Simulation of ^{13}C Labeling Effects in ^{1}H MRS with different Sequences at 9.4 T

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Introduction Glutamate related metabolism can be measured considering the ^{13}C labeling effects from an administered ^{13}C labeled substrate in ^{1}H MR spectra without ^{13}C channels. The advantage of this technique is that some challenges of ^{13}C MRS like non-standard hardware modifications etc. are avoided and the simultaneous observation of ^{12}C- and ^{13}C-coupled protons is possible. On the other hand the latter also complicates the spectra. In this work, different sequences will be compared to optimize spectral resolution for glutamate and glutamine at 9.4 T.

Methods Basis sets were simulated using VeSPA[1,2] for an FID sequence, a Spin-Echo with TE=6.5 ms to match with MC semi-Laser sequence[3] for *in vivo* data, and two echo-time optimized PRESS sequences with (TE1/TE2 = 69/37ms)[4] and (TE1, TE2 = 37/63 ms)[5] which were optimized for metabolite resolution enhancement (e.g. Glu, Gln) at 7T. Initial concentrations were adjusted to a typical 9.4 T human brain spectrum. A two-compartment model[6] is used to calculate, with CWave[7], the turnover time course of nonlabeled to labeled Glu, Gln and brain Glc concentrations and percent enrichments with plasma [1-^{13}C]Glc as source of ^{13}C in the metabolites.

Results The simulated time course of concentration and percent enrichment of labeled and nonlabeled brain Glc, Glu and Gln are used to scale the basis sets for the above mentioned sequences. The displayed difference spectra for all sequences in Fig. 1 show the peak changes around 2.5 ppm after 2h: It can be seen that the [4-^{12}C]Glu peak at 2.345 ppm is decreased with time while the [4-^{13}C]Glu peaks at 2.503 ppm and 2.187 ppm increased. The same holds true for the decreased [4-^{12}C]Gln peak at 2.443 ppm, while [4-^{13}C]Gln peaks at 2.604 ppm and 2.282 ppm increase with time. The comparison of the different sequences shows that the [4-^{12}C]Glu and [4-^{12}C]Gln peak can easily be resolved in all difference spectra and the peak height of [4-^{12}C]Glu is reduced by about 15% after approximately 2h. In the FID and the SE results the [4-^{13}C]Glu peaks changes exhibit stronger characteristics than the [4-^{13}C]Gln peaks, while both PRESS results provided slightly better resolved [4-^{13}C]Gln peaks. As a result, this work indicates the fastest possible acquisition can be obtained with an FID sequence, while the best resolution possible can be obtained with a PRESS sequence.

Conclusion With these simulation results, it can be shown that at 9.4T [4-^{12}C]Glu and [4-^{12}C]Gln peaks can be resolved in difference spectra considering realistic line width in the human brain and the peak splitting due to the additional ^{13}C label incorporation can be quantified with all used pulse sequences. Even a simple FID sequence provides sufficient resolution to quantify [4-^{13}C]Glu and [4-^{13}C]Gln peaks from which Glu-Gln cycle rates could be calculated. Furthermore, the FID MRSI sequence will potentially enable mapping of metabolic turnover rates.

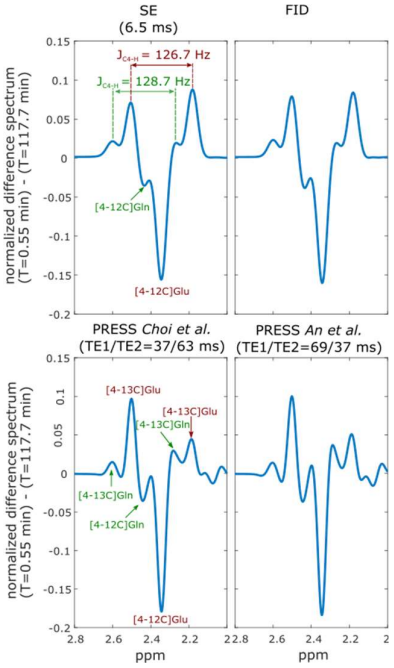

Fig.1: Difference spectra for 4 sequences after 2h after ^{13}C administration with indicated [4-^{12}C]Glu, [4-^{12}C]Gln, [4-^{13}C]Glu and [4-^{13}C]Gln peaks. Spectra are normalized to the [4-12C] Glu peak in the initial spectrum, using VeSPA and CWave. Gaussian-line broadening: 20 Hz, spectral data points: 8192, spectral sweep width: 8000 Hz.

References

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