Simultaneous Measurement of Unobstructed Glutamate and Glutamine Signals in TE-Averaged PRESS Spectra at 3T Using An Optimized Filter Function

S. Yang[1], E. A. Stein[1], Y. Yang[1]

[1]Neuroimaging Research Branch, National Institute on Drug Abuse, NIH, Baltimore, MD, United States

Introduction

Noninvasive detection of Glutamate (Glu) and Glutamine (Gln) using MR spectroscopy has been of great interest. However, the measurement is challenging due to the overlapping spectral signals between Glu and Gln using conventional one-dimensional (1D) ^{1}H spectra at low field. To address this problem, a TE-averaged PRESS technique has been proposed, in which the Glu signal at 2.35 ppm appears as a pseudo-singlet and the neighboring Gln signal (around 2.45 ppm) is minimal [1]. A recent report showed that the Gln signal can be recovered from the same multiple-TE data set while the Glu signal is suppressed by applying a simple filter function [2]. In this study, we extended the above techniques to obtain Glu and Gln pseudo-singlet signals simultaneously from the same multiple-TE data set.

Theory and Methods

Spectral Simulation in GAMMA. GAMMA NMR simulation [3] was utilized to simulate the individual PRESS spectra of Glu, Gln, and other compounds at 128 different TEs, from 35 ms to 352.5 ms with a step size of 2.5 ms, using chemical shifts and coupling constants from the literature [4]. Simulation results (Fig.1) show that the Glu signal around 2.35 ppm generally appears as a pseudo-triplet, with the central peak almost always positive, but the two sidelobes changing their signs periodically. For the Gln signal around 2.45 ppm, the two sidelobes have the same periodical variation as Glu, but the central peak does not remain positive with TEs. These phenomena suggest the possibility of obtaining a pseudo-singlet for Glu while keeping Gln signal minimal by simply summing up spectra collected at various TEs. On the other hand, using a different scheme to combine the spectra at different TEs, it might be possible to obtain the positive Gln signal while maintaining a sufficient level of Glu signal from the same data set.

Phantom and Human Experiment. Data from a phantom were acquired on a Siemens Allegra 3T scanner with a quadrature head coil. The phantom includes two containers filled with a buffered solution (pH=7.4) of 12.3 mM/L Choline (Cho) plus 40.6 mM/L Glu or 40.6 mM/L Gln. Human experiments were performed with a voxel in the anterior cingulate cortex (ACC). The sequence was derived from a single-voxel TE-averaged PRESS, which is able to save the individual PRESS spectrum at each TE. Sequence parameters: TR = 2000 ms, voxel size = 20×20×20 mm^3, spectral bandwidth = 2000 Hz, sampling points = 2048, number of TEs = 128 (from 35 ms to 352.5 ms with a step size of 2.5 ms), and NEX = 2.

Filter Function and Its Optimization. A filter function was determined to optimally select weighting coefficients for combining the data acquired at different TEs. To guarantee similar noise characteristics in the composite spectrum as the TE-averaged PRESS spectrum [1], we constrained the weighting coefficients to ether 1 or -1. Furthermore, due to the periodicity with TE (Fig.1), we also constrained the number of transition steps (at which the weighting coefficients change between 1 and -1) to 1, 2, or 3. Another degree of freedom in optimization was the final TE (from the 1st to 128th step) included in the combining process. A full search in the constrained 2-, 3-, or 4-dimensional parameter space was conducted to find the optimized parameters. We tested four different cost functions in the optimization: 1) $-\boldsymbol{F}_{Glu}\cdot\boldsymbol{F}_{Gln}$, 2) $-\boldsymbol{B}_{Glu}\cdot\boldsymbol{F}_{Glu}\cdot\boldsymbol{F}_{Gln}$, 3) $-\boldsymbol{F}_{Glu}$-$\boldsymbol{F}_{Gln}$, and 4) $-2\cdot\boldsymbol{F}_{Glu}$-$\boldsymbol{F}_{Gln}$, where $\boldsymbol{F}_{Glu}=\boldsymbol{B}^2_{Glu}/(\boldsymbol{A}_{Glu}+\boldsymbol{C}_{Glu})$, $\boldsymbol{F}_{Gln}=\boldsymbol{B}^2_{Gln}/(\boldsymbol{A}_{Gln}+\boldsymbol{C}_{Gln})$, and $\boldsymbol{A}$, $\boldsymbol{B}$, and $\boldsymbol{C}$ stand for the areas of the left sidelobe, the central peak, and the right sidelobe of the pseudo-triplets of Glu (around 2.35 ppm) and Gln (around 2.45 ppm) in the respective composite spectra. The boundaries of the three regions for each compound were determined from the respective spectra acquired at the shortest TE (i.e., 35 ms). These cost functions were designed to suppress the sidelobes and enhance the central peaks for both Glu and Gln at the same time.

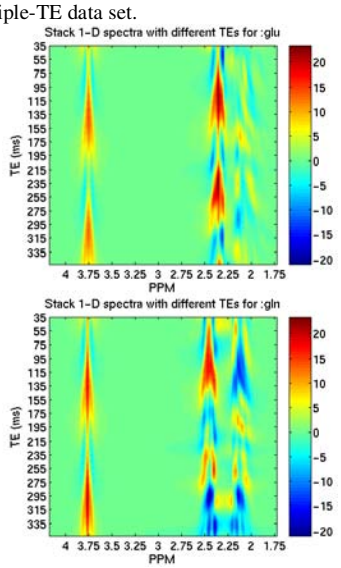
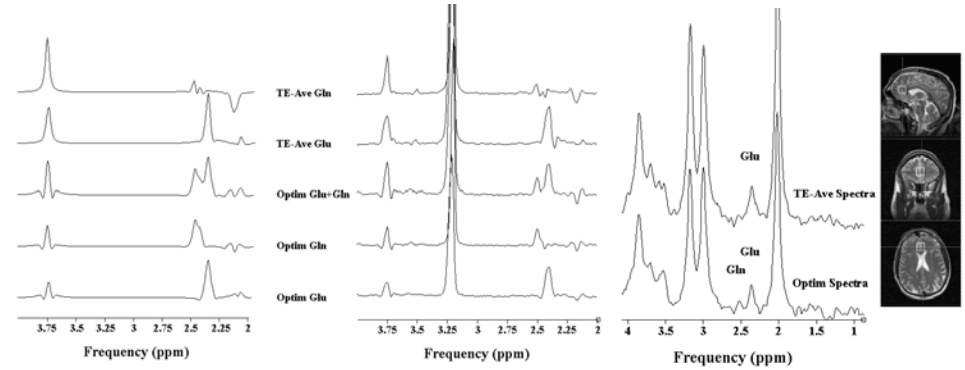


Fig. 1. Stacked GAMMA-simulated 1D spectra (real part) of Glu and Gln.

Results and Discussions

Optimizations for the filter function were first performed on the simulated data (with a 5-Hz line broadening). In the one-transition case, generally, no difference in the transition position and the final TE was observed among the four cost functions. Interestingly in the two-transition case, the obtained second transition point was coincident with the final TE position when using the cost function 1), reducing the results to those of a one-transition case. This suggests that the two-transition arrangement may not be suitable for the current TE range (128 steps) due to the intrinsic quadruple periodic variation of the spectra around 2.3-2.5 ppm with TEs (Fig. 1). The results from a three-transition optimization showed improvement primarily in the reduced spectral overlap between Glu and Gln over those from the one-transition case. The optimization results from the three-transition case using cost function 2) are shown in Fig. 2a. The associated filter function design was as follows: transition-point 1 = 87, transition-point 2 = 91, transition-point 3 = 97, and the total TE steps = 119 (all out of the 128 steps). The same optimization procedures were then applied on the phantom data (with a 5-Hz line broadening), and the optimization results in the three-transition case with the same cost function are shown in Fig. 2b. The associated filter function design was: transition-point 1 = 91, transition-point 2 = 101, transition-point 3 = 108, and the total TE steps = 128 (all out of the 128 steps). The peak at around 3.2 ppm was from Cho contained in the phantom. Two factors may contribute to the differences between the simulation and phantom data, relaxation effects not included in simulated data and a different filter function design. Fig. 2c shows the optimized *in vivo* spectrum obtained from a voxel in ACC using the same filter function as that in the phantom, with the TE-averaged PRESS spectrum as a reference. Glu and Gln signals are clearly shown in a single spectrum. These results demonstrate that the Gln signal can be successfully recovered with minimal Glu overlap using the optimized filter function, while Glu signal remains sufficiently strong for detection *in vivo*.



(a) (b) (c)

Fig. 2 Comparison between the TE-averaged PRESS spectra and the spectra obtained using an optimized filter function from (a) simulation in GAMMA, (b) phantom experiment, and (c) *in vivo* human data in ACC.

References

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