Feasibility of GABA spectral editing at TE=136 ms using MEGA J-difference editing approach

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Introduction

Spectroscopic measurement of GABA (γ-aminobutyric acid (NH_2-$^{\alpha}CH_2$-$^{\beta}CH_2$-$^{\gamma}CH_2$-COOH)) has drawn much attention in recent years due to the importance of GABA as the major inhibitory transmitter in human brain. However, due to the very low concentration of GABA in brain, it has a very low signal to noise ratio in spectroscopy, making it a very difficult task to have a reliable and reproducible standard GABA measurement technique. The methylene groups form $A_2M_2X_2$ system, while the γ (C^4H) and β (C^3H) protons are weakly coupled A_2X_2 system, with the coupling constant J = 7.3 Hz. The primary barrier to overcome in the *in vivo* measurement of GABA in cerebral nervous system involves the suppression of other overlapping resonances. The spectroscopic techniques used GABA editing essentially involves J-difference editing [1, 2, 3, 4], 2D J-resolved spectroscopy [5], multiple quantum filtering [6,7,8], and combination of longitudinal scalar order editing and J-difference editing [9].

One major problem in GABA editing is co-editing of macromolecules and glutamate because of finite bandwidth of the frequency selective pulses. It is beneficial to employ a high TE to achieve lower bandwidth of the editing pulses; however, for theoretical reasons, to date the scans are done at TE = 1/2J = 68 ms. Here, we present phantom data at TE = 1/J = 136 ms using 21 Hz bandwidth editing pulse in a sequence based on MEGA approach as in [4] showing effective GABA editing. This result is of critical importance in the selection of TE in *in vivo* measurements for effective GABA editing.

Methods

All MR scans were performed using a 3 Tesla Siemens head-only Allegra scanner (Erlangen, Germany). We performed spectroscopy scans using a phantom (HMRI, Pasadena, CA) containing 10 mM creatine and GABA each, which is ideal because it is creatine that needs to be suppressed to observe the GABA resonance at 2.88 ppm (in phantom). Two scans based on MEGA approach [4] consisted of the following parameters: TR = 3000 ms, TE = 68 and 136 ms, water suppression bandwidth = 35 Hz, editing pulse frequency = 1.77 ppm (this parameter was adjusted from that used in *in vivo* studies because of the temperature difference between the phantom solution and human body), editing frequency-selective pulse bandwidth = the lowest allowable bandwidth (40 Hz and 20 Hz at the TE = 68 ms and 136 ms respectively), voxel size = 5.8 mL (1.8 cm × 1.8 cm × 1.8 cm), NEX = 64, total acquisition time = 6.8 min.

Results and Discussion

The outer peaks of the triplet at 2.88 ppm are resolved and displayed in the difference spectra of Fig.1 for both TE = 68 and 136 ms. Creatine suppression is clearly evident at TE = 136 ms (as in TE = 68 ms), demonstrated by the absence of the second creatine peak as well as splitting of the GABA triplet. It should be noted that for an A_2X_2 spin-coupled system (C^2H and C^4H coupling), there will be full J-evolution at TE = 1/J, which should result in no remaining GABA signal in the subtracted spectrum at a TE of 136ms. However, our phantom data clearly shows (Fig. 1) effective GABA editing at TE=136 ms. Careful observation reveals that the outer members of the 2.88 ppm (A_2) triplet are reversed at TE = 136 ms when compared to that at TE = 68 ms. This results in the cancellation of the central peak in the difference spectrum (as in TE = 68 ms), while the outer members appear reversed in the subtracted spectrum. In Fig. 1, the zero order phase was shifted by 180^0 in the subtracted data in order to have positive GABA signal at TE = 136 ms. We have observed ~25% reduction in area of the outer peaks of the 2.88 ppm triplet at TE = 136 ms. The nature of the 2.16 ppm (M_2) triplet also differs at the two TE's. Non-cancellation of the central peak of this triplet at TE=136 ms is interesting as well, since the M_2X_2 J-coupling constant is also 7.3 Hz. At this narrow bandwidth the co-editing of glutamate and macromolecule will be negligible. Also, since the T_2 of glutamate (40 – 50 ms) is much smaller than that of GABA (200 – 300 ms) [10], at TE = 136 ms, glutamate signal will be about 78% lower.

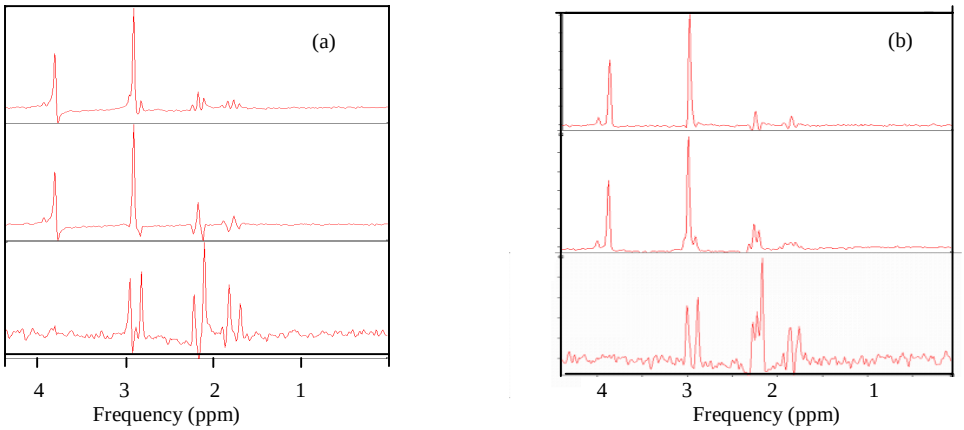

Fig. 1. Subspectra and the difference spectra at (a) TE = 68 ms, (b) TE = 136 ms. The top panels show the subspectra with the acquisition performed using the 1.77 ppm inversion pulse; the center panels display the subspectra with the inversion pulse set at a frequency symmetrically on the other side of the water resonance. The difference spectra are shown in the bottom panel.

Conclusion

Using MEGA-editing at 3 Tesla, we have demonstrated the feasibility of performing GABA editing at TE = 136 ms with frequency selective pulse bandwidth of 20 Hz (~0.16 ppm). Although from a theoretical perspective this result is unexpected, the advantages of spectral editing at the longer TE make this observation potentially important in its potential application

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