J-difference editing of GABA with extended echo-times

Jamie Near[1,2] and Chathura Kumaragamage[3]

[1]*Department of Psychiatry, McGill University, Montreal, Quebec, Canada,* [2]*Centre d'Imagerie Cérébrale, Douglas Institute, Montreal, Quebec, Canada,* [3]*Department of Biomedical Engineering, McGill University, Montreal, Quebec, Canada*

Target Audience. This abstract is intended for those interested in *in vivo* magnetic resonance spectroscopy (MRS) of γ-aminobutyric acid (GABA).

Purpose. GABA is the primary inhibitory neurotransmitter in the brain and is involved in the regulation of neuronal activity. MRS GABA detection is commonly performed using localized J-difference editing techniques, such as MEGA-PRESS [1], which enable separation of GABA signal from overlapping resonances. For maximum signal, the echo time (TE) of the MEGA-PRESS acquisition must be set to 1/2J (approx. 68 ms), where J is the scalar coupling between 3 ppm and 1.9 ppm GABA protons. In some cases, this requirement of a fixed TE can be limiting. Therefore, in this work we present a modified J-difference editing scheme that enables extension of the echo time (ExTE) while maintaining optimal J-difference editing efficiency.

Methods. Conventional J-difference editing of GABA involves the acquisition and subtraction of an "edit-on" scan and an "edit-off" scan. In the edit-on scan, the J-evolution of the 3 ppm GABA resonance is fully refocused using a pair of frequency selective editing pulses applied to the coupled GABA resonance at 1.9 ppm. The condition for refocusing in the edit-on scan is that the spacing between the two editing pulses must be equal to TE/2. In the edit-off scan, no editing pulses are applied, and the C4 GABA resonance is allowed to evolve until maximally inverted. Because maximal inversion occurs at TE=1/2J (or about 68 ms) and gives rise to the largest difference signal intensity, the TE of the acquisition is normally fixed at this value. We now demonstrate that instead of the conventional edit-off scan, it is also possible to achieve maximal inversion of the C4 GABA resonance using a pair of editing pulses spaced apart by (TE-1/2J)/2. Using this principle, efficient J-difference editing of GABA can be performed efficiently at extended echo times (ExTE). This is achieved using the conventionally acquired "edit-on, J-refocused" scan with TE/2 spacing between editing pulses, and a second "edit-on, J-inverted" scan with (TE-1/2J)/2 spacing between editing pulses. The ExTE MEGA-PRESS sequence is shown in Figure 1. Note that the only difference between even and odd scans is the spacing between the editing pulses. The ExTE MEGA-PRESS pulse sequence was implemented on a Siemens 3T Magnetom Trio system (Erlangen, Germany) using 10-14 ms Gaussian shaped editing pulses. Due to the finite duration of the editing pulses, crusher gradients (2.4 ms) and refocusing pulses (5.2 ms), the minimum echo time achievable with ExTE MEGA-PRESS was 115 ms. The sequence was first tested in a phantom containing 100 mM GABA in water. ExTE Editing was performed with echo times ranging from 115 ms to 445 ms in steps of 20 ms, with 16 averages per echo time. For comparison, conventional MEGA-PRESS spectra were acquired using the identical scan parameters and echo times. Finally, in-vivo data were acquired from a 3 x 3 x 3 cm^3 region in the primary visual cortex of a healthy volunteer using the ExTE MEGA-PRESS sequence with echo times of 120, 140 and 180 ms. At each echo time, the scan parameters were: TR=2400, 512 averages, spectral width = 1200 Hz, 2048 spectral points. Data preprocessing (frequency and phase drift correction [2], pre-subtraction alignment of subspectra) was performed using the FID-A processing toolbox (GitHub.com/CIC-methods/FID-A).

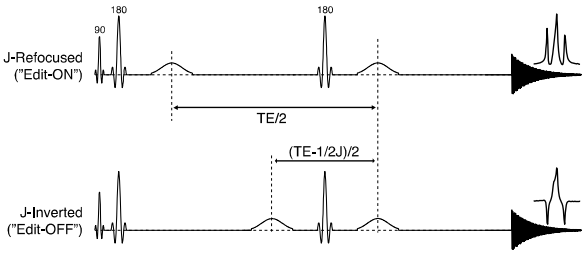

Figure 1. The ExTE MEGA-PRESS Sequence. Even and odd scans differ only in the timing of the editing pulses.

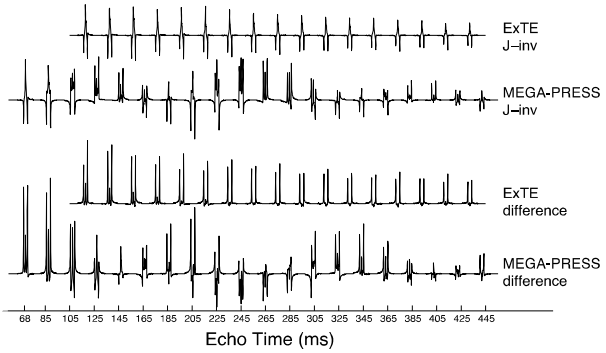

Figure 2. J-inverted and J-difference spectra acquired at different echo times using both the MEGA-PRESS sequence and the ExTE MEGA-PRESS Sequence. Using ExTE, the shape of the GABA resonance is nearly independent of echo-time. Only the 3ppm GABA resonance is shown.

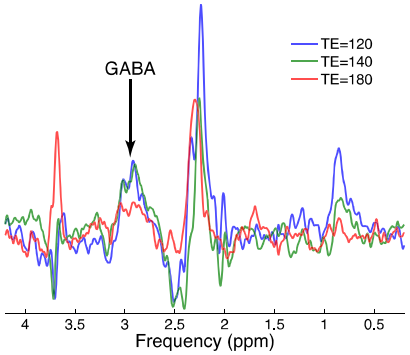

Figure 3. In-vivo data acquired with the ExTE sequence at three different TEs.

Results. Figure 2 shows phantom data acquired using the conventional MEGA-PRESS sequence and the ExTE MEGA-PRESS sequence at various echo times. Both the J-inverted/edit-off spectra and the difference spectra are shown. For the MEGA-PRESS sequence, as expected, the shapes of both the edit-off and difference spectra are strongly modulated as a function of echo time. However, for the ExTE MEGA-PRESS sequence, the shape of both the J-inverted and difference spectra are nearly independent of echo time. Figure 3 shows the results of the in-vivo GABA measurements at TEs of 120, 140 and 180 ms using the ExTE MEGA-PRESS sequence. As expected, the difference edited GABA signal is upright at each echo time. The lowest GABA signal amplitude is observed at the long echo time of 180ms, however, similar GABA amplitudes were observed at TE=120 and TE=140 ms.

Discussion. The ExTE method enables efficient J-difference editing of GABA at echo times longer than the standard 68 ms. There are a number of possible applications for this method. Firstly, use of the ExTE method would simplify the measurement of T2 relaxation of GABA; previous attempts have required sophisticated modeling of the scalar evolution of the GABA resonance [3,4]. Secondly, it is well known that conventional MEGA-PRESS GABA measures are confounded by significant macromolecular (MM) contamination. Using the ExTE method at long echo times would enable the removal of macromolecular components simply by virtue of their short T2. Finally, this technique may enable difference-edited detection of multiple coupled metabolites (GABA + Lactate) in a single acquisition. Due to the presence of editing pulses in both even and odd acquisitions, the appearance of the ExTE MRS data differs from conventional MEGA-PRESS data. Specifically, the residual NAA peak is absent.

Conclusion. The ExTE method provides efficient J-difference editing of GABA, with added flexibility in the choice of echo time.

References. 1. Mescher M et al. NMR Biomed 1998;11:266-72. 2. Near J et al. Magn Reson Med 2014; doi: 10.1002/mrm.25094. 3. Intrapiromkul J et al. J Magn Reson Imaging 2013;38(5):1224-9. 4. Edden RA et al. J Magn Reson Imaging 2012;35(1)229-34.