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Investigating the Long-Term Efficacy of Calcitonin Gene Related Peptide Monoclonal Antibodies

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Question: Calcitonin gene related peptide monoclonal antibodies (CGRP mAbs) are a promising treatment for episodic and chronic migraine. Though many real-world studies have shown benefit at an average treatment time of 3 or 6 months, little is known about its long term efficacy. The objective of this study is to examine the efficacy of CGRP mAb after 1, 2, and 3 years. This longitudinal study will provide insight on the long-term treatment use of CGRP mAb.
Methods: We extracted Electronic Medical Records (EMR) containing migraine frequency data for Cleveland Clinic patients (n =2025) with 6 consecutive months of positive treatment to a CGRP mAb between June 2018 and December 2021. This cohort's (87.5% female, 47.0 ± 13.5 years old, 1586 with chronic migraine) monthly migraine days (MMD) were examined at 1 (n = 822), 2 (n = 407), or 3 (n = 101) years of CGRP mAb treatment. The responses were differentiated into Non-responders (MMD reduction of 25% or less), Responders (MMD reduction between 26-74%) and Super-responders (MMD reduction of 75% or greater).
Results: After 1 year of treatment, 55.5% were Super-responders, 38.4% Responders, and 6.2% became Non-responders. Following 2 years of CGRP mAb use, 53.6% continued a Super-response, 37.6% responded, and 9.1% stopped responding positively. After 3 years, 59.5% maintained a Super-responder status, 29.7% were Responders, and 10.8% had a negative response.
Conclusions: We have seen great benefits in the short-term treatment of this recent agent, and our results show that CGRP mAbs do maintain efficacy after extended periods of treatment, with only a minority losing benefit over time. This longitudinal study provides some clarity for the preserved long term benefit of the use of CGRP MAB for the treatment of migraine.

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Cognition in Menstrually Related Migraine:neural correlates of working memory along the cycle

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QUESTION
Hormones play a preponderant role in triggering migraine attacks, with women having higher prevalence and severity of migraine due to their influence along the reproductive cycle[1]. The preictal, ictal and postictal phases tend to include cognitive executive difficulties along with the rest of the attack symptoms[2]. Fluctuations in neural sensitivity observed in migraine could underlie such difficulties[3]. On the other hand, functional and structural changes in brain structures related to cognitive processes along the menstrual cycle have also been documented[4].
We aim to use functional Magnetic Resonance Imaging (fMRI) to evaluate working memory at different stages of the migraine cycle and compare to a non-migraine population while controlling for their menstrual phases.
METHODS
A clinical sample of 15 women suffering from episodic migraine with menstrual-related attacks were recruited. They underwent fMRI sessions with a verbal N-back task in different phases of the migraine cycle, namely, preictal, ictal, postictal and interictal phase. 15 non-migraine controls matched for gender and age were assessed during premenstrual and post ovulation phase. A neuropsychological battery and questionnaires quantifying clinical symptoms and attack description at the time of the exam were also applied.
RESULTS
We report results for 70 sessions of acquisition in whole brain group analysis using a cluster threshold of z > 2.3. We observed left orbital prefrontal areas with significantly higher activation during preictal (z =3.44), ictal (z=3.49) and interictal (z=3.3) phases compared to postictal phase.
CONCLUSIONS
The brain activation observed in prefrontal regions during the migraine attack phases could be related to cognitive inhibition while performing a working memory task.

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Brain connectivity modifications induced by monoclonal antibodies targeting the CGRP pathway in migraine patients: a prospective HD-EEG, open-label, study

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Question: Monoclonal antibodies targeting the CGRP pathway (mAbs) proved effective and safe as migraine preventive treatment. Due to their molecular weight, mAbs act outside of the blood brain barrier, namely in the peripheral component of the trigeminovascular system. Nonetheless, a reduced sensitization of the first order neuron in the trigeminal ganglion may induce secondary effects at central level. Here we aim to study the changes induced by mAbs in cortical brain connectivity recorded by means of high-density electroencephalography (HD-EEG).
Methods: We plan to perform 5 resting state HD-EEG recordings, at baseline (before mAbs treatment), and then every 3 months for one year. Here we present data regarding 16 migraine patients (age 44.7±10.6, 14 females, 11 with CM) who completed the first three months of mAbs treatment (T3). We aim to study the connectivity changes in the nodes of the default mode network (DMN): the right and left angular gyrus (RANG and LANG), the medial pre-frontal cortex (MPC) and the posterior cingulate cortex (PCC).
Results: At T3, mAbs treatment induced an inter-nodal connectivity reduction between MPC-PCC (p=0.025), MPC-LANG (p=0.020), MPC-RANG (p=0.043), and PCC-LANG (p=0.005). By contrast, the connectivity was enhanced between PCC-RANG (p=0.005) and LANG-RANG (p=0.003). At T3, 7 patients qualified as "Responder" to mAbs (reduction in monthly migraine days of at least 50% when compared to baseline). Responders were characterized by a baseline enhanced connectivity between MPC-PCC (p=0.042) and MPC-RANG (p=0.032), and by a reduced connectivity between LANG-RANG (p=.016).
Conclusions: We described brain connectivity modifications in the DMN of migraine patients after three months of mAbs treatment. We hypothesize that a reduced sensitization of the peripheral component of the trigeminovascular system may account for the observed findings. In addition, Responder patients showed a specific baseline brain connectivity pattern.