTP) alterations in MA.

Methods: We conducted a retrospective observational study including patients with a final diagnosis of migraine with aura who were evaluated under the stroke code protocol between 2015 and 2025. Demographic variables (age, sex), clinical features (presence of aphasia, aura duration), and biochemical markers (potassium, glucose, and creatinine levels) were collected. A multivariate logistic regression model to evaluate independent variables associated with PCT alterations in MA was constructed using stepwise selection based on the Akaike Information Criterion (AIC). Odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Results: Among 5513 SC, 68 (1.23%) were MA, with median age of 42 (SD: 12.1) years old, 68% women. The most frequent aura symptom was sensitive (67%). PCT alterations were found in 15/53 (22%), with a hypoperfusion pattern mainly unilateral, not corresponding to a vascular territory. Men (OR 5.3; *P*=0.021) and aphasic aura (OR 5.8; *P*=0.016) were associated with PCT alterations. The model demonstrated good discrimination (AUC > 0.83).

Conclusion: MA as SM forms 1% of stroke code activation. Men sex, aphasia, and altered potassium levels may serve as predictors of PCT alterations in migraine with aura. Validation in larger cohorts is warranted.

P595

Plasma with added protease inhibitors improves alpha and beta-CGRP measurement as compared to serum: Towards a reliable biomarker for chronic migraine

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Objective: CGRP, mainly a-CGRP, is central in migraine pathophysiology, whereas β-CGRP is more prevalent in the gut. Although CGRP is both a therapeutic target and potential biomarker, measurement inconsistencies limit its reliability. CGRP degrades rapidly, and studies suggest adding protease inhibitors (PI) to improve accuracy. This study aims to explore factors influencing CGRP levels as a biomarker.
Methods: Chronic migraine patients (n=145) were recruited in our Headache Unit. Blood samples were collected at baseline, 6, and 12 months post-treatment. Plasma was processed with and without PI and stored at -70º. CGRP isoforms were measured with specific ELISAs. Statistical tests were made for level changes and group differences (significance $p<0.05$)
Results: PI-added plasma correlated with standard plasma ($rs=0.9310$, $p<0.0001$), but showed higher a-CGRP levels (median=21.26; PI-median=38.29, $p<0.0001$). For β-CGRP, correlation was smaller ($rs=0.8390$, $p<0.0001$), with no significant difference between samples. No correlation was found between a- and β-CGRP ($rs=0.05405$, $p=0.5662$). Plasma-PI samples showed higher CGRP concentrations than serum, for a-CGRP (serum median=13.63; PI-plasma median=38.29; $p<0.05$), and for β-CGRP (serum median=1.716; PI-plasma median=6.909; $p<0.0001$). a-CGRP levels decreased during treatment ($p<0.01$) while β-CGRP levels remained stable (p=ns). a-CGRP and age correlated negatively ($rs=-0.2317$, $p=0.0045$), but no sex-related differences were observed for neither isoform.
Conclusion: PI improved a-CGRP detection in plasma, supporting its use for a more accurate quantification. The lack of correlation between isoforms suggests independent regulation. a-CGRP levels decreased with treatment and correlated negatively with age, highlighting its role as a biomarker. b-CGRP stability and higher detection in plasma suggest it as the preferred biofluid for its measurement. These results call for implementation of PI-plasma samples in future research.

P596

Biomarkers change in patients with CM-MOH randomized to usual treatment vs mindfulness added to usual treatment

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Objective: Little is known about biomarkers of chronic migraine with MOH, but few observations of an alteration of some biomarkers of neuro-inflammation have been mad
Methods: Patients who participated to the MIND-CM phase III trial, comparing treatment as usual (TaU) to mindfulness added to TaU were analyzed with respect to variation in headache frequency, medication intake, WBC count, lymphocyte subpopulations CD3, CD4, CD8, CD19, T-Reg cells, IL-6, IFNg, TNF-a, and IL-17A. Follow-up was carried out at six and 12 months from baseline
Results: 120 patients (61 randomized to TaU and 59 to TaU+MIND) had valid information for all parameters and all time points. Patients in the TaU group had higher baseline WBC count, whereas those in TaU+MIND had higher baseline NSAIDs intake, all drugs intake and IL-17A count. Biomarkers" count was not indicative of a significant neuro-inflammation pattern. Change over time was not consistent: patients randomized to TaU+MIND overperformed those randomized to TaU for reduction in headache frequency, NSAIDs and all-drugs intake, T-Reg count (at 12 months only), and IL-17A count; vice versa, randomized to TaU overperformed those randomized to TaU+MIND for reduction in WBC count, IL-6 at 6 months only); the two groups overlapped for lymphocyte subpopulations CD3, CD4, CD8, CD19, IFNg, and TNF-a
Conclusion: Taken as a whole, our results point out some promising biomarkers of neuro-inflammation that are consistent with reduction in headache frequency and medication intake. In particular, count in T-Reg cells and IL-17A might constitute valid options for future analyses.

P597

Longitudinal EEG assessment of cortical responsivity before migraine attacks: A study of visual chirp responses

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Objective: Migraine attacks are unpredictable, often disrupting daily life. Previous research suggested that EEG responses to visual chirp stimulation (VEP-EEG)

may help detect changes in cortical responsivity during the preictal phase. This study aims to further investigate that hypothesis.

Methods: In this longitudinal, non-interventional study, participants with episodic migraine completed a validated e-headache diary for at least one month. The preictal phase was defined as the 48 hours before an attack. Each participant underwent several EEG recordings in response to 10–40 Hz visual chirp stimulation on separate days at our hospital, continuing until a migraine attack occurred. Changes from baseline in EEG spectral power were compared between interictal and preictal phases across individual stimulation frequencies (10–40 Hz), including driving, harmonic, and overall responses.

Results: Of the 31 patients who participated, 17 had at least one interictal and one preictal measurement which met the criteria for inclusion in the analysis. The mean participant age was 52 ± 15 years; 82% were female, 77% had migraine without aura, and baseline monthly migraine days (MMD) averaged 3.7 ± 2.3. Additionally, 65% of participants were not using prophylactic medication. We observed high variability in EEG responses to chirp stimulation, both between patients and between interictal and preictal measurements. No significant differences were found in EEG spectral power across the individual stimulation frequencies between interictal and preictal recordings for the driving, harmonic, or overall chirp responses (p = 0.92, p = 0.69, and p = 0.68, respectively).

Conclusion: This study did not replicate previous findings of preictal changes in cortical responsivity in migraine. We recommend increasing the sample size and number of recording days, potentially by adapting the protocol to a home-based setup.

P598

Serum levels of Pentraxin-3 as biomarkers in migraine: A systematic review and meta-analysis

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Objective: To assess serum levels of pentraxin-3 (PTX3), an acute-phase inflammatory marker, in migraine patients compared to healthy controls, and to explore differences by aura status, anti-inflammatory treatments, and clinical characteristics.

Methods: A systematic search of PubMed, Scopus, and Web of Science was conducted through June 2025 to identify studies reporting serum PTX3 levels in adult migraine patients and healthy controls. Data were pooled using a common-effects meta-analysis model. Subgroup analyses were conducted based on aura presence, anti-inflammatory interventions (curcumin or botulinum toxin A), and clinical migraine features, including disease duration and attack length.

Results: Nine studies were included, comprising 493 migraine patients (414 females, 79 males) and 259 healthy controls. The pooled mean age of migraine patients was 36.86 ± 11.58 years, and the mean BMI was 25.12 ± 3.69 kg/m². Serum PTX3 levels were significantly elevated in migraine patients compared to controls (SMD = 1.83, 95% CI: 1.59–2.06, p < 0.001). Patients without aura had slightly higher PTX3 levels than those with aura (15.10 vs. 12.85 ng/mL, p = 0.43). PTX3 levels were lower in patients receiving anti-inflammatory treatments: curcumin (0.00027 vs. 0.00016 ng/mL) and botulinum toxin A (1.28 vs. 0.49 ng/mL). Migraine characteristics such as attack frequency, duration, intensity, and disease onset were reported across studies.

Conclusion: PTX3 levels are significantly elevated in migraine, supporting its role as a marker of neuroinflammation. Variations by aura status and reductions following treatment highlight its potential utility in monitoring disease activity and therapeutic response.

Fig. 1

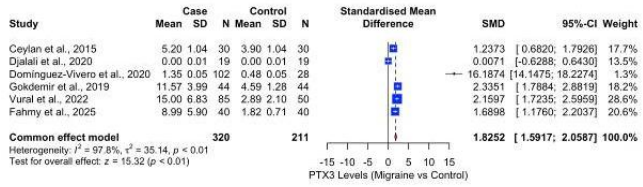


Fig. 2

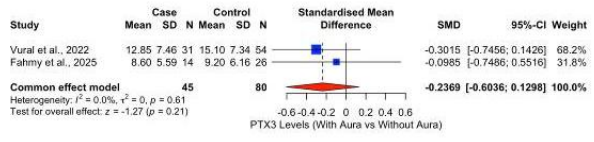
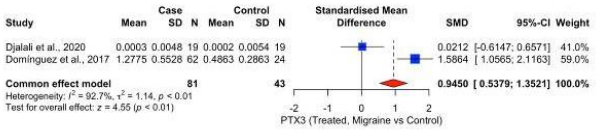


Fig. 3



P599

Early detection and monitoring of hearing loss in vestibular migraine: Extended high-frequency hearing

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Objective: Vestibular migraine (VM) mainly presents with recurrent vestibular symptoms and migraine, with many patients also reporting cochlear symptoms (tinnitus, hearing loss).While standard audiometry in VM patients is often normal or shows non-specific fluctuations,extended high-frequency (EHF) hearing loss may serve as a specific biomarker to distinguish VM from Meniere's disease, as it can reveal distinct, early cochlear damage patterns attributable to migraine-related neural excitotoxicity rather than endolymphatic hydrops.

Methods: A cross-sectional study was conducted on definite (dVM) and probable VM (pVM) patients meeting diagnostic criteria. Auditory-vestibular tests and psychological assessments were performed. Logistic regression evaluated the predictive value of EHF pure tone audiometry (PTA) for standard frequency (SF) hearing loss.

Results: Fifteen pVM and 22 dVM patients were included. The most common vertigo types were vestibulo-visual symptoms (83.8%) and internal vertigo (54.1%). Vertigo lasted <5 min in 57%, 5 min–72 h in 43%, and >72 h in 8%. Psychological disorders were present in 87%. Most patients (92%) had some EHF hearing loss, and 68% had SF loss, higher than reported complaints (43%). The mean EHF threshold (57 dB HL) predicted SF hearing loss well (AUC 0.827), outperforming distortion product otoacoustic emission (AUC 0.748).

Conclusion: Evaluating EHF hearing provides a unique window into early, subclinical cochlear damage in VM. UHF hearing loss, frequently undetectable by standard pure-tone audiometry, may represent a peripheral manifestation of central migraine mechanisms, such as cortical spreading depression or trigeminal-vascular system activation, offering invaluable insights into VM's pathophysiology and its impact on the auditory periphery.

Fig. 1

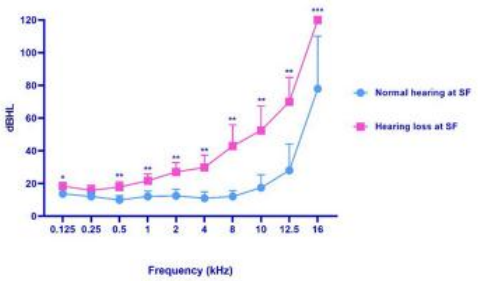


FIGURE 1
The hearing threshold of patients with SF normal hearing and patients with SF hearing loss. VM, vestibular migraine, including definite and probable vestibular migraine; SF, standard frequency (0.125–8 kHz). *p < 0.05, **p < 0.01, ***p < 0.001.

Fig. 2

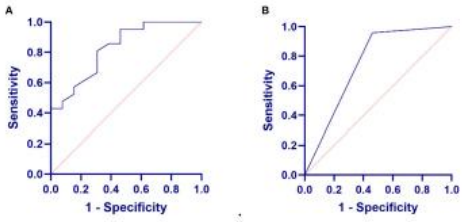


FIGURE 2
Relationship between EHF pure-tone test or distortion product optoacoustic emission (DPOAE) in VM and SF hearing loss. **(A)** The relationship between the mean EHF hearing threshold in VM and SF hearing loss. **(B)** The relationship between the DPOAE in VM and SF hearing loss.

P600

The value of subjective visual vertical in diagnosis of vestibular migraine

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Objective: To study the value of the subjective visual vertical (SVV) in the diagnosis of vestibular migraine (VM).

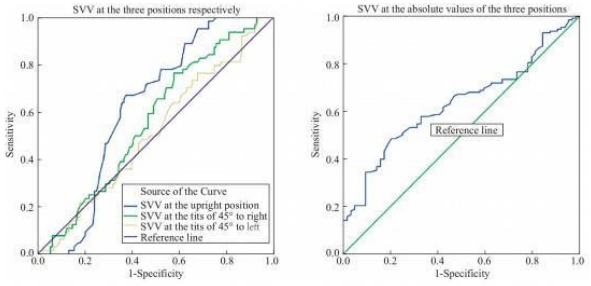
Methods: This study recruited 128 VM patients and 64 age-matched normal subjects. We detected the SVV during the interval between attacks in both groups, in sitting upright, and the head tilted at 45° to the left or right. We then examined the correlation between the SVV results with the vestibular evoked myogenic potential (VEMP) and canal paresis (CP).

Results: A significant difference in SVV at the upright position between VM patients and normal controls (P=0.006) and no significant difference was found at the tilts of 45° to the left or right between the two groups. The SVV results at the upright position were significantly correlated with cervical VEMP (P=0.042) whereas not significantly correlated with CP and VEMP. There existed no significant difference in the conformity to the Müller effect (M effect) between the two groups. ROC analysis exhibited that the sensitivity, specificity of SVVs at the upright were 67.200% and 62.500% respectively. The diagnostic value of SVV at the upright position was significantly higher than that at tilts of 45° to the left and right

(P=0.006). Nonetheless the diagnostic accuracy was relatively low.

Conclusion: Abnormality in SVV possibly stems from the lasting functional disorder of cerebellar or high-level cortical centers in VM patients or is linked to the vestibular compensation. The SVV is of low diagnostic value for VM and the value of SVV in VM warrants further study

Fig. 1



ROC curves of SVV in the study
A: SVV at the three positions respectively. blue line, SVV at the upright position; green line, SVV at the tilts of 45° to right; pink line, SVV at the tilts of 45° to left; purple line, reference line. B: SVV at the absolute values of the three positions, blue line. The green line is reference line.

P601

The peripheral blood inflammatory markers in Ménière's disease patients with and without migraine

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Objective: To investigate the peripheral blood inflammatory markers in Ménière's disease (MD) patients with and without migraine, and to explore the relationship between the inflammatory response with MD and migraine

Methods: The general physical condition, clinical manifestations, pure-tone audiometry, and peripheral blood inflammatory markers of 92 unilateral MD patients who were hospitalized in Peking University People's Hospital for surgical treatment were continuously collected. Meanwhile, 50 healthy controls matched with age and sex were included, and their general physical conditions and peripheral blood inflammatory markers were also collected. The differences in epidemical characteristics and peripheral blood inflammatory markers between MD patients and healthy controls were compared by univariate analysis. All 92 MD patients were divided into two subgroups according to whether they were accompanied by migraine. The clinical characteristics and peripheral blood inflammatory markers of MD patients with and without migraine were compared by univariate analysis. Thereafter, binary Logistic regression was used to analyze the related factors of whether MD patients were accompanied with migraine

Results: Compared with the healthy control group, the peripheral blood WBC, neutrophils and FIB of MD patients were significantly increased (all $P< 0.05$). Compared with MD patients without migraine, MD patients with migraine had higher female prevalence, longer disease history,lower low-frequency hearing threshold, higher frequency of vertigo attacks and higher HDL-C levels , meanwhile, female, frequency of vestibular attacks and HDL-C were independent related factors of whether MD patients were accompanied with migraine

Conclusion: The occurrence of MD and migraine may be related to the inflammatory response. The level of anti-inflammatory factors in the blood of MD patients with migraine are higher, suggesting that the inflammatory response status of MD patients with and without migraine is different

P602

Do migraine disorders predict cognitive decline and cortical atrophy? Preliminary findings from the ageing and brain working study group from ELSA-Brasil

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[5]Universidade de São Paulo, Psychiatric Institute, São Paulo, Brazil

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Objective: Given the conflicting findings on the link between migraine and dementia, we wondered whether migraine would be a predictor of cognitive decline and biomarkers of dementia. Thus, we explored the relationship between migraine and cognition, considering markers of cortical atrophy associated with cognitive decline in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil).

Methods: Persistent migraine (ICHD-3 criteria) from Wave 1 (2008-2010) to Wave 2 (2012-2014), considering aura symptoms (migraine without aura, MWO, and migraine with aura, MWA), was set as a predictor. The outcomes were: 1. the trajectory of

cognitive performance, as delta Wave 3 (2017-2019) – Wave 1 of CERAD battery memory, trail test, fluency, and global scores, and 2. cortical atrophy determined by 3-tesla non-enhanced magnetic resonance imaging (2023-ongoing) by entorhinal anteroposterior cortical atrophy (ERICA score, 0 vs 1, and 2-3), and medial temporal lobe atrophy (MTA score, 0 vs 1, and 2-3). β-coefficients and odds ratios (OR) with respective 95% confidence intervals (95% CI) were calculated using regression models. All models were adjusted by sex, age, educational attainment, and cardiovascular risk factors at Wave 3. All patients gave their informed consent to publish their details in an open-access journal.

Results: Among 605 adults (65.8 ± 9.3 years, 58.1% female), the prevalence of MWO and MWA was 21.5% and 11.9%, respectively. The mean (±SD) follow-up time was 11.0 (0.81) years between migraine diagnosis and neuroimaging. Compared to no migraine, overall migraine was not significantly associated with a worse cognitive trajectory in any cognitive domain (*p*-values > 0.05 for all). In contrast, MWO was associated with decreased odds of higher ERICA scores in the right entorhinal region [proportional OR: 0.45 (0.24, 0.86), p = 0.015].

Conclusion: Based on neuropsychological tests and neuroimaging markers, the preliminary findings of the ELSA-Brasil study refute a link between migraine and cognitive decline.

P603

Iron concentration in the ventral pallidum of chronic migraine with medication-overuse headache

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Objective: The correlation between iron homeostasis impairment and excessive drug use.

Methods: We recruited 38 controls (CNs) and 72 CM patients (40 wMOH, 32 woMOH). All participants underwent MRI and assessments of migraine duration, analgesic use, and health metrics. CM patients with MOH were further evaluated for one-year relapse rates and Severity of Dependence Scale scores. Quantitative susceptibility mapping (QSM) was used to measure iron content in subcortical regions, and correlations with clinical variables. ROC curve analysis was performed to evaluate the QSM"s predictive value for MOH relapse.

Results: CM patients with MOH had lower iron content in the Ventral pallidum (VeP, 0.178 ± 0.112 ppm *vs.* 0.183 ± 0.082 ppm, $p < 0.001$) compared to those without MOH. Notably, VeP iron content negatively correlated with analgesic dependence (r = -0.557, $p < 0.001$) and relapse rates (r = -0.360, $p < 0.05$). ROC analyses demonstrated significant discriminative capacity for relapse prediction (VeP: AUC = 0.880, 95% CI [0.757-1.000], $p < 0.001$) in wMOH.

Conclusion: The reduced iron in subcortical nuclei, especially the VeP, relates to analgesic dependence and relapse in MOH. This insight enhances our understanding of MOH"s neurobiological basis and supports the potential development of QSM-based biomarkers for relapse risk prediction.

Fig. 1

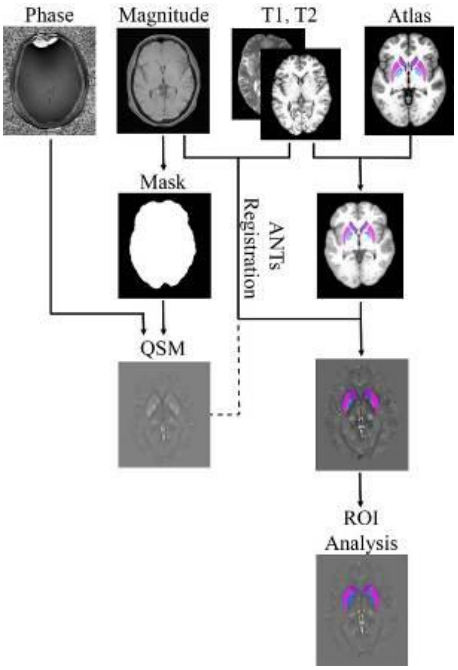


Fig. 2

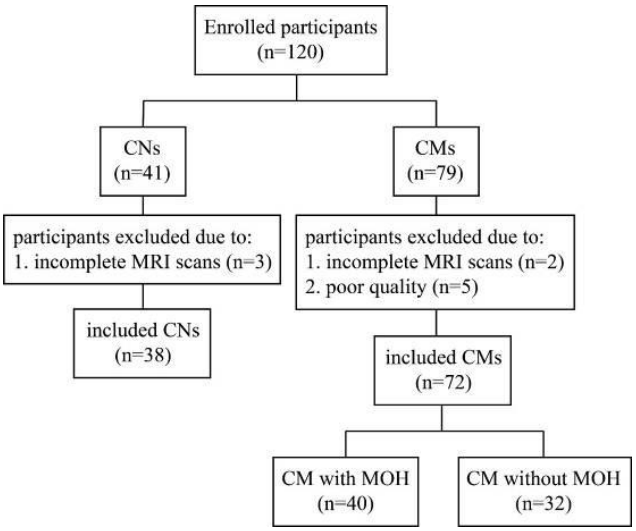
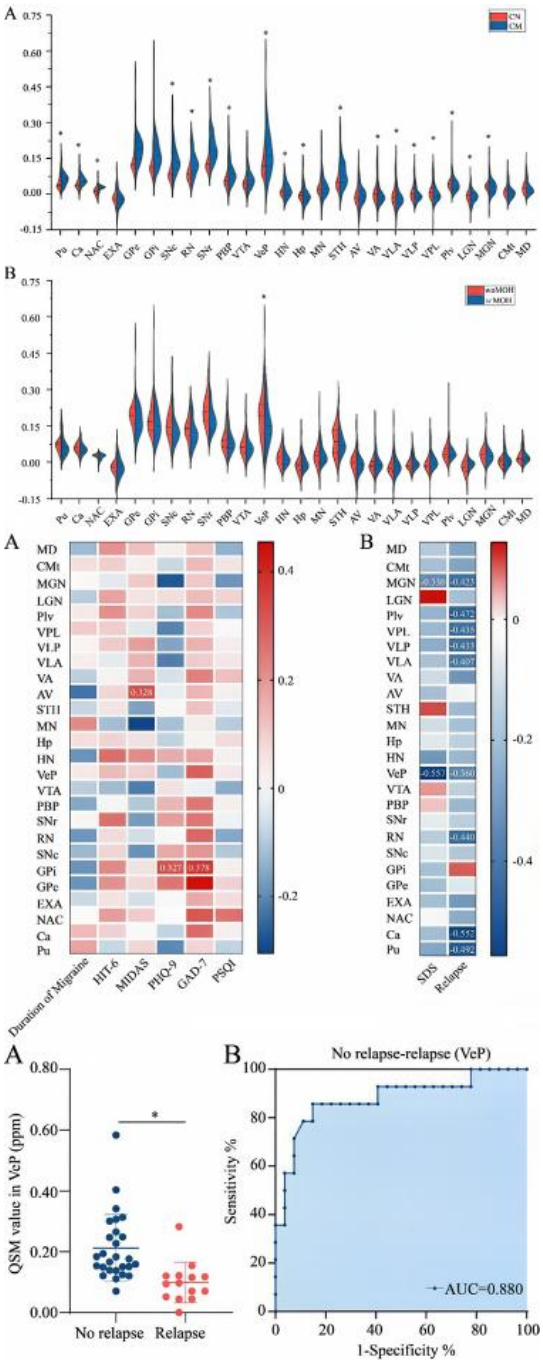


Fig. 3



P604

Tear fluid calcitonin gene-related peptide is elevated during spontaneous migraine attacks – Results from a pilot study

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Objective: Recurrent headache attacks characterize the primary headache disorder migraine. The neuropeptide calcitonin gene-related peptide (CGRP) plays a major role in its pathophysiology as it was shown that the peptide is elevated in interictal and ictal migraine patients. The detection of CGRP has been confirmed in tear fluid in interictal migraine patients and during experimentally induced migraine attacks. The aim of the present study was to investigate CGRP during spontaneous migraine attacks.

Methods: Episodic migraine (EM) patients were studied at two separate study days. At study day 1, patients were interviewed regarding their migraine history and tear fluid was sampled from both eyes (baseline). At study day 2, patients were asked to come to the study center, as soon as they experienced a migraine attack. After arrival, headache characteristics as well as tear fluid was obtained every hour. Patients were allowed to take their usual abortive medication (AM) as needed.

Results: 14 female migraine patients (28.4 9.3 years) were included. Patients arrived at the headache center 4.2 2.9 hours after migraine onset.

The first tear fluid sampling was before intake of abortive medication. Tear fluid CGRP levels were significantly higher during the migraine attack compared to baseline and after resolution of headache (baseline: 1.89 ± 1.68 ng/ml, headache: 2.34 ± 2.20 ng/ml, post headache: 1.23 ± 0.80 ng/ml; Friedman $\chi 2[2] = 11.286$, $p = 0.004$).

Rise of tear fluid CGRP levels was significantly dependent on the timepoint of sampling. Patients who reported a headache duration of less than 3h at the time of tear fluid sampling showed a higher rise in tear fluid CGRP compared to patients with a duration of 3 – 6 h or more than 6h ($p = 0.017$).

Conclusion: Tear fluid CGRP significantly rises during spontaneous migraine attacks with a higher rise at the beginning of the attack. This might be one reason for better efficacy if abortive medication is taken early.

P605

Neuroimaging biomarkers for differentiating migraine and multiple sclerosis: A systematic literature review

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[2]Medical University of Warsaw, Doctoral School, Warsaw, Poland

Objective: Migraine and multiple sclerosis (MS) are neurological diseases sharing demographic characteristics, since they most commonly affect young women. Moreover, white matter hyperintensities (WMHs) may appear on the magnetic resonance imaging (MRI) scans of patients with migraine and can be mistaken for non-active lesions of MS aetiology. Since clinical overlap sometimes occurs, diagnostic difficulties may arise. Therefore, a novel

neuroimaging biomarker could become a valuable aid in differentiation between these two conditions.

Methods: This systematic review aimed to provide an overview of the currently investigated MRI assessment methods and imaging markers as potential novel tools in migraine and MS differentiation. PubMed (MEDLINE), EMBASE and Web of Science databases were searches in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines.

Results: Among 685 records screened, we identified 22 studies eligible for inclusion. Central vein sign (CVS) positivity of lesions was significantly higher in MS patients compared to migraineurs. Volumetric markers were also able to distinguish between MS and migraine, with MS individuals having decreased thalamic and increased choroid plexus volume. Significant differences were also found in terms of lesion number and localization. Although the research covering this subject is limited, available studies provide promising results.

Conclusion: Studies suggest novel MRI approaches can become helpful tools in migraine and MS differential diagnosis, with CVS emerging as a particularly valuable neuroimaging biomarker.

P607

Efficacy and safety of prophylactic cycloxygenase inhibitor usage to prevent headache during religious fasting: A systematic review and meta-analysis

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[1]King Edward Medical University, Lahore, Pakistan

[2]Continental Medical College, Lahore, Pakistan

Objective: To evaluate the efficacy and safety of Cyclooxygenase (COX) inhibitors in preventing headache during religious fasting through a systematic review and meta-analysis of randomized trials.

Methods: A search was conducted on PubMed, Web of Science, Embase, International Clinical Trials Registry Platform (ICTRP), European Union (EU) Clinical Trials Register, and ClinicalTrials.gov till June, 2025 to retrieve randomized controlled trials (RCTs) evaluating COX inhibitor usage to prevent headache associated with religious fasting (e.g., Ramadan, Yom Kippur). Meta-analysis was performed using RStudio v2025.05.1+513. Heterogeneity was assessed using I^2 statistics. Outcomes were headache incidence during fasting, headache severity, and incidence of adverse events.

Results: Three RCTs were included in this study. Two reported on Ramadan fast, and one reported on Yom Kippur fast. A total of 556 participants (51.1% male) were involved, with mean ages ranging from 32±10 to 41.9±10.4 years. Pooled analysis showed that COX inhibitors significantly reduced fasting headache incidence on Day 2 [Risk Ratio (RR) 0.59, 95% Confidence Interval (CI) [0.38-0.93], P=0.021, I2=0%) and Day 3 (RR 0.54, 95% CI [0.32-0.91], P=0.020, I2=2.2%). However, no significant differences were observed on Days 1, 4, 5, or 6 (P > 0.05). Headache severity was lower in intervention groups across the studies; however, meta-analysis was not feasible due to substantial variation in format of reporting data. Safety outcomes were similarly not pooled due to inconsistent reporting; Nonetheless, all included trials reported comparable rates of adverse events between intervention and control groups.

Conclusion: Prophylactic COX inhibitors may reduce fasting-related headache during fasts on Days 2 and 3, without increasing adverse events. Though severity data were not pooled, individual trials showed benefit. Further trials with standardized outcomes are needed to confirm effectiveness and safety.

Fig. 1

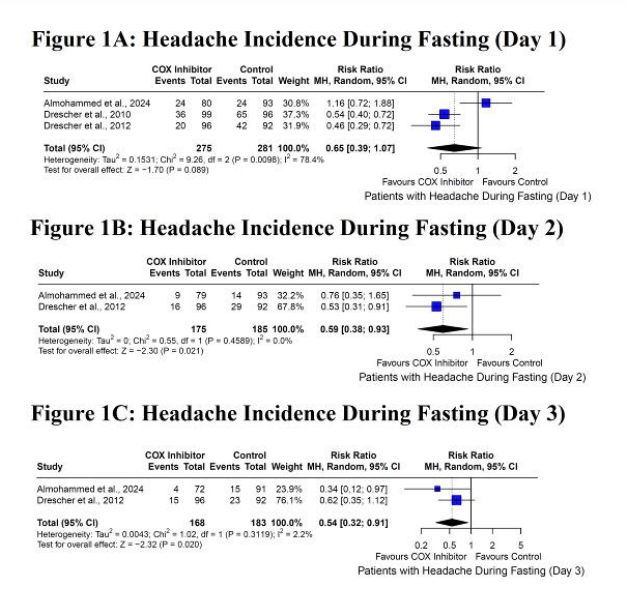
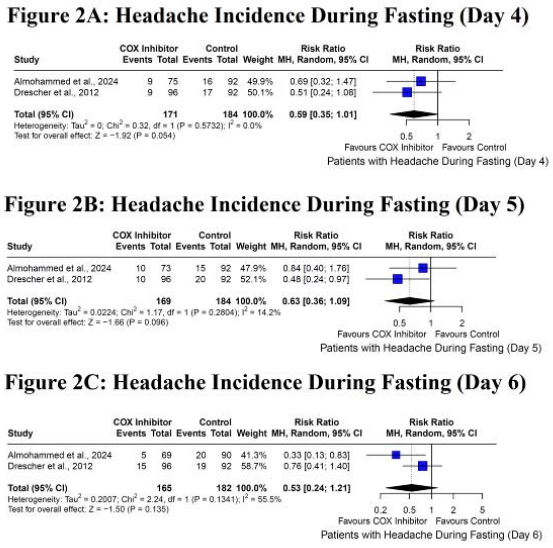


Fig. 2



P608

Program for detection, therapeutic management, and workplace impact of migraine in healthcare professionals at a terciary hospital

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[1]Hospital Clinic Barcelona, Headache and Facial Pain Unit, Barcelona, Spain

[2]Hospital Clinic Barcelona, Occupational Risk Prevention Service, Barcelona, Spain

Objective: Migraine is more prevalent in women at active working age and can be highly disabling, with significant personal, family, and occupational impact (presenteeism, absenteeism, and stigmatization). This work aimed to implement a detection and therapeutic management program for migraine aimed at professionals working at healthcare and research campus associated with a tertiary hospital. The objectives are:

To detect the number of hospital and campus employees suffering from migraine.

To implement a health program for the detection, prevention, and treatment of migraine to improve the quality of life of professionals and reduce absenteeism and presenteeism.

Methods: An anonymous 20-question self-administrated survey (Migragile-Occupational Health) was conducted to determine how many health and research workers had migraine, their disability and to plan the scope of a management program for migraine in these professionals. It includes a general education about migraine. In cases of disabling migraine, the Occupational Health Physician conducts an in-person consultation, initiates acute and first line preventive treatment, and refers the individual to its primary care physician (PCP) or the Headache Unit when appropriated. Absenteeism and presenteeism was planned to be evaluated at baseline (previous 6 months) and at 6 and 12 months after the intervention.

Results: A total of 382 workers out of 10,097 (3.8%) responded to the survey. Of these, 77.2% (n=295) had migraine (67.3% non-disabling, 7.3% disabling, and 2.6% chronic). At baseline, 25% reported presenteeism for 40 days per year, and 10% reported absenteeism of more than 4 days per year.

By now, 20 workers with disabling migraine voluntarily seek for medical consultation and were enrolled in the program.

Conclusion: The results support the need for the implementation of a migraine detection program among workers in a tertiary hospital by Occupational Health Physicians.

P609

Comparative efficacy and safety of venlafaxine versus amitriptyline for migraine prophylaxis: A systematic review and meta-analysis

S. Arsalan Wasti[1], *A. Wasti*[2]

[1]King Edward Medical University, Lahore, Pakistan

[2]Continental Medical College, Lahore, Pakistan

Objective: To compare the efficacy and safety of venlafaxine to amitriptyline in the prophylactic treatment of migraine.

Methods: We searched PubMed, Embase, Scopus, Cochrane Library (CENTRAL), International Clinical Trials Registry Platform (ICTRP), and ClinicalTrials.gov from inception to June 25, 2025 for randomized controlled trials (RCTs) comparing venlafaxine to amitriptyline for migraine prevention. All statistical analyses were done using Review Manager, version 5.4.1. Continuous outcomes were pooled as mean differences (MD), or standardized mean differences (SMD) where scales differed. Dichotomous outcomes were pooled as risk ratios (RR). 95% Confidence intervals (CI) were used. I2 statistics was used for inter-study heterogeneity. Efficacy outcomes included reduction, from baseline, in migraine frequency, migraine severity and migraine duration. Safety outcomes were incidence of adverse events.

Results: A total of 3 RCTs were included, comprising a total of 232 participants (65.5% being female). Mean age varied from 32.5 ± 7.5 years to 39.7 ± 12.7 years. Pooled analyses showed that venlafaxine usage resulted in statistically significant reduction in headache frequency during treatment, compared to amitriptyline (MD -0.39, 95% CI [-0.68 to -0.11], P = 0.006, I2 = 0%). No significant differences were observed between groups in migraine severity or duration. The incidence of adverse events, including blurred vision, dry mouth, and constipation, was comparable between the two treatments.

Conclusion: Venlafaxine demonstrated superior efficacy in reducing migraine frequency compared to amitriptyline, while both treatments demonstrated comparable efficacy in reducing migraine severity and duration. Safety profiles were similar, suggesting venlafaxine may be a clinically appropriate alternative for migraine prophylaxis. Further trials are needed to confirm these findings.

Fig. 1

Figure 1A: Reduction In Migraine Frequency During Treatment (From Baseline)

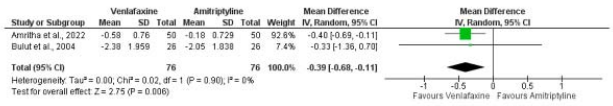


Figure 1B: Reduction In Migraine Frequency Post Treatment (From Baseline)

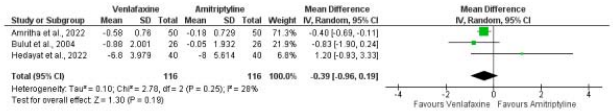


Figure 1C: Reduction In Migraine Duration During Treatment, In Hours (From Baseline)

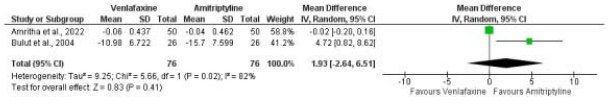


Figure 1D: Reduction In Migraine Duration Post-Treatment, In Hours (From Baseline)

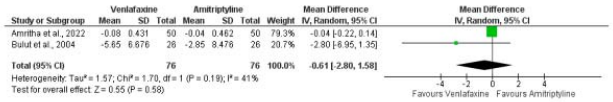


Fig. 2

Figure 2A: Reduction In Migraine Severity During Treatment (From Baseline)

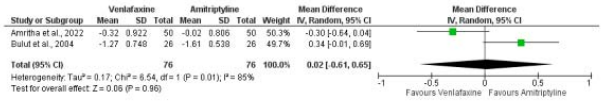


Figure 2B: Reduction In Migraine Severity Post Treatment (From Baseline)

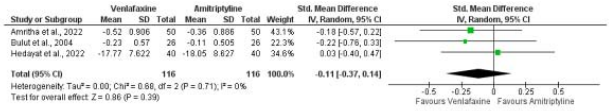


Figure 2C: Reduction In Migraine Severity Post Treatment, Ordinal Scale (From Baseline)

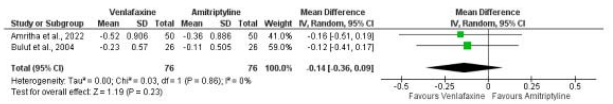


Fig. 3

Figure 3A: Incidence Of Blurred Vision

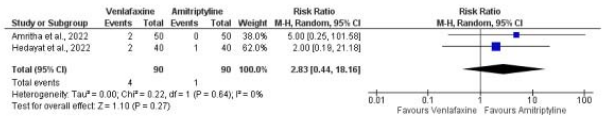


Figure 3B: Incidence Of Constipation

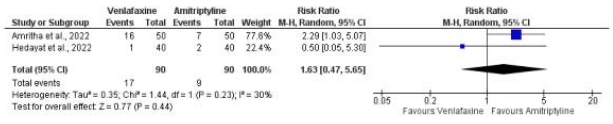
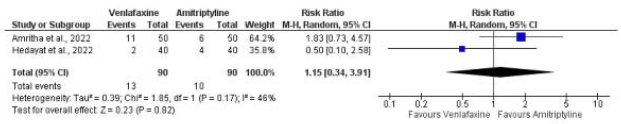


Figure 3C: Incidence Of Dry Mouth



P610

Comparative efficacy and safety of topiramate versus flunarizine in migraine prophylaxis: A systematic review and meta-analysis

S. Arsalan Wasti[1], *A. Wasti*[2]

[1]King Edward Medical University, Lahore, Pakistan

[2]Continental Medical College, Lahore, Pakistan

Objective: To systematically evaluate the effectiveness of two drugs, topiramate and flunarizine, in preventing migraine.

Methods: Systematic searches were conducted in PubMed, Scopus, Web of Science, Embase, Cochrane Library, and trial registries. Randomized controlled trials (RCTs) comparing topiramate and flunarizine were included. Continuous outcomes were pooled as change from baseline to adjust for baseline imbalances. Meta-analysis was performed using RevMan v5.4.1.

Results: A total of 6 RCTs were included, with a total of 410 migraine patients (68.5% being female). Participants" mean ages varied from 30.7±10.8 to 43.2±13.9 years. The flunarizine group had significantly lower mean headache days at 8 weeks, compared to the topiramate group (Mean Difference (MD) 2.34 days, 95% Confidence Interval (CI) [0.88-3.79], P = 0.002, I2 = 0%). No significant between-group differences were observed for other efficacy endpoints (pain intensity (VAS), attack frequency, responder rate (≥50% reduction), SOS (abortive) medication use, or mean migraine days). For incidences of overall or individual adverse events, no statistically significant differences were found, except for paresthesia which had significantly higher incidence in the topiramate group (Risk Ratio (RR) 8.62, 95% CI [1.58-46.89], P = 0.013, I2 = 0%).

Conclusion: Both topiramate and flunarizine generally demonstrated comparable efficacy in migraine prophylaxis, but flunarizine usage was associated with greater reduction in mean headache days at 8 weeks. Safety profiles were broadly similar, except that the topiramate group demonstrated higher incidences of paresthesia. Future RCTs should include larger sample sizes and use standardized reporting frameworks, including a core outcome set, to ensure consistency across studies and allow for more definitive and generalizable conclusions.

Fig. 1

Figure 1A: Change In Mean Headache Days At 8 Weeks (From Baseline)

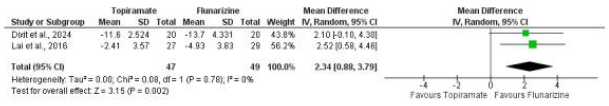


Figure 1B: Change In VAS Score At 4 Weeks (From Baseline)

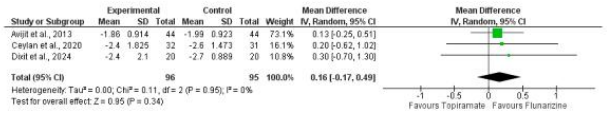


Figure 1C: Change In VAS Score At 8 Weeks (From Baseline)

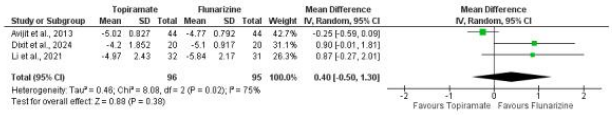


Figure 1D: Change In Abortive (SOS) Medication Usage At 8 Weeks (From Baseline)

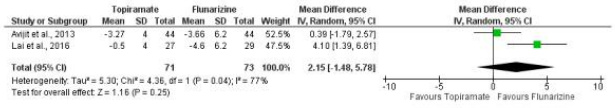


Fig. 2

Figure 2A: Change In Mean Migraine Days At 8 Weeks (From Baseline)

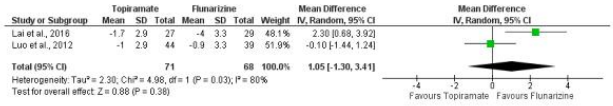


Figure 2B: Responder Rate (≥ 50% Reduction) At 8 Weeks

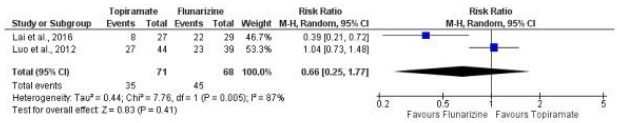


Figure 2C: Change In Attack Frequency At 4 Weeks (From Baseline)

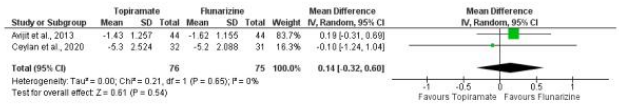


Figure 2D: Change In Attack Frequency At 8 Weeks (From Baseline)

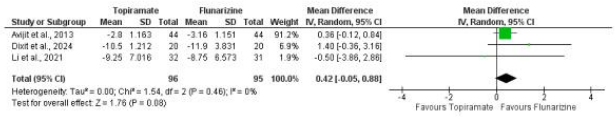


Fig. 3

Figure 3A: Incidence Of Paresthesia

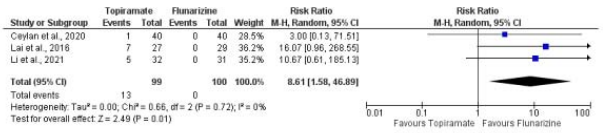


Figure 3B: Incidence Of Insomnia

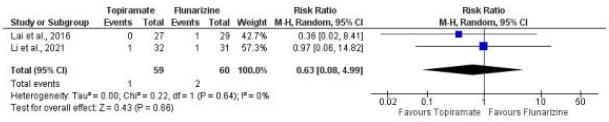


Figure 3C: Incidence Of Fatigue

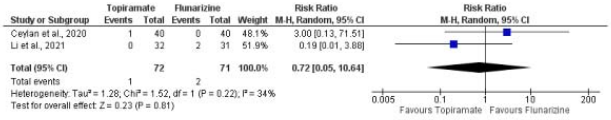
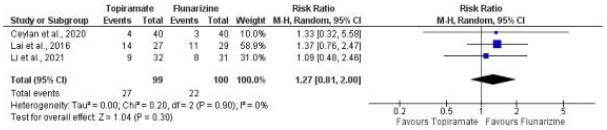


Figure 3D: Overall Incidence Of Adverse Events



P611

Prophylactic efficacy and safety of intravenous aminophylline compared to intravenous normal saline for post-dural puncture headache in cesarean section patients: A systematic review and meta-analysis

S. Arsalan Wasti[1], *A. Saes*[2], *S. ur Rahman*[2], *R. Hotak*[2], *A. Wasti*[3], *S. Noman Qayyum*[2]

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[2]Bacha Khan Medical College, Mardan, Pakistan
[3]Continental Medical College, Lahore, Pakistan

Objective: To evaluate the effectiveness of intravenous (IV) aminophylline versus IV normal saline (as comparator) in preventing post-dural puncture headache (PDPH) in people undergoing cesarean section.

Methods: We searched PubMed, Cochrane Library, Embase, Web of Science, Scopus, and clinical trial registries till June, 2025 for randomized controlled studies comparing IV aminophylline to IV normal saline in cesarean patients. Statistical analyses were performed in Review Manager (RevMan), version 5.4.1.

Results: Nine studies (N = 1029) were included. Six were conducted in Iran; others were from China, Egypt, and Iraq. Participant mean ages ranged from 24.0±3.9 to 30.5±4.9 years. Aminophylline significantly reduced PDPH incidence at 48 hours (2 days) postoperatively (Risk Ratio [RR] 0.61, 95% Confidence Interval (CI) [0.39 to 0.95]), but no significant differences were found at other time points. PDPH duration was also significantly shorter with

aminophylline use (Mean Difference [MD] -0.75 days, 95% CI [-0.88 to -0.62]). No statistically significant differences were observed in PDPH severity or intensity outcomes. Adverse event (AE) reporting was inconsistent and not suitable for meta-analysis, though no serious AEs were reported.

Conclusion: IV aminophylline use was associated with reduced PDPH incidence at 48 hours and shortened PDPH duration in cesarean patients, suggesting a low-cost prophylactic option. No consistent effect was seen on severity or intensity, and AE data remain inconclusive. These findings are hoped to inform PDPH protocols regarding low-cost alternatives to techniques such as epidural blood patches. Further high-quality, adequately powered trials with standardized outcome definitions and AE monitoring are needed, however, for more definitive conclusions.

Fig. 1

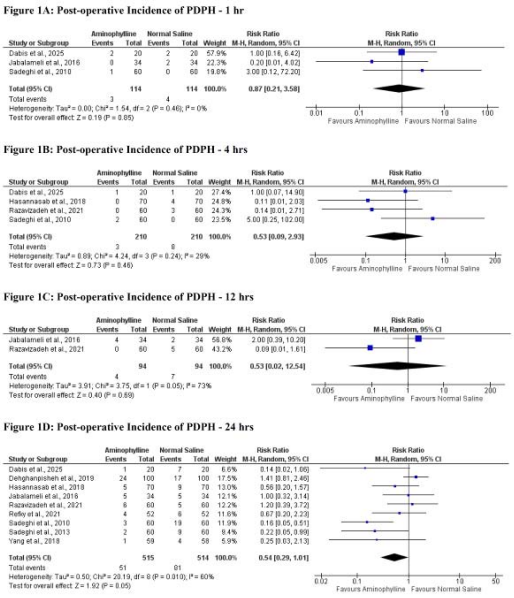


Fig. 2

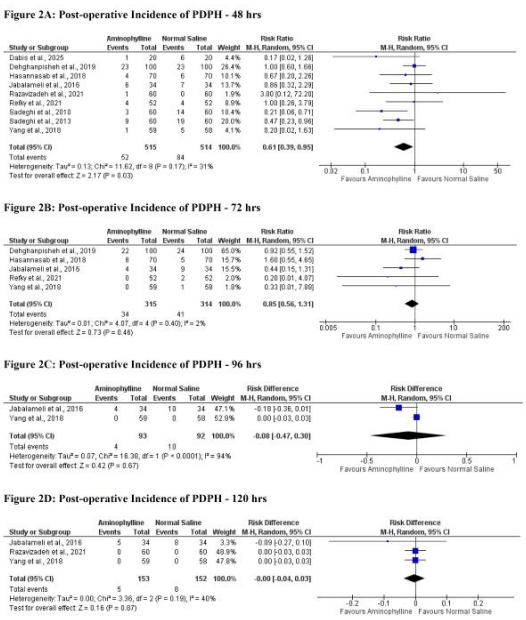
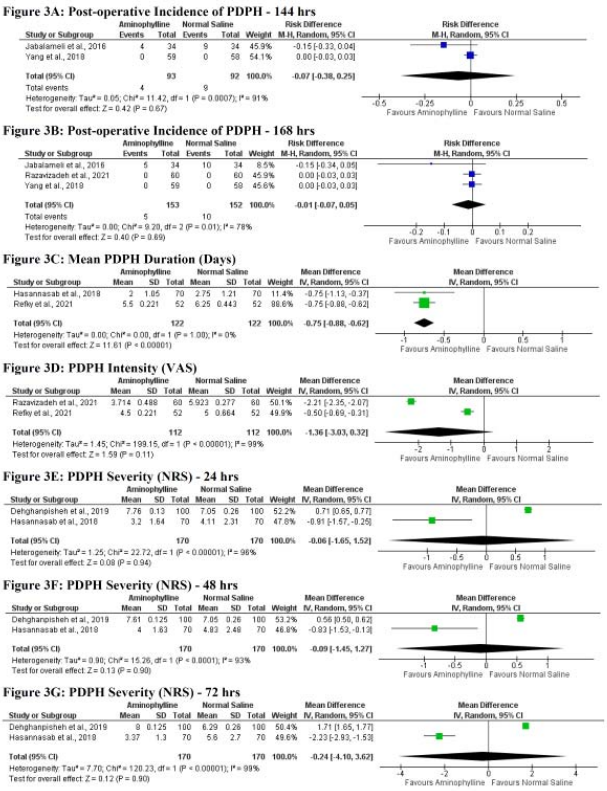


Fig. 3



P612

Prophylactic and therapeutic efficacy and safety of oral pregabalin for post-dural puncture headache (PDPH): A systematic review and meta-analysis

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Objective: To evaluate efficacy and safety of oral pregabalin in preventing and treating postdural puncture headache (PDPH).

Methods: Searches were run on PubMed, Embase, Scopus, Web of Science, Cochrane and clinical trial registries till June, 2025. Randomized controlled trials (RCTs) comparing oral pregabalin to conservative therapy or placebo (control) were included, with no language restrictions. RevMan v5.4.1 was used for all statistical analyses.

Results: 7 RCTs (N=1004) were included; 4 evaluated prophylactic use and 3 evaluated therapeutic use for PDPH. Prophylactically, pregabalin significantly reduced PDPH incidence versus control (Risk Ratio [RR] 0.47, 95% Confidence Interval (CI) [0.32-0.70]). It also reduced time to modified Bromage motor scale grade 3 (Mean Difference [MD] -3.18 minutes, 95% CI [-4.93 to -1.42]) and prolonged time to rescue analgesia (MD 45.15 minutes, 95% CI [4.06-86.25]). No significant differences were seen regarding PDPH onset, time to two-segment regression or incidence of postoperative nausea/vomiting (PONV).

Therapeutically, pregabalin significantly reduced headache intensity at 24 hours (MD -1.76, 95% CI [-3.48 to -0.03]), 48 hours (MD -1.74, 95% CI [-2.26 to -1.21]), and 72 hours (MD -1.68, 95% CI [-2.25 to -1.11]). It also lowered modified Lybecker headache severity scores at 48 hours (MD -0.57, 95% CI [-0.84 to -0.31]). Safety data, though could not be pooled due to reporting heterogeneity, showed no significant increase in adverse effects.

Conclusion: Oral pregabalin shows promise as both a prophylactic and therapeutic option for PDPH, with considerable reductions in PDPH incidence, intensity, and severity, without increased adverse events. Whilst current evidence supports its perioperative use, future research must directly compare pregabalin with established pharmacologic and non-pharmacologic strategies. In settings where therapies like epidural blood patches are impractical or delayed, pregabalin may offer a safer, non-invasive window for intervention.

Fig. 1

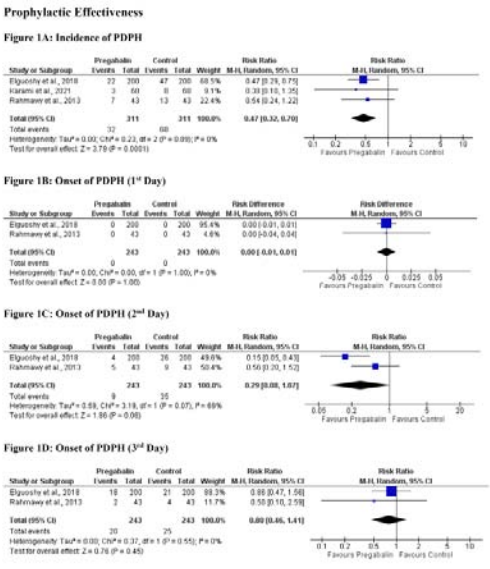
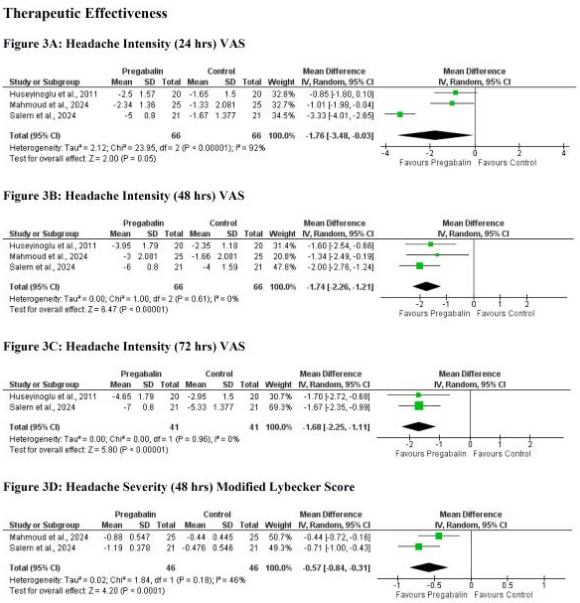


Fig. 2



Fig. 3



P613

Discontinuation of oral migraine preventives during anti-CGRP therapy: A retrospective cohort study

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[2]Espírito Santo Hospital, Neurology, Azores, Portugal

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Objective: CGRP monoclonal antibodies (mAbs) have revolutionized migraine prevention. European guidelines recommend maintaining oral preventive medications during the initial treatment period with mAbs, followed by reassessment for potential tapering after 3 months. However, real-world evidence on the feasibility of this approach remains scarce.

The aim of this study was to evaluate the proportion of migraine patients who were able to reduce or discontinue oral preventive medications within one year of initiating monoclonal antibody (mAb) therapy.

Methods: This retrospective cohort study included migraine patients treated with mAbs at a tertiary hospital center. Oral preventive medication use was monitored for 12 months. The primary endpoint was the rate of successful reduction or discontinuation of oral preventives. Secondary analyses explored patient characteristics linked to these outcomes.

Results: At baseline, each patient was, on average, under 1.4 oral preventive medications. Among 82 patients (mean age 45 years; 87% female), 56.7% reduced or discontinued oral therapies within one year. By the end of the follow-up period, there was a

significant decrease in the use of oral preventive medications ($\chi^2(2) = 23.01$, $p < 0.001$) and 34.1% had successfully discontinued all oral medications. The proportion of patients with ≤15 headache days per month increased from 30.5% at baseline to 80.5% at 12 months ($\chi^2(1) = 39.02$, $p < 0.001$). Patient with more than 15 headache days per month at baseline was significantly associated with a lower likelihood of reducing oral preventives at 12 months (OR = 0.33; 95% CI = 0.12–0.96; p = 0.042).

Conclusion: This study provides real-world evidence supporting the safety and feasibility of reducing or discontinuing oral preventive medications in mAb-responsive migraine patients. Higher baseline migraine frequency was linked to a lower likelihood of discontinuation of oral preventives, possibly reflecting greater disease burden or treatment resistance.

P614

Migraine and PFO: Correlation, coexistence, dependence

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Objective: The foramen ovale is a physiological opening in the atrial septum formed during fetal life, which closes in most people after birth. However, in some people it can be present in adulthood, and is called the patent foramen ovale (PFO). PFO is more likely to occur in patients with migraine.

The review aimed to analyze the current knowledge on the topic of the relation between migraine and patent foramen ovale and indicate the most crucial clinical implications.

Methods: Two review teams, comprising migraine experts and stroke experts, were engaged in the screening process, resulting in the inclusion of 204 relevant publications. To be considered for inclusion, an article had to cover directly the topic of PFO or migraine.

Results: In our work, we have focused on several aspects regarding the direct and indirect relationship between migraine and PFO. While analyzing migraine pathogenesis, apart from the straight link between PFO and migraine, others are also considered, such as a prominent eustachian valve or Chiari valve, causing a high-risk PFO or a paradoxical embolism. Regarding the clinical practice, the prevalence of PFO and migraine, indications for exact therapies, and subsequently, neuroimaging in the view of PFO and migraine, have been scrutinized. Another crucial aspect of this work is the risk of stroke in patients with migraine, taking into account the PFO presence. It is suggested that patients with migraine have more vascular lesions on magnetic resonance imaging and more often experience strokes. Thus, the question arises whether PFO should be closed as stroke prophylaxis in every migraine patient.

Conclusion: Several aspects have been explored; however, more research is needed to draw clear conclusions with further indications for clinical practice. Nevertheless, it seems that not in all patients with migraine with PFO should the closure procedure be performed, but when the PFO is of high-risk form or there are other indications, it should at least be considered.

Fig. 1

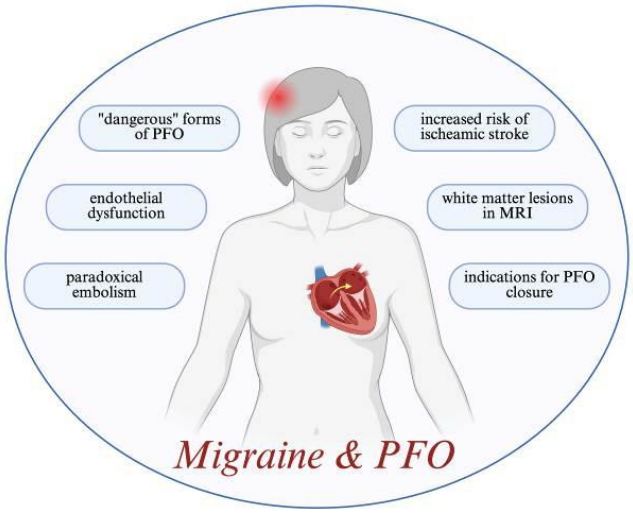
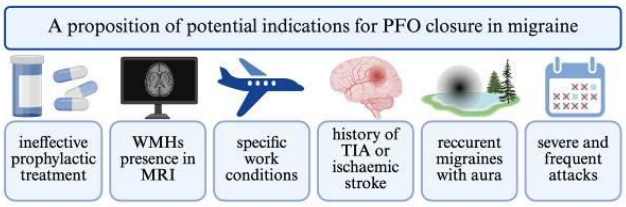


Fig. 2



P615

Therapeutic challenges in a rare trigeminal autonomic cephalalgia

M. T. Rego[1], *C. Rocha Oliveira*[1], *A. L. Pires*[1], *P. Ferreira*[1], *I. Alves*[1], *J. M. Roriz*[1]

[1]Unidade Local de Saúde Entre Douro e Vouga, Santa Maria da Feira, Portugal

Objective: To discuss therapeutic challenges associated with a probable SUNCT. It"s a rare entity with pathophysiological mechanisms that remain incompletely understood and for which evidence regarding effective treatment strategies is limited. Clinical management therefore requires an individualized, multidisciplinary approach, given the high rate of refractoriness and significant functional impact.

Methods: Clinical case report.

Results: A 39-year-old man, with no relevant past medical history, presented with continuous left-sided hemicranial headache, accompanied by dozens to hundreds of daily paroxysms of excruciating, shock-like pain lasting from seconds to a few minutes. He also had persistent ipsilateral autonomic signs/symptoms (ptosis, conjunctival injection and tearing), which began several months prior to the onset of the headache. Brain and orbital MRI revealed no structural abnormalities, nor evidence of neurovascular contact. Immunological work-up showed persistently positive antiphospholipid antibodies and HLA-B51 positivity, prompting referral to Rheumatology. A probable diagnosis of SUNCT was considered. Multiple preventive treatments were trialed without sustained benefit. A sphenopalatine ganglion block was also attempted with no lasting improvement. A discrete improvement was noted with intravenous eptinezumab 300 mg every 12 weeks, in combination with duloxetine, gabapentin, topiramate and tapentadol. He makes excessive use of fast-acting tramadol and ibuprofen to alleviate acute pain. He was referred to Neurosurgery and awaits therapeutic decision. Despite optimized pharmacological management, he continues to experience countless debilitating episodes with severe impact on functionality and mental health.

Conclusion: SUNCT remains a therapeutic challenge due to its rarity, limited evidence base, and frequent refractoriness. This reinforces the need for further research and therapeutic innovation.

P616

Efficacy and safety of single-pulse transcranial magnetic stimulation for migraine: A systematic review and single-arm meta-analysis

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[1]King Edward Medical University, Lahore, Pakistan

[2]Continental Medical College, Lahore, Pakistan

Objective: This review aims to evaluate the efficacy and safety of single-pulse transcranial magnetic stimulation (sTMS) for migraine.

Methods: We searched PubMed, Scopus, Cochrane, Embase, Web of Science, and ClinicalTrials.gov from inception to August 28, 2025. We included studies evaluating the use of sTMS for migraine. Meta-analysis was performed using R/RStudio v2025.05.1+513. Continuous and dichotomous outcomes were pooled as means and proportions respectively, with 95% confidence intervals (CI). I2-statistics were used to evaluate inter-study heterogeneity. Outcomes evaluated were patient-reported pain relief, change in HIT-6 scores, change in mean headache days, and adverse events (overall and individual [paresthesia, scalp discomfort, headache directly caused by intervention]).

Results: Four studies were included, comprising 557 participants (78.8% female, mean ages 39 to 49 years). Pooled analysis revealed the participant-reported pain relief rate to be 66% (95% CI 57%-75%). Mean reduction in HIT-6 scores at 3 months, from baseline, was -4.71 (95% CI -6.87 to -2.55) and mean reduction in headache days was -3.6 days (95% CI -4.91 to -2.28) at 3-months follow-up. Overall adverse event rate was 19% (95% CI 11%-29%), and individual adverse event rates were 1% for paresthesia, 2% for scalp discomfort, and 2% for headache.

Conclusion: Single-pulse transcranial magnetic stimulation demonstrates meaningful efficacy in reducing migraine burden with a favorable safety profile. However, high-quality trials against standard-of-care interventions are needed to further clarify its role in migraine.

Fig. 1

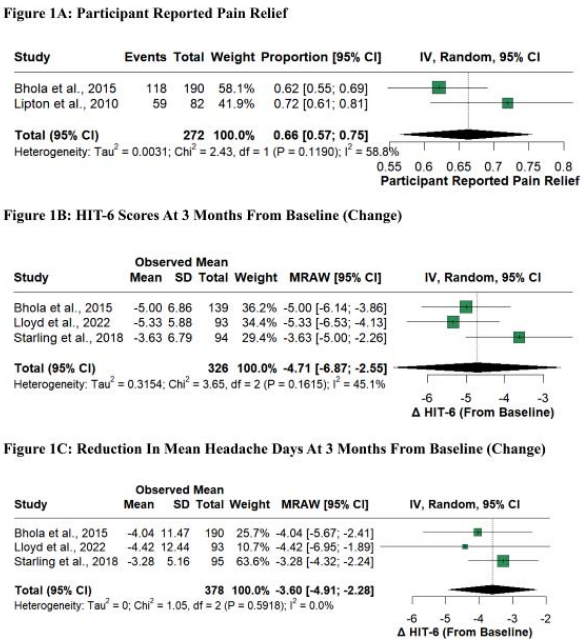


Fig. 2

Figure 2A: Overall Adverse Event Rate

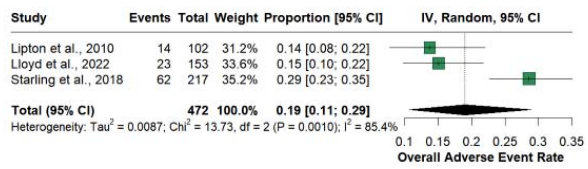


Figure 2B: Paresthesia Incidence

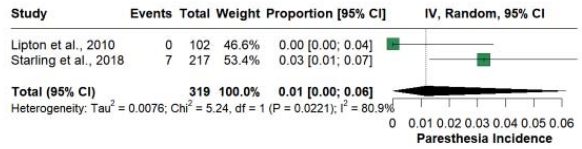


Figure 2C: Incidence Of Scalp Discomfort

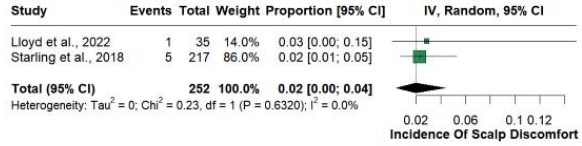
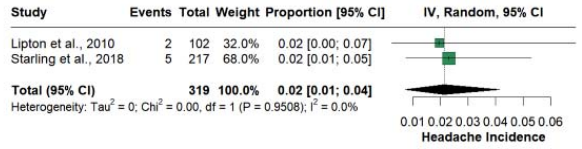


Figure 2D: Headache Incidence



P617

Comparative efficacy and safety of proximal versus distal greater occipital nerve block in managing headache disorders: A systematic review and meta-analysis

S. Arsalan Wasti[1], *A. Wasti*[2]

[1]King Edward Medical University, Lahore, Pakistan

[2]Continental Medical College, Lahore, Pakistan

Objective: This review aims to compare the efficacy and safety of proximal versus distal greater occipital nerve blocks (GONB) in managing headache disorders.

Methods: We searched PubMed, Embase, Web of Science, Scopus, Cochrane, and ClinicalTrials.gov from inception to September 9, 2025. Eligible studies were randomised controlled trials (RCTs) comparing proximal GONB to distal GONB for managing headache disorders in adults. Statistical analyses were performed in Review Manager v5.4.1. Dichotomous outcomes were pooled as risk-ratios (RR) and continuous outcomes as mean differences (MD) with 95% confidence intervals (CI). Heterogeneity was assessed using I2-statistics. Primary outcomes were block success rate and reduction in Numeric Rating Scale (NRS-11) score. Secondary outcomes were analgesic requirement and adverse event rate.

Results: Three RCTs were included in this review, consisting of a total of 270 patients (61.9% female). Mean participant ages varied from 29 ± 3.4 to 49.50 ± 12.53 years. Proximal GONB use was associated with significantly higher block success rates (RR 1.40, 95% CI 1.13-1.72, I2 = 28%) and significantly greater reductions in Numeric Rating Scale (NRS-11) scores at 24 hours post-block (MD -0.26, 95% CI -0.46 to -0.06). Proximal GONB use also resulted in significantly fewer analgesic requirements (RR 0.74, 95% CI 0.55 to 0.98). No significant differences were seen for overall adverse event rates. Heterogeneity was absent for all outcomes (I2 = 0%) other than block success rate.

Conclusion: This systematic review and meta-analysis demonstrates that proximal greater occipital nerve block provides superior clinical benefit compared to distal block in adults with headache disorders, with higher success rates and greater short-term pain relief, without increasing adverse events. Further high-quality trials with longer follow-ups are needed to confirm benefits.

Fig. 1

Figure 1A: Block Success Rate

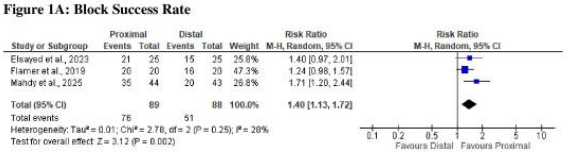


Figure 1B: Δ NRS-11 Score At 24 Hours Post-Block, From Baseline

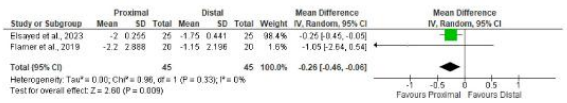
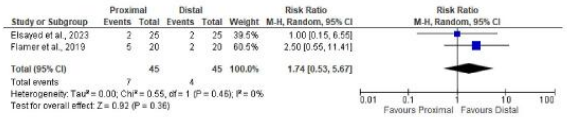


Figure 1C: Analgesic Requirement



Figure 1D: Overall Adverse Event Rate



P623

Establishment and impact of a multidisciplinary headache clinic in a tertiary hospital in southern Thailand: One-year experience from Songkhla Hospital

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[1]Songkhla Hospital / Prince Naradhiwas University, Medicine, Songkhla, Thailand

Objective: In Thailand, many migraine patients experience diagnostic delays, stigma, and medication overuse due to a lack of awareness and fragmented care.

Songkhla Hospital —a tertiary care center in Southern Thailand—established the first Multidisciplinary Headache Clinic (MDHC) in October 2023.

This study aims to evaluate the implementation and impact of a multidisciplinary headache clinic on patient outcomes, healthcare provider knowledge, and public awareness.

Methods: The Songkhla Multidisciplinary Headache Clinic (MDHC) integrates neurologists, rehabilitation physicians, Thai traditional medicine practitioners, pharmacists, and trained headache nurses. Services included structured assessments (registration forms, HIT-6, headache diaries), greater occipital nerve blocks, botulinum toxin injections, CGRP monoclonal antibodies, acupuncture, Thai massage, and educational sessions. Data was collected from October 2023 to March 2024. Outcome measures included diagnosis rates, treatment responses, and educational reach. Clinical data were monitored for six months.

Results: A total of 241 patients (F: M ratio 3.6:1) were treated. Diagnoses included migraine (65.6%), tension-type headache (3.7%), TACs (2.5%), facial pain (3.7%), and secondary headaches (24.5%). Interventions were performed in 59 patients (39 nerve blocks, 12 acupuncture, 8 Thai massage). Of those followed up, 42% had >75% reduction in monthly headache days, 35% had 50–75% reduction, and 23% had <30% reduction. Educational activities reached over 350 participants with a satisfaction rate of over 85%.

Conclusion: The Songkhla MDHC demonstrated the feasibility and benefit of a culturally adaptive, multidisciplinary approach in a low-resource setting. It improved clinical outcomes, reduced stigma, and laid the groundwork for the expansion of regional headache care. It also served as a model for professional education and community engagement

Fig. 1

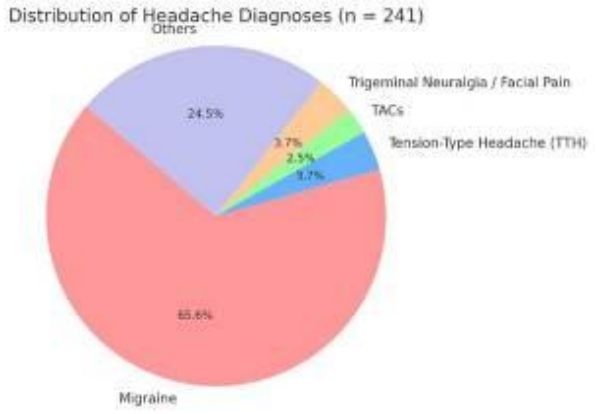


Fig. 2

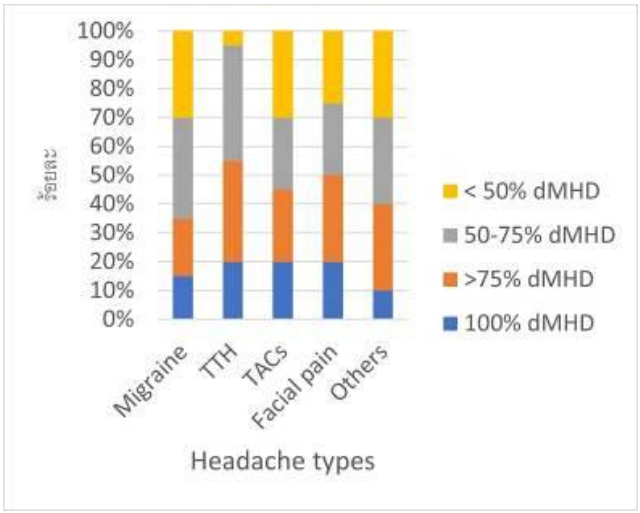
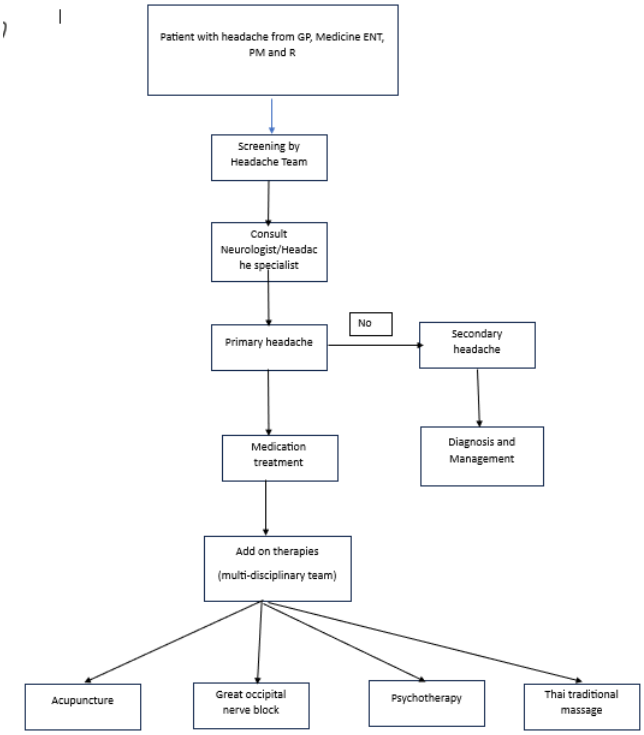


Fig. 3



P624

"Cefaleias em rede": A pilot project to improve headache management in health care

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[1]São João University Hospital, Department of Neurology, Porto, Portugal

[2]Faculty of Medicine, University of Porto, Department of Clinical Neurosciences and Mental Health, Porto, Portugal

Objective: Headache, especially migraine, is a leading cause of disability worldwide and places a significant burden on secondary care, often due to avoidable

referrals. With appropriate support, up to 90% of headache cases can be effectively managed in Primary Health Care (PHC). In our center, approximately 8% of referrals from PHC are for headache, with an average wait time of nine months for a first neurology consult. A survey among local PHC physicians revealed major gaps in diagnosis and both acute and preventive treatment.

Our goal is to empower family physicians to accurately diagnose and manage headache disorders, while optimizing referrals in line with published criteria.

Methods: Starting in 2025, over 100 family medicine residents and physicians will receive training in headache care, focusing on red flags, differential diagnosis, treatment strategies for common primary headaches, and referral guidelines. Each of five participating PHC centers will have a designated liaison family doctor serving as the main contact with the hospital"s Headache Clinic.

For referrals that can be managed in PHC with specialist input, a group consultation model will be implemented. These sessions—held without the patient—enable the neurologist to guide the family doctor on urgency, investigations, treatment, and follow-up.

Results: We expect reduced waiting times for neurology consultations and improved early diagnosis and management of headache in PHC. This will enhance patient access to timely, specialized care and improve quality of life.

Conclusion: The **"Cefaleias em Rede"** pilot project offers a scalable model to strengthen headache care within PHC. By equipping family doctors with targeted training and establishing structured collaboration with headache specialists, we aim to reduce unnecessary referrals, shorten wait times, and improve patient outcomes. If successful, this approach could serve as a framework for broader adoption in other healthcare regions.

P625

Multidisciplinary management of headaches in a Brazilian tertiary hospital

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[1]Univertisy of São Paulo, Health Sciences, Ribeirão Preto, Brazil

[2]Univertisy of São Paulo, Neurology, Ribeirão Preto, Brazil

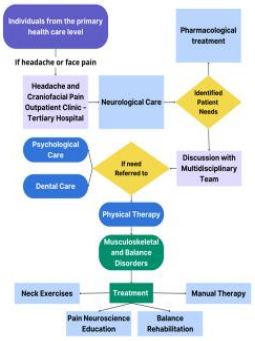
Objective: To describe how multidisciplinary management of headaches happens in a Brazilian tertiary hospital.

Methods: Medical records from the Headache and Craniofacial Pain outpatient Clinic (HCPC) were analyzed from July to December 2024.

Results: In the period of 6 months 595 individuals were treated by neurologists at the headache outpatient clinic. Of these, 56 were referred to physiotherapy. All individuals with headache were diagnosed using the third edition of the International Classification of Headache Disorders. The figure 1 shows the treatment plan for patients with headache and orofacial pain in a Brazilian tertiary hospital. After being referred to the outpatient clinic, these patients undergo a complete evaluation of the cervical spine, including the presence of trigger points, strength and cervical ROM, in addition to specific tests, such as the CCFT and FRT. In addition, evaluation of mandibular ROM and postural assessment are also included. Regarding the treatment of individuals with headache, the initial phase includes education in pain neuroscience, diaphragmatic breathing associated with cervical traction and mobilization, and release of trigger points. A second phase includes active stretching of the cervical spine and strengthening exercises for the deep flexors and cervical extensors, and cervical resistance training. In a more advanced phase, scapular strengthening exercises are included. Patients usually undergo treatment for 8 or 12 weeks, after which they are re-evaluated. At this point, there are 2 possible stages: discharge or redefinition of therapeutic goals.

Conclusion: The public and free tertiary hospital in Ribeirão Preto has a multidisciplinary team that works together for the benefit of the patient, according to their demands.

Fig. 1



P626

The role of physician associates in headache services – An example from South Tyneside and Sunderland NHS trust

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Objective: There is wide variation in the quality of headache care and access to appropriate treatment in the UK. Historically, headache conditions have been managed inconsistently due to the variation in skill

sets in primary care, and a limited number of specialist headache services, traditionally provided by consultants and nurse specialists. Due to the mismatch between demand and capacity of Headache services, there are long waiting lists, meaning patients are overusing other health services inappropriately and ineffectively. A Physician Associate joined the STSFT Neurology Department in November 2023. Job roles include providing greater occipital nerve blocks, CGRP treatment review, and assessment for advanced migraine treatments and headache diagnosis with consultant clinical supervision. Complementary roles in the idiopathic intracranial hypertension service involve review of these patients with fundoscopy and slit lamp skills and performing lumbar punctures. We assessed patient experience and satisfaction with the Physician Associate in Headache services

Methods: A survey of 30 patients were collected regarding patient satisfaction, quality of care and perception of the Physician Associate role in headache services.

Results: The overwhelming majority of responders were satisfied (93%), felt safe (97%) and had questions addressed adequately (93%) during the consultation with the Physician Associate, and 90% of service users would recommend the Physician Associate role. In particular, 87% of responders did not mind what type of health professional they saw as long as they were competent to assess their problem.

Conclusion: A multidisciplinary approach to headache management involving allied professionals provides patients with a wide support network for optimal management of their condition. It provides a benchmark for the role of Physician Associates, among other allied professionals, in Headache services

Fig. 1

	Percentage	Responses
Strongly disagree	3.4%	1
Disagree	0.0%	0
Somewhat disagree	0.0%	0
Neither agree nor disagree	3.4%	1
Somewhat agree	3.4%	1
Agree	10.3%	3
Strongly agree	79.3%	23

Fig. 2

	Percentage	Responses
Strongly disagree	3.3%	1
Disagree	0.0%	0
Somewhat disagree	0.0%	0
Neither agree nor disagree	3.3%	1
Somewhat agree	3.3%	1
Agree	10.0%	3
Strongly agree	76.7%	23
Not applicable	3.3%	1

Fig. 3

	Percentage	Responses
Strongly disagree	3.3%	1
Disagree	0.0%	0
Somewhat disagree	0.0%	0
Neither agree nor disagree	10.0%	3
Somewhat agree	6.7%	2
Agree	23.3%	7
Strongly agree	56.7%	17

P627

Acceptance-based cognitive behavioral therapy delivered via internet for migraine: 6-month follow-up results compared to treatment as usual an RCT-study

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Objective: In the current study an acceptance-based therapist-guided individually tailored internet-delivered cognitive behavioral therapy treatment program *I*nternet *A*pproach to *M*igraine (*I AM*) was developed to address migraine management in primary health care in Sweden. The aim was to evaluate whether *I AM* as an adjunct intervention to medical treatment leads to reduced migraine days, pain intensity, migraine burden and mental health.

Methods: The effectiveness of the *I AM* treatment program was assessed through a randomized controlled trial (RCT). 154 participants with episodic or chronic migraine were randomized into two groups: one receiving *I AM* in addition to treatment as usual (TAU) and the other TAU, which is medical treatment. The participants could choose modules, treatment rate and therapeutic support in collaboration with therapists based on diagnosis, needs and motivation.A Linear Mixed Model (LMM) was employed for the repeated-measures data to assess change over time while controlling for potential confounding variables

Results: Eighty percent (80%, n=125) of those randomized participated in the 6-month follow-up measurement and participants completed 88 % of the *I AM* intervention indicating high adherence. Compared to TAU, *I AM* produced a significant, lasting reduction in monthly migraine days from pre to 6 months follow- up mean difference (−2.3 days; p = 0.020) and more patients reported fewer than 15 migraine days at six months follow-up in the *I AM* group compared to TAU. *I AM* also decreased headache intensity (p = 0.013) and had a significant

effect on migraine burden (p =0. 005), mental health were better immediately post-intervention (p = 0.043), though groups converged by six months follow-up.

Conclusion: The findings of this study show that acceptance-based internet-delivered ICBT is effective in managing chronic and frequent episodic migraines in primary health care. Clinically, however, there is a need for additional biopsychosocial interventions for these patients.

Fig. 1

Table 3. Adjusted Means (SE) and p-values

	I AM n =76					TAU n= 78					Between, p-value	
	Pre M(SE)	Post M(SE)	6 months follow-up M(SE)	Within group p-value		Pre M(SE)	Post M(SE)	6 months follow-up (M(SE)	Within group p-value		Post	6 months
				Pre-post	Pre-6 months				Pre-post	Pre-6 months		
Migraine days	14.10 (0.77)	14.53 (1.02)	11.80 (1.02)	0.636	0.020*	14.88 (0.76)	13.48 (0.97)	13.41 (0.99)	.137	0.124	.381	.183
Pain intensity	6.18 (0.27)	5.51 (0.29)	5.46 (0.32)	.011*	0.013*	6.50 (0.27)	6.34 (0.28)	6.02 (0.31)	.531	0.094	.006*	.108
HIT-6	63.80 (0.83)	61.13 (1.06)	58.71 (1.31)	.005*	<0.001*	64.25 (0.82)	62.58(0.82)	61.12 (1.26)	.067	.009*	.221	.133
MHC -SF	41.65 (1.97)	44.80(2.15)	44.58 (2.40)	.115	0.196	42.37 (1.94)	40.15(2.06)	42.86 (2.31)	.255	0.826	.043*	.529

* P<0.05 Migraine days: How many migraine days per month have you had on average in the last 3 months? Pain intensity: Estimate on a scale of 1-10 how painful the headache was. 0= no pain and 10= worst pain imaginable. HIT-6 = Headache Impact Test-6, MHC SF = Mental Health Continuum Short Form

Fig. 2

Figure 1 Headache days pre, post and 6 month-follow up

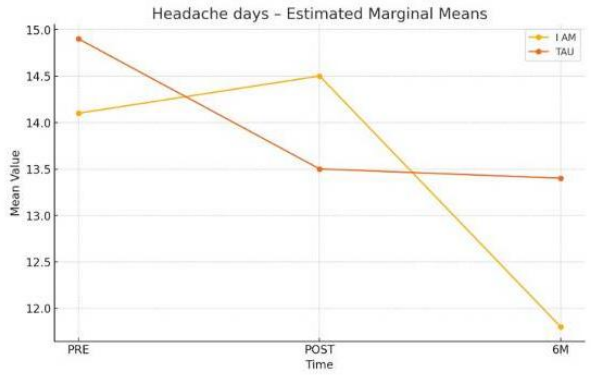


Fig. 3

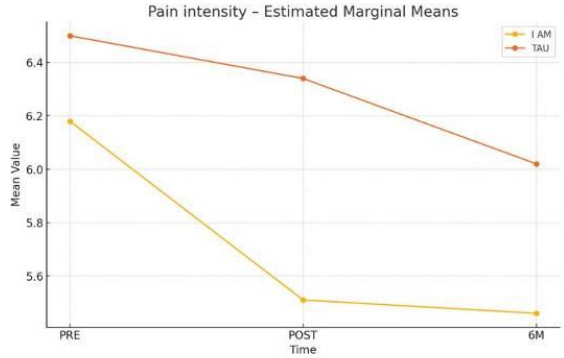


Figure 2 Pain intensity pre, post and 6 month follow up

P628

Implementing a patient-driven digital follow-up of preventives targeting the CGRP-system for migraine patients: First-of-its-kind initiative in Norway

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Objective: To develop and implement a digital outpatient model for migraine patients on CGRP-targeting treatment, focusing on safety, efficiency, and user-friendliness.

Methods: The introduction of CGRP-targeting migraine preventives has led to increased referrals, straining outpatient resources and challenging traditional follow-up models. To ensure sustainable, timely, and patient-centered care, we explored a digital, patient-driven follow-up strategy.

A multidisciplinary team from Helse Nord-Trøndelag, including healthcare professionals, IT experts (HEMIT), and a patient representative, created the model using the CheckWare platform. A digital questionnaire was developed to track migraine symptoms, treatment effect, and long-term needs. Over a 2-month pilot, patients completed the forms from home at set intervals. Clinicians reviewed responses to decide on the need for further follow-up. At the end, participants completed an evaluation form.

Results: 11 patients were invited; 10 participated. Nine completed all three scheduled forms, one only the first. All 10 answered the evaluation. They were asked if they were happy with the user-driven approach, login process, and questionnaire clarity: all answered "yes." A free-text field allowed for comments and suggestions, which were constructive. No safety concerns were reported. Based on the pilot, the model was implemented as standard care in June 2025.

Conclusion: The pilot showed that patient-driven digital follow-up is safe, easy to use, and flexible. It helped reduce unnecessary visits and saved time for both patients and staff. The model aligns with national and EU goals for digital health and will be tested for other chronic headache conditions.

P629

MIGRAGILE: A self-administered tool for early detection of disabling migraine at primary care setting

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Objective: Migraine is a common and disabling neurological disorder frequently underdiagnosed, causing delays in treatment and increased burden on patients and healthcare systems.
Aim: To evaluate a self-administered screening tool (MIGRAGILE) for early identification of disabling migraine, specifically High Frequency Episodic Migraine (HFEM) and Chronic Migraine (CM), at primary care setting.
Methods: We designed MIGRAGILE e-survey with 15 questions, self-completed by patients with headache. It allowed to characterize 1) migraine diagnosis, 2) degree of headache disability, 3) acute and preventive treatment prescribed, and 4) need to be assessed by general neurologist or more specialized headache neurologist. In a routine medical appointment, the General Practitioner provided the MIGRAGILE e-survey and recommended patients with headache to fill in the QR code survey in RedCap platform. Headache Nurse reviewed the surveys sent twice per week.
Our reference population is 540.000 inhabitants distributed in 20 Primary care centers.
Results: From July 2023 to July 2025, 332 patients completed the survey. After the learning curve, an average of 22 patients are presently evaluated every month.
False Positive (n=9) and False negative (n=1) for migraine diagnose resulted in a Sensibility, Specificity, Positive Predicting Value and Negative Predicting Value of 99.7%, 75.7%, 96.9% and 96.5%, respectively.
Headache diagnosis distribution was: 1) Low Frequency episodic migraine 50.2%, 2) HFEM and CM 37.1% 4) Medication overuse headache 2.4% and 5) Other non-migraine headaches 10.3%.
Headache nurse evaluated and sent 33.1% of patient to online educational migraine program and 30.7% to priority visits at the Headache Unit.
Conclusion: In our center, MIGRAGILE is a clinically useful self-administered screening tool for early detection of disabling migraine in primary care, integrated into headache nurse activity

P630

Real-world comparative analysis of migraine attack abortive therapies: Insights from over 59 million patient records in the Migrebot e-Diary

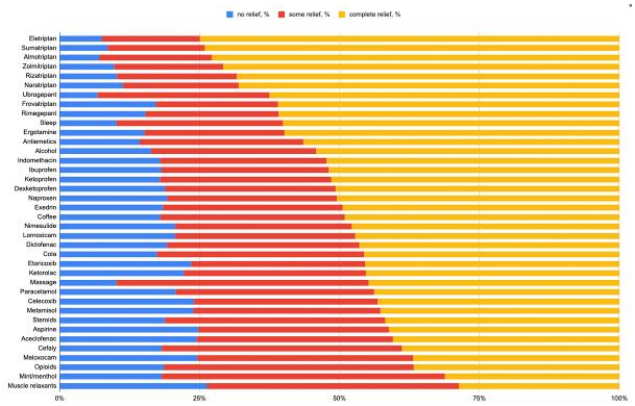
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Objective: E-diaries can characterize treatment performance at scale. Migrebot is a headache diary used by over 110,000 monthly users, with over 59 million total entries. We evaluated the real-world effectiveness of acute medications and non-pharmacological methods
Methods: We analyzed 9,278,293 anonymized medication-outcome pairs from Migrebot users between January 2022 and August 2025 (2022: 1,208,047; 2023: 1,965,543; 2024: 3,037,589; Jan-Aug 2025: 3,067,114).Drug names were standardized, and acute therapies were grouped into 10 classes:
NSAIDs and simple analgesics (4,524,131 records; 24 medications)
triptans (3,219,043; 7)
NSAID combination medications (1,370,394; n/a)
antiemetics (32,292; 2)
ergots (29,574; 5)
opioids (2,757; 4)
muscle relaxants (15,694; 4)
steroids (6,101; 2)
gepants (2,110; 2)
non-pharmacological interventions (76,197; n/a)
Patient-rated effectiveness for each attack was categorized as "no relief," "some relief," or "complete relief." The primary outcome was the percentage of attacks with "complete relief."
Results: Significant differences in effectiveness were observed between medication classes. Average "complete relief" rates were: triptans 69.99%, gepants 61.67%, NSAIDs and analgesics 46.06%, ergots 59.86%, antiemetics 56.46%, and opioids 36.71%. Across all episodes, eletriptan showed the highest proportion of "complete relief" responses (74.92%) among all medications in the dataset. We also analyzed widely used non-pharmacologic treatments. The proportion of "complete relief" was: sleep 60.09%, alcohol 54.17%, coffee 49.06%, cola 45.6%, massage 44.85%, cefaly 38.81%, mint/menthol 31.18%
Conclusion: In this very large, fully naturalistic dataset, eletriptan was associated with the greatest user-reported relief among the medications studied. While self-selection, reporting bias, attack heterogeneity, and the absence of randomization limit causal inference, e-diaries can complement clinical trials by providing rapid, global, real-world signals at scale

Fig. 1

	total records	no relief, records	no relief, %	some relief, records	some relief, %	complete relief, records	complete relief, %
Eletriptan	165855	12516	7,55%	29079	17,53%	124260	74,92%
Sumatriptan	1666067	143295	8,60%	289465	17,37%	1233307	74,03%
Almotriptan	1337	95	7,11%	269	20,12%	973	72,77%
Zolmitriptan	1203308	117721	9,78%	233783	19,43%	851804	70,79%
Rizatriptan	150525	15414	10,24%	32131	21,35%	102980	68,41%
Naratriptan	1674	190	11,35%	346	20,67%	1138	67,98%
Ubrogepant	384	26	6,77%	118	30,73%	240	62,50%
Frovatriptan	536	92	17,16%	117	21,83%	327	61,01%
Rimegepant	1726	265	15,35%	411	23,81%	1050	60,83%
Sleep	2626	268	10,21%	780	29,70%	1578	60,09%
Ergotamine	29314	4437	15,14%	7329	25,00%	17548	59,86%
Antiemetics	32292	4617	14,30%	9443	29,24%	18232	56,46%
Alcohol	2590	423	16,33%	764	29,50%	1403	54,17%
Indomethacin	11759	2114	17,98%	3490	29,68%	6155	52,34%
Ibuprofen	2519056	456576	18,12%	753232	29,90%	1309248	51,97%
Ketoprofen	140984	25369	17,99%	43145	30,60%	72470	51,40%
Dexketoprofen	39360	7399	18,80%	12019	30,54%	19942	50,67%
Naproxen	517057	99420	19,23%	156851	30,30%	260986	50,48%
Exedrin	12857	2373	18,46%	4129	32,11%	6355	49,43%
Coffee	43238	7757	17,94%	14267	33,00%	21214	49,06%
Nimesulide	338528	69768	20,61%	107118	31,64%	161642	47,75%
Lornoxicam	12310	2538	20,62%	3964	32,20%	5808	47,18%
Diclofenac	49445	9516	19,25%	16950	34,28%	22979	46,47%
Cola	2783	483	17,36%	1031	37,05%	1269	45,60%
Etoricoxib	4852	1143	23,56%	1507	31,06%	2202	45,38%
Ketorolac	174460	38681	22,17%	56843	32,58%	78936	45,25%
Massage	1224	124	10,13%	551	45,02%	549	44,85%
Paracetamol	35841	7450	20,79%	12689	35,40%	15702	43,81%
Celecoxib	13460	3228	23,98%	4418	32,82%	5814	43,19%
Metamisol	129464	31019	23,96%	43207	33,37%	55238	42,67%
Steroids	6101	1147	18,80%	2401	39,35%	2553	41,85%
Aspirine	190210	47122	24,77%	64892	34,12%	78196	41,11%
Aceclofenac	3801	931	24,49%	1331	35,02%	1539	40,49%
Cefaly	1894	345	18,22%	814	42,98%	735	38,81%
Meloxocam	5200	1280	24,62%	2007	38,60%	1913	36,79%
Opioids	2757	513	18,61%	1232	44,69%	1012	36,71%
Mint/menthol	1860	339	18,23%	941	50,59%	580	31,18%
Muscle relaxants	15694	4139	26,37%	7064	45,01%	4491	28,62%

Fig. 2



P631

Real-world analysis of headache recurrence and next-day medication use following acute migraine therapy: Insights from 3 million attacks in the Migrebot e-Diary

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Objective: To evaluate the real-world performance of acute migraine therapies based on patient-reported headache recurrence and need for next-day rescue medication using data from a digital headache diary

Methods: We analyzed 3,175,534 anonymized records from the Migrebot application (2022 – Jan-Aug 2025) where users treated a single headache attack with only one medication. Drug names were standardized and grouped into 10 classes: NSAIDs/analgesics, triptans, NSAID combinations, antiemetics, ergots, opioids, muscle relaxants, steroids, gepants, and non-pharmacological interventions. The primary outcomes were the percentage of attacks with headache recurrence within 24 hours and those requiring additional medication the next day.

Results: Significant differences were observed between drug classes. Gepants demonstrated the lowest rates of headache recurrence and next-day medication use (rimegepant 25.64%/16.8%, ubrogepant 30.82%/22.22% respectively)

Table 1. The average 24-h headache recurrence and next-day medication for different medication classes

Group	Headache recurrence, %	Next-day medication use, %
Gepants	28,23	19,51
Ergots	30,82	23,17
NSAIDs	36,41	23,7
Triptans	38,65	30,91

These efficacy patterns remained consistent and reproducible across the analyzed years (2022, 2023, 2024 and 2025)

Conclusion: This large-scale, real-world analysis confirms that gepants are not only effective in initial pain relief but are also superior in sustaining treatment response and preventing headache recurrence compared to non-specific analgesics, ergots and triptans. This may reflect the preventive potential of this class. The consistency of results across years strengthens the validity of these findings. Digital diary data provides crucial insights into long-term treatment performance, directly informing clinical practice for improved migraine management.

Fig. 1

Table 2. 24-h headache recurrence and next-day medication use

	total records	Headache next day		Abortive med next day	
		records	%	records	%
Rimegepant	1018	261	25,64%	171	16,80%
Nimesulide	218382	66819	30,60%	40088	18,36%
Ergotamine	19619	6047	30,82%	4545	23,17%
Ubrogepant	279	86	30,82%	62	22,22%
Naproxen	304817	97967	32,14%	63152	20,72%
Metamisol	67358	21980	32,63%	13561	20,13%
Exedrin	8074	2708	33,54%	1973	24,44%
Almotriptan	995	338	33,97%	269	27,04%
Ibuprofen	1820048	629367	34,58%	418352	22,99%
Ketorolac	98315	34442	35,03%	21515	21,88%
Ketoprofen	87327	30626	35,07%	20492	23,47%
Frovatriptan	357	126	35,29%	99	27,73%
Etoricoxib	2962	1051	35,48%	683	23,06%
Naratriptan	1240	440	35,48%	298	24,03%
Aspirin	82113	29288	35,67%	19280	23,48%
Dexketoprofen	22919	8220	35,87%	5549	24,21%
Diclofenac	23897	8584	35,92%	5789	24,22%
Paracetamol	217938	78703	36,11%	50094	22,99%
Eletriptan	107220	41188	38,41%	33485	31,23%
Lornoxicam	7171	2850	39,74%	2011	28,04%
Zolmitriptan	625640	259092	41,41%	218998	35,00%
Celecoxib	7711	3206	41,58%	2232	28,95%
Sumatriptan	1111090	464964	41,85%	396451	35,68%
Aceclofenac	1994	839	42,08%	525	26,33%
Meloxicam	2527	1102	43,61%	676	26,75%
Rizatriptan	91902	40549	44,12%	32766	35,65%
Steroids	1036	501	48,36%	362	34,94%
Opioids	990	480	48,48%	374	37,78%
Indometacin	6822	3717	54,49%	3036	44,50%

Fig. 2

Table 3. Consistency of results across the years

	total records	Headache next day		Abortive med next day	
		records	%	records	%
Sumatriptan 2025	286761	119172	41,56%	102118	35,61%
Sumatriptan 2024	356240	146055	41,00%	125332	35,18%
Sumatriptan 2023	282818	119275	42,17%	101592	35,92%
Sumatriptan 2022	185271	80192	43,28%	67409	36,38%
Nimesulide 2025	63735	18938	29,71%	11679	18,32%
Nimesulide 2024	71113	21246	29,88%	12676	17,83%
Nimesulide 2023	50523	15868	31,41%	9475	18,75%
Nimesulide 2022	33011	10767	32,62%	6258	18,96%
Ergotamine 2025	4917	1537	31,26%	1206	24,53%
Ergotamine 2024	6567	1959	29,83%	1471	22,40%
Ergotamine 2023	4755	1450	30,49%	1081	22,73%
Ergotamine 2022	3380	1101	32,57%	787	23,28%

P632

Intracranial incidental findings on brain Magnetic Resonance Imaging (MRI) in a pediatric population with primary headache: Our experience and management

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Objective: Headache is frequent symptom in children, which often leads to execution of neuroradiological examinations and to finding of incidentalomas. In fact, headache is often attributed to primary headache, neurological disorder common in developmental age. Recent widespread access to neuroradiological examinations has led to increase in number of incidental brain lesions in children with headache.
Methods: We reported retrospective study (28 patients under 18 years) with primary headache and incidental findings of suspected low-grade lesion at brain MRI. Data were collected on age, sex, headache characteristics. Patients were treated conservatively with neuroimaging surveillance of suspected low-grade lesion. Lesions were divided in supratentorial (thalamic) and infratentorial (cerebellar). The first follow-up MRI was performed after 6 months and follow-up were carried out every 12 to 18 months.
Results: Patients included 13 females (46%) and 15 males (54%): 67.8% presented migraine without aura, 25% tensive headache, 14.3% migraine with aura, 7% both tensive headache and migraine without aura. Average follow-up period was 43.7 months. In following period: 7% was stable at 84 months, 17.8% at 72 months, 21.5% at 60 months, 46.5% at 48 months, 64.3% at 36 months, 96.5% at 24 months. 96.5% of the patients showed radiological stability during the whole follow-up period. No significant radiological changes were found during follow-up in 27 of 28 patients.
Conclusion: With increasing detail of imaging techniques, there has been an increase in number of incidentally brain lesions in children with primary headache, leading to a management dilemma for neurologists. Incidentally low-grade lesions are not related to headache. This study reports data on long-term clinical and radiological follow-up period in patients with primary headache and occasional low-grade lesion findings during headache assessment, showing stability over time and safety of conservative management.

P633

Unveiling the hidden burden of migraine in Cape Verde: Clinical characterisation and impact assessment from a real-world care setting

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Objective: This study aims to provide aclinical and demographic characterization of a cohort of migraine patients in Cape Verde, assessing ictal, interictal, and quality of life impact.
Methods: Adults diagnosed with migraine according to ICHD-3 criteria, followed at the Neurology outpatient clinic of a central hospital in Cape Verde, were included. All participants underwent a face to-face interview to collect demographic and clinical data, including age at migraine onset, age at diagnosis, and the number of headache days—using a headache diary when available. Pain characteristics were also documented, along with therapies used during the acute phase and preventive treatments. Participants additionally completed the HIT-6 (ictal impact), MIBS-4 (interictal impact), and MSQ (quality of life) scales.
Results: Sixty patients (81.7% female; mean age 36.4±12.6 years) were included; 93.3% had episodic migraine. Regarding acute treatment, 20% used no medication during attacks, and none used triptans, differing from European standards. Prophylactic therapy was underused and mostly nonspecific, suggesting access barriers. Severe ictal impact was found in 83.3% (HIT-6), severe interictal impact in 76.7% (MIBS-4), and 70% showed severe to extreme quality of life impairment (MSQ, >53%). Limited access to specialized care, low health literacy, and barriers to treatment likely contribute to this high burden.
Conclusion: This is the first study on migraine impact in Cape Verde, highlighting the substantial disease burden—especially since most patients have episodic migraine—and showing a burden far exceeding that of European populations. This emphasizes the urgent

need to understand causes and provides data to guide tailored clinical and public health interventions.

P635

Expression of self-reported vestibular symptoms in association with migraine in autistic vs neurotypical groups

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Objective: Migraines are the third leading cause of disability, characterized by sensory disturbances and headache, affecting 10 million people in the United Kingdom. Tinnitus is more prevalent in autistic individuals and those with vestibular migraines (VM), where dizziness is a key symptom. This study explores whether autistic individuals experience increased dizziness and tinnitus, potentially indicating VM, and whether this association is stronger compared to neurotypical individuals.

Methods: A total of 56 autistic and 109 neurotypical adults completed an online survey between November 2024 and February 2025. Data were analysed using Chi-squared, Fisher"s tests, and Generalised Linear Models. The ethics application, submitted by Sultan Cadir and Prof. Hugo Critchley, was approved by the Brighton and Sussex Medical School Research and Governance Ethics Committee (ER/BSMS9HF1/1) on 28th October 2024, with approval valid until 1st June 2025.Participants who completed the questionnaires were given an honorarium.

Results: Most autistic participants (73%) reported dizziness symptoms, which was significantly higher than neurotypical respondents. Additionally, 80% of autistic participants reported tinnitus, compared to 40% of neurotypical respondents (X2 = 4.33; p = 0.04). Autistic respondents also reported increased rates of migraine alongside tinnitus (X2 = 9.98, p = 0.019). Furthermore, higher dizziness handicap (DHI) was associated with lower migraine quality of life (MSQ) with intercept at 4.24 (SE; 0.05, p<0.001).

Conclusion: These results suggest autistic adults may be more prone to dizziness and tinnitus, potentially linked to VM via shared hypersensitivity pathways. This study contributes valuable knowledge on vestibular manifestations and migraine quality of life in autistic populations- contributing to an underexplored area of research. However, further research is needed to confirm these results across larger groups and various populations.

Fig. 1

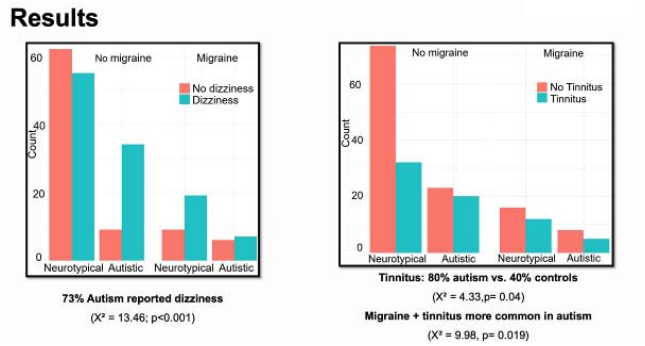


Fig. 2

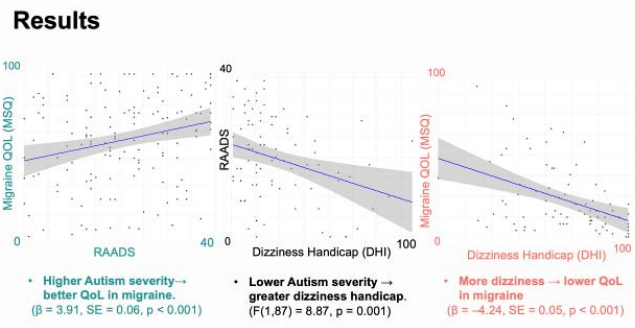


Fig. 3

Participant Demographics

Characteristics	Total
Age (mean)	38
Sex assigned at birth	
Male	48%
Female	52%
Ethnicity	
White	72%
Black	13%
Asian	6%
Other	9%
Gender identification	
Same as assigned at birth	98%
Not same as birth	2%

Highest level of education	
Primary school	0.5%
Some secondary school	1.5%
Completed GCSE	12%
Alevels or similar	14%
Attended college/ university but did not graduate	9.5%
Undergraduate degree	36.5%
Graduate degree	26%
Employment status	
Full time	69%
Part- time	12%
Unemployed	7%
Not in paid work (retired, homemaker or disabled)	7%
Other	5%

P636

Comorbid migraine and epilepsy in a UK neurology tertiary service: Clinical characteristics, treatment outcomes, and prognosis

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Objective: To describe the demographics, clinical phenotype and treatment outcomes of patients with comorbid migraine and epilepsy referred to a tertiary UK Neuroscience centre.

Methods: We retrospectively reviewed patients with both migraine and epilepsy seen at Leeds Teaching Hospitals between 2015 and 2025. Demographic, clinical, imaging, and comorbidity data were extracted

from records. Treatment outcomes were categorised as seizure free, migraine >50% improvement, or poor responder (<50%). A dual responder group captured improvement in both conditions. Associations with comorbidity, imaging findings, and clinical phenotype were analysed. Categorical variables were compared using χ^2 or Fisher's exact test.

Results: From 1160 clinical letters screened, 172 patients with comorbid migraine(episodic and chronic ICHD3) and epilepsy were identified, of whom 131 (75.3%) were female. Psychiatric comorbidity was frequent, with depression documented in 40 patients (22.7%) and anxiety in 30 (17.0%). Thirty-one patients (17.8%) had EHF 2020 criteria resistant migraine, 36% achieved being seizure free, 23% migraine patients >50% improvement and 28% had drug-resistant epilepsy. Migraine subtypes (with aura 30.8%, other subtypes(Hemiplegic, Acephalgic, Brainstem aura) 5% and Focal 42.4%, generalised 40.6%, nocturnal epilepsy 9.3%, with 20% having abnormal EEG and MRI lesions identified in 21% of patients. Topiramate was prescribed in 23.9% of patients, and linked with poorer tolerability. MRI abnormalities did not predict prognosis.

Conclusion: In our tertiary comorbid migraine and epilepsy cohort, psychiatric comorbidity, treatment resistance in epilepsy and migraine as well as EEG abnormalities and intracranial lesions were present up to one in 5 of our cohort. Lack of structured outcome documentation limited retrospective evaluation, highlighting the need for standardised recording in comorbid populations.

P637

The real pain of abuse: Not all bruises are visible

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Objective: One of the diagnostic challenges in headaches is to dissect the symptoms in patients with depressive disorders, requiring careful clinical evaluation to differentiate overlapping diseases and guide appropriate management.

Methods: Patient consent to publish details in an open access journal.

Results: A 48-year-old woman, with a medical history of hypertension, fibromyalgia and depression, was referred to neurology consult for episodes of right, stabbing, intense (10/10), frontal headache, lasting 5 minutes, recurring up to 2-3 times daily, associated with ipsilateral tearing, ptosis and miosis, and refractory to acute treatment. The hypothesis of short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) was considered, but there was no response to either lamotrigine nor topiramate at therapeutic doses. MRI was normal. Later, the characteristics of headache changed. It became right-sided hemicrania, pressure-type, constant, less intense (4/10, with paroxysmal worsening (intensity 10/10, lasting 5-10 minutes, with ipsilateral ptosis, conjunctival erythema, and tearing), 2-3 times per day. The hypothesis of hemicrania continua was considered, but again there was no response to indomethacin. When cognitive and depressive symptoms arose, psychiatry consultation was requested, where the circumstance of domestic violence was identified. One of the final diagnosis of this patient was headache attributed to psychiatric disorder, and non-pharmacologic treatment was proposed.

Conclusion: Currently, there are no established guidelines for the diagnosis or treatment of headache attributed to psychiatric disorder. Nonetheless, it is of supreme importance to systematically inquire about prior or ongoing physical, emotional, and/or sexual abuse. Emphasis is on the complex diagnostic process, the critical role of a multidisciplinary approach, and the consideration of the patients' emotional and social dimensions.

P638

The impact of migraine with aura on cardiovascular risk in women: A systematic review

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Objective: This systematic review aims to evaluate the association between migraine with aura and cardiovascular risk in women. It focuses on identifying key cardiovascular outcomes linked to migraine with aura, analyzing the impact of additional risk factors such as smoking, hypertension, and hormonal contraceptive use, and comparing cardiovascular event incidence between women with and without migraine with aura.

Methods: A systematic search was performed in PubMed, LILACS, and SciELO databases using the terms "Migraine," "Aura," "Cardiovascular Risk," and "Woman" combined with the Boolean operator AND. Studies published from 2015 to 2025 in English or Portuguese involving women with migraine with aura who developed cardiovascular diseases were included. After screening 137 articles by title, abstract, and full text, nine studies met the eligibility criteria. The selected studies were appraised according to

evidence levels from meta-analyses (Level I) to cross-sectional studies (Level V).
Results: The evidence consistently indicates that migraine with aura increases the risk of major cardiovascular events, especially myocardial infarction and stroke, in women. Prospective cohorts and meta-analyses provided the strongest support. Additional factors such as smoking, hypertension, and oral contraceptive use further increase this risk. Migraine with aura is considered an independent cardiovascular risk factor and may improve risk prediction models. Associations with vascular dysfunction and higher risk of cervical artery dissection were also reported, emphasizing the need for clinical vigilance.
Conclusion: Migraine with aura is strongly associated with increased cardiovascular risk in women, acting as both an independent risk factor and marker of vascular vulnerability. Clinical management should address modifiable risk factors to prevent adverse outcomes. Further research is essential to clarify causality and optimize personalized prevention and treatment strategies

P639

Sex differences in clinical presentation and diagnostic delay in cluster headache

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Objective: Studies suggest sex-based differences in cluster headache (CH). We analyzed clinical variability by sex, focusing on age of onset, diagnostic delay, trigeminal-autonomic symptoms (TAS), and remission periods.
Methods: A cross-sectional study was conducted in a cohort of patients diagnosed with CH. Demographic and clinical variables were collected (CH type, age of onset, diagnostic delay, attack intensity and duration, presence and severity of TAS, duration of remission periods) and compared between sexes, analyzing differences in clinical presentation.
Results: Ninety patients were included (23 women [25.6%], 67 men [74.4%]). Age of onset was significantly lower in women (28.6 ± 13.3 years) than in men (35.3 ± 13.8 years; p = 0.04). No significant differences were found in CH subtype distribution. Diagnostic delay was longer in women (8.4 ± 8.3 years) compared to men (3.6 ± 7.6 years; p = 0.0007), with immediate diagnosis in 18.2% of women and 54.5% of men. No differences were observed in attack intensity (median 9.5 vs. 10) or duration (median 60 min in both sexes). Frontal and facial redness were more frequent in women (20% and 25%) than in men (3% and 4.8%; p = 0.027 and p = 0.017). Remission periods were longer in women (20.5 ± 14.9 months vs. 11.3 ± 10.6 months; p = 0.03).
Conclusion: CH in women is associated with earlier onset, longer diagnostic delay, higher frequency of facial redness, and more prolonged remission periods.

P640

Migraine burden in postmenopausal women and the need for prophylactic treatment

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Objective: To assess the need to continue preventive treatment for migraine in women after the onset of menopause
Methods: We performed a retrospective chart review of female patients with a longstanding diagnosis of migraine according to ICHD-3 criteria. Patients aged 50 or older, who had received a clinical diagnosis of menopause between 2024 and 2025, were included. Menopause was established clinically. Patients with secondary headaches were excluded. Data were obtained from a specialized Headache Clinic in Mexico City. Treatment continuation reflected a clinical decision during follow-up.
Results: Fifty-nine patients were included. Median age was 57 years (IQR 52–59). A first-degree relative with migraine was reported in 15%. The most common comorbidities were hypertension (13%) and depression (7%). Tension-type headache was present in 10%. Twelve percent had a history of mild traumatic brain injury, without a clear relationship to migraine diagnosis or worsening. Alternating hemicranial pain was reported in 44%, side-locked pain in 25%, and frontal predominance in 16%. Median pain intensity during attacks was 7/10 (IQR 4–8.75), and median monthly migraine days were 2 (IQR 1–8). Seventy-nine percent of patients continued using preventive treatment after menopause. The most prescribed agents were amitriptyline (37%), topiramate (27%), and propranolol (10%). Acute treatment was not used in 44% of cases. The most common acute medications were zolmitriptan (10%), paracetamol (8.6%), and ketorolac (8.6%). Twenty patients used two prophylactics; 22% reported intolerance to at least one drug. Four percent had medication-overuse headache, and 5% had contraindications to triptans.
Conclusion: Our findings highlight the persistent burden of migraine after menopause and support the ongoing need for prophylaxis in a majority of patients. This may challenge assumptions of reduced treatment need post-menopause and suggests a specific phenotype of late-life persistent migraine.

P641

Hormonal changes as an etiological factor in trigeminal neuralgia in women

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Objective: To investigate the potential role of sex hormones in women with trigeminal neuralgia by exploring associations with major hormonal life events, hormone-related medications, and comorbidities that may influence hormone levels.
Methods: In this cross-sectional case-control study, women with trigeminal neuralgia aged ≤ 60 years were consecutively included and interviewed using a semi-structured questionnaire covering pain characteristics, hormonal life events, hormone-related treatments, and relevant comorbidities. Age-matched healthy female controls were recruited. All participants underwent 3.0 Tesla MRI with blinded assessment.
Results: A total of 76 women with trigeminal neuralgia and 76 age-matched healthy controls were included. Mean disease duration was 9.8 years, and 12 had classical trigeminal neuralgia. Demographics and BMI were comparable. No group differences were found in reproductive or hormonal history prior to disease onset, including age at menarche (13.4 vs 13.4 years; p = .84), infertility (19 vs 15; p = .26), number of pregnancies (1.6 vs 1.8; p = .23), months of breastfeeding (13 vs 14; p = .42), duration of perimenopause (3.4 vs 2.0 years; p = .07), or age at menopause (50.1 vs 50.3 years; p = .91). Women with trigeminal neuralgia were more likely to report comorbid headache disorders (42% vs 17%; p < .001), other chronic pain conditions (20% vs 5%; p = .01), psychiatric illness (30% vs 15%; p = .02), and over-the-counter analgesic use (22% vs 3%; p < .001). Among the eight women who experienced pregnancy after disease onset, four reported reduced pain and decreased medication use during pregnancy.
Conclusion: No significant differences were found between patients and controls regarding major hormonal life events. However, pregnancy after disease onset was associated with reduced pain and medication use, suggesting a potential modulatory effect of pregnancy-related hormonal changes and pointing to the need for further research into sex hormone influences in trigeminal neuralgia.

P642

Is sexual dysfunction the forgotten burden of migraine? A systematic review and meta-analysis

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Objective: Migraine is a significant cause of disability affecting social functioning including sexual life. Despite this, data on the presence and extent of sexual problems in individuals with migraine remain surprisingly limited. This study aims to review and analyse existing evidence on the prevalence, subtypes, and predictors of sexual dysfunction (SD) in patients with migraine.
Methods: An extensive literature search was conducted in Pubmed, Cochrane and Google Scholar, from 1987 July to October 2023. The study was registered in PROSPERO (No:CRD42024562356). After applying inclusion and exclusion criteria, the retrieved references were imported into the Rayyan platform, and the abstracts were screened blindly. Following the blind screening phase, the researchers held a consensus meeting to resolve conflicts. Full texts of the eligible studies were reviewed after quality assessment using the Newcastle-Ottawa Scale.
Results: Among the 21 studies, 18(85.7%) were cross-sectional, while 3(14.3%) were prospective in design. The majority of included studies focused exclusively on female participants (n=17); three included only males, and one included both sexes. A total of 2,096 individuals were evaluated (1,475 with migraine, 621 controls). The prevalence of SD in women with migraine was 70.9±16%, and in men, 65±39.7%. The overall prevalence of SD in migraine ranged from 41.8% to 90%, whereas it did not exceed 40% in controls. The most frequent subtype of SD was reduced sexual desire (79.35±7.99%), followed by arousal, lubrication, orgasm and satisfaction issues.
Conclusion: SD is a highly prevalent but an underestimated problem in patients with migraine. Given the substantial impact of this condition on patients" quality of life, rigorous screening and precise diagnosis of SD in individuals with migraine are essential to inform and optimize targeted therapeutic strategies

P643

Sex-related clinical differences in cluster headache

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Objective: Cluster headache (CH) is classically male-predominant. Recent cohorts suggest women may experience earlier onset, more chronic disease, and fewer alcohol-related attacks. We examined if comparable sex differences exist in a Japanese CH cohort.
Methods: We retrospectively reviewed 237 consecutive patients diagnosed with CH at Shizuoka Red Cross Hospital (ICHD-3; men=167, women=70). Variables included age at onset, family history, migraine comorbidity, HIT-6, VAS, headache varacteristics, and potential triggers (bathing, alcohol, smoking). Groups were compared using chi-square or Mann–Whitney U tests.
Results: Women tended to develop CH earlier (median 23.5 vs 29 years; p=0.079). Relative to men, women more often had bouts <1 month or chronic CH (p<0.001), year-round/multiple annual bouts (p=0.014), and longer individual attacks (≥4h vs 1–2h; p=0.011). Positive family history (p=0.031), migraine comorbidity (p<0.001), phonophobia (p=0.006), and vomiting (p=0.004) were also more frequent in women. Alcohol-provoked attacks (p=0.029) and smoking history (p<0.001) were more common in men. HIT-6, VAS, diurnal pattern, nocturnal awakening, lateralisation, daily attack frequency, typical cranial autonomic signs, and bathing-triggered attacks did not differ by sex.
Conclusion: Japanese women with CH display earlier onset, greater chronicity, longer attacks, and stronger migraine features. Men remain more strongly associated with alcohol/tobacco triggers. Recognising these sex-specific patterns may facilitate earlier diagnosis and personalised management of CH across diverse populations.

P644

Gender differences in dependence level and behaviours in patients with Medication-Overuse Headache (MOH)

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Objective: Dependence behaviours can differ between females and males with medication overuse headache (MOH) and can influence the higher prevalence of MOH in females. This prospective study aimed to characterise gender differences in dependence behaviours in MOH by using the Leeds Dependence Questionnaire (LDQ), and other dependencies, including smoking and alcohol abuse.
Methods: In total, 344 consecutive patients were recruited and professionally face-to-face interviewed, including 171 patients with MOH (mean age 43.3 years, 81.9% women, migraine 64.9%, tension-type headache 35.1%) and 173 patients without MOH (mean age 41.4 years, 74.6% women, migraine 57.8%, tension-type headache 42.2%).
Results: The presence of dependence by LDQ was significantly more often detected in patients with MOH (95.3%) than without MOH (69.4%) (p<0.001; OR 9.0; 95% CI 4.1-19.6). The mean LDQ score in patients with MOH was significantly higher than in the controls (8.2 and 2.9, respectively, p=0.004, OR 2.9; 95% CI 1.1-11.5). Among patients with MOH, no significant gender differences in the level of average LDQ scores (7.3 in females and 8.4 in males, p=0.6) and the presence of dependence (90.3% in females and 96.4% in males, p=0.1) were found and none in the control group. However, males with MOH had a more frequent medium LDQ level of dependence (10-20 points) than females (27.1% and 9.7%, p=0.04, OR 3.5; 95% CI 1.0-12.1); other levels of LDQ dependence did not differ. Besides, men were significantly more likely than women to smoke (41.9% and 23.6%, respectively; p=0.04; OR 2.3; 95% CI 1.04-5.3) and to be moderate drinkers (12.9% and 3.6%, respectively; p=0.04; OR 4.0; 95% CI 1.01-15.9).
Conclusion: In our study of age-, sex- and diagnosis-matched groups of patients with and without MOH, we found that males with MOH are more prone to smoking, moderate drinking and have a moderate level of LDQ dependence. This can"t explain the higher prevalence of MOH in females and stresses the necessity of further studies.

P645

Sex differences in the response to rimegepant for the treatment of acute migraine attacks – Insights from the multicenter GAINER study

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Objective: Clinical trial data suggest a decreased efficacy of CGRPr oral inhibitors – i.e., gepants – for acute migraine treatment in males compared with females. We aimed at assessing sex differences in the response to rimegepant for acute migraine treament in a real-world setting.
Methods: We included patients with either episodic or chronic migraine who treated at least one migraine attack with rimegepant according to clinical indications from June 2023 to April 2025. We only considered the first attack treated by patients. Our primary outcome was the proportion of pain-free patients two hours after rimegepant intake. Secondary outcomes included pain freedom at 30, 60, and 90 minutes after rimegepant intake and Patient Global Impression of Change (PGIC) scores. Results were compared between females and males via chi-square test.
Results: We included 191 patients of whom 153 (80.1%) were females. The characteristics of males and females were not different except from a lower prevalence of medication overuse in females compared with males (29 [19.0%] vs 13 [34.2%]; p=0.042). More females than males were pain-free at two hours (73 [47.7%] vs 10 [16.3%]; p=0.028). The difference in pain freedom was also significant at 90 minutes (54 [37.8%] vs 5 [14.7%]; p=0.014), while it was not significant at 30 and 60 minutees. Median PGIC score was higher in females than in males (5 [IQR 3-6] vs 3 [IQR 2-5]; p<0.001).
Conclusion: We found a higher effectiveness of rimegepant for the acute treatment of migraine in females compared with males. Nevertheless, the drug was effective in both sexes. Preclinical and clinical studies are needed to elucidate the possible mechanisms determining a sex difference in response to rimegepant.

P646

Preventive treatment of migraine in males: The role of monoclonal antibodies

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Objective: Anti-CGRP monoclonal antibody (aCGRP) trials for migraine have mostly included women, with limited data on the response of men, in both clinical trials and real-world settings. This study aimed to evaluate and compare the clinical response to and adverse effects of aCGRP use in men and women.
Methods: A retrospective observational study was conducted, including men and women who were matched by age and migraine frequency. Clinical characteristics, therapeutic response, functional improvement, and adverse effects were assessed through medical records. Statistical analysis included Student's t-test and Fisher's exact test (significance: $p < 0.05$).
Results: A total of 48 patients (24 men and 24 women) were included and matched for age (mean: 41.8 years) and migraine frequency. No significant differences were found regarding migraine type (episodic / chronic) or aura presence. After three months, migraine days decreased by a similar amount in both men and women (50.8% vs. 60.3%; $p = 0.394$), a trend that was maintained at six and twelve months. Functional improvement, as measured by a reduction in HIT-6 score of at least 5 points, was observed in both sexes, with greater reductions in women at 3 ($p = 0.002$) and 6 months ($p < 0.001$). Adverse events were generally mild, with no significant sex differences except for more gastrointestinal symptoms in women at three months ($p = 0.048$). Overall tolerability was good, with sustained adherence.
Conclusion: Despite greater reductions in HIT-6 scores and more initial adverse events in women, the overall efficacy and safety of aCGRP therapies were similar for both sexes. These results help to address the lack of male-specific data and support the applicability of aCGRP therapies regardless of sex.

P647

The impact of the menstrual cycle on migraine occurrence and quality of life in women with migraine

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Objective: To examine differences in migraine occurrence across menstrual cycle phases and to assess the association between menstrual migraine and quality of life in women with migraine.
Methods: This cross-sectional study was conducted at the Headache Clinic of the University Hospital Centre Osijek. The study included female patients with episodic migraine and regular menstrual cycles. Data were collected using an anonymous study-specific questionnaire, the 36-Item Short Form Health Survey (SF-36), and the Headache Impact Test (HIT-6).
Results: A total of 35 women with episodic migraine were included in the study. Of these, 24 (68.6%) reported that their migraines were related to the menstrual cycle, with more frequent and severe attacks occurring in the premenstrual phase (60%). Migraine attacks impaired daily functioning and quality of life in 80% of participants. A stronger influence of premenstrual syndrome on migraine occurrence was associated with lower quality of life, particularly in relation to physical pain, reduced vitality and energy, and poorer overall mental health (Table 1).
Conclusion: The findings indicate a clear association between menstrual cycle phases and migraine occurrence, as well as a negative impact on patients" quality of life, particularly regarding mental health. The presence of accompanying symptoms, diverse therapeutic strategies, and frequent use of alternative methods highlight the need for an individualized and integrated approach to the diagnosis and management of menstrual migraine.

Fig. 1

Table 1. Association between quality of life (SF-36 scores) and premenstrual features in female migraine patients

SF-36 domains	Spearman Correlation Coefficient Rho (*P* value)		
	Age of examinees	Intensity of menstruations	Effect of premenstrual syndrome on migraine occurrence
Physical functioning	0,259 (0,13)	0,247 (0,15)	-0,283 (0,10)
Role physical	0,158 (0,36)	-0,013 (0,94)	0,037 (0,83)
Bodily pain	-0,293 (0,09)	0,085 (0,63)	**-0,352 (0,04)**
General health	-0,174 (0,32)	-0,024 (0,89)	0,239 (0,17)
Vitality	-0,048 (0,78)	-0,153 (0,38)	**-0,396 (0,02)**
Social functioning	-0,123 (0,48)	-0,213 (0,22)	-0,130 (0,46)
Role emotional	0,066 (0,70)	-0,206 (0,24)	-0,265 (0,12)
Mental health	-0,244 (0,16)	-0,141 (0,42)	-0,087 (0,62)
Health transition	-0,108 (0,54)	0,035 (0,84)	-0,143 (0,41)
General physical health	-0,065 (0,71)	0,027 (0,88)	-0,194 (0,26)
General mental health	-0,056 (0,75)	**-0,343 (0,04)**	**-0,344 (0,04)**

*Mann-Whitney U test

P648

Sex differences in premonitory symptoms and triggers in migraine: Insights from a tertiary headache clinic

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Objective: To identify sex differences in migraine phenotype between men and women in a tertiary headache clinic.
Methods: A cross-sectional, single center study was conducted in consecutive patients attending a tertiary headache clinic between February-November 2024. Patients fulfilling ICHD-3 criteria for migraine were included. Data was collected on age, sex and premonitory symptoms, which were defined as symptoms occurring between 48 hours to immediately before headache onset. Data was also collected on triggers, defined as factors that were most of the time followed by migraine symptoms within four hours. Statistical analysis with Fisher"s Exact Test and Mann-Whitney U testing was performed using IBM SPSS (Version 29).
Results: A total of 101 patients were included (81 female, 20 male, median age 45 years [IQR 33–56]). Women were not more likely to report high frequency episodic or chronic migraine compared to men (74% vs 70%, *P*=0.781). Women reported a greater number of premonitory symptoms than men (6 [IQR 4-9] vs 4 [IQR 2-7], *P*=0.005) as well as more triggers (4 [IQR 3-7] vs 3 [IQR 2-5], *P*=0.046). Women were more likely than men to report premonitory symptoms of photophobia (83% vs 55%, *P*= 0.015), phonophobia (56% vs 25%, *P*=0.023), rhinorrhea or nasal congestion (23% vs 0%, *P*=0.037) and vertigo (65% vs 35%, *P*=0.021). Women were more likely to report heat as a trigger compared to men (53% vs 25%, *P*=0.027).
Conclusion: Women report more premonitory symptoms and triggers than men and are more like to specifically report premonitory photophobia, phonophobia, nasal autonomic symptoms and vertigo. Women are also more likely to report heat as a trigger. These findings may suggest sexual dimorphism in biological pathways implicated in the pathophysiology of premonitory symptoms and the influence of triggers on these pathways.

P649

Does sex impact headache diagnosis and migraine management in England? A retrospective cohort study of primary care medical records

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Objective: To examine diagnosis among people with headache in England by sex and treatment patterns, including possible risk of medication overuse and titration of preventive medication, among people diagnosed with migraine by sex.
Methods: A retrospective descriptive cohort study using the Clinical Practice Research Datalink Aurum was conducted. Adults aged ≥18 years were included in the study and indexed on the first observed migraine or other headache diagnosis between 19 September 2012 to 1 May 2023. Prescriptions 12-months post-index were analysed. Possible risk of medication overuse was defined as >10 days' (opiates/triptans) or >15 days' (analgesics/antipyretics/NSAIDs) supply in 3 consecutive months.
Results: Adults with migraine (N=476,191) or other headache (N=1,058,616) were included, the majority of whom were female (78.0% and 63.1% respectively). Primary headache disorders (including migraine) were diagnosed in 43.7% (N=454,709) of the female cohort, and 30.7% (N=104,560) of the male cohort [Figure 1A]. Migraine was diagnosed in 81.7% (N=152,191) of the primary headache disorders in females and 68.7% (N=104,560) in males [Figure 1B].
Minor differences in the percentage of the migraine cohort prescribed medication were observed by sex: any acute medication (63.6% females v 59.3% males) [Figure 2A]; any preventive medication (36.9% v 35.0%) [Figure 3A].
Differences in possible risk of medication overuse [Figure 2B] and titration of preventive medication to target dose [Figure 3B] between sexes were also numerically small.
Conclusion: In males, more headache was undifferentiated, and primary headache was less likely to be diagnosed as migraine. Differences in prescribed medication and optimisation of medication by sex were numerically small. This suggests that, although differences in diagnosis of migraine existed by sex, prescribing of migraine medication in primary care was equitable in males and females.

Fig. 1

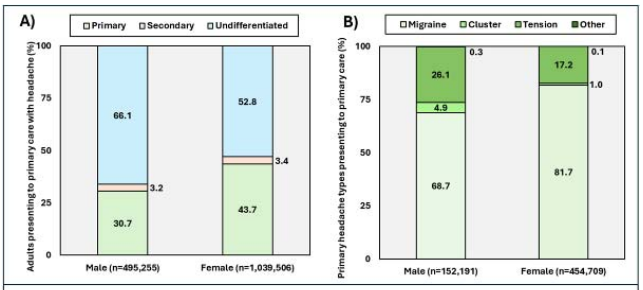


Figure 1: **A)** Percentage of adults (aged ≥18 years) presenting to primary care with headache coded as primary headache, secondary headache, or unclassified/undifferentiated by sex. **B)** Percentage of adults (aged ≥18 years) presenting to primary care with primary headache with each primary headache diagnosis by sex.

Fig. 2

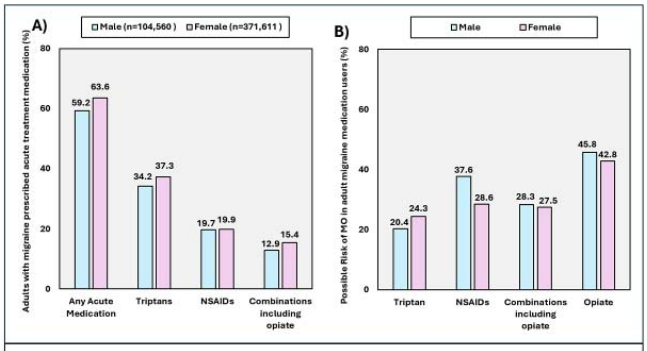


Figure 2: **A)** Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for acute treatment of migraine in the first 12 months after index by sex. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed acute medication for migraine in the first 12 months after index with prescribing patterns suggestive of possible risk of medication overuse by sex.

MO: medication overuse. Possible risk of MO was defined as >10 days' (opiates/triptans) or >15days' (analgesics/antipyretics/NSAIDs) supply in 3 consecutive months.

Fig. 3

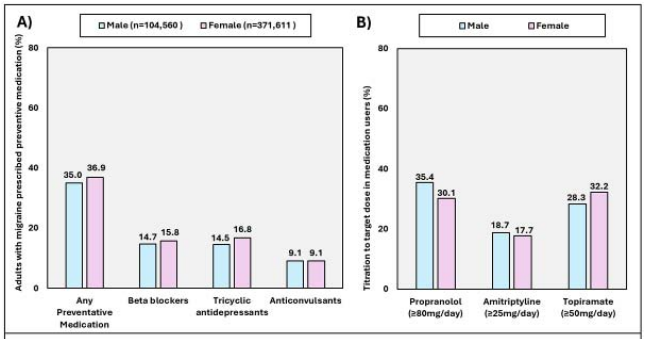


Figure 3: **A)** Percentage of adults with migraine (aged ≥18 years) prescribed medication in primary care for preventive treatment of migraine in the first 12 months after index by sex. **B)** Percentage of adults with migraine (aged ≥18 years) prescribed preventive medication for migraine in the first 12 months after index who are titrated to the NICE CKS/SIGN 155 recommended target dose.

P650

Migraine male patients: Profiling a minority using real-world data from the Italian National Migraine Registry (I-GRAINE)

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Objective: Migraine is a common primary headache disorder with a marked female predominance (female-to-male ratio 2:1–6:1). Consequently, most sociodemographic and clinical data—and the diagnostic criteria derived from them—are largely female oriented and may not fully capture the male phenotype. This study aimed to characterize male migraineurs, focusing on sociodemographic factors and attack features, using real-world data from the Italian National Migraine Registry (I-GRAINE).

Methods: I-GRAINE is an ongoing, multicenter, prospective registry involving 43 publicly funded headache centers. Since April 2021, patients with migraine have been consecutively enrolled. Data are collected through structured, face-to-face interviews conducted by trained neurologists using a dedicated electronic platform. This analysis examined the male subgroup.

Results: By 19 September 2025, 2,106 patients had been enrolled (85% female, 15% male), including 319 men. Mean age was 46 years; mean BMI 24.5 kg/m². Most had <13 years of education (57 %), were employed (79 %), were married or cohabiting (55 %) and had one child. Lifestyle factors included active smoking (19.9 %), moderate alcohol use (12 %), high coffee intake (6.6 %), regular physical activity (30 %), and sleep disturbance (26 %). Mean age at migraine onset was 18 ± 9.6 years. Attacks were mainly unilateral (71.2 %), pulsating (56.0 %), severe (mean intensity 7.5/10), and lasted <24 h (50.2 %) if untreated. Associated symptoms were photophobia (85.5 %), phonophobia (82.9 %), osmophobia (31.2 %), nausea (69 %), vomiting (24.7 %), allodynia (28.8 %), and cranial autonomic symptoms (22.4 %). Current migraine frequency averaged 10.3 days/month versus 6.3 days/month at onset. Mean MIDAS and HIT-6 scores were 47 and 61, respectively.

Conclusion: Men with migraine display distinct clinical and lifestyle profiles, underscoring the need for tailored management to improve recognition and treatment in this under-represented population.

P651

The role of sex, ethnicity, and mood disorders in older patients with primary headache

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Objective: Primary headaches in older adults remain under-investigated, particularly regarding the impact of sex, ethnicity, and psychiatric comorbidities. Identifying modifiable factors may improve prevention and management strategies in this age group.

Objective: To analyze the most frequent determinants of primary headache in outpatients aged ≥55 years and to evaluate factors negatively influencing headache chronification.

Methods: The study included 49 migraine patients from Russia and Italy aged ≥55 years. Data were collected using a structured questionnaire addressing headache features, psychiatric and sleep comorbidities, medication use, and somatic history. Statistical analyses assessed associations between chronic headache prevalence and nationality, emotional disturbances, sleep disorders, and comorbid conditions.

Results: Chronic headaches were significantly more frequent among Russian patients compared to Italian patients within the same age group. Anxiety–depressive disorders showed a strong correlation with headache chronification, particularly in the Russian cohort. Medication-overuse headache was more prevalent in Russia, associated with wide availability of combined analgesics. Conversely, insomnia was more frequent among Italian patients, despite lower rates of mood disorders. No significant associations were found between headache and cardiovascular disease, obesity, or cognitive impairment.

Conclusion: Differences in headache burden between Russia and Italy appear linked to healthcare practices, with delayed initiation of preventive treatment and limited awareness contributing to higher chronic and medication-overuse headache prevalence in Russia. The findings emphasize the importance of routine screening for anxiety and depression in older headache patients and highlight the need for tailored preventive strategies independent of cardiovascular or hormonal status.

P652

Efficacy and safety of nebulization of dexmedetomidine versus saline for treating postdural puncture headache after cesarean section: A systematic review and meta-analysis of randomized controlled trials

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Objective: This review aims to compare the effectiveness of nebulized dexmedetomidine versus saline for treating postdural puncture headache (PDPH) after cesarean section.

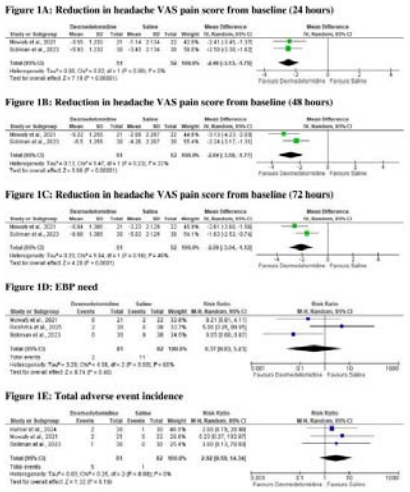
Methods: We searched PubMed, Embase, Scopus, ClinicalTrials.gov and Google Scholar from inception to September 2025 for randomized controlled trials (RCTs) comparing nebulization of dexmedetomidine versus saline for treating PDPH after cesarean section operation. Analyses were performed in RevMan 5.4.1. A P-value <0.05 was considered statistically significant. The primary outcome of this study was reduction in PDPH pain visual analog scale (VAS)

scores. Secondary outcomes included need for epidural blood patches (EBP) and overall incidence of adverse events.

Results: Four trials were included (N = 223, mean ages 24.17 to 28.77 years). Compared to saline nebulization, dexmedetomidine nebulization consistently demonstrated significantly greater reductions in VAS pain scores from baseline at 24 hours (MD -2.46, 95% CI [-3.13, -1.79]), 48 hours (MD -2.64, 95% CI [-3.50, -1.77]), and 72 hours (MD -2.08, 95% CI [-3.04, -1.12]) post-nebulization. EBP requirements and overall adverse events rates remained comparable between the two groups.

Conclusion: Nebulized dexmedetomidine may provide superior analgesic efficacy compared to saline for the management of PDPH following cesarean section, with consistent reductions in pain scores up to 72 hours. The intervention did not increase the need for epidural blood patches or the incidence of adverse events, suggesting a favorable safety profile. However, given the limited number and sample sizes of available trials, further high-quality studies are needed to confirm these findings and guide clinical practice.

Fig. 1



P653

Beyond pain: Psychological profiles in chronic migraine compared with Fibromyalgia and their comorbidity

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Objective: Chronic migraine (CM) and fibromyalgia (FM) are pain conditions marked by central sensitization and high psychological comorbidity. While they share some clinical features, evidence suggests differences in psychological functioning and symptom burden. Investigating these differences, along with transdiagnostic psychological profiles, may clarify their specificities. The present study aims to compare psychological functioning in CM, FM, and comorbid CM+FM, and to identify transdiagnostic psychological profiles beyond diagnostic categories.

Methods: This is a multicenter cross-sectional study including 318 women (97 CM, 130 FM, 91 CM+FM). Participants completed validated self-report measures of depression (PHQ-9), anxiety (GAD-7), psychological distress (SCL-90-R), mental functioning (SF-12), and defensive functioning (DMRS-SR-30). Between-group differences were tested with Kruskal–Wallis analyses. Cluster analysis was performed to identify latent psychological profiles across diagnoses.

Results: CM patients reported higher mental functioning, lower depression, anxiety, and global distress, and more adaptive defenses compared with FM and CM+FM. No differences were found between FM and CM+FM. Cluster analysis identified three profiles: vulnerable (n=73; mainly FM and CM+FM), intermediate (n=122; mixed), and resilient (n=76; predominantly CM). Cluster membership was significantly associated with diagnosis, with CM overrepresented in the resilient profile and CM+FM in the vulnerable profile.

Conclusion: CM shows a more preserved psychological profile than FM, while comorbid CM+FM aligns with the most impaired profiles. These findings support a dimensional, transdiagnostic approach to chronic pain, emphasizing psychological functioning as a key factor for personalized care.

P654

Rimegepant for the prevention of episodic migraine in adults with prior inadequate response to oral preventatives: Results from a 12-week open-label extension phase of a randomized, placebo-controlled trial

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Objective: The efficacy and tolerability of rimegepant for the prevention of episodic migraine in participants with a history of inadequate response to oral preventive medications (OPMs) was recently evaluated. This abstract reports findings from the open-label extension (OLE) phase of the multinational, randomized, placebo-controlled trial.

Methods: Participants with 4–14 monthly migraine days, <15 monthly headache days (<7 non-migraine), and documented history of inadequate response to 2–4 categories of OPM were enrolled. Following 12 weeks of randomized double-blind treatment (DBT) with rimegepant 75 mg orally disintegrating tablet (ODT) or placebo once every other day (EOD), participants entered an OLE phase to receive 12 weeks of rimegepant 75 mg EOD. Concomitant use of other preventive medications was not permitted.

Results: All participants received open-label (OL) rimegepant (N=595); 301 previously received rimegepant and 294 placebo in the DBT phase. Demographics and clinical characteristics were balanced across DBT groups (**Table 1**). In both, mean time on OL rimegepant was ~11 weeks and mean ODTs taken/month was 14. After 12 weeks of OL rimegepant (Week 24 of the trial), change from baseline in patient-reported outcomes showed participants who received placebo as DBT achieved similar benefit as those on rimegepant since the start of the trial (**Figure**). During the OLE phase, 38.2% of participants had ≥1 adverse event, including 6.6% related to rimegepant and 1.0% leading to rimegepant discontinuation (**Table 2**). One grade 4 (thrombocytopenia) and three grade 3 (hypoglycemia; hyperglycemia; hypernatremia) laboratory findings were recorded. The safety profile of OL rimegepant was comparable in both DBT groups and with previous trial findings.

Conclusion: Rimegepant 75 mg EOD is well tolerated and reduces overall disease burden when taken for the prevention of migraine in participants with a documented history of prior inadequate response to OPMs. NCT05518123

Fig. 1

Table 1. Demographics and clinical characteristics at trial baseline

	Overall n=595	Rimegepant in the DBT and OLE phases n=301	Placebo in the DBT phase and rimegepant in the OLE phase n=294
Age, mean (SD) y	42.2 (10.9)	42.4 (10.4)	42.0 (11.4)
Female sex, n (%)	506 (85.0)	262 (87.0)	244 (83.0)
Geographic region, n (%)			
Europe/Australia	524 (88.1)	269 (89.4)	255 (86.7)
North America	71 (11.9)	32 (10.6)	39 (13.3)
BMI, mean (SD) kg/m^2	24.7 (4.0)	24.6 (4.0)	24.8 (4.0)
Number of migraine days in the 28-day observation phase, n (%)[a]			
<8	232 (39.0)	120 (39.9)	112 (38.1)
≥8	363 (61.0)	181 (60.1)	182 (61.9)
Number of OPM categories with documented prior inadequate response, n (%)[b]			
<3	389 (65.4)	195 (64.8)	194 (66.0)
≥3	206 (34.6)	106 (35.2)	100 (34.0)

[a]The number of days in the 28-day observation phase (immediately prior to the DBT phase) where the participant had (i) headache lasting ≥30 min and either (a) nausea/vomiting, or photophobia and phonophobia, or (b) ≥2 of the following headache features: unilateral pain, pulsating pain, moderate or severe pain intensity, or pain aggravated by/causing avoidance of physical activity) or (ii) used acute migraine-specific medication.
[b]Prior inadequate response was defined as lack of efficacy in the previous 10 years, prior intolerance in the previous 10 years, or presence of contraindication. At least 1 qualifying incidence of inadequate response to a prior OPM must have been due to lack of efficacy or prior intolerance for study enrollment. All instances were fully documented. Categories of OPM included (i) valproic acid; (ii) other anticonvulsants, specifically gabapentin or topiramate; (iii) beta-blockers; (iv) tricyclic antidepressant, specifically amitriptyline; (v) serotonin-norepinephrine reuptake inhibitors, specifically desvenlafaxine or venlafaxine; (vi) calcium channel blocker, specifically flunarizine or verapamil; (vii) angiotensin blocker, specifically, candesartan or lisinopril; and (viii) other locally approved or recognized preventive medications.
BMI=body mass index; DBT=double-blind treatment; OLE=open label extension; OPM=oral preventive medication.

Fig. 2

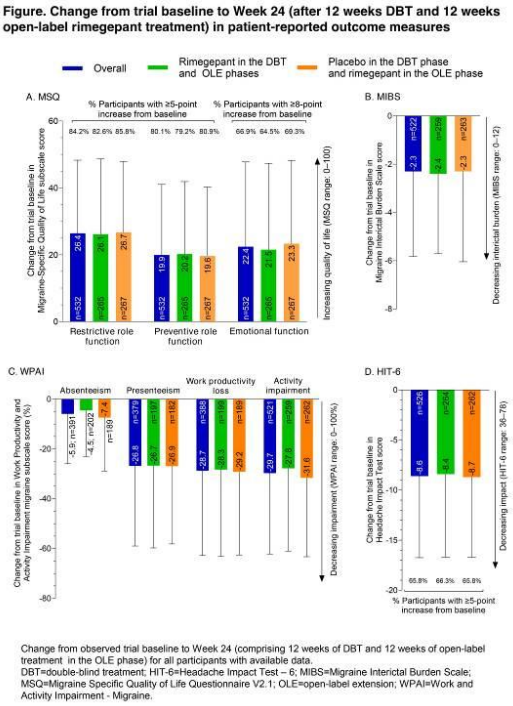


Fig. 3

Table 2. Adverse events during the OLE phase

n (%)	Overall n=595	Rimegepant in the DBT and OLE phases n=301	Placebo in the DBT phase and rimegepant in the OLE phase n=294
Any AE	227 (38.2)	121 (40.2)	106 (36.1)
Related to study medication	39 (6.6)	19 (6.3)	20 (6.8)
Leading to study medication discontinuation	6 (1.0)	3 (1.0)	3 (1.0)
In ≥2.0% of all participants			
Nasopharyngitis	34 (5.7)	22 (7.3)	12 (4.1)
Influenza	21 (3.5)	12 (4.0)	9 (3.1)
URTI	13 (2.2)	6 (2.0)	7 (2.4)
Medication error	13 (2.2)	7 (2.3)	6 (2.0)
Any mild AE	147 (24.7)	76 (25.2)	71 (24.1)
Related to study medication	26 (4.4)	12 (4.0)	14 (4.8)
Any moderate AE	104 (17.5)	52 (17.3)	52 (17.7)
Related to study medication	17 (2.9)	8 (2.7)	9 (3.1)
Any severe AE	3 (0.5)	1 (0.3)	2 (0.7)
Related to study medication	2 (0.3)	1 (0.3)	1 (0.3)
Any serious AE	6 (1.0)	2 (0.7)	4 (1.4)
Related to study medication	2 (0.3)	0 (0.0)	2 (0.7)
AEs of scientific and regulatory interest			
Medication overuse headache	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic-related AE	2 (0.3)	0 (0.0)	2 (0.7)
Leading to study medication discontinuation	0 (0.0)	0 (0.0)	0 (0.0)
Potential drug abuse AE	19 (3.2)	8 (2.7)	11 (3.7)
Cardiovascular AE	0 (0.0)	0 (0.0)	0 (0.0)
Suicidality AE	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension AE	3 (0.5)	2 (0.7)	1 (0.3)
Raynaud's phenomenon AE	0 (0.0)	0 (0.0)	0 (0.0)
Constipation AE	2 (0.3)	0 (0.0)	2 (0.7)

AE=adverse event; DBT=double-blind treatment; OLE=open-label extension; URTI=upper respiratory tract infection

P655

Associations between adherence to Mediterranean dietary pattern and the occurrence of cluster headache: A cross-sectional study

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Objective: Cluster headache is the most prevalent type of trigeminal autonomic cephalalgia (TAC) headache disorder. Cluster headaches affect approximately 0.1% of the population, and they most commonly occur in men around the age of 30. Anti-inflammatory diets can help improve cluster headaches by reducing neuroinflammation. Since the Mediterranean diet is an anti-inflammatory diet, and few studies have examined the role of this type of diet on cluster headaches, this study aimed to investigate the association between adherence to a Mediterranean diet and the occurrence of cluster headaches.

Methods: In this cross-sectional study, the case group consisted of 67 cluster patients diagnosed according to ICHD-3 criteria, and the control group comprised 200 healthy individuals with a BMI between 18 and 40 kg/m². Demographic and anthropometric information was gathered during the initial appointment. A validated 168-item semi-quantitative Food Frequency Questionnaire (FFQ) was used to examine the dietary intakes of participants. Daily energy and nutrient intakes were measured based on the USDA and Iranian food composition.

Results: A total of 267 participants were recruited in the current study. There was no significant difference between the two groups in age, gender, and BMI. Our study results showed that higher adherence to the Mediterranean diet was associated with increased consumption of vegetables, fruits, whole grains, fish, nuts, legumes, and a higher MUFA/SFA ratio. After adjustment for potential confounders, Participants who were in the fourth quartile (Q4) had a lower risk of cluster headache compared to those in the lowest quartile (Q1) (after full adjustment: OR = 0.15; 95% CI: 0.05–0.52; p for trend = 0.007).

Conclusion: The current study suggests that higher adherence to the Mediterranean diet is associated with a reduced risk of cluster headache. Therefore, this dietary pattern could be a complementary approach in the prevention and management of cluster headaches.

P656

Patient-reported outcomes through 12-weeks of double-blind rimegepant treatment for the prevention of episodic migraine in adults with prior inadequate response to oral preventatives

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Objective: A recent multinational, randomized, placebo-controlled, double-blind trial evaluated the efficacy and tolerability of rimegepant 75 mg orally disintegrating tablet (ODT) taken once every other day (EOD) in participants with episodic migraine (EM) and a documented prior inadequate response to 2-4 categories of non-migraine specific oral preventive medication (OPM). This analysis evaluated change in patient-reported outcomes (PROs) during the double-blind phase of the trial.

Methods: PROs were collected at baseline and through 12 weeks of double-blind treatment. Differences (rimegepant vs placebo) in least squares mean (LSM) change from baseline were calculated using linear mixed effects models with repeated measures.

Results: 652 participants received double-blind study treatment (328 rimegepant and 324 placebo). Findings favored rimegepant at weeks 4, 8, and 12 for the Migraine-Specific Quality of life Questionnaire role function-restrictive (LSM change [95% CI] difference at week 12: 6.6 [3.60, 9.54]; p<0.0001), role function-preventive (5.3 [2.54, 8.07]; nominal p [np]=0.0002), and emotional function domains (6.2 [2.81, 9.51]; np=0.0003); Migraine Interictal Burden score (−0.9 [−1.36, −0.38]; p=0.0006); Work Productivity and Activity Impairment: Migraine questionnaire presenteeism (−7.9 [−12.94, −2.92]: np=0.002), work productivity loss (−7.6 [−12.91, −2.26]; np=0.005), and activity impairment domains (−7.7 [−11.83, −3.53]; np=0.0003), and Headache Impact Test–6 score (−1.9 [−3.00, −0.73]; np=0.001). Average change in Migraine Functional Impact Questionnaire subscale scores also favored rimegepant at months 1, 2, and 3 across all domains (np≤0.006).

Conclusion: Rimegepant 75 mg ODT EOD is associated with reductions in disease burden when taken for the prevention of EM for 12 weeks in participants with documented prior inadequate response to 2-4 categories of non-migraine specific OPM. NCT05518123

P657

Migrain and neck pain: Effectiveness of non-pharmacological treatment

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Objective: Comorbidities and co-occurring conditions contribute to the overall burden of migraine. Treatment co-occurring condition is an important part in providing optimal care.

Aim: To investigate the effectiveness of complex non-pharmacological treatment episodic migraine and co-occurring neck pain.
Methods: We evaluated 77 patients, age from 18 to 55: group I with episodic migraine - 42 (with aura 8 and 34 without aura) and co-existing neck pain (m/f: 6/36) and group II with cervicogenic headache – 35(m/f: 12/23). Radiography of the cervical spine, VAS, "HIT-6", NDI and serum level of CGRP was by enzyme-linked immunosorbent assay ELISA principle were assessment. All patients had non-drug treatment of neck pain, which included manual methods and acupuncture, and individually selected therapeutic physical exercises. The Kolmogorov-Smirnov test was used to compare the data.
Results: Plasma level of CGRP was significantly higher in patients with episodic migraine with neck pain 242,98±5,08 пг/мл compared with the group with cervicalgia without migraine 51,96±4,46 пг/мл ($p = 0.012543$). The result of the treatment was decrease of tension in pericranial muscles: NDI (I: 4,43±0,26, $p<0,05$; 5,31±0,22, $p<0,05$). There was a significant reduction in headache intensity: VAS I: 6,93±0,11, $p<0,05$; II: 2,34±0,15, $p<0,05$). Frequency of headache attacks within 4 weeks has significantly decreased in both groups (I: 2,59±0,13, $p<0,05$; II: 2,09±0,14, $p<0,05$), number of days with headaches within 4 weeks has gone down (I: 4,71±0,29, $p<0,05$; II: 2,31±0,16, $p<0,05$) as well as number of days with simple and combined analgesics (I: 2,33±0,36, $p<0,05$; II: 1,09±0,22, $p<0,0006$).
Conclusion: Non-pharmacological treatment neck-pain in patients with episodic migraine to be effective in control of pericranial muscles tension and influence on decrease of frequency and severity migraine attacks, more significant reduce pain syndrome and psychological disorders that lead to reduce drug intake.

P658
SUNCT-like headache secondary to herpes zoster in the ipsilateral ophthalmic nerve distribution: A case report
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Objective: Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT) is an uncommon trigeminal autonomic cephalalgia. We report a secondary SUNCT-like syndrome following ophthalmic-distribution herpes zoster.
Methods: The patient provided informed consent for the case report as per ethical standards.
Results: A 52-year-old Sri Lankan male developed painful vesicular eruptions over the right ophthalmic dermatome and was treated with oral acyclovir (800 mg, five times daily). About seven days after vesicle crusting and resolution of herpetic pain, he began experiencing brief episodes of sharp right supraorbital pain radiating to the vertex and temporal region. Each attack lasted 10–15 seconds, occurred about three times per hour, with a severity of 8/10. His sleep and daily functioning were disrupted. Associated ipsilateral conjunctival injection, tearing, and partial ptosis were reported and were observed during consultation (Figure 1A). Healed vesicles and skin allodynia over the right forehead were noted (Figure 1B). Corneal reflexes and visual acuity were normal. Haemoglobin A1c was elevated at 14.2%, prompting insulin therapy. Brain imaging was unremarkable. Treatment included oral prednisolone (15 mg/day, tapered by 5 mg/week), carbamazepine (100 mg t.d.s., increased to 200 mg t.d.s. from week two), pregabalin (75 mg nocte), and tramadol (50 mg nocte). At two-week follow-up, pain severity reduced to 1/10, and he remained headache-free at one year.
Conclusion: This case underscores a SUNCT-like syndrome following ophthalmic zoster, which appears more pharmacoresponsive than primary SUNCT. Immunosuppressive states like diabetes, should be considered underlying zoster reactivation.

Fig. 1



P659
Beyond cerebrum and neurosurgery: A systematic review on Chiari Malformation Type I integrating molecular and behavioral methodologies
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Objective: Chiari malformation type 1 (CM1) radiologically defined as a caudal displacement of cerebellar tonsils exceeding 5 mm through the foramen magnum, represents the most prevalent subtype of Chiari Malformations—a group of developmental disorders characterized by congenital posterior fossa deformities. Given CM1's predominantly asymptomatic or paucisymptomatic clinical course, epidemiological data primarily reflects symptomatic cases, with prevalence traditionally estimated between 0.1-1%. We endeavor to propose a transdisciplinary conceptualization of CM1 that illuminates the cerebellum's extensive non-motor functions. This review synthesizes evidence from 60+ studies spanning genetics, genomics, neuropsychology, and neuropsychiatry.

Methods: Our analysis deconstructs the genetic, familial, and environmental factors through a framework of "CM1 Equifinality" in disease pathogenesis, methodically investigating its significant co-occurrence with neurodevelopmental and psychiatric conditions—particularly autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) in both syndromic and isolated cases, where behavioral and genomic tools are consistently validating each other,

Results: CM1 frequently presenting alongside functional impairments and problems with self-regulation, as further documented through combined measures of neuropsychology and functional neuroimaging.

Conclusion: With this work, we want to emphasize the critical need for psychiatric monitoring, neuropsychological interventions, and psychotraumatological implications in high-risk pediatric populations for CM1 within the general population. We also want to highlight how CM1 represents a unique model of study integrating developmental biology, cognition, and psychiatry through a cerebellar lens. We propose CblOs as a potential tool foreseeing the use of 3D in vitro models to recapitulate the cellular and molecular features of ASD and ADHD in CM1.

P660

COACT study: CGRPmAbs + OnabotulinumtoxinA assessment of chronic migraine treatments study

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Objective: To evaluate the safety and efficacy of combination therapy with the calcitonin gene-related peptide monoclonal antibody (CGRP mAb) fremanezumab and onabotulinumtoxinA in patients with chronic migraine (CM) who were previously treated with a stable dose of onabotulinumtoxinA.

Methods: This was a phase 4 prospective, open-label intervention conducted at the Chicago Headache Center and Research Institute. Forty-nine adult patients with CM on stable doses of onabotulinumtoxinA (155 or 195 units) received monthly fremanezumab (225 mg) over a 24-week period.

The trial aimed to assess the efficacy and safety of the combined treatment of onabotulinumtoxinA with fremanezumab. Monthly headache days (MHD), monthly migraine days (MMD), and Headache Impact Test (HIT-6) scores were assessed at baseline, week 12, and week 24. Paired t-tests were used to evaluate mean changes from baseline.

Results: Significant improvements were observed in all outcome measures. Mean reductions at 12 and 24 weeks, respectively, were:

ΔMHD: -9.00 and -14.04

ΔMMD: -8.29 and -11.63

ΔHIT-6: -7.27 and -9.88

No serious adverse events were reported. Combination therapy was well tolerated.

Conclusion: The addition of fremanezumab to onabotulinumtoxinA resulted in significant reductions in monthly migraine days at 12 weeks and 24 weeks ($p < 0.001$). Significant reductions in HIT-6 scores at 12 weeks and 24 weeks were also seen. These findings support the use of CGRP mAbs and onabotulinumtoxinA for the preventive treatment of chronic migraine.

Fig. 1

Outcome Measure	(Mean ± SD) (Week 12)	(Mean ± SD) (Week 24)	95% CI (Week 12)	95% CI (Week 24)	*p*-value (vs. Baseline)
ΔMHD	-9.00 ± 5.070	-14.04 ± 5.955	[-7.544, -10.456]	[-12.330, -15.751]	<.001
ΔMMD	-8.29 ± 4.826	-11.63 ± 4.876	[-6.899, -9.672]	[-10.232, -13.033]	<.001
ΔHIT-6	-7.27 ± 5.279	-9.88 ± 6.109	[-5.749, -8.782]	[-8.123, -11.632]	<.001

P661

Ubrogepant utilization during prodrome: A case report

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Objective: To report the successful treatment of migraine episodes with ubrogepant taken during the prodrome phase.

Methods: An extensive chart review was conducted to examine a patient"s progress over time with the treatment of migraine attacks with ubrogepant, which was taken during the prodrome phase.

Results: The patient reported experiencing neck pain followed by moderate to severe headache. This was identified as her prodrome symptom, and she was advised to take ubrogepant when she experienced

neck pain. The patient was able to recognize her prodrome symptom, neck pain, and treat her migraine episodes earlier. This early treatment opportunity largely prevented the patient from experiencing moderate to severe headaches.

Conclusion: The success the patient demonstrated with administering ubrogepant at prodrome underscores the importance of the timing of acute treatment for migraine. Educating patients on prodrome symptoms and the potential benefits of treating migraine episodes before headache onset may be a path to reducing or preventing disability and improving patients" quality of life.

P662

Comparison of functional responses to CGRP and related peptides in human middle meningeal and superficial temporal arteries

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Objective: The role of extracranial arteries during migraine attacks is unclear. Our aim was to compare the vasodilatory responses of extracranial human superficial temporal arteries (HSTA) and intracranial middle meningeal arteries (HMMA) to CGRP, the amylin analogue pramlintide, and adrenomedullin 2 (AM2), as well as the inhibition induced by the CGRP receptor-binding monoclonal antibody erenumab and the CGRP receptor antagonist olcegepant.

Methods: HSTA and HMMA were obtained from patients undergoing neurosurgery (HSTA: n=8, aged 55 ± 15 years, 38% female; HMMA: n=52, aged 54 ± 15 years, 62% female, age and sex not available for 2 donors). After precontraction with 30 mM KCl, concentration-response curves were constructed to CGRP (10 pM - 1 µM), pramlintide (10 pM – 300 nM), and adrenomedullin 2 (10 pM – 300 nM). Concentration-response curves to CGRP were constructed in the presence or absence of 1µM olcegepant or 1µM erenumab.

Results: CGRP induced similar, potent vasodilatory responses in HSTA and HMMA (pEC_{50} 8.06 ± 1.10 vs 8.25 ± 0.46, p=0.65; E_{max} 63% ± 31% vs 64% ± 19%, p=0.96). Pramlintide responses were comparable (pEC_{50} 6.33 ± 1.86 vs 6.40 ± 1.66, p=0.95; E_{max} 23% ± 12% vs 18% ± 10%, p=0.48), as were AM2 responses (pEC_{50} 6.56 ± 1.10 vs 7.03 ± 1.00, p=0.41; E_{max} 58% ± 23% vs 54% ± 24%, p=0.74).

The blocking potency of olcegepant and erenumab was similar across both arteries (olcegepant: pK_B HSTA 8.21 ± 1.36 vs HMMA 8.52 ± 1.27, p= 0.63; erenumab: pK_B HSTA 7.36 ± 0.97 vs HMMA 7.26 ± 1.02, p= 0.87).

Conclusion: The comparable responses of HSTA (innervated by V3) and HMMA (innervated by V1) to CGRP, pramlintide and AM2 do not challenge the potential role of extracranial arteries in the pathophysiology of migraine. Similar CGRP inhibition in both arteries may contribute to the antimigraine effects of CGRP receptor-targeting medications at either location. Finally, these results may also suggest that pain pathways relevant to migraine may overlap with those implicated in temporomandibular disorders.

P663

Interictal metabolic changes in episodic migraine: A voxel-based FDG-PET

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Objective: Whereas there are many H215O-positron emission tomography (PET) studies demonstrating neuronal activation during acute migraine attacks, little information is available on the interictal (headache-free period) glucose metabolic changes in migraine.

Methods: We therefore conducted voxel-based statistical parametric mapping analysis of 18F-fluorodeoxyglucose-PET to evaluate interictal metabolic differences between 20 episodic migraine patients (four with aura; three men; mean age 34.0 ± 6.4 years) and 20 control subjects. Separate correlation analyses were performed to delineate a possible relationship between regional glucose metabolism and disease duration or lifetime headache frequency in migraine patients.

Results: Group comparison showed that migraine patients had significant hypometabolism in several regions known to be involved in central pain processing, such as bilateral insula, bilateral anterior and posterior cingulate cortex, left premotor and prefrontal cortex, and left primary somatosensory cortex (uncorrected $P < 0.001$, corrected $P < 0.05$ with small volume corrections). Correlation analyses showed that regional metabolism of the insula and anterior cingulate cortex had significant negative correlations with disease duration and lifetime headache frequency (uncorrected $P < 0.001$, corrected $P < 0.05$ with small volume corrections).

Conclusion: Our findings of progressive glucose hypometabolism in relation to increasing disease duration and increasing headache frequency suggest that repeated migraine attacks over time lead to metabolic abnormalities of selective brain regions belonging to the central pain matrix.

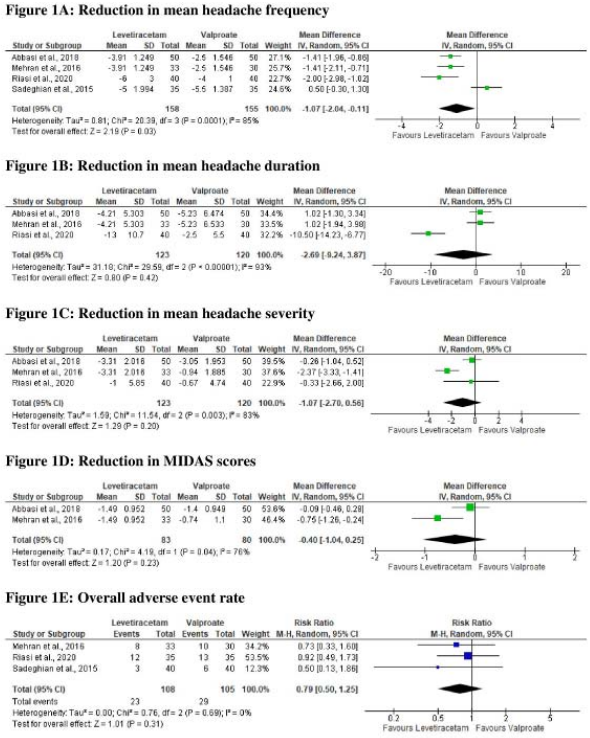
P664

Comparative efficacy and safety of Levetiracetam versus valproic acid in migraine prophylaxis: A systematic review and meta-analysis

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Objective: To systematically compare levetiracetam to valproic acid in the context of migraine prophylaxis.
Methods: We searched PubMed, Embase, Scopus, Web of Science, Cochrane, Scientific Information Database and Clinicaltrials.gov from inception to September 2025 for randomized controlled trials (RCTs) comparing levetiracetam to valproate in migraine prophylaxis. Dichotomous outcomes were pooled as risk ratios (RR) and continuous outcomes as mean differences (MD) with 95% confidence intervals (CI) in Review Manager (RevMan) version 5.4.1.
Results: Four trials were included (N = 288, 93.9% female, mean ages 33 to 36 years). Compared to valproate, levetiracetam use was associated with significantly greater reductions in mean headache frequency from baseline (MD -1.07, 95% CI -2.04 to -0.11). However, no significant differences were seen for reductions in mean headache duration, mean headache severity and MIDAS scores. Adverse event rates also remained comparable across the two treatment groups.
Conclusion: This systematic review and meta-analysis suggests that levetiracetam may provide a modest advantage over valproic acid in reducing headache frequency among individuals with migraine. However, the two drugs remained broadly comparable with respect to headache duration, severity, functional disability, and tolerability. However, larger, high-quality trials are needed to further explore the comparative efficacy and safety profiles of levetiracetam and valproic acid, so as to better inform individualized treatment strategies in migraine prophylaxis.

Fig. 1



P665

The multimodal 7T-MRI study on the mechanism of migraine chronification: Temporal evolution of driving hubs based on dynamic causal network

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[4]PLA Joint Logistic Support Force 983rd Hospital, Department of Neurology, Tianjin, China

Objective: This study aims to explore the dynamic evolution of brain structure and function in migraine patients as the disease progresses, utilizing multimodal magnetic resonance imaging (MRI). It also seeks to identify key neural networks that drive the chronicity of migraines.
Methods: Migraine patients, including those with episodic and chronic migraines, along with age- and education-matched healthy controls, were recruited from the Neurology Department"s Headache Center at the PLA General Hospital. Diagnoses were made according to the International Classification of Headache Disorders, 3rd edition, by two neurologists. Exclusion criteria included recent medication use (within 3 months) and menstrual period in females. Depression, anxiety, and sleep quality were assessed using the PHQ-9, GAD-7, and PSQI scales, respectively, and headache characteristics were recorded. 7T MRI scans were employed to capture structural and functional brain images, processed via VBM and zfALFF, with adjustments for confounding variables.

Multilevel logistic regression was used to identify migraine-related brain regions, construct a disease severity score and a target brain region set. Granger causality testing and cluster analysis were applied to identify key driving networks. Statistical analyses including ADF test and FDR correction ensured robust results. (Fig 1)

Results: 1. Participant Characteristics

The study included 345 participants: 81 healthy controls (HC), 154 with episodic migraines (EM), and 110 with chronic migraines (CM). No significant differences were found in gender, age, or education years among the groups (all $P > 0.05$); however, age and gender were considered as covariates in further analyses. Compared to the EM group, the CM group had a longer disease duration, significantly higher monthly headache frequency, shorter duration per headache episode, and a higher average medication usage per month, suggesting a higher risk of medication overuse. Psychological and sleep assessments revealed that the CM group scored significantly higher in depression, anxiety, and sleep quality issues compared to both the EM and HC groups (all $P < 0.001$), indicating more severe psychological and sleep disturbances. (Table 1)

2. Characteristics and Dynamic Evolution of Migraine-Related Brain Regions

2.1 Structural and Functional Abnormalities VBM analysis showed significant atrophy in the right thalamic reticular nucleus in both CM ($\beta = -15.294$) and EM ($\beta = -8.759$) patients ($P < 0.001$ for both). Asymmetric changes were noted in brainstem nuclei: left locus coeruleus volume increased (CM: $\beta = 4.692$; EM: $\beta = 3.313$), and right locus coeruleus volume decreased. Significant atrophy was also observed in the right amygdala and accumbens, while CM patients showed increased volume in the prefrontal and cerebellar regions.

zfALFF analysis indicates widespread neural activity suppression in EM patients, particularly in the right red nucleus ($\beta = -28.798$), bilateral pallidum, and accumbens. CM patients also demonstrated widespread suppression, but with distinct heightened activity in the left substantia nigra pars reticulata ($\beta = 15.797$).

2.2 Brain Region Changes Related to Headache Frequency Sliding window analysis revealed dynamic patterns of brain region characteristics as headache frequency evolved: - **Low-Frequency Stage (0-8 days)**: VBM indicated a negative correlation between volume of left thalamic reticular nucleus and headache severity, with a positive correlation for the left accumbens. zfALFF analysis demonstrated general suppression in the basal ganglia-thalamus system. - **High-Frequency Stage (8-14 days)**: The correlation expanded to wider networks. VBM showed negative correlations with left locus coeruleus and middle frontal gyrus volume, and positive correlations with prefrontal cortex and caudate volume. zfALFF highlighted increased activity in default mode network nodes. - **Chronic Stage (15-30 days)**: Involvement of the sensorimotor and cerebellar systems was evident. VBM identified complex volume changes in cerebellar regions related to severity, with general volume reduction in the prefrontal areas. (Shown in Fig 2 and Fig 3)

3. Dynamic Driving Network Analysis

3.1 Overall Granger Causality Analysis VBM analysis indicated the right Rolandic operculum had the strongest positive causal effect (GCA = 1.106, FDR-p = 0.008), with left subgenual anterior cingulate and middle frontal gyrus similarly showing significant positive driving roles.

zfALFF analysis identified thalamic nuclei exerting the strongest causal influences, with the right lateral posterior thalamus displaying the most prominent driving role (GCA = 1.783). Contributions from the sensorimotor areas, basal ganglia, and brainstem nuclei were also significant.

3.2 Dynamic Driving Network Identification Through sliding window GCA and cluster analysis, characteristic driving networks were identified for different headache stages: - **VBM Recognized 5 Driving Clusters**: - Clusters 1-2: Dominating low-frequency stage, involving sensorimotor and advanced association cortices - Cluster 3: Dominating transition to chronic stage, centered on limbic system and default network nodes - Clusters 4-5: Dominating chronic late stage, comprising subcortical structures and brainstem nuclei (Fig 3).**zfALFF Recognized 4 Driving Clusters**: - Cluster 4: Dominating low-frequency stage, mainly involving basal ganglia and thalamic nuclei - Cluster 2: Dominating high-frequency stage, involving cerebellar and limbic systems - Cluster 1: Dominating transition stage, focused on visual and sensory integration areas - Cluster 3: Dominating chronic late stage, with a sensorimotor cortical core. (Fig 4)

3.3 Cross-Modal Consistency Analysis revealed a cross-modal consistent neural driving evolution pathway: thalamic-driven early stage; cerebellum and brainstem participation in higher frequency dynamics; sensorimotor cortex and subcortical structure coordination sustaining chronic pain state.

Conclusion: This study is the first to systematically reveal the dynamic evolution patterns of brain structure and function as migraines progress, identifying characteristic driving networks across different disease stages, thus providing new neuroimaging evidence for understanding the chronicization of migraines.

Fig. 1

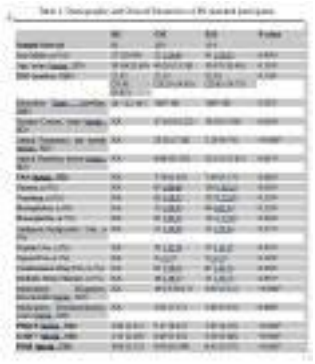


Fig. 2

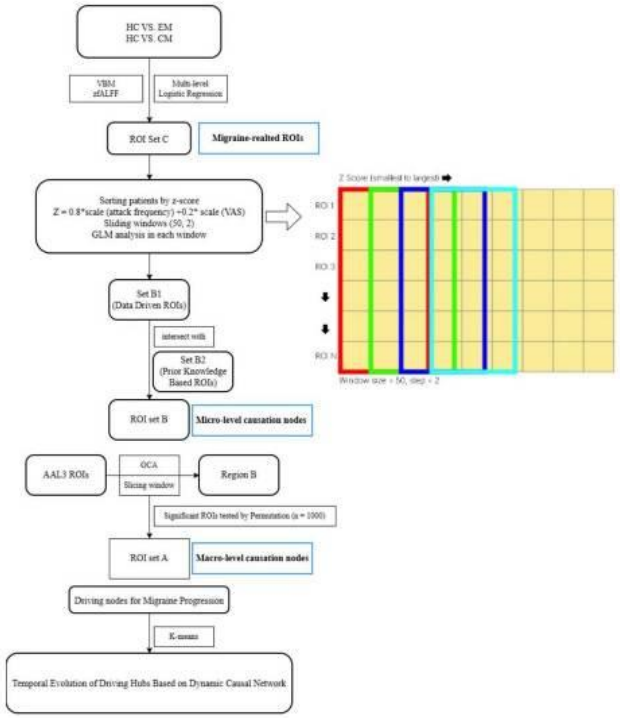


Fig. 3

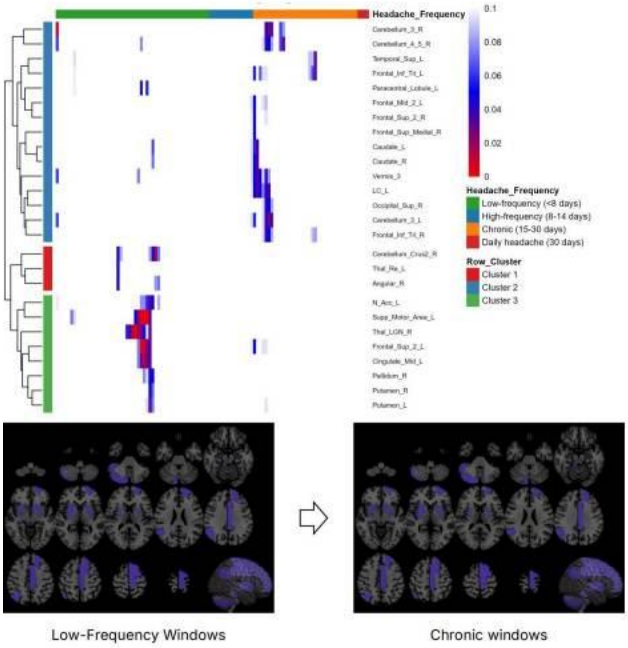


Fig. 4

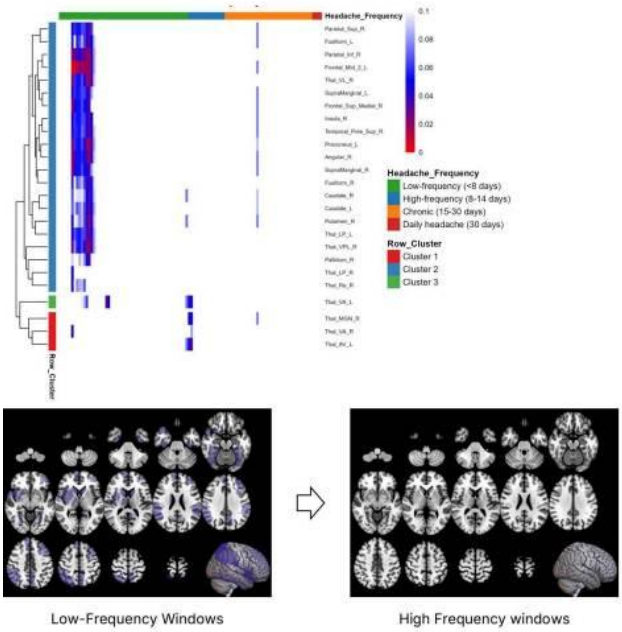


Fig. 5

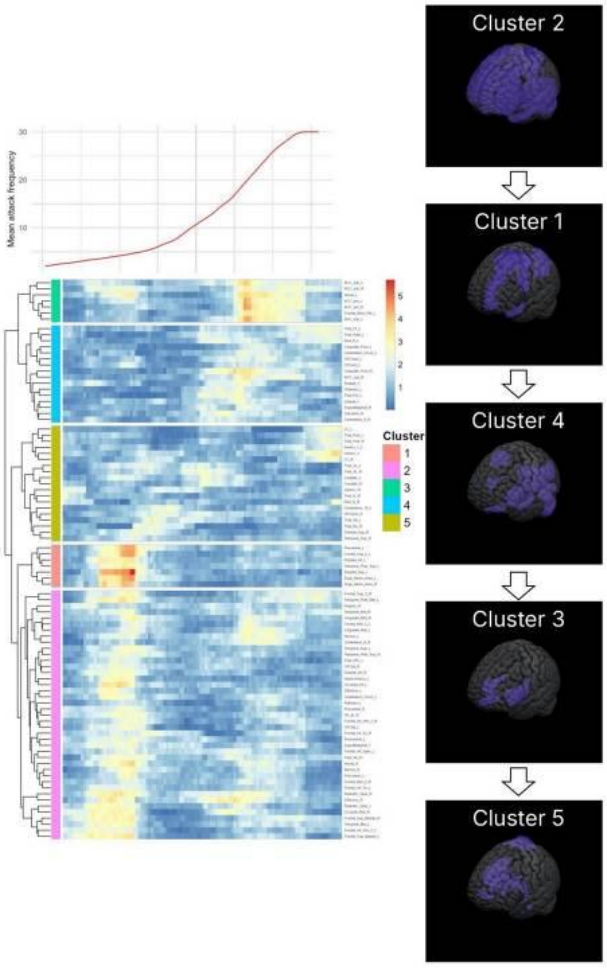
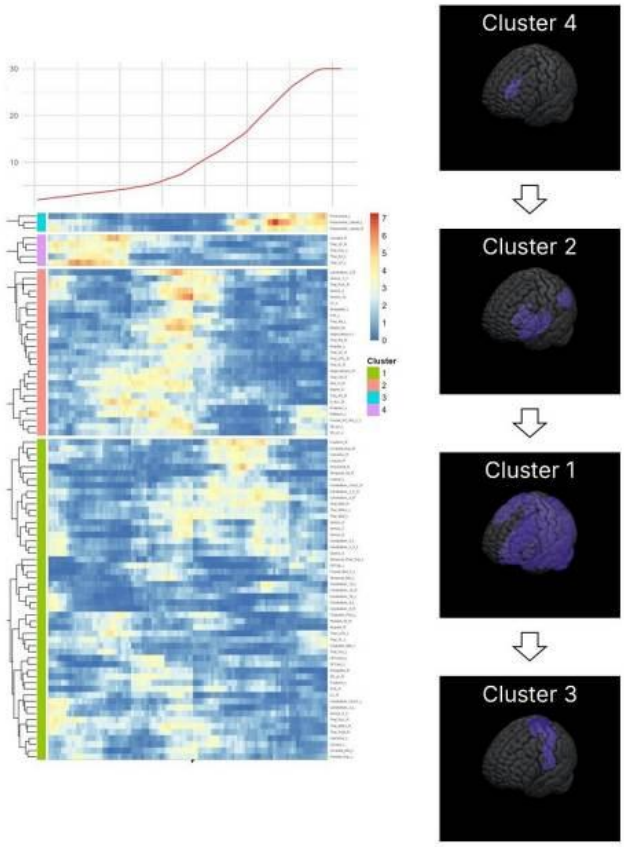


Fig. 6



P666

Structural, functional, and quantitative susceptibility mapping abnormalities in new daily persistent headache: Insights from 7T-MRI multimodal neuroimaging

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Objective: New Daily Persistent Headache (NDPH) is an extremely rare, disabling, and refractory primary headache disorder, with its pathophysiological mechanisms remaining poorly understood. According to the International Classification of Headache Disorders, 3rd edition (ICHD-3), NDPH is defined by a distinct onset, continuous pain within 24 hours, duration exceeding 3 months, and no better explanation by other diagnoses. Its prevalence in the population ranges from 0.01% to 0.3%, and it is recognized as a heterogeneous syndrome with at least three distinct phenotypes. Previous neuroimaging investigations into NDPH have been largely constrained to 3T magnetic resonance imaging (MRI) systems, which fail to thoroughly reveal microstructural changes—particularly subregional abnormalities within key neural networks such as the limbic system and perturbations in brain iron metabolism. Existing 3T MRI-based studies have yielded inconsistent findings. Furthermore, there is a critical gap in research regarding iron deposition patterns in NDPH, as no studies have systematically analyzed this aspect using Quantitative Susceptibility Mapping (QSM), an advanced MRI technique capable of non-invasively quantifying tissue iron content. The limbic system, a core neural network integrating emotion, memory, and somatic sensation, includes structures such as the thalamus, hypothalamus, hippocampus, and amygdala. Given that NDPH is frequently comorbid with emotional disorders (e.g., anxiety and depression) and that a "pain-emotion" vicious cycle significantly impairs patients' quality of life, investigating limbic system abnormalities is essential to unraveling NDPH pathogenesis.

This study aimed to address the limitations of previous research by employing 7T multimodal MRI—with its superior spatial resolution and signal sensitivity—to systematically investigate structural, functional, and iron metabolism abnormalities in NDPH patients. Specifically, the study focused on: (1) whole-brain structural volume changes and subregional alterations within the limbic system (hypothalamus, thalamus, amygdala, hippocampus); (2) functional perturbations using fractional Amplitude of Low-Frequency Fluctuations (fALFF) and Regional Homogeneity (ReHo) derived from resting-state fMRI (rs-fMRI); (3) iron metabolism dysregulation via QSM; and (4) the correlations between these neuroimaging metrics and clinical parameters (e.g., anxiety/depression scores, pain intensity, sleep quality). The ultimate goal was to provide novel insights into NDPH pathogenesis.

Methods: A total of 23 individuals with NDPH and 23 healthy controls (HCs) were enrolled. Clinical assessments included the Generalized Anxiety Disorder-7 (GAD-7) scale (anxiety), Patient Health Questionnaire-9 (PHQ-9) (depression), Pittsburgh Sleep Quality Index (PSQI) (sleep quality), and Visual Analog Scale (VAS) (pain intensity).

Results: No significant differences in age or sex were observed between individuals with NDPH and HCs. However, NDPH patients had significantly higher GAD-7, PHQ-9, and PSQI scores than HCs. After FDR correction, NDPH patients showed significantly reduced volumes in the right accumbens area and left caudal anterior cingulate cortex (cACC) compared to HCs, with no significant correlations between these regions and clinical indicators. In limbic subregions: **Thalamus**: Increased volume in the left nucleus reuniens (L-MV(Re)); **Hippocampus**: Increased volume in the molecular layer of the bilateral hippocampal head and body, but reduced volume in the Granule Cell and Molecular Layer of the Dentate Gyrus (GC-ML-DG) head/body and Cornu Ammonis 1 (CA1) head. Notably, volumes of left hippocampal subregions (molecular_layer_HP-head, CA1-head, GC-ML-DG-head, parasubiculum) were negatively correlated with

history (P<0.05), indicating more severe atrophy with longer disease history. NDPH patients exhibited widespread increased fALFF values in the frontal lobe, parietal lobe, temporal lobe, occipital lobe, cerebellum, and limbic structures (bilateral amygdala, hippocampus) after FDR correction. Correlation analyses revealed: Positive correlations between fALFF values in the right accumbens area, right hippocampus, and left lateral occipital cortex and GAD-7 scores (P<0.05); Negative correlation between fALFF values in the left transverse temporal cortex and VAS pain intensity scores (P<0.05); Positive correlation between fALFF values in the left frontal pole and PHQ-9 scores (P<0.05); Negative correlation between fALFF values in the left inferior parietal cortex and headache duration (P<0.05). After FDR correction, ReHo values were significantly increased in the left supramarginal gyrus, left pars triangularis, left inferior parietal gyrus, and other frontal/parietal regions, while reduced in the right pallidum, left ventral DC, right parahippocampal gyrus, and multiple limbic subregions. Correlation analyses showed: Negative correlations between ReHo values in the left parahippocampal gyrus, left superior parietal gyrus, left inferior parietal gyrus, left supramarginal gyrus, and left pars opercularis and headache duration (P<0.05); Positive correlation between ReHo values in the left frontal pole and PHQ-9 scores (P<0.05); In limbic subregions: positive correlation between ReHo values in the left amygdala medial nucleus and GAD-7 scores (P<0.05); positive correlation between ReHo values in the right hypothalamic anterior inferior subregion and headache duration (P<0.05); negative correlation between ReHo values in the right thalamic MV(Re) and VAS scores (P<0.05). Compared to HCs, individuals with NDPH (n=19) showed significantly decreased QSM values (reduced iron content) in the right paracentral lobule, right cuneus, and left precentral gyrus, and increased QSM values (elevated iron content) in the left rostral middle frontal gyrus after FDR correction. Within the limbic system, QSM values were significantly increased in the left amygdala central nucleus and left hippocampal parasubiculum (FDR<0.05). No significant correlations were observed between QSM values and clinical indices.

Conclusion: This study is the first to systematically explore structural, functional, and iron metabolism abnormalities in NDPH using 7T multimodal MRI, focusing on whole-brain networks and limbic subregions. The findings reveal widespread structural atrophy (e.g., right accumbens area, left cACC, hippocampal subregions), functional hyperactivation/hyposynchrony (dysregulated fALFF/ReHo), and abnormal iron deposition patterns. These abnormalities are closely correlated with clinical parameters such as headache history, anxiety/depression scores, and pain intensity, highlighting a "pain-emotion-metabolism" pathological cycle underlying NDPH. The limbic system subregional changes, in particular, emphasize its critical role in pain-emotion interaction. Abnormal iron metabolism provides a novel insight into NDPH"s refractory nature, suggesting targeted iron regulation (e.g., iron chelators) may be a potential therapeutic strategy. Limitations include a small sample size, cross-sectional design, and lack of phenotypic stratification. Future large-scale longitudinal studies are needed to validate these findings, clarify causal relationships, and translate neuroimaging insights into clinical practice. These results advance our understanding of NDPH pathogenesis and offer potential therapeutic targets for this refractory disorder.

Fig. 1

Tables

Table1.Demographic information and clinical characteristics in structural and functional analysis.

	HC(n=23)	NDPH(n=23)	*P*
Age (median [IQR])	30.00[26.00, 47.00]	30.00[20.00, 47.00]	0.2911
Male (n)	15	18	0.5125
Headache history (months)	NA	24.00 [12.00, 78.00]	
VAS (0-10)	NA	5.48 (1.47)	
Gad-7 (median [IQR])	4.00 [0.00, 7.00]	8.00 [4.00, 12.50]	0.0070
PHQ-9 (median [IQR])	4.00 [0.00, 9.00]	11.00 [8.00, 15.50]	0.0013
PSQI (mean (SD))	6.35 (4.34)	10.17 (4.79)	0.0069

Abbreviations: VAS, Visual Analogue Scale; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder; PSQI, Pittsburgh sleep quality index.

Fig. 2

Table2. Demographic information and clinical characteristics in QSM analysis.

	HC(n=23)	NDPH(n=19)	*P*
Age (median [IQR])	30.00[26.00, 47.00]	30.00 [20.00, 49.00]	0.4327
Male (n)	15	14	0.7984
Headache history (months)	NA	24.00 [12.00, 78.00]	
VAS (0-10)	NA	5.32 (1.49)	
Gad-7 (median [IQR])	4.00 [0.00, 7.00]	8.00 [4.00, 11.00]	0.0112
PHQ-9 (median [IQR])	4.00 [0.00, 9.00]	11.00 [8.00, 15.00]	0.0028
PSQI (mean (SD))	6.35 (4.34)	10.37 (4.56)	0.0059

Abbreviations: VAS, Visual Analogue Scale; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder; PSQI, Pittsburgh sleep quality index. QSM, quantitative susceptibility mapping.

Fig. 3

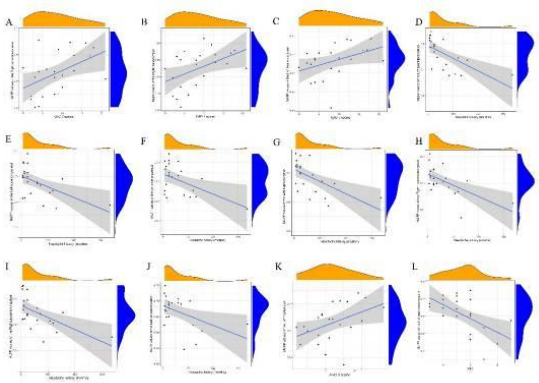


Fig. 4

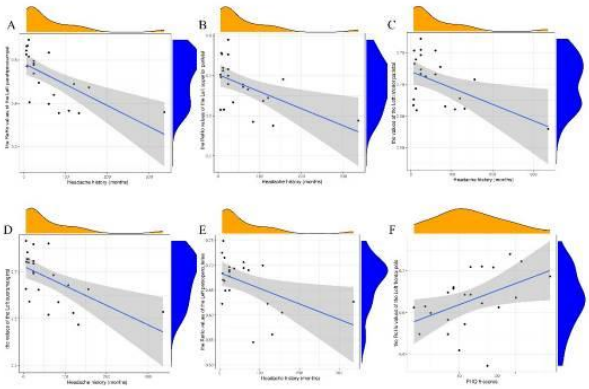


Fig. 5

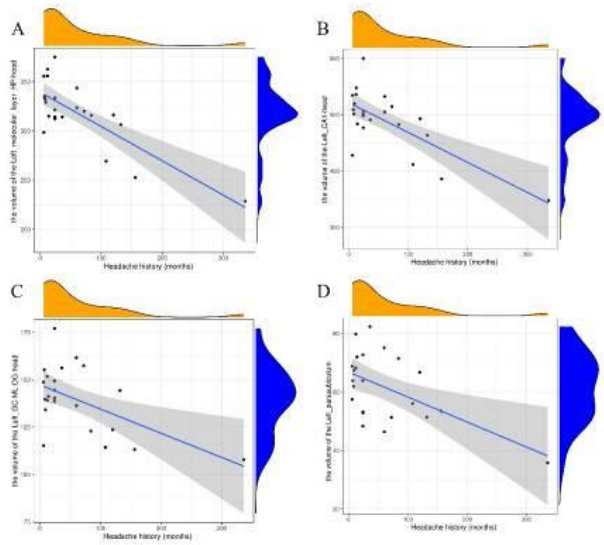
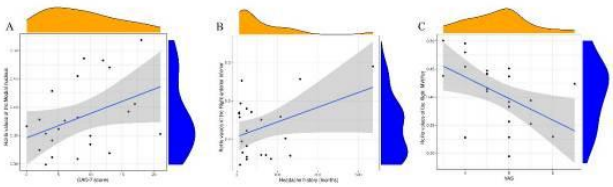


Fig. 6



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Mechanistic study of dopamine and D2 receptors in the medial orbitofrontal cortex involved in migraine

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Objective: Chronic Migraine (CM) is a neuropathic pain disorder characterized by recurrent attacks and protracted course, whose pathogenesis is closely associated with brain network dysfunction. The current brain network dysregulation model of migraine reveals that this disorder results from the disruption of dynamic balance between the "top-down" control network (represented by the prefrontal cortex) and the "bottom-up" sensory network (represented by the insula, thalamus, and brainstem). Among them, the functional decline of the prefrontal cortex leads to impaired filtering and inhibition of pain signals, causing hyperactivity and enhanced connectivity in pain-processing regions such as the insula, anterior cingulate cortex, and thalamus, which amplifies pain signals and their affective components, potentially participating in the pathophysiological mechanism of migraine.

The orbitofrontal cortex (OFC), as a vital component of the prefrontal cortex, has gradually attracted attention for its role in chronic migraine. The dynamic changes of the midbrain dopamine (DA) system play a crucial role in pain modulation. Previous studies have shown that alterations in DA release affect pain perception. Our team's previous clinical study found that patients with chronic migraine complicated by medication overuse exhibited reduced metabolic levels of dopamine transporter (DAT) in the OFC, particularly in the medial OFC (mOFC), suggesting that dynamic changes in DA in the mOFC may be involved in the pathophysiological mechanism of migraine.

Our study focuses on the function of dopamine and its receptors in the medial orbitofrontal cortex, aiming to deeply elucidate the specific mechanism of the midbrain dopamine system in the orbitofrontal cortex in pain regulation of chronic migraine, and to provide new theoretical basis and potential targets for targeted therapy of chronic migraine.

Methods: A chronic migraine mouse model was established by repeated administration of glyceryl trinitrate (GTN). In vivo fiber photometry was used to monitor the dynamic changes of dopamine in the mOFC. Calcium imaging and immunofluorescence co-staining of c-Fos were used to detect the signal changes of DRD2+ neurons in this brain region; chemogenetic methods were used to activate and inhibit DRD2+ neurons in the mOFC, and immunofluorescence staining was used to identify the types of DRD2+ neurons. Finally, chemogenetic methods were continued to regulate different types of DRD2+ neurons. Behavioral assessments included pain sensitivity (Von-Frey test) and anxiety-like behavior (elevated plus maze test and light-dark box test).

Results: Firstly, repeated GTN injection successfully induced migraine-like phenotypes in mice: compared with the normal saline control group, model mice exhibited significantly decreased periorbital and hindpaw withdrawal thresholds (indicating tactile allodynia) and displayed anxiety-like behaviors—

including reduced time spent in the open arms of the elevated plus maze and decreased entries into the light compartment of the light-dark box. Fiber photometry recordings showed a significant increase in dopamine release in the mOFC of model mice. Molecular biological analyses (Western blot and quantitative real-time polymerase chain reaction [qPCR]) demonstrated that the expression of DRD2 in the mOFC of model mice was significantly upregulated, while the expression of DRD1 showed no significant change. Calcium imaging combined with c-Fos co-staining further revealed that the calcium signal amplitude and c-Fos-positive rate of $DRD2^+$ neurons in the mOFC of model mice were significantly lower than those in the control group, suggesting that the function of $DRD2^+$ neurons was inhibited in the migraine model.

In addition, chemogenetic inhibition of mOFC $DRD2^+$ neurons (via hM4Di) significantly alleviated GTN-induced tactile allodynia: both periorbital and hindpaw withdrawal thresholds were increased compared with model mice treated with normal saline, confirming the analgesic effect of inhibiting mOFC $DRD2^+$ neurons. Subsequent immunofluorescence co-staining showed that mOFC $DRD2^+$ neurons were predominantly excitatory: $Camk2a^+$ excitatory neurons accounted for 87.3712±0.90787% of total $DRD2^+$ neurons, while GABAergic interneuron accounted for only 10.3226±0.56701%. Finally, subtype-specific chemogenetic manipulation revealed that inhibition of excitatory $DRD2^+$ ($Camk2a^+/DRD2^+$) neurons significantly improved both GTN-induced tactile allodynia and anxiety-like behaviors. However, inhibition of inhibitory $DRD2^+$ ($GABA/DRD2^+$) neurons had no significant effect on migraine-related behaviors.

Conclusion: This study clarifies the key role of dopamine and D2 receptors in the mOFC in chronic migraine: in CM model mice, dopamine release in the mOFC is increased, which activates dopamine D2 receptor and inhibits excitatory DRD2+ neurons dominated by $Camk2a^+$, thereby improving pain hypersensitivity and anxiety-like behavior. This finding supplements the specific mechanism of the prefrontal control network in the migraine brain network dysregulation model, provides the excitatory DRD2+ neurons in the mOFC as a potential target for targeted therapy of CM, and also lays a foundation for subsequent exploration of the interaction and effect of this pathway with other analgesic systems.

Fig. 1

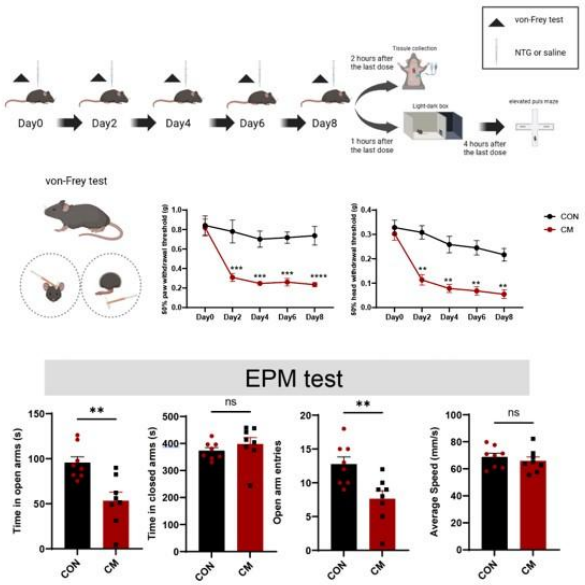


Figure 1

Fig. 2

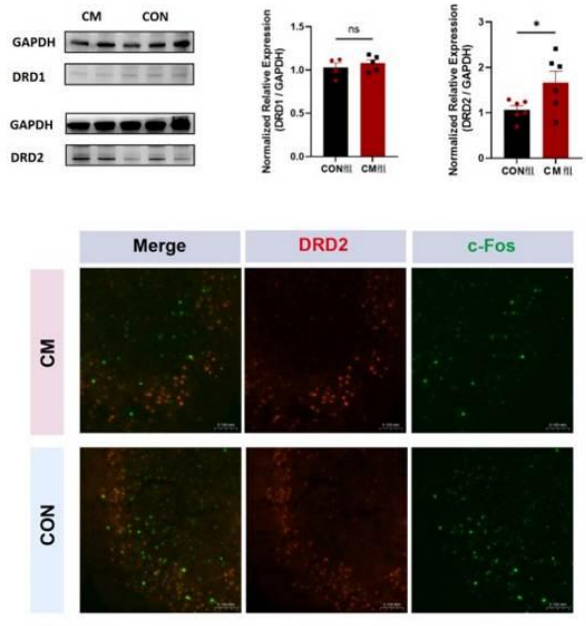


Figure 2

Fig. 3

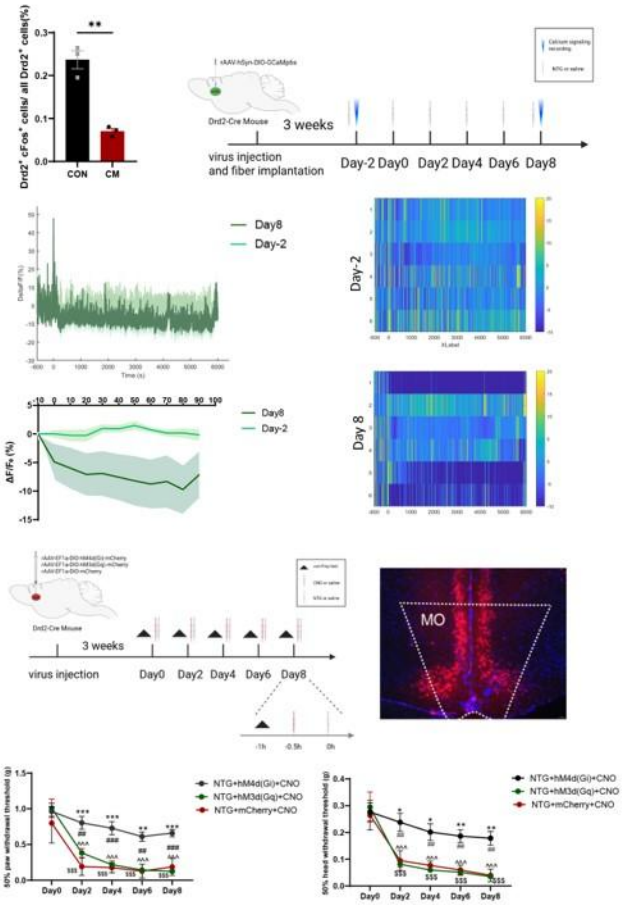


Figure 3

Fig. 4

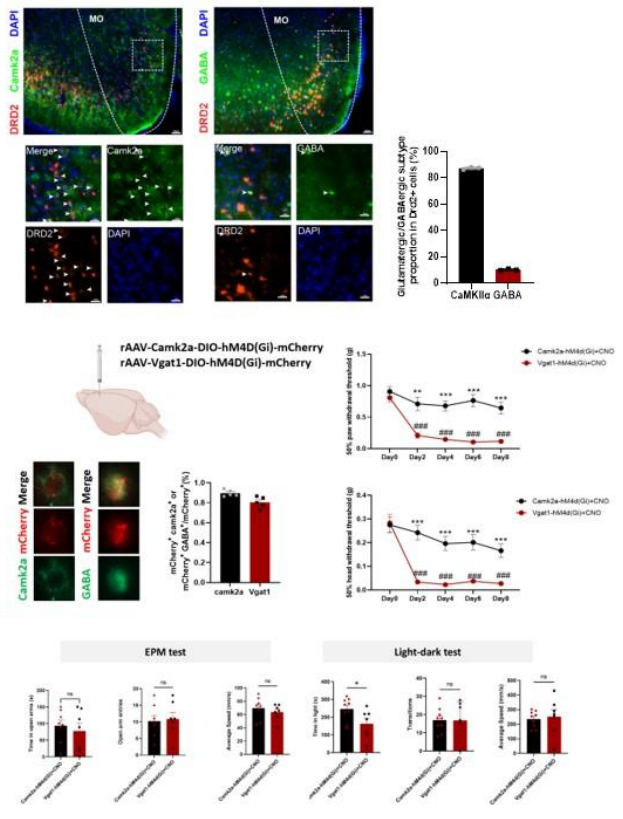


Figure 4