Behavioural correlate of GABA concentration in visual cortex

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Introduction

Recent experiments have shown a close relationship between the concentration of the inhibitory neurotransmitter GABA and visually stimulated gamma-band oscillations, as measured by MEG[1]. In addition, animal experiments have long shown a relationship between the orientation discrimination of individual neurons and GABAergic neurotransmission[2]. This study aims to test the hypothesis that the relationship between GABA and gamma-band oscillations is not merely a neuroimaging epiphenomenon, but has behavioural consequences in terms of an individual's ability to discriminate orientation, as measured by psychophysical staircase methods.

Methods

Thirteen healthy volunteers were recruited for this study, with local ethics board approval.

MR Spectroscopy

Editing methods can harness scalar couplings to reveal low intensity, or heavily overlapped signals in the MR spectrum. In the case of GABA, applying a frequency selective pulse to the CH_2 spins at 1.9 ppm allows the signal at 3 ppm to be separated from the overlying creatine signal. In this study, MEGA-PRESS[3] spectra were acquired of a (3 cm)[3] volume in the occipital lobe (as shown in Figure 1B), centred on the midline with the lower face aligned to the cerebellar tentorium. The following experimental parameters were used: TE = 68 ms; TR = 1.8s; acquisition time 16 min; 16 ms editing pulse.

MEG

Data were acquired using a CTF-Omega 275-channel radial gradiometer system with an additional 29 channels for noise cancellation. An 18-minute duration visual paradigm was presented during recording, consisting of periodic display of a high-contrast single-quadrant grating. Synthetic aperture magnetometry was used to create differential images of source power for 1.5s periods of baseline and visual stimulation. Gamma peak frequency was extracted from time-frequency spectrograms (e.g below left) of virtual sensors reconstructed in the primary visual cortex.

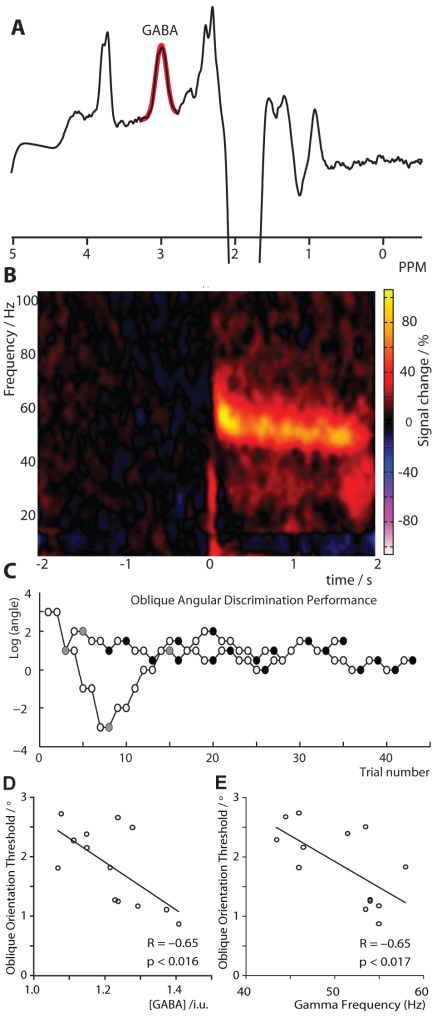

Figure 2: *(A) MEGA-PRESS spectrum showing model (red). (B) Time-frequency plot showing sustained gamma response. (C) Behavioural staircase closing on orientation threshold. Correlations of threshold against GABA (D) and gamma frequency (E).*

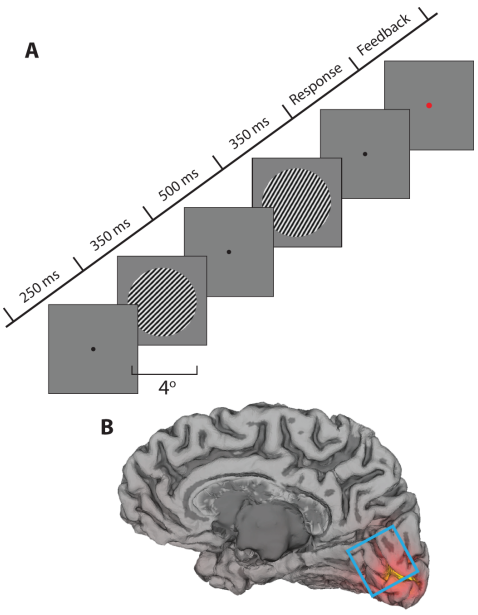

Figure 1: *Methods: orientation discrimination task (A) and occipital MRS voxel location overlaid on reconstruction of gamma power (B).*

Behavioural measurements

Two circular patches filled with a black and white sinusoidal grating (spatial frequency 3 cpd; diameter 4°) of differing orientation were presented separated by a 0.5s fixation delay (as shown in Figure 1A). Participants were instructed to fixate centrally, and to determine whether the second patch was oriented clockwise or anticlockwise relative to the first. Repeated presntations were performed as interleaved staircases. Six runs were recorded, alternating between oblique and vertical discrimination. The threshold was determined by averaging staircase reversal points for the final two staircases (black circles; Fig 2C).

Results

High-SNR edited spectra (e.g. Figure 2A) were acquired in all subjects. GABA concentration was calculated by fitting the MEGA-PRESS GABA signal with a Gaussian function (shown in red) and quantifying relative to the unsuppressed water signal from the same volume. Time frequency plots of the virtual MEG sensor (e.g. Figure 2B) allowed the frequency of the sustained gamma oscillation to be determined in all subjects. Oblique, but not vertical, orientation discrimination threshold correlates with both GABA concentration (Figure 2D; $p < 0.016$) and gamma frequency (Figure 2E; $p<0.017$).

Conclusion

GABA has long been known to play a central role in orientation discrimination at a cellular level; however this is the first study to draw a link between regional GABA concentration and behavioural orientation discrimination. Interpretation of the correlation of gamma frequency with orientation discrimination is complex: it may be simply be associative (as gamma frequency correlates with GABA concentration), but it may also be causatively linked to performance as gamma oscillations are thought to play a role in preserving neural sychrony.

References

1. SD Muthukumaraswamy et al. Proc Nat Acad Sci. 2009; 106(20):8356-61. 2. AM Sillito. J. Physiol. 1979; 289:33:53. 3. M Mescher et al. NMR Biomed. 1998;11(6):266-72.