

O'Hare*¹, L., Hibbard, P.B. Wilkins, A.J. (in press) Evidence for increased background neural noise in migraine aura: hyperactive but not hyperresponsive. *Headache: The Journal of Head and Face Pain* DOI: 10.1111/head.15046

Abstract

Objective: To investigate the contrast gain in migraine and compare it to that in photosensitive epilepsy. To explore any effects of coloured spectacles (Precision Ophthalmic Tints, POT) on contrast gain.

Background: Individuals with migraine with aura typically show high amplitude electrophysiological responses, but poor performance on visual tasks. One possible explanation is increased neural "noise" in the visual cortex in migraine with aura. "Noise" is neural activity that does not carry information about the stimulus.

Methods: This is a case-control study of individuals with migraine with aura (MA) and controls with no family history of migraine, as there is a tendency for migraine to run in families. We measured the steady-state visual evoked potential in response to a sinewave grating (striped pattern) that varied in contrast (appeared to flicker on and off) at 5 and 17Hz in 15 MA and 15 control participants. The maximum contrast (stimulus intensity) increased progressively from 10% to 90% in nine equal steps. We also measured the effect of coloured spectacles (Precision Ophthalmic Tints, POTs) on the EEG response. The experiment was a mixed factorial design, with one between-participants factor (experimental versus control group) and two within-participants factors (contrast and lens type (none, POT or control)). The dependent variables were the SSVEP response, and the background EEG activity. In Experiment 2, discomfort judgements on a rating scale of 0-9 from a separate set of 12 MA and 12 control participants were also collected during the EEG session. Data were collected between February 2022 and August 2024.

Results: At the faster flicker rate of 17Hz (appearing on and off 17 times per second), the electrophysiological response of the migraine with aura (MA) group showed increased background activity (EEG power at frequencies other than the stimulation frequency) (Experiment 1: mean for the migraine group = -666.45 dB/Hz, SE = 116.69, mean for the control group = -1100.50 dB/Hz, SE = 164.99, coefficient estimate = 434.09, $p = 0.016$, CI = [82.24, 735.94], estimated Cohen's d of 0.94, CI = 0.14, 1.73; Experiment 2: migraine group mean = -500.01 dB/Hz, SE = 122.99, control group mean = -741.88 dB/Hz, SE = 126.12, coefficient estimate = 265.04, $p = 0.049$, CI = [1.52, 528.56], estimated Cohen's d of 0.95, CI = 0.05, 1.84). The increase in EEG power with contrast at the stimulation frequency was similar in both migraine with aura and control groups. The MA group experienced more discomfort compared to the control group (median rating for migraine group = 4, IQR = 4, median rating for control group = 3, IQR = 3, coefficient estimate = 3.58, $p = 0.003$, CI = [1.18, 6.00]) and faster flicker (17Hz) was judged more uncomfortable than slower flicker (5Hz) by both groups (median rating for 5Hz = 3, IQR = 3, median rating for 17Hz = 4, IQR = 4, coefficient estimate = 0.97, $p < 0.001$, CI = [0.49, 1.45]). There was no specific reduction in EEG response in the MA group compared to controls with Precision Ophthalmic Tints.

Conclusions: The increased EEG responses in MA show evidence that in migraine the brain is "noisier" compared to controls. As the contrast response was similar in both migraine with aura and control groups, this suggests typical contrast gain control, as distinct from the abnormality seen previously in photosensitive epilepsy. The chosen colour of Precision Ophthalmic Tints can reduce discomfort judgements under some circumstances, although this does not appear to be specific to migraine with aura.