

UNRAVELING THE SPECTRUM OF MIGRAINE RESISTANT TO TREATMENT: THE ROLE OF MRI RESTING-STATE FUNCTIONAL CONNECTIVITY IN MIGRAINE SUBJECTS TREATED WITH ANTI-CGRP MONOCLONAL ANTIBODIES

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Background. Around 30% of individuals with migraine fail to achieve sufficient disease control (Non-responders) using monoclonal antibodies targeting the CGRP pathway (mAbs). Functional magnetic resonance imaging (fMRI) allows a non-invasive characterization of alterations in resting-state networks, including default mode network, salience, executive control, and sensory systems, defining migraine as a network-level brain disorder. fMRI has also been explored as a predictor of response to mAbs, but definite conclusions are lacking. Our aim was to assess if Non-responders bears a distinct functional connectivity fMRI profile.

Methods. Fifty-seven migraine individuals were enrolled (age 46.0 ± 14.0, 80% female). Subjects were evaluated with fMRI at baseline (T0), and after underwent a 3-month mAbs treatment (T1). Non-Responders were defined as those who did not achieve a reduction of at least 50% in monthly migraine days (MMDs) at T1. Resting-state fMRI was analysed using Independent Component Analysis (ICA) and graph theory, to identify resting-state networks and characterize functional connectivity patterns.

Results. At T1, 24 subjects were classified as Non-responders. At a global level, Non-responders showed stronger functional connectivity between the right superior frontal gyrus and the left cerebellar lobule VI/crus II ($p<0.01$, tfce corrected), whereas Responders exhibited higher connectivity between the right occipital pole, the right inferior frontal gyrus pars triangularis and the right insula ($p<0.01$, tfce corrected). Within resting-state networks, Responders showed increased connectivity in the right precuneus, the left cingulate gyrus, and the right intracalcarine cortex and lingual gyrus ($p<0.01$, tfce corrected), while Non-responders showed higher connectivity in the left paracingulate gyrus ($p<0.05$, tfce corrected). Graph-theoretical analysis indicated a diffuse, less segregated frontal organisation in Non-responders, whereas Responders showed greater thalamic centrality and a more efficient network architecture ($p<0.05$).

Conclusions. We identify a brain connectivity and organization of migraine individuals with a future meaningful response to mAbs treatment. Future Responders are characterized by a more efficient network architecture with the thalamus acting as central hub.