Simultaneous Detection of Unobstructed Glutamate and Glutamine Using Standard STEAM with Optimized Sequence Parameters at 3, 4, 4.7, 7, and 9.4 Tesla - A Simulation Study

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Introduction

Glutamate (Glu) and Glutamine (Gln) are two important neurotransmitters in the central nervous system (CNS). In standard one-dimensional ^{1}H MR spectroscopy, however, the signals of the two compounds around 2.3-2.5 ppm usually overlap, particularly at low field strengths, which impairs accurate and reliable quantification. A recent report suggested the possibility of simultaneously detecting Glu and Gln (and GABA in pathological conditions) in standard STEAM spectra with minimized spectral overlap around 2.3-2.5 ppm at 4T [1]. The essential idea was to find sequence parameters for STEAM, at which the PQ-multiplets of the AMNPQ spin systems of Glu and Gln appeared as pseudo-singlets (with suppressed sidelobes) and thus reduce the overlap between the sidelobes of the two compounds or between the sidelobes of one compound and the central peak of the other compound. In that report, however, the sequence parameters were optimized by searching in a limited set of phantom experiments, which would be tedious and inefficient for a full search in large experiments. In this study, we performed spectral simulation for STEAM using the GAMMA NMR library [2] and optimized sequence parameters for suppressing sidelobes while maintaining the central-peak signal. Besides verifying the reported optimized sequence parameter set at 4T [1], we also extended the optimization process to other magnetic field strengths, i.e., 3, 4.7, 7, and 9.4 Tesla.

Methods

Spectral Simulation in GAMMA. The spectral response of each compound to the standard STEAM sequence throughout the two-dimensional {TE, TM} parameter space was calculated at each magnetic field strength, using the publicly available GAMMA NMR library [2]. A range of 0 to 200 ms with a step size of 2 ms was covered for TE and a smaller range of 0 to 140 ms with the same step size for TM. The three 90º pulses in STEAM were simulated using ideal pulses for computation efficiency, since a realistic selective 90º pulse does not deviate far from the ideal case. For the effects of gradients in the two TE/2 periods and the TM period, a more complete simulation was used, in which a cubic voxel of 20x20x20 mm^3 was divided into 1000 sub-voxels (10 steps each in the x-, y-, or z-direction), and the signals from the sub-voxels were summed up. The gradients applied in the simulation were equivalent in effect to those of a realistic STEAM sequence. After a 5-Hz line broadening, the spectral data were input into a Java-based magnetic resonance user interface (jMRUI) software package [3] for further processing. The ^{1}H NMR chemical shifts and coupling constants for the brain metabolites were obtained from the literature [4].

Search for Optimized STEAM Parameter Sets. For each compound, a total of 7000 spectra with different {TE, TM} parameter sets were simulated at each magnetic field, from which a full search was performed to find out optimal parameter sets for unobstructed detection of Glu and Gln. An index or cost function was defined for the optimization procedure. Fig. 1 shows the simulated STEAM spectra of Glu and Gln at 4T with {TE, TM} = {10 ms, 10 ms} and a line broadening of 5 Hz. The shaded bars indicate the regions of the central peaks of the two pseudo-triplets. Simulation revealed that the two central peaks are separate from each other at 4T and at other magnetic fields from 3T to 9.4T. However, overlap exists between the sidelobes of the two pseudo-triplets and/or between the central peak of one pseudo-triplet and the sidelobes of the other one. The former happened at 3T, 4T, and 4.7T, but much less at 7T and 9.4T, and the latter mainly at 3T. Regardless of field strength, if the sidelobes of the pseudo-triplets can be suppressed while maintaining the two central peaks, the spectra of the two compounds should be readily separated from each other. Based on the above observation and analysis, an index was defined, for each compound, as $\boldsymbol{F} = [\boldsymbol{b}]^2/([\boldsymbol{a}]+[\boldsymbol{c}])$, where $[\boldsymbol{b}]$ is the area of the central peak of the pseudo-triplet, $[\boldsymbol{a}]$ and $[\boldsymbol{c}]$ are the areas of the two sidelobes, as shown in the top frame of Fig. 1. The boundaries of the three regions were determined based on the simulated spectra at {10ms, 10ms}. The ultimate index used for the optimization was the product of the individual indices for Glu and Gln, i.e., $\boldsymbol{F} = \boldsymbol{F}_{\mathrm{Glu}}\cdot\boldsymbol{F}_{\mathrm{Gln}}$, which was the combined contribution from the two compounds.

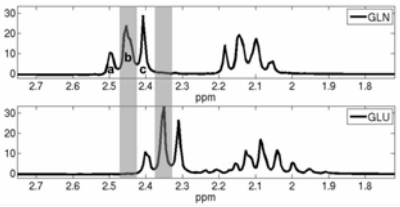

Fig. 1. Simulated STEAM spectra of Glu and Gln at 4T with {TE, TM} of {10ms, 10ms} and a 5-Hz line broadening. In the top frame, **a**, **b** and **c** stand for the three regions of the pseudo-triplet.

Results and Discussions

A set of contour diagrams, in the {TE, TM} space of the STEAM sequence, of the ultimate index $\boldsymbol{F} = \boldsymbol{F}_{\mathrm{Glu}}\cdot\boldsymbol{F}_{\mathrm{Gln}}$ at the five magnetic fields are shown in Fig. 2a-e. The contours were individually normalized to the maximum at each field strength. The maximum ultimate indices at each field are shown in Fig. 2f. At 4T the optimized {TE, TM} sets were distributed in the range of 40-60 ms for TM and 70-90 ms for TE, and the maximum index appears at {82ms, 48ms}. This confirms the previous results of phantom experiments [1], which found the optimized parameter set at {80ms, 50ms}. Fig. 3 shows the spectra using the optimized sequence parameters (associated with the maximum ultimate indices in Fig. 2f) at each field strengths, along with the 3T-spectra at {10ms, 10ms} as a reference. The spectra were normalized to the maximum individually at each field. Compared with the corresponding spectrum at {10ms, 10ms}, the spectra at the optimized sequence parameters appear as pseudo-singlets, especially at 4T, 4.7T, 7T, and 9.4T. A low level of sidelobes remains at 3T. These results indicate that simultaneous detection of the pseudo-singlets of Glu and Gln signals using standard STEAM sequence is possible at these field strengths. On the other hand, due to increased spectral separation at 7T and 9.4T (the J-coupling constants are B_0-independent) [5], spectral overlap between the coupled spin systems of Glu and Gln at higher magnetic fields is not as critical as in the lower fields. Therefore, this technique will be mostly useful at middle field strengths (3-4.7T).

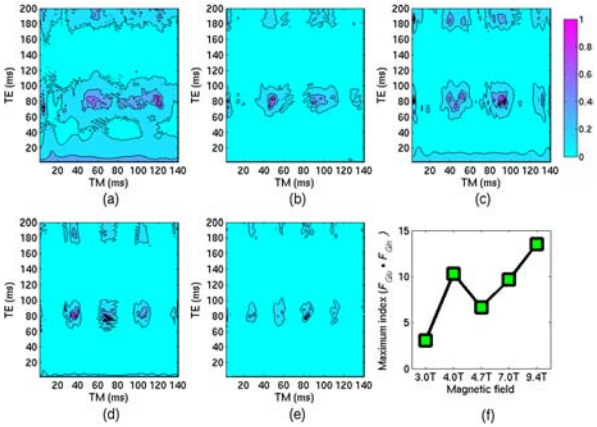

Fig. 2. Contour diagrams, in {TE, TM} parameter space, of the ultimate index calculated at (a) 3T, (b) 4T, (c) 4.7T, (d) 7T, and (e) 9.4T, normalized to the maximum in each data set. The maximum ultimate indices at individual magnetic fields are shown in (f).

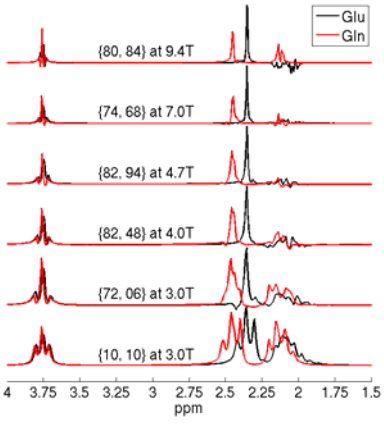

Fig. 3. STEAM spectra using the optimized sequence parameters at the five fields and the 3T-spectra at {10ms, 10ms} at bottom as a reference.

References

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[4] Govindaraju V et al., NMR Biomed 2000;13:129-153. [5] Tkáč I et al., MRM 2001; 46:451-456.