Introduction

Short echo time (TE) PRESS spectroscopy allows non-invasive in vivo investigation of brain metabolites and is beneficial in the detection of strong, unobstructed signals. However, due to the narrow spectral range inherent in proton in vivo spectroscopy, many important metabolites have comparable frequencies which can produce quantification confounds or completely obscure the resonance peaks in highly overlapped signals. In particular, the important neurotransmitter γ-aminobutyric acid (GABA; a six-spin system) is difficult to detect in vivo due to the strong signal contaminations of creatine (Cr), glutamate (Glu) and N-acetylaspartate (NAA). Several spectral editing methods have been proposed to detect GABA including subtraction-based schemes (1,2) which have gained popularity recently but introduce complexities due to application of spectral selection pulses that can adversely affect metabolite responses. In this work, we propose a new GABA detection method based on subtraction spectroscopy without the addition of spectral pulses, termed J-Editing via homonuclear polarization transfer (JET). The technique provides robust detection of coupled spins in general with minimal changes to the PRESS sequence and also benefits from maintenance of an unedited addition spectrum for quantification of non-varying resonances. The method is compared to the MEGA subtraction technique (2) in healthy volunteers at 3 T.

Methods

The proposed method is based on subtraction of two spectra (denoted S1 and S2) acquired at an identical echo time, defined with PRESS timings of TE1+TE2 = TE. In contrast to standard PRESS, the JET technique employs a variable refocusing pulse with flip angle θ1 and the resultant signal S is determined by:

\[ S = S_1(θ_1) - S_2(θ_2) = S_1(90° - θ_1 - 180°) - S_2(90° - 180° - θ_2). \]

The varied placement of the θ pulse in S1 and S2 allows contributions of homonuclear coherence transfer from J-coupled spins producing signal variation dependent on chemical shift and/or J-coupling evolution resulting from a specific TE1 and TE2. The dissimilar spin evolution between the 180° pulse and the θ pulse in S1 and S2 results in a phase difference which is detected by subtraction. The maintenance of pulse flip angles between S1 and S2 ensures equal singlet contributions in both. The amount of polarization transfer due to the θ pulse (Eθ), maximization of the antiphase input term immediately prior to the θ pulse, and the chemical shift and J-modulations of the polarization transfer term can be expressed as Eθ = (cosθ−1)sinθ/2, resulting in a compromise between editing (with optimum at θ = 90°) and refocusing (θ = 180°) efficiencies. In the ideal case, the targeted metabolite resonance will experience a lineshape phase shift of 180° between S1 and S2 to produce the greatest signal yield upon subtraction. For increasingly complex systems such as GABA, this simple framework does not describe the interactions in entirety, and therefore numerical simulations (3,4) of 16 metabolites with optimization based on Cramer-Rao lower bounds (CRLBs) were performed for detection of the GABA resonance at 3.0 ppm for TE1 and TE2 increments of 5 ms up to a maximum of 200 ms, and θ increments of 10° from 90° to 170°. The value of θ = 110° was replaced by 109°, which was the predicted optimum in accordance with the relation for Eθ given above. In addition to yield maximization, the CRLB optimization ensures the least amount of contamination due to neighbouring resonances. The optimized parameters were used in the in vivo measurements, which were performed using a Siemens 3 T Magnetom Trio System (Erlangen, Germany) on healthy subjects giving informed consent. Other parameters included a voxel size of 20x20x25 cm³, a TR of 1500 ms and 2x512 averages (512 for each S1 and S2). The JET method was compared to MEGA with standard parameters of TE = 68 ms and a 44 Hz spectral pulse located at 1.9 ppm. Spectral analysis was performed by LCMModel (5).

Results and Discussion

The JET optimization for GABA resulted in TE1 = 20 ms, TE2 = 85 ms, and θ = 109°, with the corresponding spectra displayed in Fig. 1. The calculated value of θ agreed with the predicted value of 109°. As indicated by the blue trace in Fig. 1, the GABA peak at 3.0 ppm is readily visible. The voxel placement for the in vivo measurements is shown in Fig. 2, with measured JET and MEGA spectra illustrated in Fig. 3. To emphasize the peak locations in the subtraction spectra, the LCMModel GABA fit is overlaid in blue. GABA in both JET and MEGA is easily identifiable visually at 3.0 ppm. The JET method resulted in a substantially better CRLB compared to MEGA (11% vs. 14%) as illustrated in Table 1. Also included in Table 1 are other metabolites that were detected with significant accuracy (CRLBs < 20%).

Conclusion

The JET method provides a viable alternative to existing GABA detection techniques, as shown by the reduced CRLB for GABA vs. the MEGA approach. As JET does not require spectrally selective pulses, the method is easy to implement on clinical scanners and the addition spectrum can be used for better quantification of non-varying resonances. Although this initial study was focused on GABA, the optimization of JET via the CRLB approach can be adapted to other metabolites of interest. The JET method is of particular interest for spin systems with very similar Larmor frequencies (e.g. ascorbate) as long spectral selection pulses with very low bandwidths are required for MEGA.

References