GABA detection in vivo: J-editing via homonuclear polarization transfer (JET)

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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.

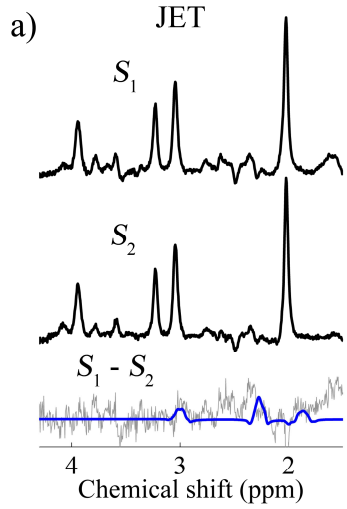

Figure 3: In vivo JET (a) and MEGA (b) data. The GABA fit by LCModel is highlighted in blue in the subtraction spectra. Note the MEGA subtraction spectrum has been truncated to increase the GABA scale.

Table 1: LCModel CRLBs (%)

	JET	MEGA
GABA	**11**	**14**
Glu	7	15
Gln	-	6
mI	14	-
NAA	12	2

Methods

The proposed method is based on subtraction of two spectra (denoted S_1 and S_2) 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 θ, and the resultant signal S is determined by:

$$S = S_1(\theta) - S_2(\theta) = S_1\left(90^\circ_x - \theta_y - 180^\circ_y\right) - S_2\left(90^\circ_x - 180^\circ_y - \theta_y\right).$$

The varied placement of the θ pulse in S_1 and S_2 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 *TE*1 and *TE*2. The dissimilar spin evolution between the 180° pulse and the θ pulse in S_1 and S_2 results in a phase difference which is detected by subtraction. The maintenance of pulse flip angles between S_1 and S_2 ensures equal singlet contributions in both. The editing efficiency is determined by the amount of polarization transfer due to the θ pulse (E_{PT}), maximization of the antiphase input term immediately prior to the θ pulse, and the chemical shift and *J*- modulations of the polarization transfer term. The amount of polarization transfer can be expressed as $E_{PT}(\theta) = (\cos\theta - 1)\sin^2\theta/2$, 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 S_1 and S_2 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 *TE*1 and *TE*2 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 E_{PT} 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 cm^3, a TR of 1500 ms and 2x512 averages (512 for each S_1 and S_2). 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 LCModel (5).

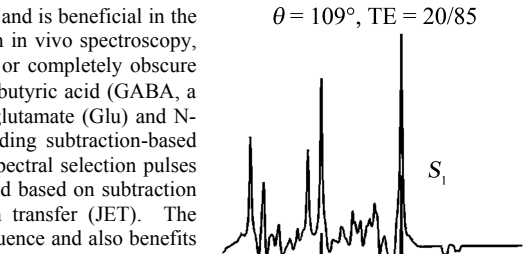

Figure 1: Results of the JET optimization. The theoretical GABA response is overlaid on the resultant subtraction spectrum.

Results and Discussion

The JET optimization for GABA resulted in *TE*1 = 20 ms, *TE*2 = 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 LCModel 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%).

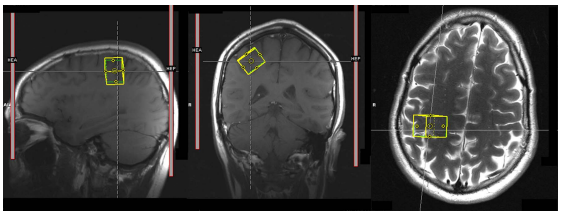

Figure 2: Voxel location (yellow) for the JET and MEGA experiments.

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

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