Selective Measurement of Brain Glutamate and Glutamine In Vivo by Spectrally-selective Refocusing at 7T

C. Choi[1], C. Zhao[1], I. Dimitrov[1,2], A. Stan[3], and C. Tamminga[3]

[1]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [2]Philips Medical Systems, Cleveland, OH, United States, [3]Psychiatry, University of Texas Southwestern Medical Center, Dallas, Texas, United States

INTRODUCTION

Similarity between the glutamate (Gln) and glutamine (Gln) spin systems causes spectral overlap, making it difficult to measure the metabolites reliably using conventional short-TE ^{1}H-MRS methods. With its relatively low concentration and the overlap with additional neighboring resonances of N-acetylaspartate (NAA) and with the macromolecule baseline signals, precise measurement of Gln is limited even at 7T, unless exceptionally good shimming is achieved [1]. It was reported recently that the C4-proton resonances of Glu and Gln can be separated by means of spectrally-selective refocusing at 3T [2], which utilized the spectral difference between the C4-proton resonances of Glu and Gln, i.e., ~0.1 ppm. In addition to enhancement of spectral resolution, high field is beneficial to spectral editing because the increased spectral distance enables to use relatively short RF pulses for spectrally-selective excitation. This reduces the coherence evolution during the RF pulse and may increase the editing yield. We have investigated the performance of spectrally-selective refocusing for Glu and Gln measures at 7T. Preliminary results of sequence optimization by density-matrix simulation and in vivo tests are presented.

METHODS

Spectrally-selective refocusing has been employed for selective measurement of Glu and Gln on a Philips Medical Systems 7T spectrometer. A 50-ms long single-band Gaussian 180° RF pulse (truncated at 10%) was implemented between the slice-selective 180° RF pulses of PRESS. Spatial localization was obtained with a 13-ms long frequency-modulated 90° RF pulse ("fremex05"; BW = 3.2 kHz) and two 16-ms long optimized 180° RF pulses ("refoman6"; BW = 1.0 kHz). Density matrix simulation was used to investigate the responses of Glu, Gln, and NAA spin systems to the filtering sequence, incorporating slice-selective RF and gradient pulses. The carrier frequency of the Gaussian 180° pulse and the echo time were optimized using numerical calculations. Published chemical shift and coupling constants [3] were used. T_1 and T_2 effects were not included in the simulation. In vivo tests of the filtering sequences were conducted on the anterior cingulate cortex of a healthy volunteer (50×15×15 mm^3 voxel) (see Fig .3). A standard quadrature birdcage head coil was used for RF transmission and reception.

RESULTS AND DISCUSSION

Fig. 1(left) displays the numerically-calculated Glu and Gln peak amplitude versus the carrier of the filtering Gaussian 180° pulse. At carriers of 2.35 and 2.45 ppm, the difference in signals from Glu and Gln becomes maximal. **Tuning** of the spectrally selective refocusing pulse to these frequencies permits the discrimination of the Glu and Gln signals in separate scans. Fig. 1(right) shows the calculated TE dependence of the Glu and Gln peak amplitude. At TE = 100 ms, which is the shortest possible TE under the given durations of RF pulses, the Glu and Gln peak amplitude is 60% and 36% with respect to 90°-acquired spectra from an identical voxel. However, the coherence evolution leads to greater signal return at later TE. The computer simulation indicates that, at TE = 137 ms, the peak amplitude is, ignoring T_1 and T_2 effects, 67% and 53% relative to 90°-acquisition for Glu and Gln, respectively.

Fig. 2 presents calculated spectra of Glu, Gln and NAA (Asp moiety) for 90°-acquisition and Glu-Gln filtering (TE = 137 ms). For equal concentration between Glu, Gln and NAA, the Glu filter generates a Glu target multiplet at 2.35 ppm, with negligible contamination (< 2%). In the Gln-filtered spectrum, NAA causes spectral overlap with the target Gln multiplet. Fig. 3 shows spectrally-selective refocusing (SSR) filtered spectra of NAA, Cre, Glu and Gln. The Glu-to-Cre peak area ratio is ~0.62. With a simulation value of 0.44 for identical concentration, assuming same T_1 and T_2 between Glu and Cre, the Glu concentration is estimated as 11 mM for [Cre] = 8.0 mM. For Gln, the NAA contamination can be separated using its 2.01-ppm singlet intensity. The simulation indicates that the area of the coedited NAA aspartate peak is 7.4% with respect to the NAA 2.01-ppm singlet. Excluding the NAA portion from the filtered signal in the brain SSR-Gln spectrum, the remaining portion, which is the pure Gln signal, is estimated as 16% relative to the Cre 3.03-ppm peak (SSR-Cre). With a simulated Gln-to-Cre peak area ratio of 36% for equal concentration, the Gln concentration is estimated to be 3.6 mM for [Cre] = 8.0. A short-TE STEAM spectrum from the same voxel is shown for comparison in Fig. 3. Further in vivo studies of SSR filtering are currently underway.

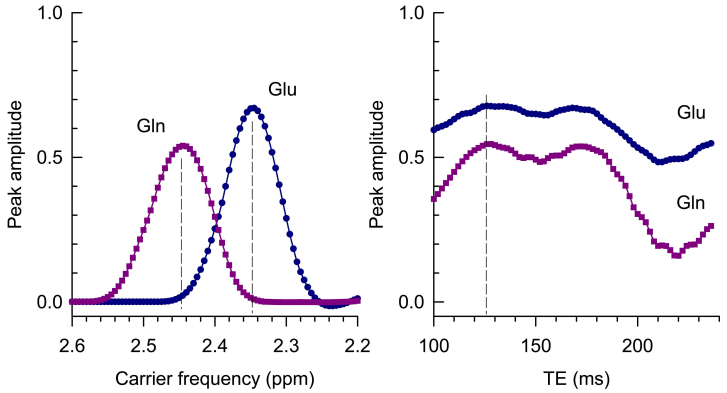

FIG. 1. (**Left**) Numerically-calculated carrier frequency dependence of the amplitude of the Glu and Gln C4-proton multiplets, for a 50-ms long Gaussian (truncated at 10%) 180° RF pulse within PRESS. Separation of Glu and Gln signals is achieved at carriers of 2.35 and 2.45 ppm, indicated by vertical dashed lines. (**Right**) Numerically-calculated TE dependence of Glu and Gln peak amplitude, for the spectrally-selective refocusing method. The y-axis is all normalized with respect to 90°-acquired signals. TE = 137 was chosen for in vivo tests for both Glu and Gln.

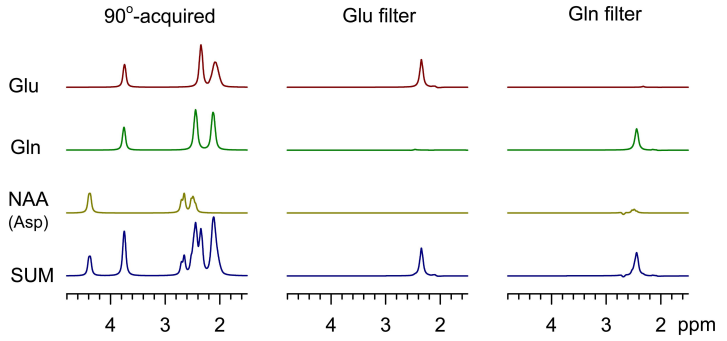

FIG. 2. Calculated spectra of Glu, Gln and NAA, following 90°-acquisition and spectrally-selective refocusing Glu and Gln filters are shown for equal concentration. Spectra are broadened to match the in-vivo linewidth (~13 Hz).

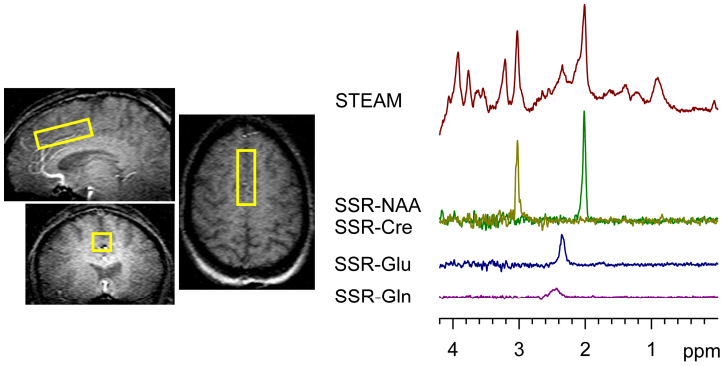

FIG. 3. In vivo human brain spectra, obtained with STEAM {TE, TM} = {19, 25} ms, and spectrally-selective refocusing (SSR) tuned for NAA, Cre, Glu and Gln. Number of averages was (from the top) 64, 16, 16, 64 and 128. TR = 2.4 s. The data were filtered with a 1-Hz exponential function.

REFERENCES

1. Tkac I *et al.*, Magn Reson Med 2001;46:451-456.
2. Choi C *et al.*, Magn Reson Med 2006;55:997-1005.
3. Govindaraju V *et. al.*, NMR Biomed 2000;13:129-153.