GABA concentration in frontal eye field predicts oculomotor distractibility

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Introduction

Inhibitory neurotransmission cannot be generally mapped onto behavioural inhibition, however in the area of motor planning for eye movements, there is clinical and pharmacological evidence that the two processes are closely linked (e.g. [1,2]). In this study, we combine edited MRS measurements of GABA, the principle inhibitory neurotransmitter in the human brain, with behavioural psychophysics to measure eye movement distractibility. Both eye movements[3] and GABAergic neurotransmission[4] are known to be altered in a number of neurological disorders; this study develops the necessary multimodal tools to investigate whether the two observations are causally linked, demonstrating for the first time a correlation between a behavioural measure and GABA within an fMRI-localised, functionally relevant brain region.

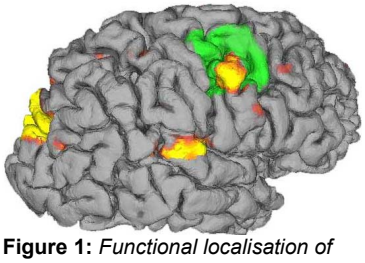

Figure 1: *Functional localisation of FEF and GABA MRS voxel.*

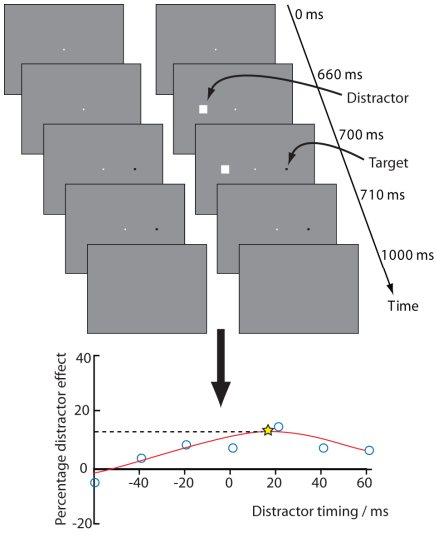

Figure 2: *Distractor task (above) and fitting of typical behavioural results to determine the maximum distractor effect.*

Methods

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

MR Imaging and Spectroscopy

Eye movement planning is carried out in the frontal eye fields (FEF), bilateral regions close to the junction of the superior longitudinal sulcus and the precentral sulcus (see activation in Figure 1). In order to plan MRS measurement in the region of functional interest, a BOLD-fMRI localiser was used to locate FEF. A 10-minute lateral tracking task (15s moving; 15s fixation) was used; imaging parameters: (1 mm)^2 in-plane resolution, 3 mm slices (to facilitate co-registration with anatomical landmarks for MRS planning); TR 1.5s TE 80 ms. A (1mm)^3 isotropic resolution, T1-weighted FSPGR was carried out to allow segmentation of the MRS voxel and reconstruction of the cortical surface. A MEGA-PRESS spectrum was acquired of a (3 cm)^3 volume centred on FEF and an occipital control volume; parameters: TE 68 ms; TR 1.8s; editing pulse length 16ms applied at 1.9 ppm and 7.5 ppm; acquisition time 10 min.

Psychophysics

Participants were instructed to fixate centrally, and to look at the black square (target) when it appears, ignoring the white square (distractor; see Figure 2). Stimuli were presented and eye movements recorded using a CRS visage and video eyetracker. Trials in which the participant looked at the distractor (errors) or made a two-step saccade to the target were omitted from the latency analysis. Relative timings of the distractor and target were sampled from -60 to +60 ms, to obtain the peak distractor effect (the percentage increase in response time of the trials with a distractor over those without, yellow star in Fig 2)[5].

Results

The functional localiser allowed right FEF to be located in all 12 participants and high-quality edited MRS spectra were acquired in each case (e.g. Figure 3). GABA concentration was quantified in institutional units using the unsuppressed water signal from the same volume as an internal standard. The MRS voxel was overlaid on the segmented, structural MRI and a concentration correction was made for the voxel CSF percentage (which ranged from 6% to 12%). Behavioural measurements of the distractor effect correlated strongly with GABA concentration in FEF ($p = 0.001$; see Figure 3) but not the occipital control region, demonstrating the functional specificity of the MRS measurement.

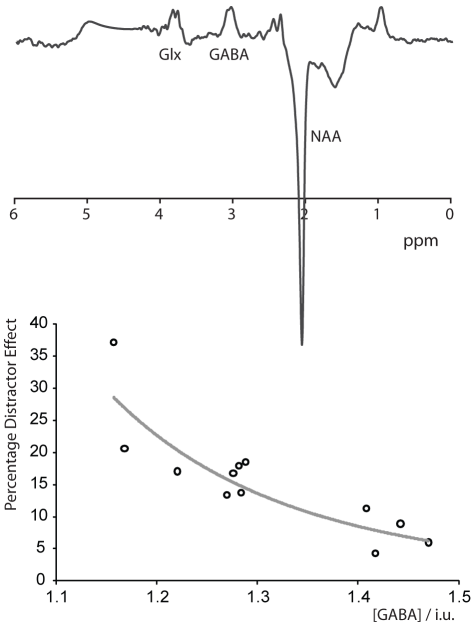

Figure 3: *Typical edited MRS spectrum (above) and correlation of GABA concentration and distractor effect (below) showing top-down reactive inhibition model.*

Conclusion

This novel study combines edited MRS with a functional localiser for the first time to measure GABA in a volume of interest related to a specific process. This is the first study to investigate GABA concentration in the region of human FEF, and there have been no published studies combining MRS of GABA with behavioural psychophysics to investigate the relationship between behavioural inhibition and GABA concentration.

This study has demonstrated a strong correlation between GABA concentration and a low-level property, oculomotor distractibility. This approach is currently being developed for applications in schizophrenia, a disorder in which oculomotor abnormalities are widely reported. The direction of the correlation between GABA and the distractor effect, i.e. high GABA corresponds to low distractibility, is interesting, associating individual differences in GABA with top-down suppression of distractor activity, rather than mutual inhibition between regions of target and distractor activity.

References

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