Differences in GABA to Creatine ratio between the Occipital and the Medial Pre-Frontal Cortices

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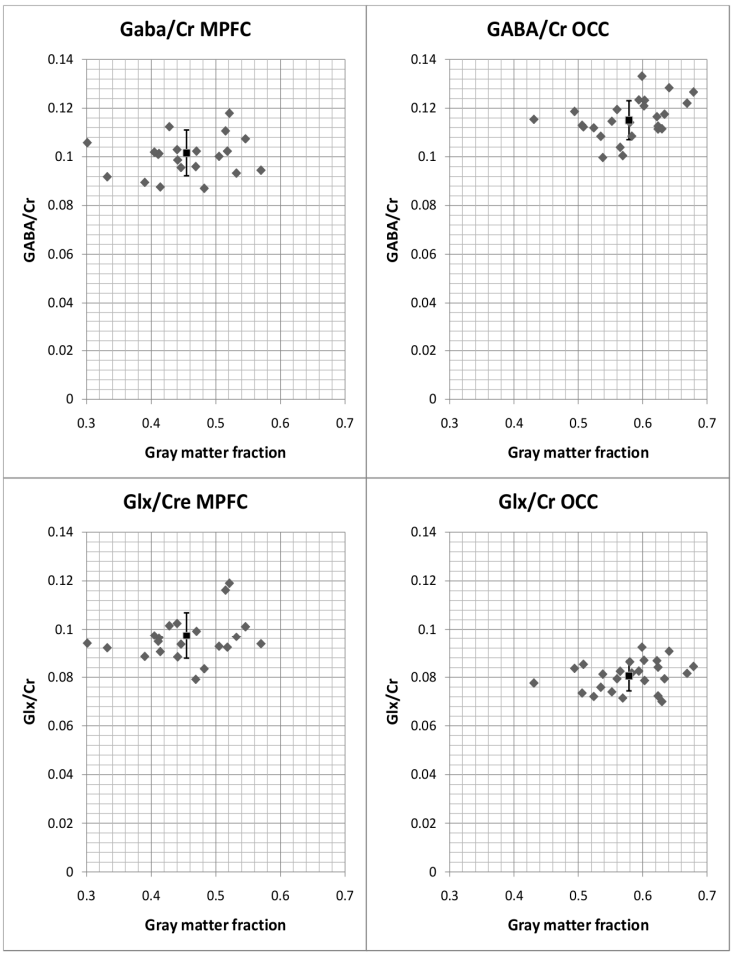
Introduction: Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in the CNS which is believed to be involved in a variety of psychiatric and neurological disorders. GABA can be measured using proton MRS with a PRESS-based two step editing sequence (1-4). Initially only the occipital lobe GABA was measured. Recently GABA measurement has been extended to the frontal lobe (5-7). The frontal lobe is considered to be more directly connected to psychiatric disorders. To compare the results of these two regions we examined the differences in GABA/creatine ratio between the occipital cortex (OCC) and the medial pre-frontal cortex (MPFC).

Methods: All experiments were performed on a 3 Tesla GE whole body scanner (GE, Milwaukee, WI) running on the 14M4 platform. A Medical Advances (Intermagnetics General Corporation) RF coil (transmit/receive, 25cm id) was used. The scan started with an anatomical scan to be used for tissue segmentation using MPRAGE (spoiled gradient echo, TE = 2.1 ms, inversion-recovery delay 725ms, flip angle 12 degrees, FOV 22cm, and slice thickness 1.2mm). A voxel (S/I = 20 mm, R/L = 30 mm, A/P = 30 mm) was placed along the midline in the frontal lobe and anterior to the ventricles (n=23). A second voxel (S/I = 30 mm, R/L = 30 mm, A/P = 30 mm) was placed along the midline in the occipital lobe and superior to the cerebellum (n=28). The GABA editing pulse sequence was modified from a standard PRESS sequence (4). NS = 512, TR/TE = 3000/68 ms, NEX = 2. The editing pulse (14.4 ms, $\gamma B1max$ = 160 Hz) has a top-hat frequency profile with a bandwidth spanning the 2.2 ppm – 0.6 ppm range (4) covering both GABA β-H2 and M4. The GABA editing pulse was switched on and off during even- and odd-numbered scans. A total of 512 edited and non-edited FID pairs were acquired for a total of 26 minutes.

The anatomical MPRAGE scan was segmented using SPM5 (Wellcome Trust Centre for Neuroimaging, UCL, UK) and a homewritten macro used the voxel coordinates to calculate the gray matter, white matter, and CSF fractions of the voxel. GABA data were processed in two steps. First, NAA, Cre, and Cho were fitted in the unedited spectrum. Then the GABA (3.0 ppm) and the co-edited Glx (3.74 ppm) signals were fitted in the subtracted data using position and linewidth information from the unedited spectrum. GABA and co-edited Glx to Cre ratios were plotted as a function of gray matter fraction.



Results and Discussion: Figure 1 shows the GABA/Cre and the co-edited Glx/Cr ratios for the MPFC and OCC areas as a function of gray matter fraction. The editing pulse co-edits a fixed portion of Glx H2 protons at 3.74 ppm which can be used to evaluate Glx (5, 6). The OCC voxel has a higher ($P<0.001$) gray matter fraction, 0.58 (stdev=0.064) than that of the MPFC 0.46, (stdev=0.068). Both GABA/Cr and co-edited Glx/Cr and are significantly ($P<0.001$) different between the two different voxels. The average GABA/Cr ratio is 0.102 (stdev=0.0094) in the MPFC and 0.115 (stdev=0.008) in the OCC. The average co-edited Glx/Cr ratio is 0.0974 (stdev=0.0095) in the MPFC and 0.0806 (stdev=0.006) in the OCC. Since the reported difference in Cre between frontal and occipital lobes (8) are much greater than the corresponding difference in GABA/Cre ratios found in this study we expect that both GABA and Glx are significantly different between MPFC and OCC. Absolute quantification using water as a reference is currently in progress.

Figure 1. GABA/Cre and the coedited Glx/Cr ratios for the MPFC and OCC areas as a function of gray matter fraction. Diamonds represent data from individual subjects; squares and bars represent mean and standard deviation.

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