In Vivo Detection of Gray and White Matter Differences in GABA Concentration in the Human Brain using Chemical Shift Imaging of GABA

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INTRODUCTION

GABA is the major inhibitory neurotransmitter for normal brain function and its dysfunction has been associated with many psychiatric and neurological disorders. Assessment of regional alterations of GABA concentration should greatly aid the diagnosis of these diseases. GABA may also serve as a surrogate marker for monitoring treatment efficacy, particularly that related to GABAergic drug treatments. However, due to high technical challenges, the development of *in vivo* chemical shift imaging (CSI) of GABA has been very limited without any clinical applications published so far (1). *In vivo* GABA CSI using selective multiple quantum (MQ) filtering methods (1) enables us to investigate its *in vivo* regional distribution e.g., gray and white matter differences as suggested by previous autopsy and biopsy studies. Therefore, we sought to develop a selective MQ GABA CSI in combination with a circularly polarized ^{1}H RF coil (2) to enable the measurements of GABA in regions other than the occipital lobe where most of GABA measurements were performed.

METHODS

Ten healthy subjects were studied (31 ± 9 years old, mean ± SD) on a 3 Tesla whole-body SMIS system using a helmet coil with several of them being scanned multiple times. The ^{1}H GABA CSI sequence is based on a single shot selective MQ filtering method. During MQ preparation period, a double-band spectrally selective 180^o pulse was used for improved selection of GABA-4 (3.0 ppm) and GABA-3 (1.9 ppm) (2,3). For *in vivo* studies, T_1-weighted images were acquired using an MPRAGE sequence. The T_1-weighted images were used to calculate the gray and white matter ratio of the CSI voxels. The CSI slice was positioned across prefrontal to parietal lobe. The MR parameters for GABA CSI were FOV = 18 cm x 18 cm, Slice thickness = 3 cm, 6 x 6 PE steps, nt = 20-30. *In vivo* GABA concentration was estimated by the external reference method using a phantom with known concentrations of GABA. For each subject, B_1 map was acquired using a dual excitation gradient echo sequence (4) to correct B_1 inhomogeneity for each voxel. The CSI slice was shimmed using an automatic slice shimming method, which corrects all first- and second-order in-slice shims and the first-order through slice shims to ensure a uniform B_0 field across the CSI slice (5,6).

RESULTS AND DISCUSSION

Figure 1 shows a partial view of an *in vivo* axial GABA image of the human brain at 3 Tesla overlaid on the T_1-wighted anatomical MPRAGE image. Clear GABA doublets were observed throughout the slice as seen from those in the single-voxel measurements (2). Similar results were obtained from all human subjects. To the best of our knowledge, this is the first report of a GABA CSI with the MQ filtered GABA peaks at 3.0 ppm appeared as doublets, indicating complete suppression of overlapping Cr, glutathione throughout the entire GABA CSI slice and the first report of detection of GABA concentration distribution between gray and white matters in the living brain. Based on our single voxel measurements using the same sequence without the phase-encoding gradients, the contamination from overlapping macromolecules should be minimal. As shown in Fig. 1, the position of the GABA doublets are well-aligned indicating excellent B_0 homogeneity achieved across the CSI slice, consistent with that of the corresponding Cr CSI map and the phase map (data not shown).

As shown in Fig. 1, the GABA doublet intensity is consistently larger in the voxel with more gray matter than that in the voxel of similar B_1 profile and with more white matter. A preliminary quantitative analysis of the GABA distribution was shown in Fig. 2 using the external reference method. Clearly from Fig. 2, GABA is more concentrated in the gray matter than in the white matter, consistent with autopsy findings and those using surgically removed brain tissues. Based on the quality of the data achieved in this report, we expect that GABA CSI will soon become a very valuable tool for investigating GABAergic function in normal brain and in a variety of psychiatric and neurological diseases.

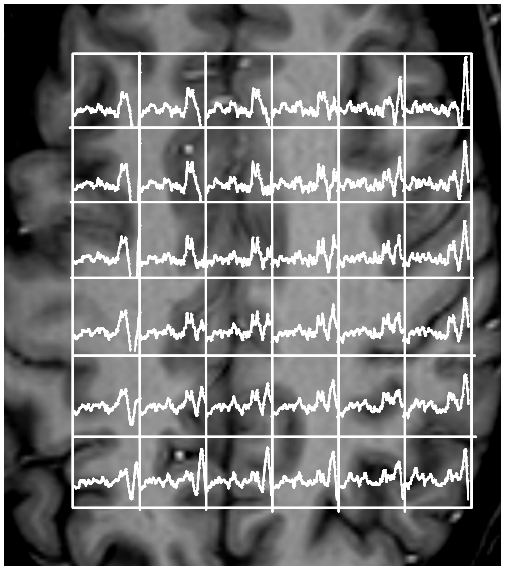

Fig. 1 GABA CSI of the human brain *in vivo* at 3 Tesla.

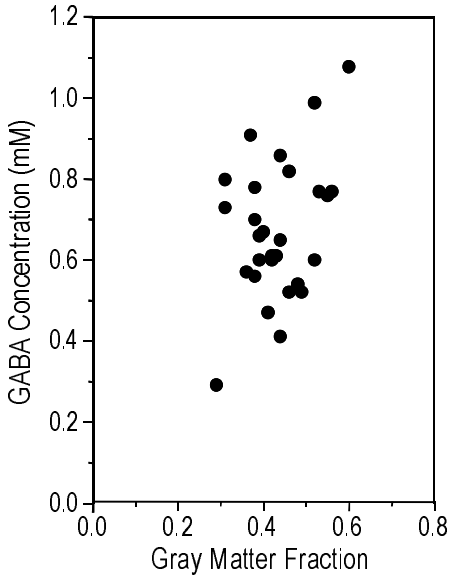

Fig. 2 GABA concentration plot as function of percentage gray matter from each CSI voxel.

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