GABA concentration in visual cortex correlates with individual differences in γ-band oscillation frequency

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Introduction

As the principle inhibitory neurotransmitter, GABA is implicated in a number of pathological processes in the brain, and modulation of the GABA system is a possible treatment mechanism e.g. in epilepsy. Although the GABA signals are not resolved in the localised ^{1}H magnetic resonance (^{1}H-MRS) spectrum, editing methods such as MEGA-PRESS[1] can selectively reveal GABA signals through manipulation of known scalar couplings within the molecule. Magnetoencephalography (MEG) is the direct detection of magnetic fields caused by neuronal events within the brain. This study applies GABA-edited MRS to investigate individual differences in γ-band (30-100 Hz) oscillations as detected by MEG. These results, which demonstrate a range within healthy volunteers, are immediately applicable to studies of the disease mechanism and treatment of epilepsy, and demonstrate the power of a combined MRS-MEG approach.

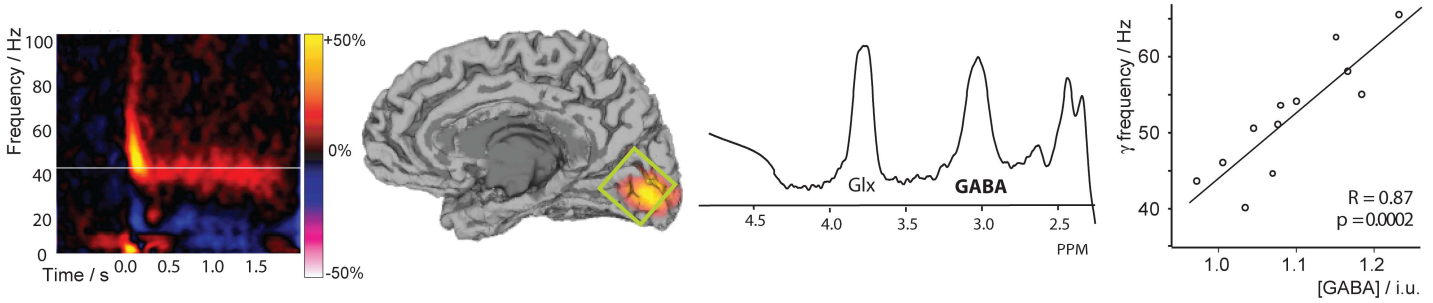
Methods

12 healthy male (aged 34.8 ± 4.8 yrs) volunteers were recruited to the study in accordance with local ethics board procedures. Females were excluded to remove the possible confound associated with hormonal effects on GABA[2].

Two MEGA-PRESS GABA spectra per volunteer were acquired of a 3x3x3 cm^3 volume within the occipital lobe (see green box below, consistent with the MEG source localisation) with the following parameters: 512 scans of 2k datapoints per 15-minute acquisition; TR 1.8s TE 68 ms; 20 ms Gaussian editing pulse offset from water by ±356 Hz; 3T GE Signa HDx scanner using 8-channel phased array head coil for receive, body coil transmit. The repeated measurement provided additional robustness to volunteer movement compared to a single long scan, and reduces variability in the data associated with peak integration. GABA concentration was calculated relative to the internal standard provided by the unsuppressed water signal. Whole brain FSPGR images (1 mm isotropic resolution) were also acquired for colocalisation to the MEG data and to quantify cortical thickness and volume. 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[3] 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.

Results

The visual paradigm elicits a sustained reproducible response at a range of frequencies in this cohort (40 – 66 Hz), as shown for one volunteer in the frequency power plot below left (44 Hz sustained response shown by white line). Localisation of this signal to the occipital lobe is shown below centre with the acquired MRS voxel (green). High-quality edited MRS spectra (e.g. below centre right) were acquired in each volunteer. There is a strong correlation between the frequency of this visual gamma response and GABA concentration (below right).



No correlation was found between gamma frequency and Glx (combined glutamine and glutamate) concentration, occipital grey matter volume, cortical thickness or gamma amplitude. No correlation was found between gamma amplitude and GABA or Glx concentration, or the structural measures.

Discussion

This result clearly demonstrates the possibilities arising from the combination of the non-invasive biochemical measurements of MRS and direct detection of neuronal events by MEG for studying the nature and origin of neuronal oscillations. The MRS-MEG approach can be easily transferred to patient populations for the study of disease processes and treatment efficacy. Mechanistically, it has been suggested that gamma oscillations in visual cortex are generated in local re-entrant networks of neurons, including GABAergic inhibitory interneurons. The findings presented here support this conclusion, and suggest that MRS and MEG can combine to give important information regarding excitation-inhibition balance in cortex. Further work is planned to investigate whether the same relationship holds in patients with epilepsy and whether pharmaceutical modulation of GABA also effects gamma oscillation frequency.

References 1. Mescher et al. *NMR Biomed* (1998) 266. 2. Epperson et al. *Arch. Gen. Psych.* (2002) 851 3. Robinson & Vrba, *Rec Adv Biomagnetism* (1999) 302.