Frontal and Occipital Lobe GABA Changes in Depression, Measured with 1H-MRS

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Introduction

Previous studies have measured reductions in the concentration of the inhibitory neurotransmitter γ-aminobutyric acid, GABA, in the occipital lobes of subjects with depression [1]. These changes have not been observed in the frontal lobes of recovered depressed subjects [2], even though this region is closely related to mood disorders, suggesting regional variations in GABAergic function in depression. However, it is difficult to generalise the current data in literature due to potential variations in the patient groups. The aim of this study was to measure the GABA concentrations of healthy controls and recovered depressed subjects in the frontal and occipital lobes to investigate both regional variations and differences between the subject groups.

Methods

22 subjects were scanned on a 3T Varian INOVA system, with Magnex head gradient and a head-only transmit/receive birdcage rf coil. The subject groups comprised of 11 recovered depressed (RD) subjects and 11 healthy controls (C). All subjects in the RD subject group had suffered from an affective illness in the past, but were euthymic and medication free for a period of at least 3 months prior to the time of the study. Standard PRESS spectra were acquired at TE=26ms and 68ms for quantification. GABA measurements were made using a MEGA-PRESS sequence [3] for voxel localisation, water suppression and editing of the 1.9ppm GABA resonance, to reveal the GABA+ peak at 3ppm while suppressing the overlapping Creatine (Cr) singlet (TR=3s, TE=68ms, 128 averages, ~7min acquisition time). As the GABA+ peak can contain up to 50% macromolecular contamination, spectra were acquired with an additional inversion pulse before the MEGA-edited sequence to null the metabolite signal, providing an estimate for the macromolecular contribution to the peak at 3ppm. All spectra were analysed with LCmodel [4] using phantom-generated basis-functions for the PRESS and MEGA-edited spectra. Typical occipital lobe spectra from control subjects are shown for PRESS (Fig. 1A) and GABA-edited (Fig. 1B) sequences. 3D T_1-weighted structural images were acquired in a subset of subjects to quantify the grey matter fraction within the occipital and frontal lobe MRS voxels of the subjects.

Results

The GABA/Cr ratios were significantly lower in the recovered depressed subjects than in controls (p=0.04), and were significantly lower in the frontal lobe voxel than in the occipital lobe (p<0.01). The interaction between voxel position and subject group was not significant (p=0.70). Age was a significant covariate (p<0.01) but there were no significant effects of gender nor grey matter voxel content on the results.

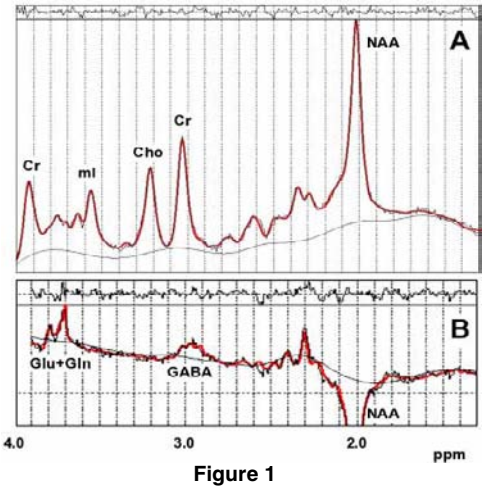

Figure 1

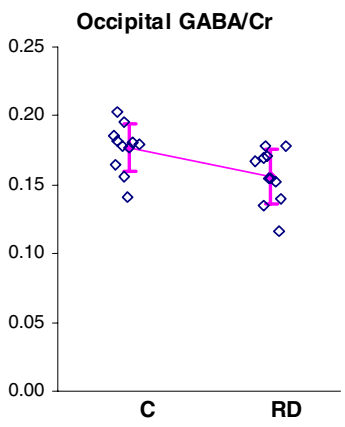

Figure 2

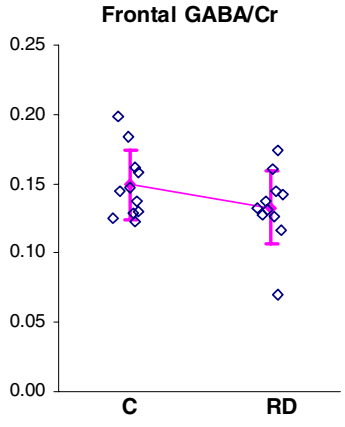

Figure 3

Discussion

The previously reported decrease in the GABA levels of depressed subjects [1] was replicated in this study. The mean GABA/Cr of the RD subjects was 11.3% lower in occipital lobe and 11.4% lower in the frontal lobe, and there was no statistical interaction observed between voxel position and group in our analysis. These data suggest that the reduced GABA/Cr levels in the occipital lobes of depressed subjects are accompanied by similar changes in the frontal lobes.

References

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[3] Mescher *et al*, NMR Biomed. 11, 266 (1998) [4] Provencher, Magn. Res. Med. 30, 672 (1993)