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 ^{1}H 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 ^{1}H STEAM localization pulse sequence. The sequence parameters, besides a variety of chosen (TE, TM), were TR = 2 s, bandwidth = 2 kHz, voxel-size = 2x2x2 cm^3, and NEX = 256. The phantom set consisted of two phantoms containing either 50mM Gln or 50mM Glu in a buffered solution (pH = 7.2), and the solutions were put in plastic spheres with a 4.38" diameter. In the study reported in [2], 7000 spectra were simulated for each metabolite, covering a large range of TE (0 – 200 ms) and TM (0 - 140 ms) with a step of 2 ms in each parameter. If the same size of phantom experiments were performed using the above mentioned sequence parameters, it would take 1.5-months for one metabolite, which is obviously unfeasible in reality. Therefore, a limited (although still large) set of phantom experiments was carried out. We used the contour diagram of the cost function (or index) defined in [2] to select three most promising TE and TM ranges for phantom experiments. The chosen (TE, TM) ranges, as shown in the white boxes of Fig. 1, cover (60-80 ms, 6-10 ms), (70-90 ms, 44-70 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 un-degraded. 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 larger difference in the chemical shifts of the $^4CH_2$ protons of Gln (0.022 ppm) than that of the Glu $^4CH_2$ protons (0.015 ppm) [5]. The outer-wings of the Glu C4 resonance were significantly suppressed at multiple isolated 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 Gln C4 resonance, especially the upfield one, did decrease in amplitude at two parameter "islands" around (70 ms, 06 ms) and (76 ms, 130 ms). One of the common optimal TE/TM parameters for Glu and Gln matched the optimal 3T parameters predicted in [2], i.e., (72 ms, 06 ms). The corresponding phantom spectra acquired at (72 ms, 06 ms) and (84 ms, 58 ms) are shown in Fig. 2 and these spectra were multiplied with a filter to render them representative of typical *in vivo* line widths. A low level of upfield outer-wing of Gln C4 resonance still remains, which is well consistent with the simulation prediction [2].

Besides the above qualitative evaluation, quantitative analysis is needed for a better evaluation of these phantom spectra. As relatively long echo times are used in the STEAM sequence, the T_1 and T_2 relaxation effects may be considerable in *in vivo*. Considering the relaxation effects in evaluation of either simulated or phantom data may help bring about more realistic timing parameters of a standard STEAM sequence for the *in vivo* application, which is the next step of this study. In the *in vivo* spectra of healthy people, the Gln signal is usually rather lower, sometimes even completely immersed in the background or just with a small bump, while the Glu signal is much stronger, especially in the frontal gray matter of human brain. As such, using the most optimal STEAM timing parameters for Glu only may be more practical in these situations. Fig. 3 shows *in vivo* STEAM spectra from a single voxel encompassed the ACC of a healthy volunteer using the sequence timing parameters of (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.

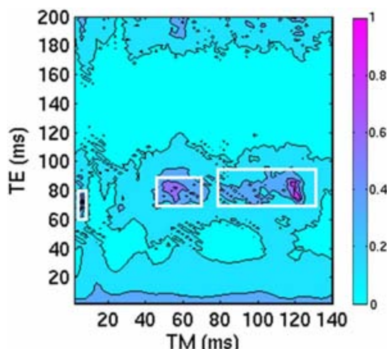

Fig. 1. Contour diagram of the cost function designed in [2] for unobstructed Glu and Gln detection with chosen (TE, TM) regions in white boxes for phantom experiments.

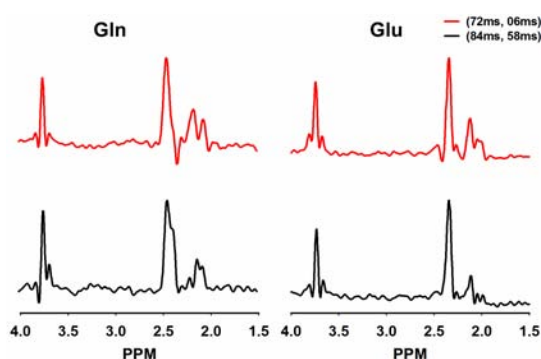

Fig. 2. *In vitro* STEAM spectra of Glu and Gln acquired at (72ms, 06 ms) and (84 ms, 58 ms) at 3T and multiplied with a filter to render them representative of typical *in vivo* line widths.

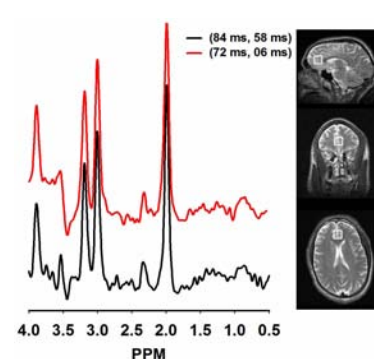

Fig. 3. *In vivo* STEAM spectra acquired from a voxel including the ACC of a healthy volunteer with the sequence timing parameters of (72 ms, 06 ms) and (84 ms, 58 ms), respectively, at 3T.

References

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