Constant-TE difference editing of serine at 3T: Simulation and phantom Study

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INTRODUCTION

Activation of the N-methyl-D-aspartate (NMDA) receptor requires both glutamate binding and binding of an endogenous co-agonist at its glycine site. Accumulating evidence suggests that serine (Ser) is a potent agonist for the NMDA-glycine site [1]. Noninvasive measurements of Ser levels in human brain could therefore be important, particularly for the study of schizophrenia and its treatment with serine administration. Ser has three coupled resonances at 3.98, 3.96, and 3.83 ppm [2], forming an ABX spin system. Ser in human brain is difficult to measure due to its relatively low concentration (~0.5 mM) and the spectral overlap primarily with the creatine (Cr) 3.92 ppm resonance. Following the first attempt to detect Ser (4T) [3], measurement of Ser by constant-TE triple-refocused difference editing at 7T was reported recently [4]. This constant-TE difference editing strategy [5] has been explored for both PRESS (point-resolved spectroscopy) and triple refocusing at 3T. The feasibility of the methods is demonstrated with computer simulated and phantom data.

METHODS

The spectral pattern and signal intensity of coupled spins depend on subecho times of a multiple refocusing sequence, enabling difference editing of coupled resonances overlapped by uncoupled resonances (whose signal depends on the total echo time only). Subecho time dependence of the Ser multiplet at 3T was investigated, for both PRESS and triple refocusing, using density-matrix simulation incorporating the slice-selective RF pulses. A triple refocusing sequence had a 50-ms non-spatially selective RF pulse (bandwidth 326 Hz; tuned to 3.0 ppm) between the 180° pulses of a PRESS sequence. Spatial localization RF pulses included a 9.8-ms 90° RF pulse (BW = 4.2 kHz) and a 13.2-ms 180° RF pulses (BW = 1.3 kHz), at an RF field intensity of 13.5 μT. Phantom confirmation of the simulation results was carried out on a whole-body 3T scanner (Philips Medical Systems), using a body RF coil for transmission and an 8-channel phased-array coil for reception. Two phantoms were prepared at pH = 7.2; one with Ser 30 mM and glycine (Gly) 20 mM and another with Ser 1 mM and Cr 16 mM.

RESULTS AND DISCUSSION

For individual total echo times, difference between Ser multiplets was calculated for all possible pairs to obtain a pair of subecho time sets that gives maximum difference peak amplitude. The peak amplitude increases with TE for both PRESS and triple refocusing, as shown in Fig. 1. For PRESS, a maximum editing yield of 42% with respect to 90°-acquisition (for a voxel) is predicted at TE = 268 ms. It appears that triple refocused difference editing is more efficient in terms of editing yield, giving ~2-fold greater signal at TE = 345 ms. Fig. 2 displays simulated and phantom sub-/difference-spectra of Ser, Gly, and Cr, obtained at three pairs of subecho time sets of PRESS and triple refocusing. The spectral pattern and signal intensity of Ser are in good agreement between simulation (Fig. 2a) and experiment (Fig. 2b). Figure 2c presents spectra from a phantom with a Ser-to-Cr concentration ratio of 1/16. With complete suppression of the large Cr 3.92 ppm singlet via subtraction, the edited Ser multiplets agree well with those in Fig. 2b.

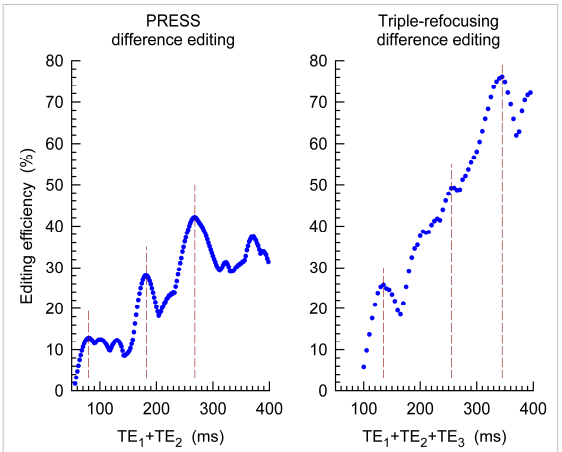

FIG. 1. The simulated difference editing yield of Ser is plotted vs. total echo time TE for PRESS and triple refocusing. The amplitude was obtained from the Ser multiplet broadened with a 5-Hz exponential function. Vertical lines indicate TE of spectra shown in Fig. 2.

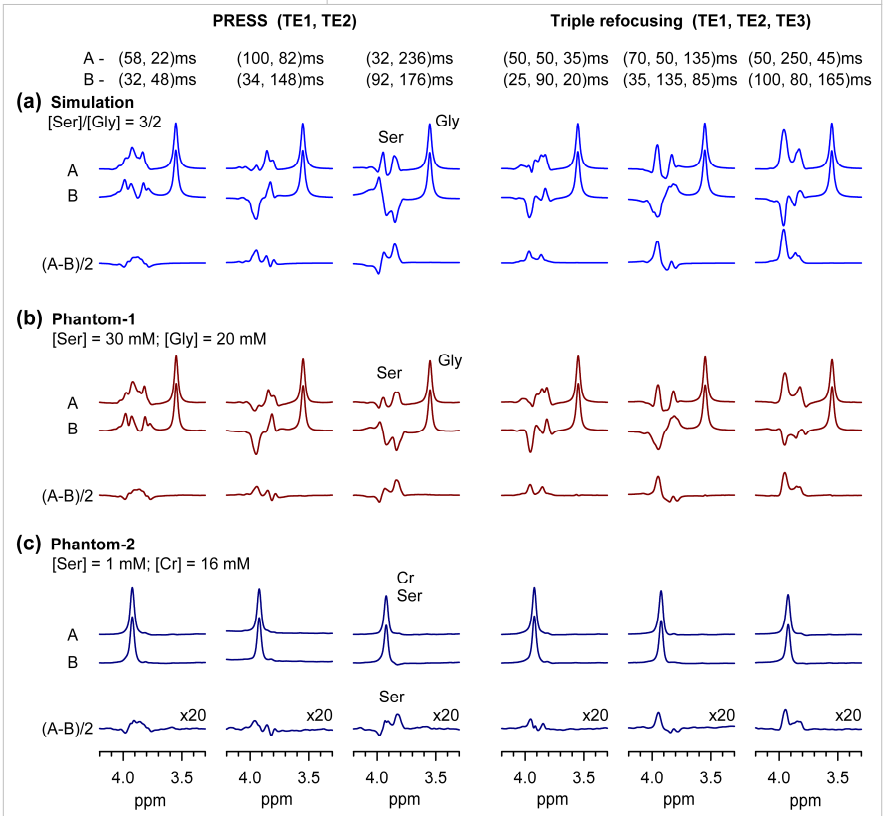

FIG. 2. Simulated and phantom spectra of Ser, Gly, and Cr. Sub- and difference-spectra, labeled A, B, and (A-B)/2, are shown for three pairs of subecho time sets of PRESS (left) and triple refocusing (right). Spectra are broadened to 5 Hz.

Several factors may have to be taken into account for *in vivo* Ser measurement. First, T_2 signal loss *in vivo* is much greater than in phantom solutions, so the *in vivo* signal yield will be different than in Figs. 1 and 2. Ser T_2 is not known, but presumably published T_2 values of brain metabolites [6] may be used for determining a TE for *in vivo*. Second, co-editing of macromolecule (MM) resonances is inevitable in this type of editing. It appears that MM resonances are fairly abundant in the proximity of the Ser resonances [7]. Since MM signals decay rapidly with increasing TE, long TE may be beneficial for minimizing MM contamination. Third, in addition to its greater signal yield compared to PRESS editing, triple refocused editing has an advantage that the additional 180° pulse within PRESS can be utilized for further water suppression, as in the present study. Complete water suppression is important especially for Ser editing since the Ser resonances are close to the water resonance. Lastly, several metabolites have coupled resonances in the proximity of the Ser resonance [2]; *i.e.*, aspartate, phosphoethanolamine, glycerophosphocholine, ethanolamine, etc. Further echo time optimization will be required for minimizing their potential contaminations. This is currently underway.

REFERENCES

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