Macromolecular and Lipid Contributions in Short Echo Time 1H MRS at 4 Tesla: 1) Reliability in Normal Controls and 2) Comparative Study Between Amyotrophic Lateral Sclerosis Patients and Controls

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BACKGROUND: A ^{1}H MR spectrum at short echo time in the human brain is characterized by contributions from metabolic (MET) and macromolecular (MM) and lipid (LP) components. MM/LP resonances may contain valuable information about pathological conditions, as shown previously (1). The majority of the ^{1}H MRS studies focus on the MET resonances, therefore little is currently known about the role of the MM/LP spectral content in the human brain. The first goal is to estimate the reliability of quantifying MM/LP in the human brain using a parameterized prior knowledge fitting routine. The second goal is to explore if systematic differences between patients with Amyotrophic Lateral Sclerosis (ALS) and controls could be detected within MM/LP contributions to the MR signal, which would imply that ALS is also characterized by the altered MM/LP constituency of brain tissue in addition to MET contributions.

METHOD: A group of younger subjects (N=10, mean age=27 years) was scanned twice within one week. To address a second goal, a group of ALS patients (N=16, 12 men and 4 women, mean age = 54 ± 12 years) and normal controls (N=16, 10 men and 6 women, mean age= 55 ± 9 years) was scanned once. ^{1}H MRI/MRS experiments were performed on a 4T Inova Infinity Varian system, as previously described (2). A ^{1}H MRS STEAM (Stimulated Echo Acquisition Mode) sequence (TE/TM/TR=15/10/2000 ms, voxel size=8 mL) was used to acquire MR spectra from corona radiata (COR). Typical experimental in vivo data from normal control is shown in Figure 1A,B. MET and MM/LP fitting was performed automatically with FITT software (3). Prior knowledge of chemical shifts for MET and MM/LP and scalar coupling constants for the MET was derived from the literature values (1,4) and our own saturation recovery experiments in healthy controls. The concentration for MM/LP was calculated assuming that each separate MM/LP resonance is due to one proton and ignoring relaxation.

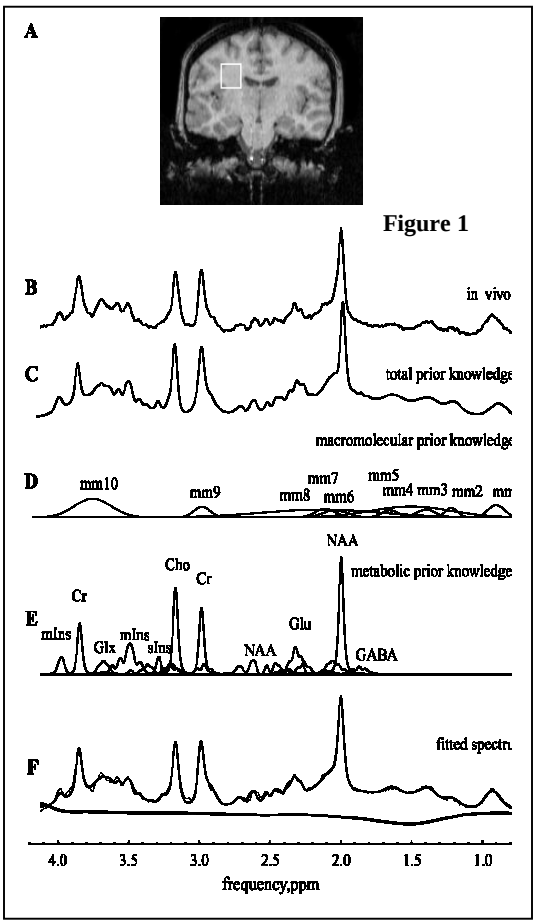

Figure 1

RESULTS: Based on tissue segmentation, the COR voxel contained significantly more white matter (~ 80%) than gray matter (~19%) and cerebrospinal fluid (~1%), therefore MM/LP reported here represent primarily white matter composition. Test-retest results are summarized in Table I (Study 1). Three MM/LP components displayed the most reproducible results - the resonance at 0.90 ppm (CV=11%), at 1.40 pmm (CV=9%), and at 3.0 ppm (CV=8%). Two of these resonances (at 0.90 and at 1.40 ppm) yielded the largest concentration compared to other MM/LP components. The most unreliable component was at 1.61 ppm (CV=41%). ALS comparison results are summarized in Table I (Study 2). Overall, ALS patients had lower MM/LP concentrations than normal age-matched controls, but only three MM/LP contributions at 0.90, 1.61 and 2.11 ppm demonstrated statistically significant decreases compared to controls ($p<0.05$).

DISCUSSION: Higher reproducibility for MM1 and MM3 contributions was expected, since they exhibit the highest signal to noise and no overlap with MET, but was unexpected for the MM9 resonance. Compared to previously published CVs for MET at 4 T, all three above-mentioned components had similar reproducibility relative to NAA, Cr and Cho. Two reduced peaks in ALS subjects at 0.90 and 2.11 ppm detected in this study are most likely signals from neighboring protons in the same protein, since it was demonstrated previously that these protons are connected via J-coupling in the rat brain 2-D spectra (5). In summary: Inclusion of parameterized MM/LP components into the quantification routine enhances the diagnostic potential of in vivo ^{1}H MR spectroscopy.

Table 1. Study 1.Coefficients of variation and MM/LP concentrations[&] (mean ± standard deviation, mM). Study 2. MM/LP concentrations for ALS and controls. Spectral location in ppm is shown for each individual MM/LP peak in parenthesis ( ).

Study	MM1 (0.90)	MM2 (1.22)	MM3 (1.40)	MM4 (1.55)	MM5 (1.61)	MM6 (2.05)	MM7 (2.11)	MM8 (2.15)	MM9 (3.0)	MM10 (3.7)
1) CV,%	11%	28%	9.0%	18%	41%	22%	26%	16%	8%	18%
CNT (age=26)	23.7±1.8	14.7±2.6	23.9±1.5	18.7±2.4	16.5±4.41	19.6±3.5	20.4±4.7	18.4±2.6	13.0±0.8	18.3±2.2
2) ALS(age=54)	22.4±2.3*	12.9±1.1	23.3±1.8	18.6±3.1	14.1±2.8*	19.8±3.7	18.4± 4.3*	19.2±2.3	12.8±1.3	18.1±3.8
CNT (age=55)	24.0±1.2	14.5±4.2	23.5±2.9	18.7±3.4	18.3±4.8	20.6±3.5	21.9±4.0	18.9±2.6	13.1±0.8	17.6±2.6

[&] referenced to cerebral water (assuming 1 proton/macromolecular peak), * significant difference between ALS and control subjects ($p<0.05$)

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