Optimized MRS of Neurotransmitters: How far do you need to go?

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Introduction: A number of reports have appeared recently concerning optimal techniques for the measurement of neurometabolites with J-coupled resonances using proton magnetic resonance spectroscopy (^{1}H-MRS). Editing techniques are often proposed as the best method to unambiguously detect glutamate (Glu), glutamine (Gln), or gamma amino butyric acid (GABA). In the present study, we compare one such technique, optimized for glutamate, to standard point resolved spectroscopy (PRESS) in the anterior cingulate gyrus, a region of interest in many brain disorders or conditions.

Aim: Comparison of glutamate detection reproducibility among 1) a single voxel TE averaged PRESS technique (*1*) optimized for Glu, 2) a standard PRESS acquisition at the commonly reported echo time (TE) of 30 ms, and 3) a PRESS acquisition at TE = 40ms, previously shown to be optimal for Glu detection at 1.5T(*2*).

Methods: Six normal healthy subjects volunteered to be subjects in this study. MRI and MRS was performed on a Siemens 3T TRIO system (SIEMENS Karslrue) using the standard phased array head coil. Sagital T1-weighted anatomical images were obtained with a 3D MPRAGE (TR/TE/TI = 1500/3.87/700 ms, flip angle = 10°, field of view (FOV) = 256x256mm, matrix = 256x256, 1 mm thick slice, total scan time = 6 mins). The T1 images where used both for voxel prescription and for partial volume correction. Conventional ^{1}H-MRS spectra were acquired using the PRESS sequence provided with the scanner. TE averaged spectra where collected using a modified version of this sequence based on the concept introduced by Hurd et al (2), in which spectra at different TEs are summed before analysis. In our application, only the last 180 pulse is moved to increment TE by the required amount (10 ms step size in this case). All spectra where collected in the same session from the same voxel location, with the same shim adjustment. This reduced the effects of repositioning on the reliability measures. Spectra from each PRESS technique were collected along with reference water scans twice, back to back. The voxel for all spectroscopy scans was 2 mm X 2 mm X 3mm and comprised mostly of grey matter in the anterior cingulate (Figure1). For the TE average PRESS, TE was incremented over 16 steps (16 scan averages per step) at an TE increment of 10 ms per step, starting at a TE of 30 ms. TR was 2 s to provide an appropriately short scan time (just under 9 min). Standard PRESS with TE = 30 ms and TR = 2 s, and TE = 40 ms and TR = 2 s were then collected (128 averages). MRS data were analyzed using LCModel software (*3*) using simulated basis sets created in jMRUI (*4*) for all acquisition schemes. The results from LCModel were corrected for partial volume and relaxation effects as outlined previously (*5*).

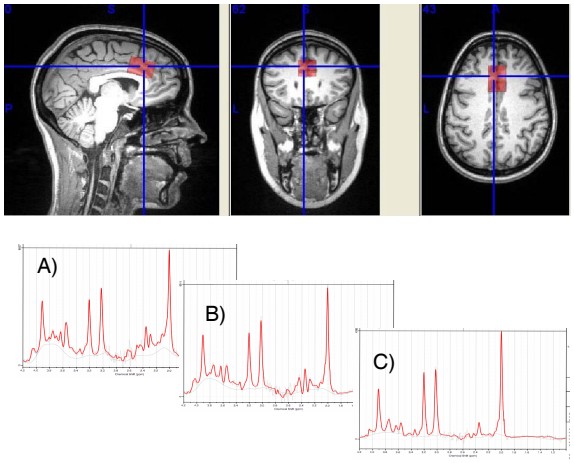

Figure 1: Voxel location and Representative PRESS spectra and LCmodel fit. A) TE = 30 ms B) TE= 40 ms C) TE Average

Results: All three techniques produced good quality spectra from the region of interest (Figure 1). LCModel fits for all were acquired with average Cramer Rao lower bounds (CRLB) of less then 5% for N-acetylaspartate (NAA), choline groups (Cho), and creatine (Cre), and a CRLB of ≤ 8% for glutamate. Coefficients of variation from scan to scan are displayed in Table 1. The 40-ms TE PRESS scans produced the lowest measures of variance for each metabolite. Mean concentration measures did not vary greatly among the three sequences for any metabolites, with the exception of Glu and GABA. Metabolite concentrations of Glu measured with the TE average sequence were lower than those calculated from 30- and 40-ms PRESS (9.15 mM v's 12.73 or 13.14 mM, respectively).

Table 1: Mean concentrations (mM), Cramer Rao lower bounds (CRLB) and Co-efficient of Variation (CV).

Metabolite	TE Average			TE 30 ms			TE 40 ms		
	Conc.	CRLB	CV	Conc.	CRLB	CV	Conc.	CRLB	CV
NAA	9.48	2%	9%	9.81	3%	4%	10.82	3%	3%
Cho	2.11	3%	9%	2.03	4%	3%	2.30	3%	3%
Cr	9.09	2%	9%	9.54	3%	3%	10.52	3%	3%
Glu	9.15	8%	10%	12.73	7%	7%	13.14	8%	5%
Gln	2.27	38%	83%	1.95	49%	64%	2.35	29%	37%
GABA	1.84	27%	50%	0.63	169%	74%	1.89	29%	13%
Myo-Ins	6.91	9%	16%	7.14	5%	15%	7.14	6%	15%

Discussion: There are several MRS techniques presently employed to detect Glu and Gln concentrations in vivo. Here we examine one such technique, TE averaged PRESS and compare it to typical and optimized TE PRESS. Our results show that while these techniques all produce roughly equivalent measures of metabolite concentration, they differ in terms of repeatability of measures of J-coupled metabolites. While our application of the TE average technique provided good quality spectra for Glu detection, the method did not prove to be the most reproducible from scan to scan. Instead, the 40-ms TE PRESS was the most reproducible technique in this study. This was also the case for GABA measures, suggesting that changes in both Glu and GABA may be investigated using standard 40-ms TE PRESS. The observed increase in reproducibility at TE=40 ms may be a result of reduced underlying macomolecule signals, as compared to 30-ms PRESS, as well as improved separation of the main peaks for the coupled resonances, due to J modulation of the mutliplets for Glu, Gln, and GABA in the 2.6 – 2.0 ppm range. In addition, at 40 ms relaxation effects are reduced compared to the longer effective echo time of TE averaged PRESS, providing greater signal-to-noise.

Conclusion: Standard PRESS with an optimized echo time and appropriate line fitting techniques is a reliable and reproducible technique to measure Glu and other neurometabolites in spectroscopy studies.

References

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