7T MRS in Patients with 1.5T Normal Medically-Refractory Temporal Lobe Epilepsy

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Target Audience: Scientists interested in measuring metabolic changes in neuropathological conditions with heightened signal-to-noise (SNR) and spectral dispersion provided at 7T and clinicians studying temporal lobe epilepsy.

Purpose: The purpose of this preliminary 7T study was to characterize metabolite levels in the hippocampus of 1.5T- MRI negative temporal lobe epilepsy (TLE) patients. Using high field ^{1}H magnetic resonance spectroscopy (MRS) high quality quantifiable hippocampal spectra can be obtained from these patients. Metabolites such as *N*-acetylaspartate (NAA), glutamate (Glu), glutamine (Gln), choline (Cho) and myo-inositol (Myo) are markers for partial epilepsy[1] and may help localize the seizure origin in the 1.5T MRI negative cases.

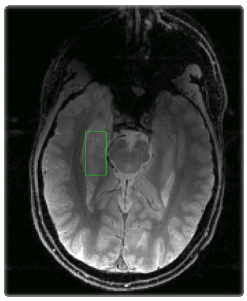

Figure 1: Axial T_2-weighted MRI image with a 2.7x1.3x1.3 cm^3 voxel in green.

Methods: A 7T Agilent/Siemens MRI system with a 16-channel transmit and receive head coil (built in-house) was used to acquire single-voxel short-echo-time ^{1}H MR spectra as previously described,[2] from 2.7x1.3x1.3 cm^3 voxels in the left and right hippocampi (Figure 1). Eight MRI negative TLE patients (mean age 26 ± 8 years) and eight healthy controls (mean age 32 ± 8 years) were studied. T_2-weighted 2D FLASH images (TR = 1000 ms, TE = 6.5 ms, α = 30°, 1x1x2 mm^3 resolution) were used for voxel placement (Figure 1). A conventional localization by adiabatic selective refocusing (LASER) sequence[3] was modified as described by Marjanska *et. al.*.[4] Briefly, the sequence consisted of a 2 ms slice-selective 90° excitation pulse followed by two pairs (one pair for each remaining orthogonal dimension) of slice-selective adiabatic full-passage pulses (hyperbolic secant, R10, 3.5 ms) (TR/TE = 3700/38 ms). Eight global 5 ms Gaussian pulses were used for variable pulse power and optimized relaxation delays (VAPOR) water suppression.[5] Water (8 averages), water suppressed (full - 128 averages), and water and metabolite suppressed (macromolecule - 128 averages) data were acquired. Double inversion recovery[6] (two non-selective 5 ms adiabatic full-passage pulses) was used to suppress the metabolite signal when acquiring the macromolecule spectra. Prior-knowledge based fitting using the fitMAN software[2] was used to measure metabolite levels. Metabolite ratios normalized to Cr were compared between patients and healthy controls using a two tailed unequal variance t-test (p<0.05 considered significant).

Table 1. Demographics of Patients and Controls

Characteristics	Patients	Controls
N	8	8
Age		
Mean	25.3	32.9
Range	20-45	23-45
Gender	male	male
Handedness	right	right

Results: Table 1 summarizes the demographic and clinical characteristics of all participants in the study. Table 2 shows the metabolic ratios (mean and SD) in all patients and controls as well as their respective p-values. Figure 2 shows metabolite ratios in controls and patients (combined left and right hippocampi). Significantly higher Glu/tCr (p=0.05), tCho/tCr (p=0.01), and Tau/tCr (p=0.02) along with lowr Peth/tCr (p=0.04) was observed in patients relative to controls (Table 2).

Discussion and Conclusion: The semiLASER MRS protocol was used to measure metabolite concentrations and calculate metabolite ratios. Using short echo time MRS Semi-LASER at 7T significant differences were detected in hippocampal metabolite concentrations in patients with normal 1.5T MRI scans compared to healthy controls. The identification of structural and metabolic abnormalities using high field MRI could improve surgical selection of patients with temporal lobe epilepsy. Better localization of the epileptogenic focus will also improve surgery outcome.

Table 2. Comparison of metabolites between MCD patients and controls

Metabolites and ratios	Patients Mean	Patients SD	Controls Mean	Controls SD	p-value[a]
NAA/tCr	1.0	0.2	0.9	0.3	0.34
Glu/tCr	1.4	0.3	1.2	0.3	0.05
Peth/tCr	0.2	0.1	0.3	0.2	0.04
Tau/tCr	0.1	0.1	0.0	0.1	0.02
GPC/tCr	1.0	0.2	0.8	0.2	0.002
tCho/tCr	1.2	0.2	1.0	0.1	0.01

SD, standard deviation.
[a] p-value obtained from two tailed ttest

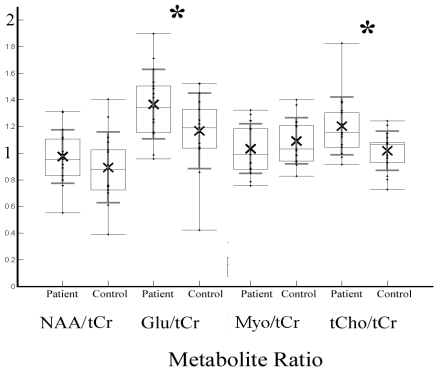

Figure 2: Comparison of average metabolite ratios in eight patients and eight age matched controls (left and right hippocampi). Whisker plot. Band in the center represents the median, top and bottom of the box are first and third quartiles (median of lower and upper half of the data). Bold lines are error bars of +/- STDEV.

References:1. Hetherington HP et al. Magn Reson Med 63(1):9-19 (2010); 2. Kassem, M. et al. Magn Reson Med 49(5):918-27 (2003); 3. Garwood, M. et al. J Magn Reson 153:155-177 (2001); 4. Marjanska, M. et al. Proc Intl Soc Mag Reson Med 2343 (2009); 5. Tkac, I. et al. Magn Reson Med 41:649-656 (1999); 6. Dixon, W. et al. Magn Reson Med 18:257-68 (1991).