Reproducibility of Multi-slice 2D Proton MRSI at 3.0 T

T. J. DeVito[1], R. Nicolson[2], Y. Bureau[3], P. C. Williamson[2], D. J. Drost[1]

[1]Medical Biophysics, University of Western Ontario, London, Ontario, Canada, [2]Psychiatry, University of Western Ontario, London, Ontario, Canada, [3]Radiology and Nuclear Medicine, Lawson Health Research Institute, St. Joseph's Health Care, London, Ontario, Canada

Introduction Recent studies have reported on the variability of metabolic concentration measurements made using ^{1}H MRSI (1, 2, 3) at 1.5 Tesla. The goal of this study is to examine the variation of fitted metabolite amplitudes between subjects, and within subjects on repeat scans at 3.0 Tesla. The experimental protocol under investigation is presently being used to study regional brain metabolism in children with autism and Tourette syndrome (4, 5). Estimates of subject-to-subject and session-to-session variability, and potential sources of such variation, are of particular interest in determining limitations of the protocol for cross-sectional and longitudinal ^{1}H MRSI studies.

Methods Nine healthy adults (mean age 29.6 (6.2) years, range 24 – 40 years; 5 male, 4 female) were imaged using a combined MRSI/MRI protocol, twice on the same day. After the first session, patients were removed from the magnet and repositioned after ~15 minutes for the second session. This was done to include the effects of patient positioning in the repeatability analysis, while minimizing temporal biological variation within each subject. This study was approved by the local human ethics review board.

A 3.0-T head-only research scanner (IMRIS, Winnipeg, Canada) with a quadrature head coil was used for all imaging experiments in this study. Standard T_1-weighted localizer images and axial multi-echo images for radiological assessment were initially acquired. This was followed by a 3-D MP-RAGE acquisition (1.2-mm isotropic voxels, TI/TE/TR=200/5/11 ms, flip angle 12 degrees, inter-segment repeat time 3.3 s), used for MRSI partial volume correction. Localized proton spectra were acquired with an interleaved, multi-slice spin-echo MRSI sequence using slice-selective adiabatic inversion for extra-cranial lipid nulling (TI/TE/TR=230/135/1800 ms, FOV=280 mm, 35x35 circularly-bounded k-space acquisition, 512 ms acquisition time, 30 minute total scan time) (6). Two 10-mm thick oblique-axial slices (Figure 1a) were excited with numerically optimized RF pulses, yielding nominal voxel size of 8x8x10 mm (~1.0 cc effective voxel size after k-space filtering). Water suppression was performed during the inversion time, using the adiabatic WASHCODE technique (7), providing good insensitivity to RF inhomogeneity. T_1-weighted images were acquired at the same slice positions as the MRSI acquisition for anatomical correlation, and B_1-maps (8) were acquired to correct MRSI signal levels for RF field inhomogeneity. Each session took approximately 1 hour; the full 2-session experiment took ~2.5 hours.

MRSI data sets were first processed using k-space extrapolation to reduce ringing artifact from residual extra-cranial lipid signal (9). Using the T_1-weighted anatomical correlation images, voxels were selected for spectral analysis from nine regions, comprising various tissue types: cerebellar vermis, insular gray matter, frontal white matter, posterior hippocampus and thalamus (Figure 1b). Except for the vermis, which is a mid-line structure, spectra were analyzed from both left and right hemispheres for each region. After subtraction of the residual water signal, fit using HLSVD, unfiltered spectra were fit in the time domain using prior knowledge from *in vitro* metabolite solutions using a constrained Marquardt-Levenberg minimization algorithm (10). The fitted metabolite signal amplitudes were corrected for coil load (11) and B_1 inhomogeneity. For each voxel, paired *t*-tests were performed to assess differences between sessions in fitted metabolite amplitudes for NAA, total creatine (Cre) and choline-containing compounds (Cho). Inter-subject metabolic variation was assessed using coefficients of variation (CV), calculated as the standard deviation divided by the mean (3). Reproducibility of repeat MRSI sessions was examined using CVs defined as standard deviation of the difference between test and retest measurements divided by the mean values from the measurements (2). Intra- and inter-subject mean CVs across all voxels were also calculated.

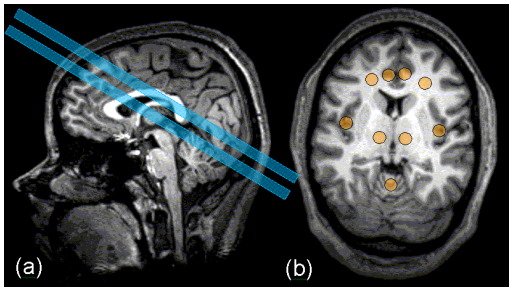

Figure 1: MP-RAGE images showing (a) MRSI slice positions and (b) voxel positions from lower slice used in repeatability analysis.

Results No significant differences were observed in fitted metabolite amplitudes from session 1 to session 2 in any region examined. Intra- and inter-subject CVs are shown in Table 1 for each metabolite and region. The spread of intra- and inter-subject CVs across brain regions is illustrated in Figure 2. In general, intra-subject CVs were less than inter-subject CVs for all metabolites and regions. Mean intra-subject CVs were measured to be 12.6% (NAA), 24.6% (Cre) and 18.4% (Cho). Inter-subject mean CVs were slightly higher: 17.2% (NAA), 25.0% (Cre) and 21.3% (Cho).

	ver	hcl	hcr	igl	igr	thl	thr	fwl	fwr	mean
NAA (Intra)	13.5	10.9	15.7	8.0	8.0	11.2	19.2	11.0	16.0	12.6
NAA (Inter)	12.5	11.4	19.5	15.0	11.9	16.1	19.8	18.4	26.2	17.2
Cre (Intra)	12.1	21.6	29.0	20.3	13.1	26.8	29.4	26.3	42.4	24.6
Cre (Inter)	13.5	17.9	24.4	20.3	14.2	33.7	25.6	26.9	48.8	25.0
Cho (Intra)	17.8	30.2	17.0	13.7	23.0	16.4	19.2	17.1	11.5	18.4
Cho (Inter)	15.6	23.6	18.1	17.9	25.9	20.7	21.9	22.3	25.6	21.3

Table 1: Intra- and inter-subject CV (%) for NAA, Cre, Cho in each of the nine regions examined: cerebellar vermin (ver), left/right hippocampus (hcl/hcr), left/right insular grey matter (igl/igr), left/right thalamus (thl/thr), and left/right frontal white matter (fwl/fwr). Mean %CV across all regions (mean) is also indicated.

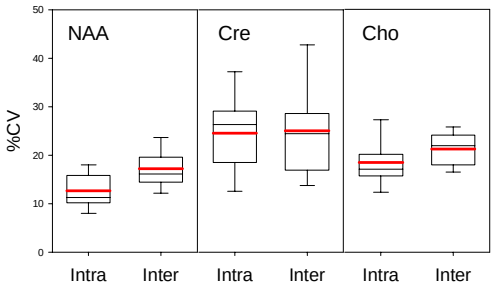

Figure 2: Box plots of Intra- and inter-subject %CVs for NAA, Cre and Cho for all 9 voxels. Mean is indicated by the red line.

Discussion Intra- and inter-subject CVs observed for this MRSI protocol are in accord with values reported in the literature (2, 12). The observed similarity between session-to-session and subject-to-subject variance suggests that biological variability due to gender and age differences is not the main contributor to the overall variations. In fact, biological metabolite level variation has been reported to be relatively low, up to ±3.8% for Cre, ±6.5% for Cho, and zero for NAA (3). As suggested by Li et al. (3), a likely major contributor to measurement variance is poor reproducibility of voxel positioning. Even small errors in choice of voxel location can lead to large differences in the grey/white/CSF content of a voxel, which can lead to large variation in the observed metabolite levels. Wiedermann et al. (2) found very good reproducibility by regressing fitted metabolite levels against the gray-matter fraction of each voxel. Further experiments on phantoms will assess the contribution to variance of the MR system and analysis technique. A partial volume analysis using the 3D volumetric data collected at each session will be undertaken to determine the variation in voxel tissue content at each location, and its contribution to the observed variation.

References

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