

Regional Variations in GABA Measured with MEGA-PRESS

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Introduction

GABA, the main inhibitory neurotransmitter, has been implicated in many disorders, e.g. depression (review in 1), schizophrenia (review in 2), and correlates with the performance of individuals on a variety of behavioural tasks (3,4). However, most studies measure GABA in a single area, or occasionally in a region of interest plus a control area, thus there is sparse literature on the natural variation in GABA levels across the brain in healthy controls. In this work we report the findings from a study measuring GABA in six different brain regions, within the same participant group, demonstrating that there are significant differences in GABA levels across the brain. Our data show a correlation in GABA between motor and parietal regions, but weak (or absent) correlations between other regions.

Methods

MRS: All MRS measurements were performed on a 3T GE HDx. GABA levels (GABA+macromolecules) were measured using a MEGA-PRESS editing sequence (5), (TR/TE = 1800/68ms, 400 transients). The six areas were studied (Fig 1); inferior frontal gyrus (IFG), dorsolateral pre-frontal cortex (DLPFC), supplementary motor area (SMA), parietal lobe, occipital lobe (all 3x3x3cm³), and anterior cingulate cortex (ACC) 2.5(SI)x3(LR)x4(AP) cm³. In each session, a 1mm isotropic T₁-weighted structural image was acquired. **Analysis:** All spectra were processed using locally written Matlab software. GABA levels were calculated from a fit of the 3ppm peak, with unsuppressed water used as an internal concentration reference. The GABA level was scaled to account for fraction of CSF within each voxel. For each voxel, the tissue fraction of grey matter, f_{GM} , was calculated.

Participants: Two cohorts of participants were scanned, all male aged 19-35. Cohort 1, N=12: data from all six MRS voxels acquired in two sessions; cohort 2, N=12: data from three voxels (SMA, IFG, parietal) acquired in a single session. Local ethics committee approved all procedures.

Results

Mean GABA and grey matter fractions for each voxel, along with number of scans for the region are reported in Table 1. Fig. 2 shows all spectra included in the study, by region. Three spectra were excluded due to participant motion. The baseline fluctuations in the DLPFC and parietal spectra are not reflected in increased variance in the data in these voxels. The scatter plot of the participants' GABA levels (both cohorts) is shown in Fig 3. Analysing the whole dataset (both cohorts) using a 2-way ANOVA (voxel location, voxel grey matter fraction), showed a significant effect of voxel location ($F=2.9$, $p<0.02$, $df=5$), and of grey matter fraction ($F=5.7$, $p<0.02$, $df=1$). Correlating between all regions (in the first cohort) yielded significant correlation between SMA and parietal GABA ($p=0.003$, significant after correcting for multiple comparisons).

Discussion

This study is the first to measure GABA using a single-voxel technique in six regions of the brain. The results demonstrate that there are regional differences in GABA, which cannot be explained by differences in grey matter between these regions. However, this result is strongly driven by the low GABA measured in the IFG. We measured a significant correlation between GABA in SMA and parietal lobe across participants. Interestingly, correlations between GABA levels in other regions are weak or absent, even in voxels with some overlap (e.g. SMA-ACC, DLPFC-IFG).

References: [1] Croarkin et al., 2010, Neuroscience and Biobehavioral Reviews, [2] Lewis, D.A, 2005, et. al. Nat. Rev. Neurosci. 6, 312-324, [3] Edden et. al., 2009, J Neurosci., 29 15721; [4] Sumner et. al., 2010, Nature Neuroscience 13 825; [5] Mescher et. al., 1998, NMR Biomed., 11 266

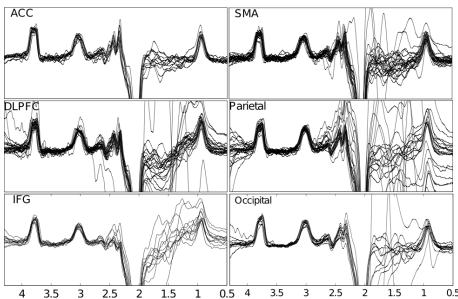


Figure 2: All GABA spectra

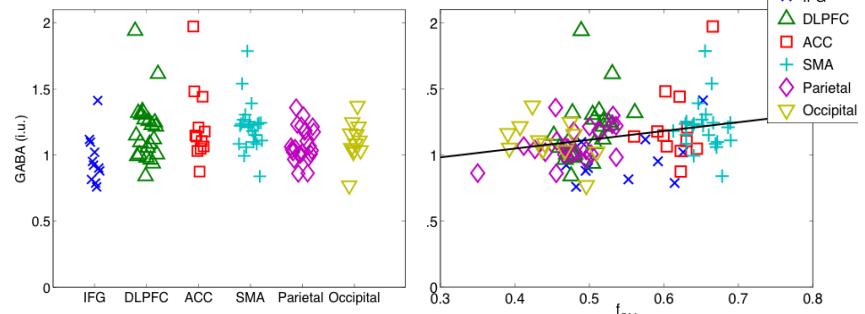


Figure 3: GABA levels (institutional units, i.u.) for all individuals, by region

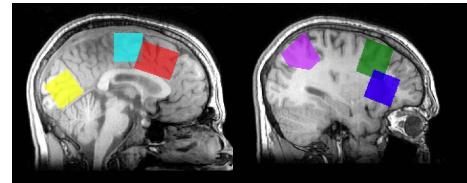


Figure 1: Voxel positions. Blue-IFG; green-DLPFC; purple - parietal; red-ACC; blue-SMA, yellow-occipital

Region (N)	GABA (i.u.) Mean±StDev	f_{GM} Mean±StDev
IFG (11)	0.97±0.19	0.55±0.07
DLPFC (23)	1.23±0.29	0.50±0.03
ACC (12)	1.22±0.29	0.61±0.03
SMA (24)	1.21±0.19	0.65±0.02
Parietal (23)	1.08±0.13	0.48±0.04
Occipital (12)	1.10±0.15	0.45±0.04

Table 1: Mean GABA levels and grey matter tissue fractions, by region