Optimization of GABA Double-Quantum Filtering with Dual-Resonance Refocusing: Its Application to Human Prefrontal Brain In Vivo

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Introduction

Proton double-quantum filtering (DQF) is an effective method for selective detection of metabolites with coupled spins, because signals from uncoupled spins can be completely eliminated in a single scan. Recently, Shen *et. al.* have reported a GABA DQF with a dual-resonance selective 180° pulse (3.01 and 1.89 ppm) in the first echo period [1]. This pulse was designed and implemented for the suppression of unwanted signals, especially the macromolecule (MM) signal, when detecting the GABA resonance at 3.01 ppm. Here, we further investigate the effects of this 180° pulse on GABA editing. The editing efficiency can be enhanced to 50% if the echo time is optimized. Measurements of GABA in prefrontal cortex are presented.

Backgrounds and Experimental

At 3 T, the GABA spin system can be approximated by a weakly-coupled $A_2M_2X_2$ system, where A, M and X spins resonate at 3.01, 1.89 and 2.28 ppm, respectively, and J = 7.3 Hz. Fig. 1 depicts the GABA DQF sequence and the evolution of the target antiphase coherences of the A and M spins during TE_1 for a dual-resonance selective 180° pulse (D180), tuned to 3.01 and 1.89 ppm, together with the predicted signal return ratio with respect to the A_2 spin triplet following a 90°-acquire sequence. Because the X spins do not experience 180° rotation, the J evolution (of A and M spins) associated with the X spins evolves back during the second half of TE_1, resulting in maximal $2M_xA_z$ coherence equal to that of $2A_xM_z$ coherence. DQ editing of these two coherences gives rise to a GABA doublet at 3.01 ppm with efficiency of 50% with respect to the A_2 triplet. The TE_1 value that gives such enhanced yield is not given by 1/2J, but depends on the type and duration of the 180° pulse. The present method utilizes a 28.6 ms single rectangular r.f. waveform that incorporates successive r.f. phase variations [2], governed by the frequency separation between 3.01 and 1.89 ppm. Fig. 2 shows the refocusing profile and the generation of the target antiphase coherences at TE_1. Both $2A_xM_z$ and $2M_xA_z$ maximize at TE_1 = 49.4 ms with a maximum sum of 0.94, predicting a maximum yield of 0.47. Mixing time TM was set at 9 ms, the shortest allowable. The second echo time TE_2 was 32.6 ms, which gave the largest signal in phantom tests. The DQF sequence was tested on a 2.5×3×3 cm^3 voxel of two 6-cm diameter spherical phantoms (pH = 7.1), one containing GABA (100 mM) and the other with GABA (10 mM) and Cr (80 mM). In vivo tests were performed on ten healthy subjects (TR = 2.4 s, NEX = 512). A 2.5×3×3 cm^3 voxel was selected in prefrontal cortex (Fig. 5). The r.f. phase of the second 90° pulse was optimized using the water signal. To minimize unwated signals, the phase of the r.f. pulses was cycled with 512 steps. Experiments were carried out at 3.0 T in an 80-cm bore magnet (Magnex Scientific PLC), interfaced to a SMIS console. A 28-cm diameter quadrature birdcage coil was used for r.f. transmission and reception. The density-matrix simulation was programmed with Matlab (The MathWorks, Inc.).

Results and Discussion

GABA editing yield was evaluated in two ways. First, the GABA edited doublet from a localized volume was compared with the A_2–spin triplet following a hard 90-Gaussian180 (28ms, tuned to 3.01 ppm) sequence with echo time of 82 ms. The resulting triplet from the whole phantom was rescaled with the volume ratio given by the PRESS water signal ratio, Fig. 3(a). The area under the edited doublet is estimated to be 0.43 with respect to that of the A_2 triplet. The discrepancy between the experimental and predicted yield (0.47) is due to signal loss resulting from the non-zero TM and finite bandwidth of the slice-selection r.f. pulses. Second, the edited doublet was compared with the PRESS Cr singlet at 3.01 ppm from an identical voxel, Fig. 3(b). The area ratio of the peaks from the phantom with GABA to Cr concentration ratio of 1:8 is 3.3×10^{-2}. Considering the difference in T_2 decay of GABA ($T_2 \cong$ 500ms) and Cr ($T_2 \cong 1$ s) signals in the phantom solution, the GABA to Cr signal ratio gives the same yield as for the first method, within the experimental error. Fig. 4 displays calculated DQF spectra of GABA and homocarnosine (HC), assuming the GABA to HC concentration ratio of 3:1. The sum of the two calculated spectra is in excellent agreement with the experimental data. For estimation of MM contamination in vivo, both ordinary and metabolite-nulled DQF tests were carried out, Fig. 5. At 3 T, for TR = 2.4 s, following a 740-ms long inversion recovery delay, the PRESS Cr 3.03 ppm singlet is suppressed >100-fold. This will also be the case for the GABA signal, assuming a similar T_1 to Cr. No discernible signal is observed at ~3 ppm in the metabolite-nulled DQF spectrum, indicating that MM contamination is negligible. In Fig. 4, HC contribution to the edited signal at ~3ppm is 20%, therefore GABA contributes 80% of the observed signal. Based on these data, the GABA concentration in the prefrontal voxel = 0.77±0.13 µmol/g, estimated with respect to Cr (9 µmol/g).

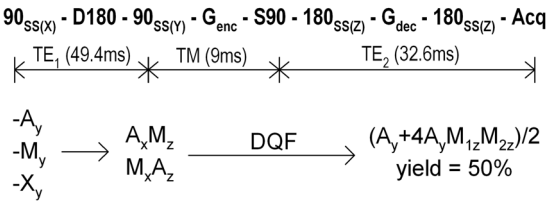

FIG 1. Overview of the DQF sequence and the GABA target coherence evolution. Localization is obtained with the first and second 90° pulses, and a pair of adiabatic 180° pulses during TE_2. D180 (28.6ms long) is tuned to 3.01 and 1.89 ppm, and S90 (9ms-long, Gaussian) to 1.89 ppm. The decoding gradient G_{dec} is twice the encoding gradient G_{enc}.

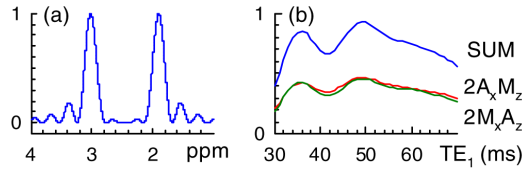

FIG 2. (a) Refocusing profile of D180 (28.6ms). (b) TE_1 dependence of GABA coherences, $2A_xM_z$ and $2M_xA_z$, and the sum, for D180.

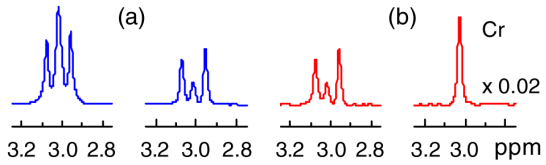

FIG 3. Phantom spectra from solutions (a) with GABA (100 mM) and (b) with GABA (10 mM) and Cr (80 mM). TR was set at 12 s, which is > $6T_1$ for both GABA and Cr.

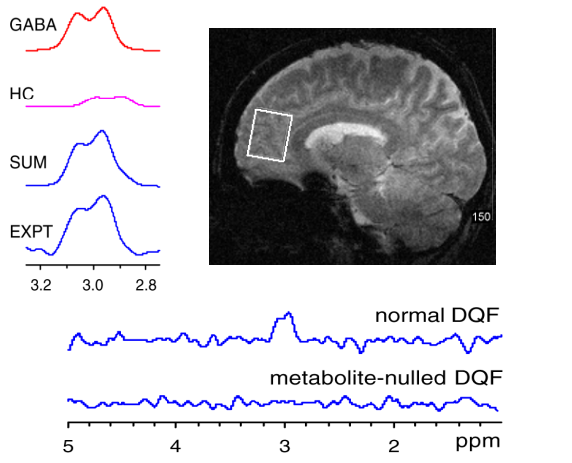

FIG 4. (left) (top to bottom) Calculated DQF spectra of GABA and homocarnosine (HC). Here, it is assumed that HC concentration is one-third that of GABA. Sum of the two spectra. In vivo prefrontal cortex GABA spectrum.
FIG 5. (right) (top) Voxel (2.5×3×3 cm^3) position in prefrontal cortex. (bottom) DQ filtered spectra without and with metabolite-nulling inversion recovery.

References

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2. H. Green *et. al.*, J Magn. Reson. **81**, 646 (1989).

Acknowledgments

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