Multi-Volume GABA-Edited Spectroscopy of the Human Brain

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INTRODUCTION: Here, a novel method is presented for acquiring J-difference edited GABA signal from multiple interleaved spectroscopic voxels. Interleaved multi-volume spectroscopy has only recently been reported for more than two volumes in non-edited spectroscopy, and has never been reported for GABA or any other type of edited spectroscopy (1). This is not at all due to a lack of clinical value, but due instead to technical difficulties inherent in this approach in localization and especially shimming. In this study, multi-volume edited spectroscopy is demonstrated in-vivo at 4T for three volumes located in the occipital cortex, corpus callosum, and baso-frontal cortex. From additional anatomical scans each voxel was segmented into gray matter, white matter, and CSF. Metabolite and GABA concentrations were calculated for gray and white matter using the water signal from a non-water suppressed scan as a concentration reference.

METHODS: Eight normal human subjects (five men, three women, ages 28 ± 4, mean ± SD) were studied in accordance with institutional review board guidelines for research in human subjects. All experiments were performed on a 4.0 T Magnex (Oxford, UK) magnet interfaced to a Bruker (Ettlingen, Germany) Avance console. A Magnex whole-body gradient system housed actively shielded linear gradients, a Z_0 coil, and first through third order shims (shim diameter = 72 cm). Reception and transmission were carried out by a Bruker birdcage coil. A dynamic shim updating system was custom built on this system consisting of a shimming interface capable of storing multiple sets of shim settings, pre-emphasizing, and changing all first through second order shims during a scan (2).

In each subject, three cubic voxels of side length 2.6-2.8 cm were placed along the midline of the brain in the occipital cortex, corpus callosum, and baso-frontal cortex. Localization was achieved by PRESS with phase cycling and additional pre-excitation OVS. Double-oblique localization gradients were used to prevent cross-excitation of voxels (3). Local first and second order shim settings were calculated using FASTMAP over spheres of diameter 4 cm centered on each of the three voxels (4). These shim settings were loaded into local hardware memory, and shim settings were updated between each interleaved voxel acquisition.

Two T_2 -weighted anatomical MRI images (192 x 192, FOV = 19.2 x 19.2 cm, slice thickness = 4 mm), were acquired at echo times of 32 and 70 ms, TR = 2000 ms. These were used to determine the gray, white matter, and CSF fractions of each voxel by B_1-correcting and thresholding the images.

J-difference editing was accomplished with 20 ms dual frequency Gauss pulses selective for both the GABA 1.9 ppm resonance and water. In alternating scans these pulses selected either the 1.9 ppm GABA resonance or the resonance symmetrically around the water peak. This method of simultaneous spectral editing and water suppression has been shown by Mescher et al to give very minimal macromolecule contamination of the edited GABA resonance at 4.0 T (5). Spectra were collected with TR/TE = 3000/68 ms in circa 16 minutes, with a total scanning time of 50 minutes.

GABA, creatine, choline, and NAA signal was determined by peak integration following baseline correction. Metabolite concentrations were calculated using the water signal from an additional non-water suppressed scan as a concentration reference. Water concentration for each voxel was calculated based on literature gray, white matter, and CSF water volume fractions of 0.78, 0.65, and 0.97, respectively (6). The water and metabolite signals were corrected for differing T_1's and T_2's, editing efficiency, receiver gain, and number of averages. In-vivo metabolite T_1's and T_2's were taken from average literature values. GABA was assumed to have an in-vivo T_1 and T_2 similar to that of the other metabolites (5).

RESULTS AND DISCUSSION: In all subjects, the multi-voxel J-difference edited GABA sequence provided spectra with good shimming and SNR. The linewidth (mean ± s.d.) for the ~2.8 cm^3 voxels was 8.5 ± 2.5 Hz over all subjects and was similar for all three volume locations. A clear GABA signal at 3.02 ppm was identifiable in all subjects with a SNR of 9 ± 3 (mean ± s.d.). The resulting major metabolite and GABA concentrations were found to be consistent with both single volume and MRSI studies in the literature.

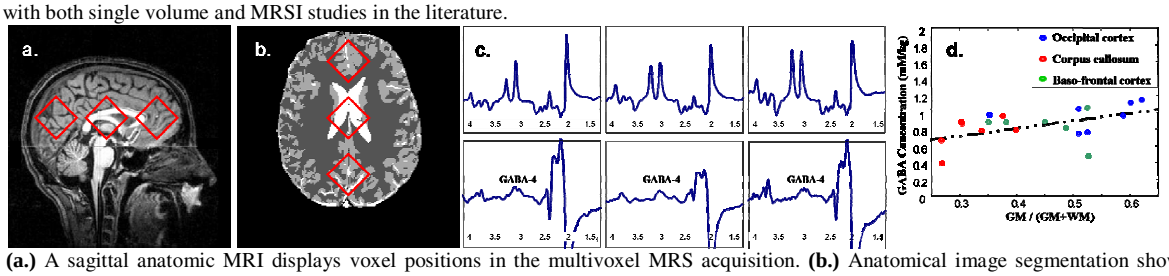

Figure 1: (a.) A sagittal anatomic MRI displays voxel positions in the multivoxel MRS acquisition. **(b.)** Anatomical image segmentation showing gray matter (light gray), white matter (dark gray), and CSF (white). **(c.)** Unedited (top) and difference (bottom) spectra from the three voxels- from left to right: occipital, corpus callosum, and baso-frontal cortex, from a single subject. The bottom row is shown at 5x scale compared to the top row. **(d.)** Relationship between GABA concentrations and percent gray matter fraction of the voxels.

Table 1: Metabolite Concentrations in Gray and White Matter:

Creatine (mM/kg)		Choline (mM/kg)		NAA (mM/kg)		GABA (mM/kg)	
Gray	White	Gray	White	Gray	White	Gray	White
7.8±2.3	6.3±1.0	0.6±0.4	2.7±1.0	10.7±2.6	9.5±1.2	1.26±0.32	0.54±0.15

Although it is possible to acquire spectra from multiple volumes with global or first order (gradient) shimming in some locations in the brain, in regions of high native inhomogeneity such as our frontal cortex volumes, second order shims were necessary in all subjects. Large first and second order shim changes were needed between voxels (up to 40% of maximum shim strength) across all subjects.

In this study, we demonstrate the feasibility of edited, interleaved multi-voxel spectroscopy for GABA detection from multiple brain regions. This represents a novel modality for in-vivo spectroscopy that has been previously confined to either single volumes or whole slice spectroscopic imaging. Many applications exist where neither of these is optimal. For instance, 'whole slice' MRSI works well for areas that can be shimmed well with a single global shim, but field homogeneity that is adequate for edited MRSI can not currently be achieved in the frontal cortex. Multi-voxel spectroscopy is viable for a very large diversity of in-vivo experiments.

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