

MEETING ABSTRACTS

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# Abstracts from the 18 th European Headache Congress (EHC)

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## AL001

### Overuse of analgesics can affect the fertility biomarker Anti-Müllerian hormone in females. A translational study

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**Objective:** Over-the-counter analgesics (OTC) have been associated with disrupted male endocrinology, while effects on female endocrinology remains nearly unknown. The aim was to understand the effect of long-term analgesic exposure in females with medication overuse headache (MOH) on Anti-Müllerian Hormone (AMH), a surrogate measure of female fertility.

**Methods:** Using a translational approach, an observational prospective clinical study was conducted to determine AMH-levels in females with MOH, in combination with pre-clinical investigation of primary granulosa cells (GC) to understand the effects of analgesics on GC-function.

**Results:** We included 21 females (mean-age 30.0 years; SD (7.3)) for AMH-measurement. AMH increased by 21% from baseline (mean 20.1 pmol/L; SD (8.7)) after withdrawal of analgesics ((mean 24.3pmol/L; SD (12.0));  $p=0.0023$ ). Exposing primary GCs to analgesics (acetaminophen (100 and 200  $\mu$ M,  $n = 9-10$ ) and ibuprofen (150 and 200  $\mu$ M,  $n = 12-13$ )) did not reduce AMH-levels. In contrast, *de novo* DNA synthesis in GCs ( $n=6$ ) exposed to acetaminophen was reduced with 78% ( $p=0.0036$ ) compared to controls, suggesting that cellular proliferation was restricted.

**Conclusion:** Frequent use of OTC was associated with repressed AMH-levels likely through disruption of GC proliferation. Further research is crucial to investigate a potential effect of analgesics on adult female reproductive endocrinology.

## AL002

### Sex differences in RAMP1/RAMP2 expression in the human middle meningeal artery match functional response to CGRP

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**Objective:** CGRP induces vasodilation after binding to the CGRP receptor (CLR-RAMP1), but can activate the adrenomedullin receptor (CLR-RAMP2) as well. Previously, age-dependent sex differences were observed for CGRP-induced relaxation of human middle meningeal arteries<sup>1</sup>. In addition, RAMP1 and RAMP2 mRNA expression was highly variable between patients<sup>2</sup>. The current study aims to investigate whether RAMP1 and RAMP2 expression differs between men and women and varies throughout life.

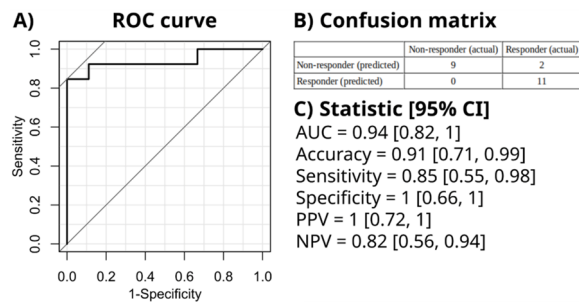
**Methods:** RNA was isolated from homogenized human middle meningeal arteries (14 F, 12 M, age  $51 \pm 3$  years) and qPCR was performed for RAMP1 and RAMP2 mRNA expression. The ratio between RAMP1 and RAMP2 expression with increasing age was investigated for men and women separately.

**Results:** The RAMP1/RAMP2 ratio significantly decreases with age in men, while a positive trend can be observed for women. These findings match the pattern of maximum relaxation to CGRP as observed in a previous study<sup>1</sup>, with a significant decrease with age in men and a trend for increased maximum relaxation with age in women.

**Conclusion:** The current study suggests that the maximum effect of CGRP-induced relaxation of human middle meningeal arteries matches the ratio of RAMP1/RAMP2 expression, and changes in a sex-dependent manner with increasing age. Interestingly, migraine is generally most prevalent in pre-menopausal women. Here, these young women show a relatively high RAMP2 and low RAMP1 expression, suggesting predominance of the adrenomedullin receptor over the canonical CGRP receptor in this population. Possibly, increased exposure of CGRP in young women results in downregulation of RAMP1. Future research should investigate whether RAMP1 and RAMP2 expression is altered in migraine patients.



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**Fig. 3 (Abstract P311).** Results of the multivariate prediction model. A) Receiver Operating Characteristics (ROC) curve. B) Confusion matrix. C) Statistic values to evaluate the prediction model with the 95% confidence interval (95% CI). AUC = area under the curve; PPV = positive predictive value; NPV = negative predictive value

### P312

#### Uncovering functional connectivity variations throughout the migraine cycle

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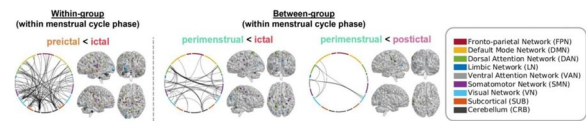
**Objective:** Lack of case-control fMRI studies covering the migraine cycle hinders the understanding of brain functional connectivity (FC) in migraine. Our goal was to determine how the migraine cycle affects individual FC fingerprints.

**Methods:** We studied resting-state FC in 10 patients with low frequency episodic menstrual-related migraine without aura across 4 sessions (preictal, ictal and postictal phases; and interictal phase) and 14 matched healthy controls (HC) in 2 sessions (perimenstrual and post-ovulation, matching the peri-ictal and interictal phases, respectively). fMRI was preprocessed and parcellated into cortical, subcortical and cerebellar regions. We computed individual FC matrices and the corresponding identifiability matrix (correlation between all pairs of FC matrices). Next, we employed a multilevel clinical connectome fingerprinting approach, by combining the differential identifiability within-subject, within-session and within-group. The FC fingerprints were analyzed to identify variations in FC within-group and between groups.

**Results:** We observed increased FC heterogeneity in the preictal/ictal phases, which decreased with the progression of the attack. Interictally, patients were more homogeneous, and this homogeneity did not differ from the HC. FC significantly increased among migraine patients during the ictal phase compared to the preictal, as well as compared to HC in the same menstrual cycle phase, observed during both the ictal and postictal phases (Figure 1).

**Conclusion:** Our findings of FC fingerprint variations across the migraine cycle may help fill the gap on the occurrence of migraine attacks and lead to more personalized treatments built upon clinical fingerprinting. [This work was supported by LARSyS FCT funding (DOI: 10.54499/LA/P/0083/2020, 10.54499/UIIDP/50009/2020, and 10.54499/UIIDB/50009/2020), PRR project Center for Responsible AI C645008882-00000055 and FCT grants PD/BD/150356/2019, PTDC/EMD-EMD/29675/2017, LISBOA-01-0145-FEDER-029675.]

The patient gave their explicit informed consent to publish their information in an open access journal.



**Fig. 1 (Abstract P312).** FC analysis within-group and within menstrual cycle phase (Left) and between-group (Right), using NBS (based on extent, cluster threshold = 4;  $\alpha = 0.05$ ; 5000 permutations). For each comparison, two representations are shown: a chord diagram with the edges that significantly and four brain views showing the nodes that contribute to significantly different edges. For each comparison, the node size is scaled according to the node degree, which corresponds to the sum of the number of significantly different edges linked to that node. The networks are represented by colors, as indicated in the legend

### P313

#### Brain dural arteriovenous fistulas – a case study and literature review

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**Objective:** To review the literature on dAVF based on a case study.

**Methods:** Case report

**Results:** A 39-year-old male, with a history of active smoking and right transverse and sigmoid sinus thrombosis six months prior, presented with progressive worsening of residual symptoms. Initial investigations included a follow-up brain MRI at four months post-thrombosis, revealing partial recanalization. The patient reported visual disturbances (myodesopsia and inferior altitudinal visual field defect) and oppressive holocranial headaches occurring 1–2 times per week, partially responsive to acetaminophen. Ophthalmological evaluation found papilledema, raising clinical suspicion of dural fistula. Subsequent angiography confirmed the presence of a Cognard Type 2A dAVF, with arterial supply from branches of both external carotid arteries and vertebral arteries, draining into the superior sagittal sinus and torcula.

The patient provided consent for the use of all images

**Conclusion:** dAVFs with bilateral and posterior arterial supply are exceedingly rare. Treatment options include arterial embolization and neurosurgery. These fistulas should always be considered in patients with compatible clinical symptoms and a history of venous sinus thrombosis, as untreated cases may lead to intracranial hemorrhage

### P314

#### Contralateral cranial autonomic symptoms in migraine patients, in Azerbaijani population

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**Objective:** Migraine is a complex neurological disorder characterized by a range of symptoms beyond headache, including cranial autonomic symptoms typically associated with trigeminal autonomic cephalalgias. These symptoms encompass conjunctival injection, lacrimation, nasal congestion, rhinorrhea, eyelid edema, forehead and facial sweating, miosis, and ptosis.