

PRESS Difference Spectroscopy Optimization Applied to GABA and Tau at 3 T

J. Snyder¹, T. Lange¹, J. Hennig¹, and M. Zaitsev¹

¹Dept. of Diagnostic Radiology, Medical Physics, University Hospital Freiburg, Freiburg, Germany

Introduction

Detection of γ -aminobutyric acid (GABA), an important inhibitory neurotransmitter, at 3 T via Magnetic Resonance Spectroscopy (MRS) generally requires a spectral editing technique as the peaks of the GABA signal are obscured by overlapping metabolite resonances including glutamate (Glu), glutamine, creatine (Cr) and N-acetylaspartate (NAA). Several spectral editing techniques have been proposed including multiple quantum filtering and application of spectrally selective pulses. (1-3). A recent study proposed a method to detect GABA in vivo by constant echo time (TE) difference spectroscopy (subtraction of two spectra with asymmetric PRESS timings and constant total TE) and inclusion of variable PRESS flip angles (4). In this study, we propose a method of difference spectroscopy based on flip angle variation only, with both spectra acquired at the same PRESS timings (TE₁ = first echo time; TE₂ = second echo time). The timings and flip angles are also optimized to produce the largest yield and smallest overlap with adjacent metabolites upon subtraction, and the treatment can be extended to any arbitrary metabolite, although weakly coupled systems are expected to provide the best results (4).

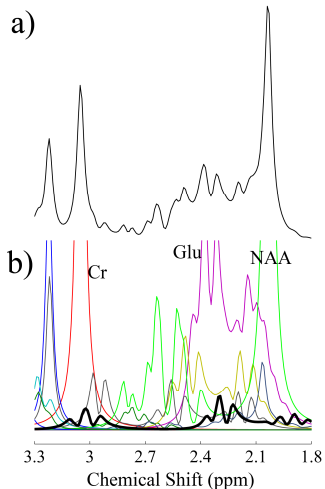


Figure 1: Simulated short echo time (TE = 30 ms) spectra: a) the resultant spectrum from all 16 metabolites, and b) individual contributions. The GABA spectrum is shown in black in b).

Methods

The signal variation required for difference spectroscopy for weakly coupled spins is produced by deviation of the refocusing pulse flip angles from the standard 90°-180°-180° PRESS sequence; the first spectrum is acquired at 90°- α -180° and the second at 90°-180°- α . To determine the best values of TE₁, TE₂ and α , the procedure was optimized as follows. First, numerically simulated spectra for sixteen metabolites were calculated for TE₁ and TE₂ values of 10-205 ms using 5 ms increments for both sets of spectra. This procedure was repeated for values of α from 90° to 180° with 5° increments. For each difference spectrum acquired, the extent of the overlap of GABA with the other 15 metabolites was determined on a point by point basis. The deviation of each metabolite value from the summed (actual spectral value) was calculated for each point, and weighted by the metabolite value height (normalized to each metabolite) as well as the actual spectral point value. This procedure allowed cancellation of overlapping metabolite signals without interfering with the actual spectral value, as an absolute value approach would overestimate the amount of overlap. The weighting with peak height eliminated spectral regions with low signal dominating the overlap calculation, and placed greater emphasis on points with greater signal, thus improving the sensitivity of the analysis to yield. The entire procedure can be repeated for each metabolite to be investigated. The constant parameters of linewidth and metabolite concentrations will also influence the outcome of the experiment. In addition, it was beneficial to restrict the analysis to a certain range in the spectrum determined by the metabolite resonance frequencies. In the case of GABA, the ranges chosen corresponded to narrow bandwidth selections centered on the A₂ (3.01 ppm), M₂ (1.88 ppm) and X₂ (2.28 ppm) frequencies. To approximate in vivo conditions, the simulations used healthy adult parietal gray matter metabolite concentrations (where available) (5,6), and spectral linewidths were broadened to 6 Hz.

Results and Discussion

Figure 1 illustrates simulated symmetric (TE₁ = TE₂) PRESS spectra at short TE (TE = 30 ms, α = 180°) for the resultant spectrum (1a) and individual contributions from the sixteen metabolites (1b). The detection of many metabolites at standard short TE PRESS is hindered by the massive overlap at 3 T, as shown in Fig. 1b. The target resonance of GABA is highlighted in black. The GABA difference experiment is shown in Fig. 2, with the first (90°- α -180°) and second (90°-180°- α) individual metabolite spectra shown in 2a and 2b, respectively, and the difference spectra shown in 2c. The GABA spectra are highlighted in black, with the grey columns denoting the target resonances. The resultant spectrum from summation of all metabolite signals is given in 2d. The optimal parameters were determined to be α = 120°, TE₁ = 20 ms, and TE₂ = 95 ms, resulting in less than 10 % contribution of overlapping resonances to the A₂ (left grey column) and X₂ (right grey column) peak areas, and an overall yield of 34 % compared to the equivalent two averages of a short echo PRESS experiment with TE = 30 ms. As shown in 2c, the prominent singlet resonances of Cr (3.03 ppm) and NAA (2.02 ppm) are removed upon subtraction, and the GABA signals are relatively unobstructed, with the major residual components being glutathione (GSH) at 2.95 ppm and Glu at 1.95 ppm.

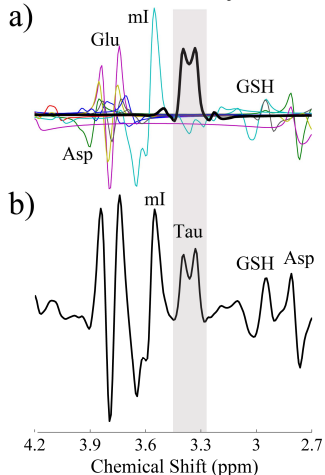


Figure 3: Tau optimization: a) difference spectra, and b) resultant summed difference spectrum. The target resonance is shown in black in a)

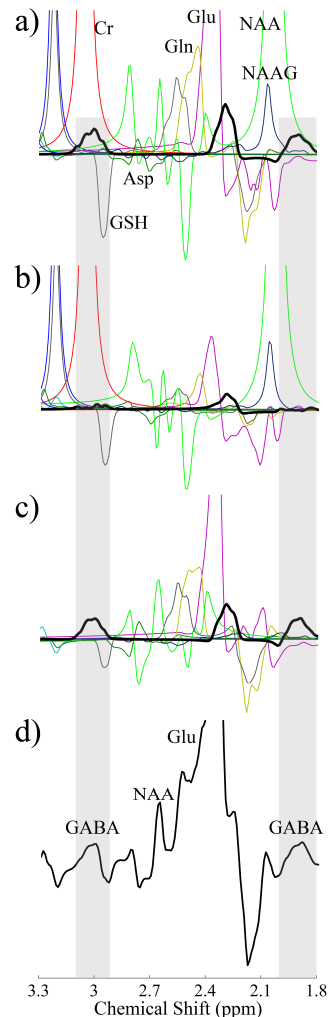


Figure 2: Simulated difference spectra for 16 metabolites at TE₁ = 20 ms, and TE₂ = 95 ms, and pulses of a) 90°-120°-180°, and b) 90°-180°-120°. The difference spectra are shown in c), with the resultant summation in d). The GABA spectra are shown in black, with the target resonances in grey columns.

A second example of the difference spectroscopy optimization procedure is shown in Fig. 3, with taurine (Tau) as the target metabolite (a four spin weakly coupled A₂X₂ system with multiplets around 3.25 and 3.42 ppm). The difference spectra are shown in 3a, with the Tau signal emphasized in black. The major overlapping signal is mI, which reduces the Tau signal by 26 %. The resultant summed difference spectrum is shown in 3b. The spectrum for the targeted region for Tau is in good agreement with the lineshape in 3a. The optimal parameters were determined to be TE₁ = 30 ms, TE₂ = 65 ms, and α = 120°. Note that GSH and aspartate (Asp) are also partially optimized concurrently with Tau for these specific parameters.

Conclusion

These results show that optimization of a difference spectroscopy experiment based on varying flip angles in PRESS can dramatically reduce the overlap of adjacent resonances allowing for detection of obscured metabolites including GABA and Tau at 3 T, without requiring specialized pulse sequences. The inclusion of other signals such as macromolecules may also improve the applicability to in vivo situations. The end goal of improving quantification of obscured metabolites is currently being investigated using this method in healthy volunteers.

References

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