J-difference editing of GABA: simulated and experimental multiplet patterns

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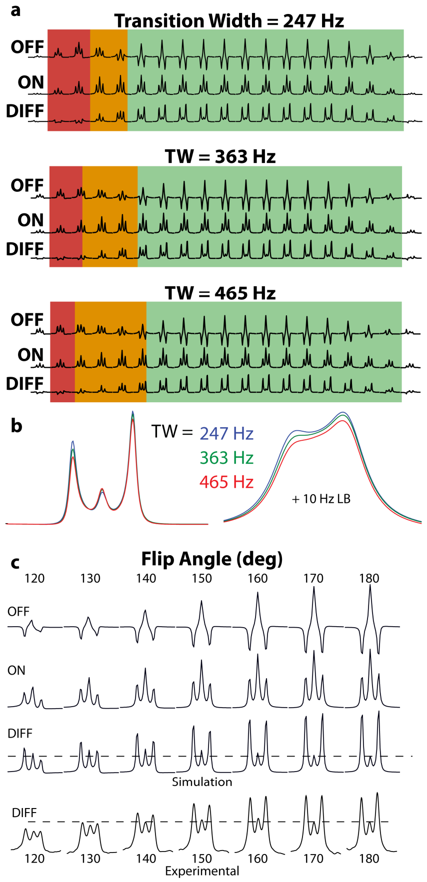
TARGET AUDIENCE Researchers interested in applying J-difference editing for detecting the neurotransmitter GABA in the brain.

PURPOSE J-difference editing of GABA is widely applied in clinical and cognitive neuroscience. For simple spin systems, the multiplet patterns detected by editing can be predicted from theory, particularly if ideal RF pulse behavior is assumed. However, for more complicated spin systems, spin systems containing strong-coupling, and in the presence of 'imperfections' in the RF pulses, the expected multiplet pattern can only be determined by numerical calculation. Simulations of multiplet patterns are important for MEGA-PRESS if they are to be used as basis functions for spectral fitting routines, as well as to recognize the presence or absence of artifacts in experimental spectra, so as to distinguish the 'true' GABA signal from those of subtraction artifacts. In this abstract, density-matrix simulations of the evolution of the GABA spin system are used to investigate the form of the 3 ppm GABA multiplet as a function of properties of the slice selective refocusing pulses of the MEGA-PRESS experiment. This investigation was motivated by two factors: firstly, MEGA-PRESS implementations on different scanners have variable center-peak intensities; and secondly, the expectation of a pseudo-doublet leads to the view that seeing a doublet splitting in *in vivo* edited spectra is a marker of data quality.

METHODS Simulations were performed using an in-house MATLAB-based (MathWorks, Natick MA) implementation of the density-matrix formalism. The chemical shifts and coupling constants of the GABA spin system were taken from (1). The MEGA-PRESS experiment was simulated by following the evolution of the density matrix ($\sigma(t)$) under the influence of a time-independent Hamiltonian corresponding to either free precession, or rotation about an RF field. Both excitation and editing pulses were assumed to be ideal rotations, while amplitude-modulated slice-selective refocusing pulses were simulated in full. The bandwidth of the slice selective refocusing pulses was set to 1050 Hz. Simulations were run to investigate the effect of transition bandwidth (TW); i.e. making the slice profile less rectangular) and the flip angle (FA) of slice selective pulses. TW simulations were run over a 19x19 spatial grid of positions; FA simulations were run for the voxel center. Phantom experiments were run to match FA simulations.

RESULTS The center row of the spatially resolved TW simulations is shown in Figure 1a. Where the flip angle applied to the 1.9 ppm spins is between 0˚ and 180˚ (shown in orange), there is more center-peak contribution to the edited signal. As the profile of slice-selective refocusing pulses becomes less rectangular, the spatial extent of the orange transition region is increased. Within this region, the OFF spectra have reduced amplitude, whereas the ON spectra are unaffected, with the net effect that the difference spectra look like the ON spectra, with full intensity center peaks in addition to the outer peaks. The sum over the whole 19x19 array is shown in Figure 1b, with the relative contribution of the center peak increasing with TW. With 10 Hz additional line broadening to simulate the in vivo case, it can be seen that the appearance of a doublet splitting is dependent on center-peak intensity. Figure 1c shows the simulated signal at 3 ppm for flip angles from 120˚to 180˚. There is a global reduction in signal intensity for flip angles below 180°, caused by reduced efficiency of refocusing. In addition, the center peak of the difference spectrum is relatively increased in the reduced flip angle case relative to the outer lines, largely due to reduced signal in the OFF spectrumT the experimental results for the same flip angles show similarly increased relative center-peak intensity at reduced flip angles.



DISCUSSION The simulations and experiments performed here illustrate several points about the 3 ppm GABA multiplet observed at 3T using the MEGA-PRESS editing sequence: namely, (a) even under conditions of ideal flip angle pulses, a small 'center' peak is present due to the presence of magnetically inequivalent methylene groups in the AA'MM'XX' spin system and unequal coupling constants between the 3, 3' and 4, 4' spins; (b) the multiplet is asymmetric (with the downfield outer line of lower intensity that the upfield at refocusing flip angles close to 180°) due to strong coupling effects; (c) that the relative intensities of the outer and central lines are dependent on the flip angles of the slice selective refocusing pulses - as the flip angle decreases from 180˚ the relative amplitude of the center line increases; (d) these effects will also be observed in the 'transition zone' of the slice selective pulses where the flip angle deviates from 180˚.

CONCLUSION The observed multiplet structure depends on multiple low-level acquisition parameters inherited from the base PRESS acquisition. Given the variability of center-peak intensity, the observation of the pseudo-doublet in itself is not a good metric for the 'quality' of an edited spectrum.

REFERENCES (1) Near et al. Proc ISMRM 2012, p.4386.