

Area-Specific GABA Concentration Predicts Tactile Discrimination Performance In Humans

R. A. Edden¹, N. A. Puts², C. J. Evans³, and D. J. McGonigle^{2,3}

¹Russell H Morgan Department of Radiology and Radiological Science, The Johns Hopkins University, Baltimore, MD, United States, ²School of Biosciences, Cardiff University, Cardiff, United Kingdom, ³CUBRIC, School of Psychology, Cardiff University, Cardiff, United Kingdom

Altered somatosensory perception is an important aspect of several neuropsychiatric disorders in which abnormal GABAergic neurotransmission is proposed to play a role, such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (AD/HD)¹. We have recently shown that, in the visual domain, orientation discrimination performance correlates with GABA concentration in the occipital lobe². In this study, we investigate the relationship between somatosensory discrimination and GABA, using MEGA-PRESS MRS to measure GABA concentration in sensorimotor cortex and tactile psychophysics to determine the threshold of frequency discrimination to vibrotactile stimuli in healthy adults.

Hypothesis: Vibrotactile frequency discrimination thresholds will correlate with GABA concentration in the sensorimotor region, and not in the occipital control region.

Methods

15 healthy subjects (9 male) aged 27.3±4.35 years were recruited to this study with local institutional ethics committee approval. All subjects were right handed and had no history of neurological disorder.

MRS Edited MRS measurements of GABA were made in a (3x3x3) cm³ 'sensorimotor' volume centred on the right hand knob³, and a midline occipital control region, as shown in Figure 1. MEGA-PRESS sequence parameters were: TE 68ms; TR 1800 ms; 16 ms Gaussian editing pulse applied alternately at 1.9 and 7.46 ppm (ON and OFF experiments); 320 transients; 2k datapoints; 2 kHz spectral width. GABA concentration in 'institutional units' was quantified from the ratio of the integral of the edited GABA signal (determined by fitting to a Gaussian model) to the integral of the unsuppressed water signal from the same volume (determined by fitting to a Lorentzian-Gaussian model) and a constant multiplier used to account for differences in T1 and T2 relaxation times of water and GABA and the editing efficiency. In addition, GABA levels were controlled for amount of GM, WM and CSF.

Tactile Psychophysics The frequency discrimination task is shown in Figure 1c. Vibrotactile stimulation was delivered using a piezoelectric stimulator. A static surround limited stimulation to the region directly contacted by the 8mm diameter tip (the left index finger, LD2). Subjects were asked to determine which of two stimuli was higher in frequency in a two alternative forced choice (2AFC) design with paired estimated stepwise tracking algorithm (PEST) to determine the frequency discrimination threshold of 75% correct across two tracks. In each trial, one of the frequencies was always 25Hz (50% chance) and the other stimulus either higher or lower. 50 trials per track were completed in a total measurement time of approx. 15 min. Discrimination performance was quantified by the Weber fraction (a measure of discrimination ability; $\Delta f/f$), calculated as the average last 20 trials across tracks.

Results

Good quality edited MRS spectra were acquired in all 15 subjects. Discrimination performance is shown to correlate significantly ($r=0.58$, $p<0.02$) with GABA concentration in sensorimotor cortex, with higher GABA concentrations occurring in subjects with the best vibrotactile discrimination thresholds. As predicted, there was no relationship ($r=0.04$, $p=0.44$) between GABA in the control region and behavior.

Discussion

This is the first time that individual differences in GABA concentration in sensorimotor cortex have been shown to correlate with any facet of tactile function, and suggests that GABA is an important driving force in controlling the fidelity of vibrotactile representation in early somatosensory cortex. In addition, the finding that there is no relationship between GABA in occipital cortex and tactile discrimination show that this relationship is region-specific. Given the interest in somatosensory deficits, particularly in developmental disorders such as ASD, this is a significant result.

References 1. Tommerdahl et al. *Neurosci Biobehav Rev* 34: 160 (2010)
2. Edden et al. *J Neurosci* 29:15721 (2009). 3. Evans et al. *JMRI* 31:204 (2010).

