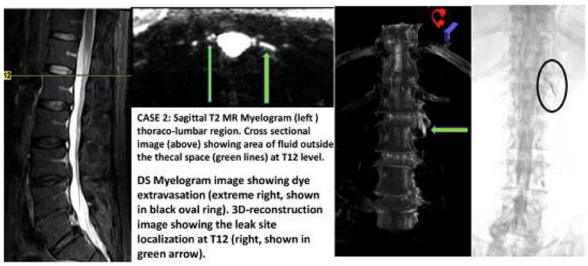

Fig. 2 (abstract P0253). See text for description

P0255

Cortical spreading depression alters transcriptomic profile in meninges and associated vasculature of rats

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The Journal of Headache and Pain 2021, **22(Suppl 1):**P0255

Objectives: Cortical spreading depression (CSD) induces activation of the meninges and associated vasculature (MAV), a key process leading to trigeminal nerve activation and migraine pain. However, how CSD mediates these phenomena in migraine is poorly understood. The aim of this study is to examine CSD-mediated transcriptomic profile of the MAV.
Methods**:** CSD was recorded using electrophysiology in rats. RNA-seq analysis and qPCR were applied for gene expression analysis.
Results: RNA-seq analysis showed that multiple CSD rapidly induced profound changes in gene expression profile in the ipsilateral MAV of rats. CSD induced a total of 1126 genes with altered expression levels, of which 953 CSD-induced DEGs were upregulated and 173 CSD-induced DEGs were downregulated in the rat ipsilateral MAV. All these genes were, for the first time, identified to be altered by CSD in the MAV. These transcriptomic changes accounts to 4.8 % of genes identified in the MAV of rats. Furthermore, these changes of transcriptomic profile were largely associated with altered pathways in synaptic transmission, ion transport and neuroinflamma-tion.
Conclusions: These data implied that MAV activation may be attributed to changes in its transcriptomic profile which are markedly induced by CSD.
The authors declare that there is no conflict of interests.

P0256

TRPA1/SFK signaling in trigeminal ganglion contributes to migraine pathophysiology

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The Journal of Headache and Pain 2021, **22(Suppl 1):**P0256

Background and objective: TRPA1 is a promising therapeutic target in migraine by responding to migraine triggers and regulating migraine pathogenesis. However, TRPA1-invovled signaling events in migraine are poorly understood. In this study, we explored the potential role of Src family kinases (SFK) in TRPA1-mediated migraine pathophysiology in trigeminal ganglion (TG), the key anatomical region for migraine pain transmission from periphery to brain.
Methods: A mouse trigeminal ganglia (TG) tissue culture model was applied. The level of SFK activation was detected using Western Blot; calcitonin gene-related peptide (CGRP) release was detected using ELSIA and IL-1β gene expression was detected using qPCR.
Results: The results showed that activation of TRPA1 by umbellulone increased the level of phosphorylated SFK at Y416 in TG, which was reduced by inhibition of protein kinase A by PKI (14-22) amide. Moreover, inhibition of SFK activity by saracatinib reduced umbellulone-enhanced CGRP release and IL-1β gene expression in TG.
Conclusions: These findings suggest that SFK participate in TRPA1 signaling in TG to mediate neuropeptide release and neuroinflammation, leading to peripheral sensitization and the development of migraine.

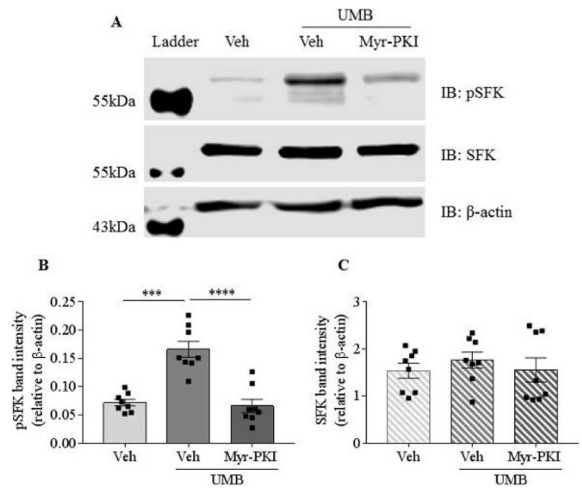

Fig. 1 (abstract P0256). See text for description

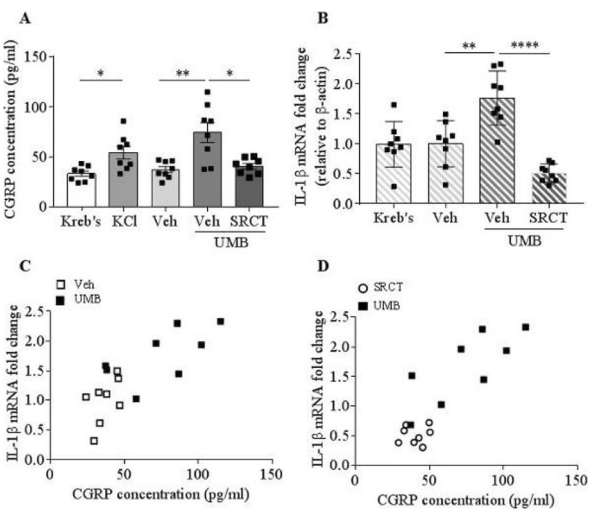

Fig. 2 (abstract P0256). See text for description

P0257

Is there a link between pain chronification, and allodynia and vitamin D deficiency in headache?

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The Journal of Headache and Pain 2021, **22(Suppl 1):**P0257

Objective: The vitamin D deficit has been associated to pain chronification, and chronic migraine is frequently associated with allodynia. The aim of this study was to assess the potential role of VitD in pain chronification and its relation to the occurrence of allodynia.
Methods: We recruited 76 consecutive patients: 32 belonged to the episodic migraine (EM), 34 to the chronic migraine and medication overuse (CM-MOH) groups and 10 to the tension-type headache (TTH) group. All patients underwent neurological and physical examination and anamnestic data collection including allodynia and serum calcifediol (25(OH)D) assessment.
Results: The occurrence of patients with vit D deficit was significantly higher in the CM-MOH (46%), than in the EM groups (25.7%) and in the TTH group (11.4%). The Vit D deficit was not significantly associated with any of the other variables. Allodynia also was more frequent in CM-MOH (66.7%) than in the EM (29.2%) and TTH groups (6.7%). On the contrary the occurrence of allodynia was independent from the vit D deficit (allodynia occurred in 42.4% of patients with and 57.6% without vit D deficit)
Conclusion: Prevalence of VitD deficiency and allodynia were significantly higher in patients suffering from CM-MOH, however the co-occurrence of allodynia and VitD deficiency were not correlated, thus suggesting that chronification and allodynia do not stem from the same pathophysiological mechanism.

P0258

COmbining UbRogepAnt and preventives for miGrainE (COURAGE) study using the Migraine Buddy application: A novel, entirely remote design for collecting real-world evidence

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The Journal of Headache and Pain 2021, **22(Suppl 1):**P0258

To describe COURAGE, a novel, mobile (Migraine Buddy) app-based, study evaluating the real-world effectiveness of ubrogepant for the acute treatment of migraine when used with an approved preventive.
Eligible adults (≥3 ubrogepant-treated attacks, ≥3 migraine attacks in last 30 days) used ubrogepant with onabotulinumtoxinA (ub+obA), or with anti-CGRP monoclonal antibody (ub+mAb), or with both medication (ub+both). Over 30 days, participants reported treatment outcomes at <1, 1-2, 2-4, or >4 hrs post-ubrogepant. Interim marginal odds of achieving meaningful pain relief (MPR) for the 1st ubrogepant-treated attack by 2 and 4 hrs post dose were modeled via logistic regression. Covariates were age, MIDAS, ubrogepant dose. As of 01/2021, 492 respondents consented, with 461 screened and then 354 enrolled; users with baseline treated ≥1 attack with ubrogepant) were ub+obtA, n=88 (83); ub+mAb, n=206 (175); ub+both, n=60 (51). 237 completed the study and 177 logged ≥3 ubrogepant-treated attacks. Interim data suggests many patients achieving MPR by 2 hrs post-treatment with a larger majority achieving MPR at 4 hrs. Adjusted odds were significant (p<0.001) for ub+obA and ub+mAb.
COURAGE has successfully assessed treatment value and usage patterns remotely to keep patients and HCP safe during the COVID-19 pandemic. Interim findings suggest that ubrogepant is effective when used with approved migraine preventives; final data may inform clinicians how best to optimize treatment.

P0259

Real-World Efficacy, Tolerability and Safety of Ubrogepant

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The Journal of Headache and Pain 2021, **22(Suppl 1):**P0259

Objective: To assess the real-world efficacy, tolerability, and safety of ubrogepant in a tertiary headache center.
Method: This was a cohort study conducted at Mayo Clinic Arizona. All patients prescribed ubrogepant were tracked and contacted 1-3 months after the prescription to answer a list of standardized questions.
Results: We obtained eligible responses from 106 patients; 86.8% had chronic migraine. Complete headache freedom, and headache relief for ≥75% of all treated attacks at 2 hours after taking ubrogepant was achieved in 19.0% and 47.6% patients, respectively. 31.1% patients were being "very satisfied" with ubrogepant. Adverse events were reported in 39.6% patients, including fatigue 27.4%, dry mouth 7.5%, nausea 6.6%, constipation 4.7%, dizziness 2.8%, and others 6.6%. Predictive factors for being a "good responder" to ubrogepant included migraine with aura, episodic migraine, <5 prior unsuccessful preventive or acute treatments, successful responses to a CGRP monoclonal antibody and onabotulinumtoxinA. For the 62 (58.5%) patients concurrently using a CGRP monoclonal antibody, there was no difference in the "good responder" rate or adverse event rate compared to those who were not on a CGRP monoclonal antibody, though the rate of moderate adverse events was higher.
Conclusion: Our study confirms and extends the efficacy profile and tolerability of ubrogepant in a real-world tertiary headache clinic and identifies factors that may predict efficacy.

Table 1 Efficacy of Ubrogepant

% of all treated attacks	Number (%) of patients experienced headache **freedom** at 2 hours after taking ubrogepant N=105	Number (%) of patients experienced headache **relief** at 2 hours after taking ubrogepant N=105	Number (%) of patients experienced headache **freedom** at 2 hours for **mild headache** N=56
0%	63 (60.0%)	28 (26.7%)	19 (33.9%)
> 0%	42 (40.0%)	77 (73.3%)	37 (66.1%)
≥50%	33 (31.4%)	62 (59.0%)	27 (48.2%)
≥75%	20 (19.0%)	50 (47.6%)	23 (41.1%)
100%	13 (12.4%)	32 (30.5%)	18 (32.1%)

Table 1 (abstract P0259). See text for description

Table 2 Factors predictive of being a "good responder" to ubrogepant

	Odds Ratio (95% CI)	p
Migraine with aura	2.27 (1.01-5.12)	0.048
Chronic migraine	0.205 (0.05-0.78)	0.021
Previously tried and failed <5 preventive medications	2.98 (1.30-6.86)	0.010
Previously tried and failed <5 acute medications	2.42 (1.10-5.30)	0.028
Had > 50% decrease in headache frequency from a CGRP mAb	4.5 (1.45-13.95)	0.009
CGRP mAb non-responders (<30% decrease in frequency)	0.242 (0.09-0.62)	0.003
OnabotulinumtoxinA non-responders (<30% decrease in frequency)	0.369 (0.14-0.95)	0.040

Table 2 (abstract P0259). See text for description

P0260

Adding sodium bicarbonate to bupivacaine in occipital nerve blocks improves injection related pain

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The Journal of Headache and Pain 2021, **22(Suppl 1):**P0260

Objective: Our aim was to analyze if addition of sodium bicarbonate (SB) to bupivacaine for occipital nerve block (ONB) relieves injection related pain.