In vivo detection of Serine in Human Brain by Constant-TE Difference Editing at 3T

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INTRODUCTION

Serine (Ser) is an endogenous amino acid in brain which functions as a co-agonist with glutamate at the NMDA receptor. In disorders of cognition, especially psychosis, alterations in glutamate transmission have been found, possibly including serine signaling [1]. Noninvasive measure of Ser in brain could be pivotal in defining regional tissue pathology. Ser has three coupled resonances at 3.98, 3.96, and 3.83 ppm [2]. Ser is difficult to measure due to its relatively low concentration (~0.5 mM) and the spectral overlap with the creatine (Cr) 3.92 ppm resonance. Following the first attempt to detect Ser (4T) [3], measurement of Ser by constant-TE triple-refocusing difference editing at 7T was reported recently [4]. Here, we have exploited this editing method for measurement of Ser at 3T. A preliminary *in vivo* result from a healthy volunteer is presented.

METHODS

The spectral pattern and signal intensity of coupled spins depend on subecho times of multiple refocusing at a constant total echo time. This affords difference editing of coupled resonances overlapped by a singlet since the singlet can be eliminated via subtraction between spectra obtained using a pair of constant-TE subecho time sets [5]. We have explored difference editing of Ser using triple refocusing at 3T. A 50-ms non-spatially selective RF pulse with bandwidth of 326 Hz, tuned at 3.0 ppm, was applied between the 180° pulses of a PRESS sequence. Volume 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. Editing performance was investigated, with computer simulations, for all possible pairs of subecho time sets (TE_1, TE_2, TE_3) for TE between 100 – 350 ms. An *in vivo* test of Ser editing was carried out on a whole-body 3T scanner (Philips Medical Systems). A body RF coil was used for transmission and a single-turn surface coil for reception. *In vivo* data were obtained from the occipital cortex of a healthy subject (voxel size 25×35×35 mm^3). Data were acquired with sweep width of 2.5 kHz (number of sampling points = 2048). Data were corrected for frequency drift and residual eddy current artifacts. The total echo time of the editing was 255 ms. Repetition time was 2 s. LCModel software [6] was employed to analyze sub- and difference-spectra, using numerically calculated model spectra.

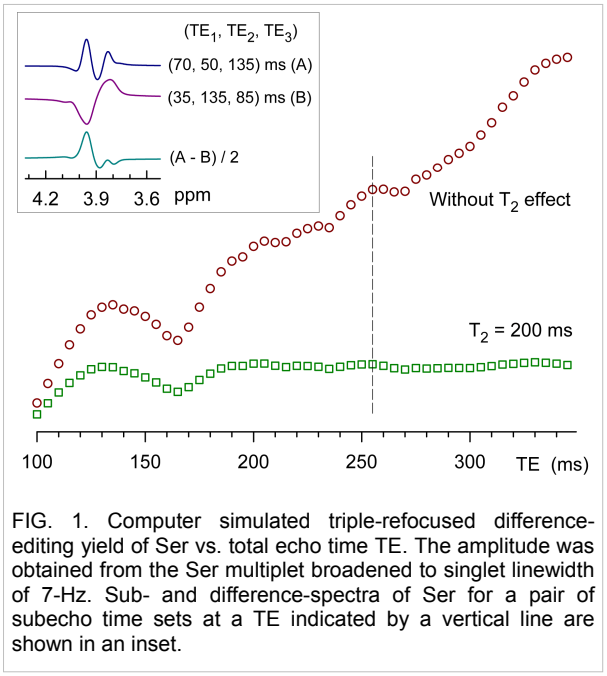

FIG. 1. Computer simulated triple-refocused difference-editing yield of Ser vs. total echo time TE. The amplitude was obtained from the Ser multiplet broadened to singlet linewidth of 7-Hz. Sub- and difference-spectra of Ser for a pair of subecho time sets at a TE indicated by a vertical line are shown in an inset.

RESULTS AND DISCUSSION

Figure 1 shows TE dependence of the Ser difference-edited peak amplitude. The peak amplitude increases with TE, leading to a maximum difference editing yield of 76% at TE = 345 ms with respect to 90°-acquisition for a localized volume, ignoring T_2 signal loss. Assuming an in vivo T_2 of Ser at 200 ms, which is a mean value of published Cr and NAA T_2's [7], the peak amplitude remains about the same at TE > 200 ms. We selected a pair of subecho time sets at TE = 255 ms since the edited Ser multiplet is relatively narrow, as shown in an insert.

Figure 2a displays simulated sub- and difference-edited spectra of brain metabolites at the physiological concentrations and the individual difference spectra of 12 metabolites that have coupled resonances close to the Ser resonances and consequently could interfere with Ser editing. Major contaminants may include aspartate, phosphoethanolamine, ethanolamine, and glycerophsphocholine since these compounds have coupled resonances that overlap with the Ser CH_2 resonances. For a concentration ratio shown in the figure, the peak amplitudes of these compounds do not exceed 30% of the Ser peak. Figure 2b presents *in vivo* spectra from the occipital cortex, together with LCModel fits for both sub- and difference spectra. The *in vivo* spectra were reproduced by the fits, leading to residuals at the noise levels (not shown). The Ser to NAA concentration ratio was measured as 0.05. This result is in good agreement with a prior study at 7T [4]. Macromolecule resonances appear to be fairly abundant near the Ser resonances [8]. With the long TE used for the *in vivo* tests, the contamination from coupled macromolecule resonances may be negligible. Further echo time optimization is currently underway to minimize the coediting of the overlapped resonances.

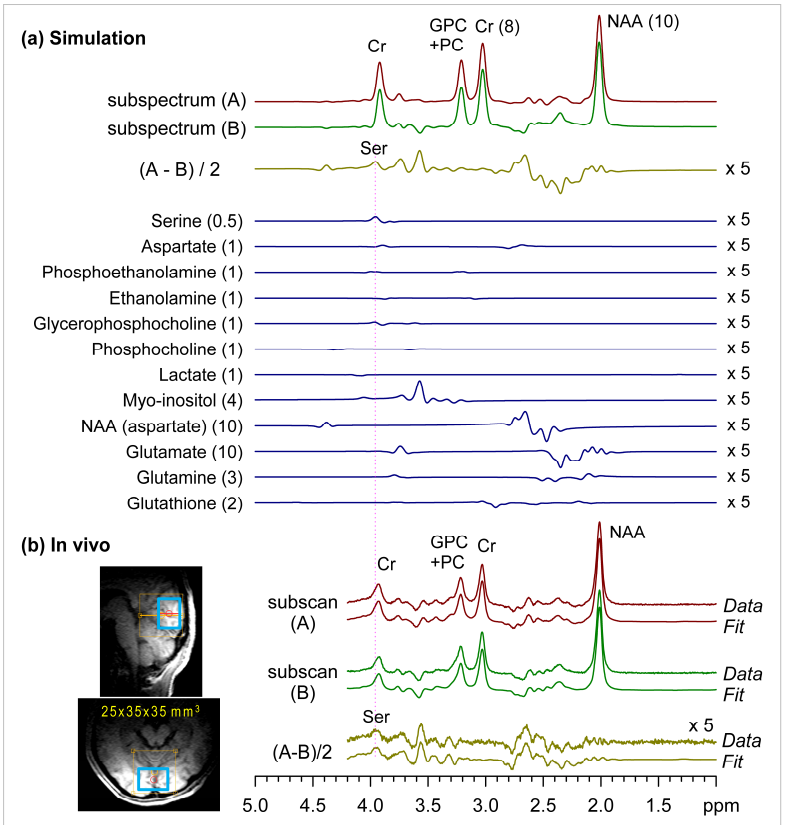

FIG. 2. Simulated (a) and *in vivo* (b) spectra of Ser difference editing. The concentrations of compounds used for simulation are shown in brackets. For *in vivo*, sub- and difference-spectra are shown together with LCModel fits. Difference spectra are 5-fold magnified. Voxel positioning (25x35x35 mm^3) is shown in the images. TR = 2 s. NEX = 256 (subscan).

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