Spatial interference in localized J-difference GABA editing

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Introduction: One of the main problems with GABA detection *in vivo* in human brain is its inherent low concentration, which results in poor SNR. The low SNR can be further reduced by less than optimal experimental settings and detection methods. MEGA-PRESS implementation (1) of homonuclear J-difference editing is a very popular technique for measuring GABA *in vivo*, due to its relatively easy implementation and analysis. However, PRESS-based volume selection of this implementation introduces a spatial interference (also known as "4 compartment") artifact (2), which constitutes one of the most significant mechanisms for GABA signal loss. This artifact takes place in parts of the selected volume where J-coupled spin partners are not affected equally by the volume selective RF pulses. The first goal of this study was to use numerical simulations to examine how MEGA-PRESS editing sequence is influenced by the spatial interference artifact. The second goal was to examine alternative combinations of editing with PRESS (PRESS+4) to evaluate the ability to reduce this artifact.

Methods: The simulations and experimental verifications were carried out at 4 Tesla. Simulations were performed for sequences depicted in Fig.2 A (MEGA-PRESS) and Fig. 3A (PRESS+4) using C++ code which incorporated the GAMMA library. To reduce the complexity, the PRESS simulations assumed an ideal 90° excitation pulse without the volume selection gradient and were carried out for the two-dimensional plane, localized by the identical spin echo 180° pulses (with ideal square magnetization profile, bandwidth=900Hz). The simulation method used for the gradient volume selection with 180° pulses is described in detail elsewhere (3). The RF editing pulse (duration=18 ms) with gaussian shape (bandwidth=60 Hz) was initially generated in MATPULSE and digitized to 180 points. The frequency shifts for EDIT ON and OFF conditions (to 1.9 and 7.5 ppm) were accomplished prior to importing into GAMMA by multiplying the time domain pulse shape by the appropriate exponential function containing the corresponding frequency. All experiments were carried out with TE= 72 ms (For MEGA-PRESS: τ_1=6 ms, τ_2=36 ms, τ_3=30 ms; for PRESS+4: τ_1=τ_4=6 ms, τ_2=τ_3=30 ms). MEGA-PRESS simulations were compared to phantom GABA solution (100mM) spectrum acquired on a Bruker MedSpec 4 T whole body MRI system.

Results/Discussion: Figure 1 compared MEGA-PRESS simulation results (a) with experimental GABA solution (b). Overall, Figure 1 demonstrated good agreement between simulations and experimental data. The small deviations between the simulation and the phantom data were likely caused by T_2 differences between different GABA proton groups and line shape distortions from eddy currents (not accounted for in the simulations). Also apparent was the significant reduction of GABA outer peaks at 3.0 ppm in both simulations and phantom spectra for the EDIT OFF scan (middle) compared to EDIT ON scan (top). Figure 2b illustrated distribution of GABA outer peaks at 3 ppm at 4 Tesla for the MEGA-PRESS selected volume. While there was no observed signal loss during the EDIT ON acquisition, there was a substantial signal loss during EDIT OFF due to GABA phases in compartments 2 and 4 adding destructively with compartments 1 and 3. The spatial interference artifact in the MEGA-PRESS sequence induced signal loss of 40% in the EDIT OFF spectrum compared to non-localized conditions, resulting in the overall 20% loss in the difference spectrum. Figure 3b showed the GABA outer peak distributions in "PRESS+4" volume selection. Unlike in MEGA-PRESS experiment, GABA in all 4 compartments in the EDIT OFF case exhibited similar spectral appearances. The signal loss in PRESS+4 difference spectrum was only 2% compared to the non-localized simulation; this was mainly due to a small reduction in signal intensity during EDIT ON scan in compartment 1. Therefore, the GABA signal intensity acquired with PRESS+4 was 18% higher compared to the MEGA-PRESS sequence. This improvement would be even more dramatic at higher fields (i.e. 7 Tesla), since the amount of signal loss due to spatial interference is directly proportional to the frequency separation between GABA J-coupled spins (2).

Summary: In conclusion, numerical simulations of GABA J-difference editing were carried out and shown to be in good agreement with experimental data. It was shown that the MEGA-PRESS method of GABA J-difference editing suffers significant signal loss (~20% for the difference spectrum) due to the spatial interference artifact at 4T. Numerical simulations demonstrated that it is possible to preserve almost all of GABA signal by addition of the non-selective 180 pulse to PRESS localization. In summary, numerical simulations of realistic experimental components provide a powerful tool for optimization of spectral editing and quantification of edited metabolites.

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