SLIM-based Multiple Quantum Chemical Shift Imaging for the Measurement of GABA in the Human Brain In Vivo

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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. Based on data from postmortem studies, the GABA levels in the human brain are heterogeneous (e.g., different lobes, gray/white matter differences) and a GABAergic defect and lowering in GABA concentrations in disease are region/tissue-type specific. Therefore, assessment of regional alterations of GABA concentration is of importance for the diagnosis and treatment of the diseases. To characterize the metabolite concentration difference in gray and white matters in the human brain, the application of single voxel techniques has been rather limited due to the difficulties in the selection of pure gray or white matter. The difficulty has been overcome by the use of CSI techniques in conjunction with tissue segmentation methods. We have recently developed *in vivo* GABA CSI using selective multiple quantum (MQ) filtering methods [1, 2] and demonstrated for the first time gray and white matter differences of GABA in the human brain *in vivo*. In this study, we further develop the GABA CSI technique into a SLIM-based [3] GABA CSI for rapid assessment of GABA distribution in the living human brain.

METHODS: Seven healthy subjects were studied (30 ± 9 years old, mean ± SD) on a 3 T SMIS system using a helmet circularly polarized ^{1}H RF coil. The SLIM-based MQ GABA CSI sequence is based on the selective MQ GABA CSI [2]. The gray/white matters and CSF compartments for SLIM were generated by an automatic segmentation algorithm, FAST software in the FSL package (Oxford University, Oxford, UK), from high-resolution 3D MPRAGE images (FOV = 20 × 20 × 15 cm^3, matrix = 256 × 160 × 120, TI = 1.1 s, TR/TE = 12/5 ms). The SLIM reconstruction was performed using an in-house written IDL program. For *in vivo* studies, the CSI slice was positioned across the prefrontal to parietal lobes. The MR parameters for GABA CSI were FOV = 20 x 20 x 6 cm^3, effective slice thickness = 3 cm, matrix = 4 x 4 x 4, nt = 16. *In vivo* GABA concentration was estimated by the external reference method by comparing the *in vivo* signal intensity to that of *in vitro* with known concentrations in the solution phantom. 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 [4, 5].

RESULTS AND DISCUSSION: The SLIM-based MQ GABA CSI technique was tested on a tri-compartment phantom sample containing solutions of GABA (A: 100 mM, B: 25 mM, C: 50 mM). Figure 1 shows spectra of a compartmented solution phantom reconstructed using the SLIM-based MQ GABA CSI technique. Compartmental boundaries are shown in the MR image (left) and localized spectra were reconstructed for each compartment. Various GABA concentrations in each compartment were well reflected in the peak integration of GABA at 3.02 ppm (Fig. 1 right). Since the MQ filtering method was used, singlets such as creatine signals at 3.03 ppm and 3.93 ppm were completely suppressed. Minimal spectral leakage among compartments was demonstrated with the well-localized lactate signal in the compartment C (Fig. 1C).

GABA levels in the GM and WM were measured from 29.5 ml and 47 ml volumes, respectively (Fig. 2A). The GABA doublet intensity is consistently larger in the volume with gray matter (Fig. 2A top) than that of white matter (Fig. 2A bottom). As can be seen from the segmented brain images in Fig. 2, it is difficult to assess GM and WM contributions to GABA accurately using conventional 2D CSI, especially since coarse spatial encoding is necessary due to the low concentration of GABA. As demonstrated by Figs 1 and 2, with prior knowledge of the boundaries of gray matter, white matter and CSF compartment from the segmented images, SLIM reconstruction allow determination of the mean concentration of GABA in gray and white matters without the necessity to use very high resolution CSI. SLIM requires far less phase encoding steps than conventional k-space based CSI methods. Because the overall size the gray and white compartments are relatively larger than the voxel size in conventional CSI, SLIM allows for rapid measurement of the concentrations of GABA in gray and white matters.

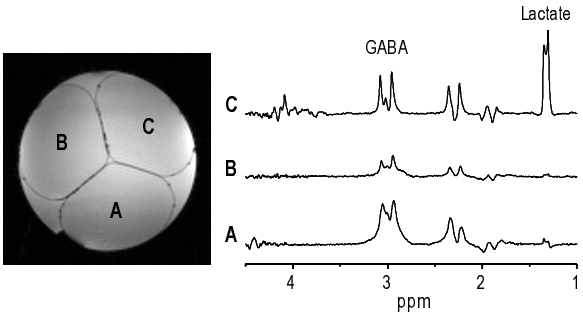

Fig. 1 Spectral reconstruction using MQ SLIM in solution phantoms. (A) Spectra were reconstructed for a phantom containing GABA 100 mM, (B) GABA 25 mM and creatine 50 mM (C) GABA 50 mM and lactate 50 mM.

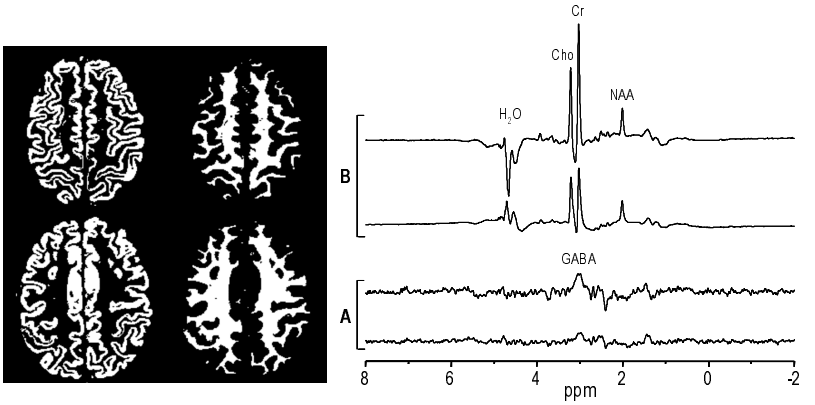

Fig. 2 SLIM-based MQ GABA CSI of the human brain *in vivo* at 3 T. Image segmentation of the human brain in two different slices. (A) *In vivo* GABA measurements from the gray (top) and white (bottom) matters. (B) The corresponding Cr measurements from the gray (top) and white (bottom) matters.

REFERENCES

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