Residual water as a navigator in GABA editing spectroscopy

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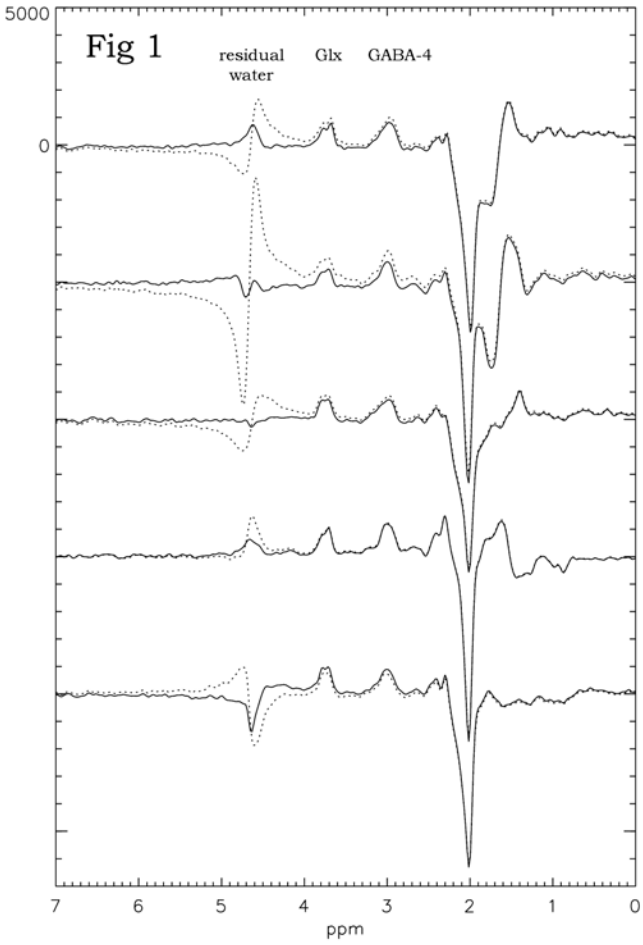
Introduction: GABA is the primary inhibitory neurotransmitter involved in a variety of psychiatric and neurological disorders including schizophrenia, depression, and epilepsy. In the normal brain, the concentration of GABA is approximately 1 mM. At field strengths available for clinical studies, all GABA resonances are overlapped by more intense signals. Several subtraction editing techniques have been developed to measure the γ-H_2 signal of GABA (GABA-4) at 3.0 ppm which is overlapped by creatine, glutathione and macromolecules (1-4). Due to the intense creatine methyl signal at 3.0 ppm, small movements of the subject and carrier frequency drift can lead to severe subtraction errors using the conventional two-step subtraction editing methods. Subject movement is a major problem for studying certain patient groups including certain psychiatric patients. Although the intense singlets in the unedited spectra can provide some indication of phase shifts caused by subject movement, accurate and objective phase correction requires a phase marker with much higher SNR and an automatic routine with minimal user intervention. Here we report a robust phase correction method for GABA editing using residual water as the internal navigator signal.



Methods: All experiments were performed on a GE whole body scanner (GE, Milwaukee, WI) running on the 3T VH3 platform. A standard GE head coil (transmit/receive, 28-cm i.d.) was used. Spectroscopy voxels (5 x 3 x 2 cm^3) were placed in the anterior frontal lobe. For GABA editing experiments, NS=1024, TR/TE=1500/68 ms, NEX=2 (two scans summed by scanner). 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). The β-H_2 of GABA (GABA-3) at 1.91 ppm was inverted by the editing pulse. The GABA editing pulse was switched on and off during even- and odd-numbered scans. Each NEX-times-summed scan was stored separately for off-line data processing. A total of 256 odd- and 256 even-numbered scans were acquired for each study.

Results and Discussion: Fig. 1 shows the results of five 26-min editing experiments obtained from five different healthy volunteers. The edited spectra were shown which were resulted from subtracting the odd-numbered scans from the even-numbered scans. The large NAA signal at 2.0 ppm is inverted due to the action of the editing pulse in the even-numbered scans. The Glx-2 signal at 3.8 ppm and the Glx-4 signal at 2.4 ppm were also detected due to their J-coupling to Glx-3 at 2.1 ppm which lies in the frequency range of the GABA editing pulse. The co-edited Glx-4 peak is partially overlapped by the negative NAA signal at 2.0 ppm. The Glx-2 signal at 3.8 ppm is cleanly co-edited, allowing simultaneous determination of Glx without contamination from GABA. The edited GABA-4 signal is located at 3.0 ppm which is the target for quantification of GABA. The co-edited GABA-2 signal at 2.3 ppm was overlapped by the residual Glx-4 signal at 2.35 ppm and by the dominant NAA signal at 2.0 ppm.

To correct for phase error caused by subject movement and scanner carrier frequency drift, the zero order phase of each single odd or even scan was corrected in the time domain according to the zero order phase of the residual water signal compared to the average phase of all the odd or all the even scans as a reference. The intensity of the residual water was at least ten times higher than the NAA signal at 2.0 ppm. Specifically, for each pair of odd- and even-numbered scans their difference in zero order phase was corrected before subtraction was made to generate the edited spectrum. In Fig. 1, the solid-line spectra are phase-corrected; the corresponding dotted-line spectra are without phase correction. The larger subtraction error at the water frequency is evident in the dotted-line spectra, indicating larger overall subtraction error. The much reduced subtraction error in the solid-line spectra demonstrates that significant improvement was achieved using the phase correction procedure proposed in this study. The reduction of the residual water signal in the edited spectra also improves their baseline, facilitating the quantification of the GABA-4 and the co-edited Glx-2 signals.

References: 1. Rothman, et al, PNAS, 90:5662 (1993) 2. Mescher et al, NMR Biomed, 11:266 (1998). 3. Hetherington, et al, MRM 39: 6 (1998). 4. Sailasuta, Proc ISMRM 9:1011 (2001).