Motor Control Predicted by GABA Concentration in the Supplimentary Motor Area

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Introduction

The concentration of inhibitory neurotransmitter GABA in functionally-relevant brain regions has been demonstrated to predict participants' performance in visual behavioural tasks(1,2). In this work, we demonstrate that participants performance on motor reaction-time task is related to GABA concentration in the supplementary motor area (SMA) – a region previously associated with the inhibition of motor planning (3,4) – but is not correlated to the GABA concentration in other brain regions.

We used a visual priming paradigm; in which participants' reaction times to target stimuli are delayed by another stimulus presented below conscious perception (Fig 1) - an effect known as the Negative Compatibility Effect (NCE).

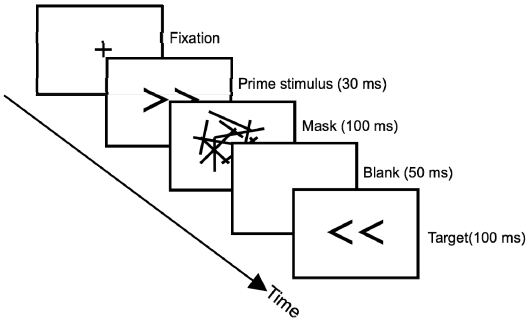

Figure 1: *The masked priming paradigm.*

Methods

Two experiments were performed: (i) *N*=12, all male, aged 21-32 (ii) a replication in an independent cohort, *N*=13, all male, aged 19-35 years. Local ethics committee approved all procedures.

MRS: All MRS measurements were performed on a 3T GE HDx, with body coil transmit and an 8-channel head coil. GABA levels (GABA+coedited macromolecules) were measured using a MEGA-PRESS editing sequence(5), (TR/TE = 1800/68ms, 400 transients). Data were acquired from 3x3x3cm^3 voxels in the following regions: SMA, dorsolateral prefrontal cortex (DLPFC) and parietal lobe. In each session, a 1mm isotropic T_1-weighted structural image was acquired. All spectra were processed using locally written Matlab software. A model with Gaussian, linear and constant baseline terms was fitted to the 3ppm GABA peak over the region 2.81-3.55ppm, and the integral under the Gaussian component calculated. The unsuppressed water signal was used as an internal concentration reference. Structural scans were segmented using *FSL FAST* and the GABA integral was scaled to account for fraction of CSF within each voxel.

Behavioural Paradigm: Participants were asked to indicate whether target stimuli (Fig 1) were left or right pointing arrows by pressing a button, and reaction times were measured.

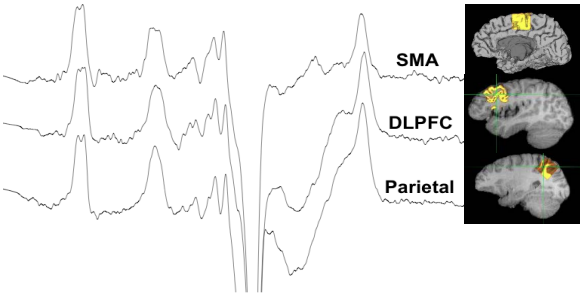

Figure 2: *Typical MEGA-PRESS GABA spectra and the corresponding voxel positions.*

Results

Representative spectra from a single participant are shown in Fig 2, demonstrating excellent spectral quality for the three regions studied. Fig 3 shows the correlation between GABA and magnitude of the NCE (the reaction time delay for a compatible prime stimulus) for all participants. There is a significant correlation for both cohorts – demonstrating that this is a robust finding. No correlation was found between GABA and the NCE in either the DLPFC or the parietal lobe, for either cohort. In this group of young, healthy participants, no correlation was found between GABA in the SMA and age or grey matter.

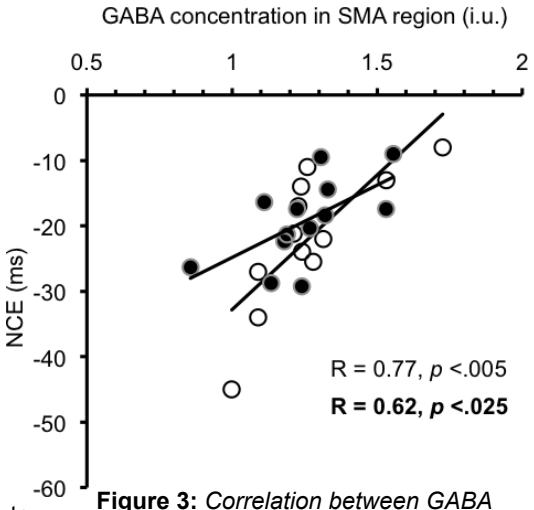

Figure 3: *Correlation between GABA (institutional units) and NCE (the reaction time delay, ms). White circles: experiment 1, black circles: experiment 2*

Discussion

As the brain's major inhibitory neurotransmitter, GABA is a likely candidate to mediate the *behavioural* inhibition reflected in the NCE. This work demonstrates that the magnitude of an individual's NCE when responding to stimuli is related to their GABA concentration in the SMA.

References

[1] Edden et. al., 2009, *J Neurosci.*, 29 15721; [2] Sumner et. al., 2010, *Nature Neuroscience* 13 825; [3] Sumner et. al., 2007, *Neuron*, 54 679 [4] Boy et al, 2010, Experimental Brain Research, 206 441; [5] Mescher et. al., 1998, *NMR Biomed*, 11 266