Detection of Resolved Glutamate and/or Glutamine Using Optimized STEAM at 3T – A Verification Study by Phantom Experiments

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Introduction
Glutamate (Glu) and Glutamine (Gln) are two important neurotransmitters in the central nervous system (CNS). In conventional one-dimensional 1H MR spectrum at 1.5-4.7 Tesla, the C4 multiplet resonances of Glu and Gln usually overlap around 2.3-2.5 ppm, which may impair accurate, reliable quantification [1]. A recent study, through density-matrix simulation and parameter optimization, suggested the possibility of simultaneously detecting unobstructed Glu and Gln in standard STEAM spectra at 3, 4, 4.7, 7, and 9.4 Tesla [2]. The underlying idea was to find optimal TE and TM timing parameters of a standard STEAM sequence, at which the C4 multiplet resonances of Glu around 2.35 ppm and Gln around 2.45 ppm turned into pseudo-singlets (i.e., with suppressed outer-wings), thus reducing the overlap either between the outer-wings of two target C4 multiplet resonances or between the outer-wing of one resonance and the central peak of the other resonance. In the present study, we carried out a set of phantom experiments to verify the simulation-predicted timing parameters of a standard STEAM sequence at 3 Tesla, the most commonly-used magnetic field in basic and clinical application. We also demonstrate the feasibility of this technique with preliminary in vivo examples.

Methods
Phantom experiments were conducted on a Siemens Allegra 3T scanner using a quadrature head coil and a standard 1H STEAM localization pulse sequence. The phantom was taken out from the refrigerator a day before the scan, which allowed sufficient time for the solution to reach the room temperature. Also there was a one-minute interval between every six continuous scans to avoid any potential temperature change in the solution, which may induce a frequency shift. With these precautions, stable spectroscopic data were observed during the experiments. Besides the phantom experiments, we also carried out preliminary in vivo tests on the anterior cingulate cortex (ACC) of healthy human brain.

Results and Discussions
The in vitro spectral raw data were first preprocessed in the Java-based magnetic resonance user interface (jMRUI) software package [3] and were evaluated on the patterns of the C4 multiplet resonances of Glu and Gln at 2.3-2.5 ppm. Generally, the Glu C4 multiplet resonance yielded more like a triplet [4], while the Gln C4 resonance mostly had a nearly-split “central-peak”. Part of the reason of the above phenomenon is related to a relatively large r difference in the chemical shifts of the CH2 protons of Gln (0.022 ppm) than that of the Glu 4CH2 protons (0.015 ppm) [5]. The outer-wings of the Glu C4 resonance were significantly suppressed at multiple parameter “islands” in the (TE, TM) space, including a small “island” around (72 ms, 06 ms) and two larger “islands” around (84 ms, 56 ms) and (82 ms, 122 ms). It was relatively more difficult to suppress the outer-wings of the Gln C4 resonance than that of the Glu C4 resonance [6]. The outer-wings of the Glu C4 resonance mostly had a nearly-split “central-peak”. Part of the reason of the above phenomenon is related to a relatively large r difference in the chemical shifts of the CH2 protons of Gln (0.022 ppm) than that of the Glu 4CH2 protons (0.015 ppm) [5]. The outer-wings of the Glu C4 resonance were significantly suppressed at multiple parameter “islands” in the (TE, TM) space, including a small “island” around (72 ms, 06 ms) and two larger “islands” around (84 ms, 56 ms) and (82 ms, 122 ms). It was relatively more difficult to suppress the outer-wings of the Gln C4 resonance than those of Glu C4 resonance. However, the outer-wings of the Glu C4 resonance, especially the upfield one, did decrease in amplitude at two parameter “islands” around (70 ms, 06 ms) and (70-96 ms, 80-130 ms), respectively, with a 2-ms step in each parameter. As a result, a total of 551 scans were carried out for each metabolite and the experiments for each metabolite were done within one week, a time period for Glu and especially Gln to stay undegraded. Considering the overlap from the background and other overlapping metabolites, it was obtained that only 9 scans were acquired from the spectrum acquired at (72 ms, 06 ms) and (84 ms, 58 ms), respectively, at 3T. A virtual singlet peak of Glu C4 resonance, especially in the spectrum acquired at (84 ms, 58 ms), is clearly visible at 2.35 ppm and well-resolved from the background and other overlapping metabolites.

References