Quantification of Co-Edited Macromolecules in GABA J-Editing

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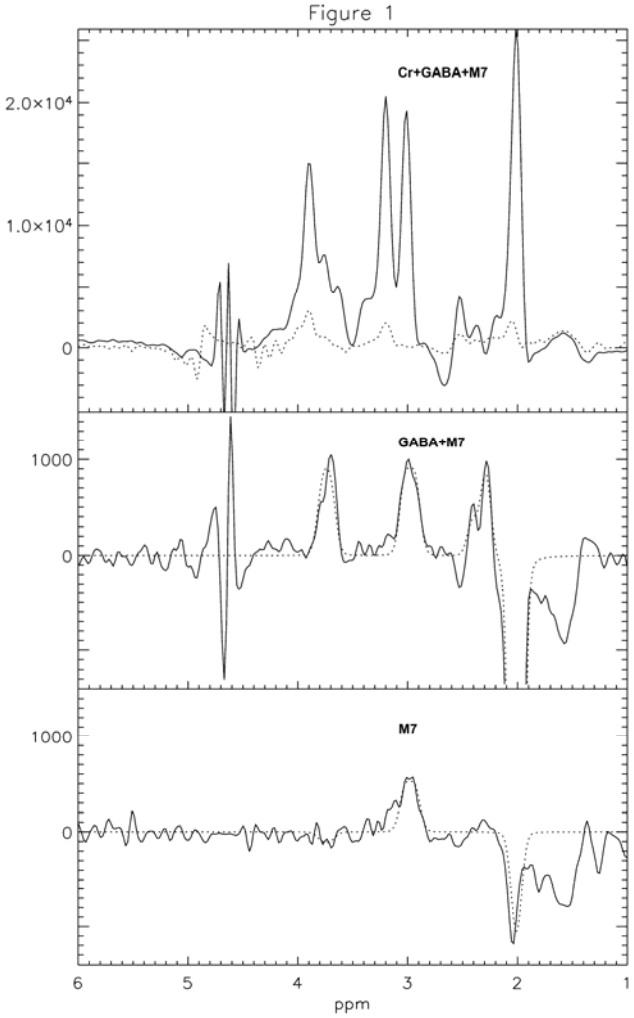
Introduction: Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in the CNS which is involved in a variety of psychiatric and neurological disorders. Several two-step J-editing techniques have been developed for measuring GABA γ-H2 at 3.0 ppm. These techniques (1-4) use a very selective 180° editing pulse on GABA β-H2 at 1.9 ppm, but the signal from macromolecules (M7 at 3.0 ppm) which is coupled to M4 at 1.7 ppm (5), is co-edited. Previously, co-edited macromolecules were analyzed either by placing the editing pulse at 1.7 ppm (1, 2) or using the metabolite null method with the editing pulse at 1.9 ppm (3). In all cases, M7 was not fully co-edited because of the narrow frequency profile of the editing pulse used, complicating quantification of M7 due to the broad chemical shift dispersion of M4 components. Also, only macromolecules in the occipital lobe were analyzed previously. We report determination of macromolecules in the frontal lobe by the use an editing pulse with a top-hat frequency profile which fully excites GABA β-H2 and M4 (4). Since M7 is fully co-edited here, it can be easily quantified using the metabolite null method.

Methods: All experiments were performed on a 3 Tesla GE whole body scanner (GE, Milwaukee, WI) running on the VH3 platform. A standard GE head coil (transmit/receive, 28cm id) was used. A voxel (S/I = 25 mm, R/L = 25 mm, A/P = 40 mm) was placed in the left frontal lobe with predominantly gray matter. NS = 512, TR/TE = 3000/68 ms, NEX = 2. The GABA editing pulse sequence was modified from a standard PRESS sequence (4). The GABA editing pulse (14.4 ms, γB_{1max} = 160 Hz) has a top-hat frequency profile with a bandwidth spanning the 2.2 ppm – 0.6 ppm range (4) covering both GABA βH2 and M4. The GABA editing pulse was switched on and off during even- and odd-numbered scans. The inversion pulse for metabolite null is a modified hyperbolic secant pulse (bandwidth = 2453 Hz, pulse length = 3 ms, field strength = 25 μT). The default slice selection gradient was switched off. Two editing experiments were performed, one with and one without the metabolite null.

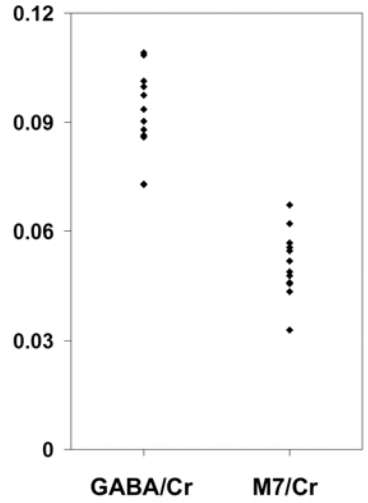
Figure 1



The data were first corrected for eddy currents using singular value decomposition to fit the water reference scans. Only components in a 3 ppm range around the water frequency with amplitude greater than 1/1000 of the maximum intensity were used for eddy current correction (6). Even and odd frames were subtracted to obtain the edited signal (6). Then, choline, creatine (Cr), and NAA in the non-edited frames were fitted. The frequency offset and linewidth parameters were used to construct a GABA doublet reference signal that was fit to the GABA signal in the edited signal and to the macromolecular signal acquired at the metabolite null for quantification of the co-edited macromolecules.

Results and Discussion: The inversion-recovery delay for generating the metabolite null was found to be 824 ms. Fig 1. top frame shows the unedited signal at TE = 68 ms with the dotted line representing corresponding spectrum acquired with the inversion pulse switched on. The middle frame shows the edited spectrum without the inversion pulse. The dotted line represents the fit to the edited spectrum. In the middle frame, residual water at 4.6 ppm, co-edited glutamate + glutamine (Glx) α-H at 3.75 ppm, GABA γ-H2 + M7 at 3.0 ppm, as well as the inverted NAA at 2.0 ppm were observed. The bottom frame shows the edited signals acquired with the metabolite-nulling inversion pulse switched on. The Glx signal at 3.75 ppm was completely suppressed by the inversion pulse as expected. Therefore, the edited signal at 3.0 ppm in the bottom frame was assigned to M7 only. Figure 2 shows the GABA/Cr and the M7/Cr ratios acquired from thirteen normal volunteers. The fully co-edited M7 fraction in GABA without the metabolite null was estimated to be 0.56 ± 0.11 in the frontal lobe voxel.

Figure 2



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