GABA Detection Via PRESS Constant Echo Time Difference Spectroscopy

J. Snyder[1], R. B. Thompson[2], and A. H. Wilman[1,2]

[1]Physics, University of Alberta, Edmonton, Alberta, Canada, [2]Biomedical Engineering, University of Alberta, Edmonton, Alberta, Canada

Introduction

In the human brain, γ–aminobutyric acid acts as an inhibitory neurotransmitter, and its quantification aids in understanding many neurological disorders. However, detection via proton magnetic resonance spectroscopy is inhibited due to spectral overlap with other metabolites including glutamate, glutamine, creatine (Cr) and N-acetylaspartate. In particular, the A_2 multiplet of GABA is completely obscured by the strong A_3 singlet of Cr in the 2.9-3.1 ppm range. Several spectral editing techniques have been proposed including multiple quantum filtering and application of spectrally selective pulses (1-3). These methods improve previous quantification schemes, but may be difficult to implement clinically due to complex sequence design. This preliminary study proposes application of PRESS constant echo time (TE) difference spectroscopy to detect the A_2 resonance of GABA while suppressing the Cr singlet. The method exploits signal variations in TE space due to refocusing flip angles other than 180° in the PRESS sequence. The sequence uses no spectrally selective pulses as in previous difference spectroscopy (4). The technique is demonstrated using numerical simulation at optimized timings.

Methods

Constant TE difference spectroscopy relies on signal variations in TE space (TE1, TE2) along constant lines of TE, which are not produced in weakly coupled systems using a standard 90°-180°-180° PRESS sequence. However, the necessary variations can be introduced by altering the flip angle of one of the refocusing pulses. In the case of GABA, a weakly coupled system at 4.7 T, signal variations in TE space were calculated using an in-house numerical simulation program (5). The program was run for a range of TE1 and TE2 values (10-205 ms) for GABA and Cr using a PRESS scheme of 90°-180°-α, where α was varied from 90° to 180° in increments of 5°. For each value of α and TE1/TE2 combination, GABA A_2 areas were calculated and visualized as TE space area maps. By analyzing all constant TE lines in each area map (19 in total, dependent on the number of flip angle iterations), the optimal flip angle and echo times can be determined. The two time points from the optimal area map were chosen to simulate constant TE difference spectroscopy. The spectra were broadened by a 6 Hz exponential filter, and GABA and Cr were combined using a parietal gray matter physiological concentration ratio of 4:1 (6).

Results

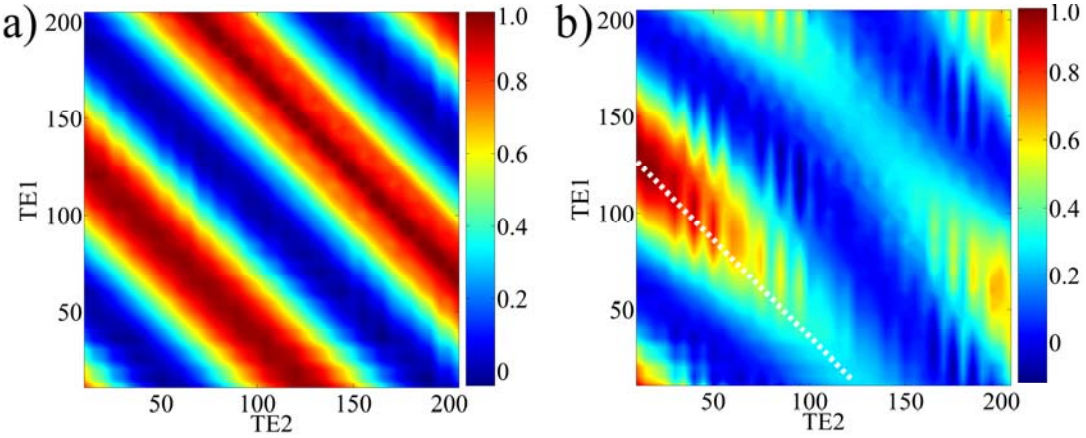

Figure 1: TE space area maps produced by the simulator at 4.7 T for the A_2 group of GABA under PRESS excitation and flip angles of 90°-180°-α with a) α = 180°, and b) α = 120°. The dotted line denotes the line of constant TE with greatest signal variation (TE = 130 ms).

Figure 1 illustrates TE space area maps for the A_2 multiplet of GABA. The values are normalized to the case when TE1 = TE2 = 10 ms, and relaxation effects are not considered. In a), α = 180°, resulting in a symmetric pattern in TE space. The period between two similar points in the map is 1/J (J = 7.3 Hz) or 137 ms in either the TE1 or TE2 direction. The optimal signal difference along a line of constant TE was determined to occur for α = 120°, as shown for GABA A_2 in b). Note the asymmetries in TE space caused by the reduction in flip angle, and specifically, the period along the TE1 direction remains 1/J as in a) due to complete refocusing, but is altered along the TE2 direction. The dotted white line shows the constant TE line with greatest asymmetry (TE = 130). Two time points from this line were chosen to simulate difference spectroscopy, illustrated in Figure 2 for GABA (solid lines) and Cr (dashed). The spectra in a) show the full Cr A_3 signal obscuring the relatively small GABA signal at 3 ppm at timings of TE1 = 120 ms, TE2 = 10 ms. Figure 2b shows the spectra taken at timings of TE1 = 120 ms, and TE2 = 10 ms, corresponding to the strongest yield along the dotted line in Fig. 1b. The second calculated time point with values of TE1 = 20 ms, TE2 = 110 ms produces the largest signal upon subtraction from the spectra in Fig. 2b. The subtraction spectra are shown in Fig. 2d. Note the large signal variation between GABA spectra in b) and c), producing a large remnant in the difference spectrum. As expected, no signal variation was observed in the simulations for the Cr A_3 singlet at the reduced flip angle, and therefore it has a negligible contribution in d). Analysis of the GABA A_2 areas in b) and c) result in a 60% GABA yield in the subtraction spectrum compared to the equivalence of two pulse acquire experiments. Due to the large remaining yield, in vivo experiments should be feasible.

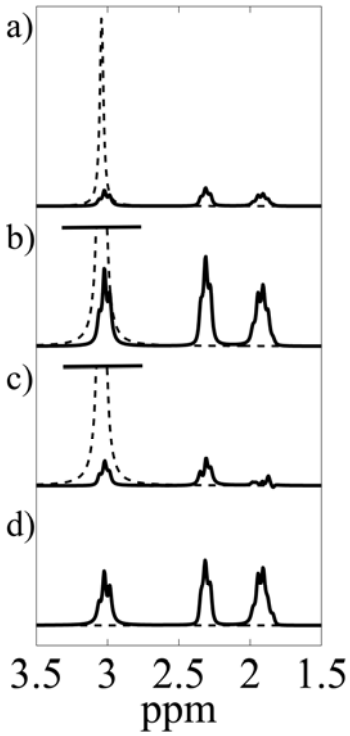

Figure 2: Spectra from the subtraction simulations with α = 120° at timings of a,b) TE1 = 120 ms, TE2 = 10 ms, and c) TE1 = 20 ms, TE2 = 110 ms. The subtraction spectra are shown in d). The Cr peak has been truncated in b and c.

Discussion

These results show that it may be possible to detect GABA at 3 ppm via constant TE difference spectroscopy at 4.7 T, by varying the flip angle of the second refocusing pulse and producing signal asymmetries in TE space. This technique is simple to implement with a standard PRESS sequence, and is therefore available for clinical use. The same results are obtained if the first refocusing pulse is varied, although the asymmetries are flipped in TE space. The addition spectrum maintains all spectral information resulting in a method with no lost information, as can be the case in multiple quantum filtering.

References

1. Choi CH, *et al.* MRM 58:27-33 (2007). 2. Shen J, Rothman DL, Brown P. MRM 47:447-454 (2002). 3. Hetherington HP, Newcomer BR, Pan JW. MRM 39:6-10 (1998). 4. Rothman DL, *et al.* PNAS 81:6630 (1984). 5. Thompson RB, Allen PS. MRM 41:1162-1169 (1999). 6. Pouwels PJW, *et al.* Ped Res 46:474-485 (1999).