

SIFI FISSION PROFILE IN MIGRAINE PROPHYLAXIS: MIXED ANOVA RESULTS

F. Brighina, P. Alonge, A. Torrente, V. Portera, I. Cutrò, A. Meli, A. Vignoli, C. Camarda

Department of Biomedicine, Neuroscience and Advanced Diagnostics (Bi.N.D.) - Section of Neurology - University of Palermo, Italy

Background. Changes in cortical excitability have been extensively described in migraine and may represent an expression of pain sensitization, potentially contributing to migraine chronicization. Anti-calcitonin gene-related peptide monoclonal antibodies (anti-CGRP mAbs) and anti-CGRP small molecules, such as atogepant do not cross the blood--brain barrier and are thought to act predominantly at the peripheral level, with no evidence of direct effects on the central nervous system (CNS). The sound-induced flash illusion (SIFI) paradigm provides a simple and affordable method to assess visual cortical excitability, as illusion perception depends on cortical excitability: fewer illusions occur when visual cortex excitability is increased. The aim of this study was to evaluate changes in cortical excitability in patients treated with anti-CGRP therapies.

Methods. We analyzed the Sound-Induced Flash Illusion (SIFI) fission profile in three groups of patients receiving monoclonal antibodies targeting the CGRP pathway (mAbs), atogepant, and botulinum toxin (Botox). Five variables were assessed at baseline (t0) and at 3 months (t3): 1F0B (1 flash, 0 beeps), 1F1B (1 flash, 1 beep), 1F2B (1 flash, 2 beeps), 1F3B (1 flash, 3 beeps), and 1F4B (1 flash, 4 beeps). A physiologically monotone-increasing profile is expected, as increasing beep count should elicit greater fission illusion. To exclude unreliable responses, we set a validity criterium (score 0–2, valid if ≥ 2): (1) 1F0B mean response between 0.8 and 1.2; and (2) 1F4B > 1F0B (overall rising profile). Only patients meeting both t0 and t3 validity criteria were included in the analysis.

Results. Valid paired sample: mAbs n = 32, Atogepant n = 13, Botox n = 12. A 3 × 2 mixed ANOVA was performed for each SIFI variable (between-factor: group; withinfactor: time), using pingouin.mixed_anova with partial eta-squared (ηp^2) as effect size measure. Significant effects of Time were observed for 1F3B (F = 7.34, p = 0.009) and 1F4B (F = 10.07, p = 0.003), indicating a significant reduction in fission perception at 3 months, independent of treatment group. No significant between-group effect was detected for any variable (all p > 0.29).

Conclusions. These preliminary findings suggest that anti-CGRP therapies induce measurable changes in visual cortical excitability, consistent with a reduction in cortical hyperexcitability. The effect does not appear to depend on the specific treatment. Further studies are warranted to confirm these findings and clarify their clinical relevance.