# Measurement of Heterogeneous Distribution of GABA in Gray and White Matters in the Human Brain using Selective Multiple Quantum Chemical Shift Imaging of GABA

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## INTRODUCTION

GABA is the major inhibitory neurotransmitter in the mammalian central nervous system. The importance of the role of GABA has been suggested in normal brain function and its dysfunction has been associated with many psychiatric and neurological disorders (1). Heterogeneous distribution of amino acids throughout the brain is well recognized even though the mechanisms and functional significance have yet to be elucidated. Particularly, the difference in GABA concentration is known to be up to over 20-folds in the human brain based on postmortem biochemical analysis (2). Assessment of regional alterations in GABA concentration should be very useful in characterization of brain diseases and to monitor their progression and the efficacy of treatment targeting GABAergic mechanism. Therefore, we sought to measure the distribution of GABA in gray and white matters in the human brain *in vivo* using our recently developed selective multiple quantum (MQ) filtering GABA CSI method (3,4). The selective MQ GABA CSI method has been further developed for simultaneous detection of multiple quantum filtered GABA and single quantum creatine (Cr) signals using a two-echo acquisition scheme (5).

## METHODS

Thirteen healthy subjects were studied (31 ± 11 years old, mean ± SD) using a 3 T whole-body SMIS system and a helmet coil (6). The $^1$H GABA CSI sequence is based on a single-shot two-echo selective MQ filtering method (STEMS) (5). The simultaneously measured Cr singlet served as a navigator for the spectral phase of GABA and any frequency shift during measurements, and as an internal concentration reference. In addition, a double-band spectrally selective 180$^o$ pulse was used during MQ preparation period for improved selection of GABA-4 (3.0 ppm) and GABA-3 (1.9 ppm). The gray and white matter ratio in the CSI voxels was calculated using $T_1$-weighted images acquired using an MPRAGE sequence. The CSI slice was positioned across the prefrontal-parietal lobes. MR parameters used for GABA CSI were FOV = 20 cm x 20 cm, Slice thickness = 3 cm, 8 x 8 PE steps, nt = 8. *In vivo* GABA concentration was determined using an internal reference method and the simultaneously measured Cr signal from the second echo as described below. Automated slice shimming was used to adjust all first- and second-order shims to ensure a uniform $B_0$ field across the CSI slice (7,8). Gray matter fraction of each voxel was obtained from segmented 3D-MPRAGE images. Peak integration was performed using an in-house peak fitting routine written in IDL. The GABA-to-Cr concentration ratio was calculated using integrated peak intensity ratio and a correction factor obtained from phantom calibrations. GABA concentrations in gray matter and white matter were calculated using a nonlinear least square fit of the ratio data to the equation, $[Gb]/[Cr] = \{f_G [Gb]_G + (1-f_G)[Gb]_W\}/\{f_G [Cr]_G + (1-f_G)[Cr]_W\}$, where [Gb] and [Cr] are concentration of GABA and Cr, and subscript G and W indicate gray and white matter, respectively. $f_G$ is the gray matter fractions at a given CSI voxel.

## RESULTS AND DISCUSSION

Figure 1 shows a partial view of *in vivo* axial GABA and Cr images of the human brain acquired at 3 T using the selective MQ STEMS method. The phase of GABA in each CSI voxels was corrected based on that of Cr in the corresponding Cr CSI map. The positions of the GABA and Cr signals in the two CSI maps are well-aligned in all CSI voxels, indicating excellent $B_0$ homogeneity achieved across the CSI slice. The excellent $B_0$ homogeneity was further confirmed using conventional phase mapping. The distinctive GABA doublet observed in all CSI voxels indicates excellent suppression of overlapping metabolite signals such as Cr, glutathione and potentially macromolecules.

A quantitative analysis of the GABA distribution was shown in Fig. 2 using Cr as the internal reference. GABA and Cr concentration ratio showed an approximately linear relationship with gray matter fraction. Higher GABA concentration in gray matter compared to white matter was found in Fig. 2. The GABA concentration in gray matter and white matter were 1.00 ± 0.22 μmol/g and 0.34 ± 0.06 μmol/g (mean ± SD, n = 13), calculated based on Cr concentration of 8.2 and 6.0 μmol/g in gray matter and white matter, respectively. The Cr concentrations in gray and white matter used here were averaged from literature values. As demonstrated in Fig. 2, the selective MQ STEMS CSI method allows determination of tissue-specific distribution of GABA in the human brain. Since altered GABA intensity has been detected using single-voxel GABA editing in many brain disorders, which are also associated with gray matter deficit, it is important to determine any tissue-specific changes in GABA using GABA CSI.

## REFERENCES

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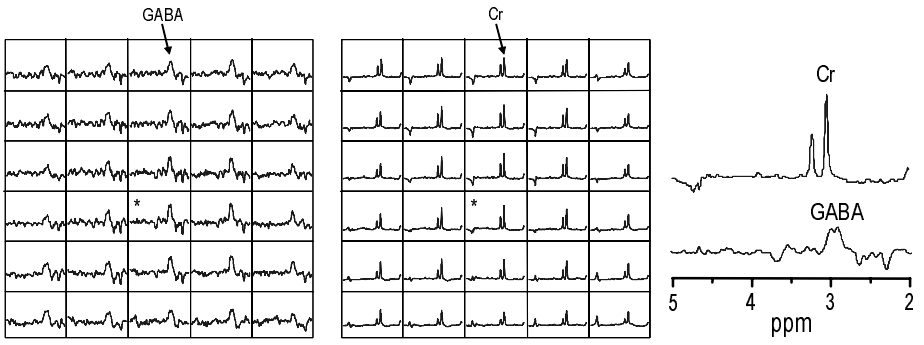


**Fig. 1 *In vivo* $^1$H selective MQ CSI of GABA (left) and Cr (middle) of the human brain at 3 T. Spectra in the 2-5 ppm range are shown. Spectra on the right are extracted from the CSI voxel indicated with *.**

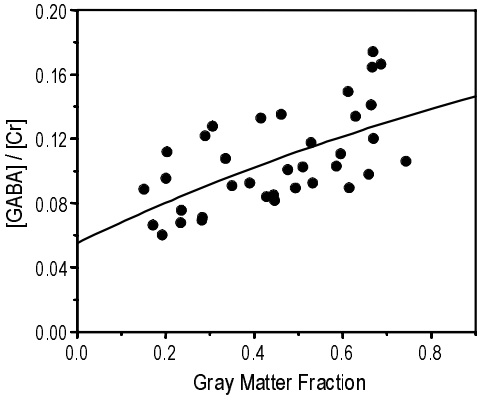


**Fig. 2 Representative plot of GABA-to-Cr concentration ratio as a function of gray matter fraction from one subject.**