Biochemical and Anatomical Characterization of Minimal HE

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Introduction: Signal abnormalities in the globus pallidus (GP) regions of T_1-weighted and in other regions of T_2-weighted magnetic resonance imaging (MRI) of chronic liver patients with and without hepatic encephalopathy (HE) have been reported earlier (1-2). One-dimensional (1D) MR Spectroscopy (MRS) has been shown to detect decreased myo-inositol (mI) and choline (Ch), and increased glutamate/glutamine (Glx) in the parieto-occipital region of HE patients (3). Spectral overlap, a major problem in 1D MRS, has been demonstrated to be minimal in two-dimensional (2D) MRS due to the added 2nd dimension (4). The goals of this study were to investigate the neuro-metabolite changes in the prefrontal and occipital white matter regions using 2D L-COSY, and to compare with the anatomical changes using T_1-weighted and T_2 values of HE patients and healthy human subjects.

Methods: MR Imaging and MRS were performed using a 1.5 Tesla scanner (Siemens Medical Systems, Erlangen, Germany) with a body coil "transmit" and a 2-surface coil phased array "receive" assembly for MRS, and a head 12-channel head matrix "receive" assembly. Sixteen minimal HE patients (mean age = 50 yrs) awaiting liver transplantation and eighteen healthy volunteers (mean age = 49.5 yrs) have been investigated so far. **2D MRS**: One of the surface coils was placed directly on the forehead and the other facing the occipital cortex of the subjects. A 27-ml voxel was placed on two locations: the right prefrontal dorsolateral white/gray and the left visuo-occipital white/gray matter. Spectra were recorded with the following parameters (4): TE = 30ms, TR = 2s and total-scans = 784. **MRI**: High-resolution T_1-weighted images using a magnetization prepared rapid acquisition gradient-echo (MP-RAGE) sequence were acquired using the following parameters: (TR = 1,660 ms; TE = 3.9 ms; inversion time = 900 ms; average = 1; matrix size = 256 × 256; FOV = 230 × 230 mm^2; slice thickness = 1.2 mm; number of slices = 176) were collected. Proton-density (PD) and T_2-weighted images were also collected using a dual-echo turbo spin-echo sequence (TR = 7,500 ms; TE_1, TE_2 = 17, 134 ms; flip angle = 150°; matrix size = 256 × 256; FOV = 230 × 230 mm^2; slice thickness = 4.0 mm; number of slices = 42; average = 1). All the subjects also participated in a neuropsychological test battery on the same day before MRS and MRI.

2D L-COSY spectra were processed using Felix-2000 (Accelrys, San Diego, CA). Anatomical MRI data were processed using the statistical parametric mapping package SPM2 (Wellcome Department of Cognitive Neurology, UK), and Matlab-based (The MathWorks Inc, Natick, MA) custom software. Using T_2 and PD-weighted images, T_2 maps were computed voxel-by-voxel. In addition to GP region, median T_1 signal changes and T_2 relaxation values were calculated from the locations that were selected for MRS voxels. Relative T_1 signal changes were calculated in selected regions of the patient group compared to controls. T_2 values obtained from different regions were compared for significant difference between the groups using paired t-test.

Results: Analysis of anatomical MRI data revealed 23% increase in the globus pallidus signal intensities in the T_1-weighted images, however, there was no significant change in T_2 values in this region (Table 1). T_1 signal changes for the right frontal white matter (FWM-R) and left occipital white matter (OWM-L) were minimal compared to controls, however, T_2 values showed increasing trend in patient group compared to controls although it was not significant (Table 1). Table 2 includes the cerebral metabolite ratios that were calculated using the 2D L-COSY spectra recorded in the right frontal and left occipital white/gray matter regions. Increase of Glx/Cr combined with decrease of Ch/Cr, mI/Cr and Tau/Cr were observed in both locations in agreement with an earlier report that included only the anterior cingulate gray/white matter (4).

Table 1. GP hyper-intensities and T_2 values calculated in the right and left GP, right frontal and left occipital white matter regions.

	T_1 signal changes		T_2 Relaxation values (ms)			
	GP-L	**GP-R**	**GP-L**	**GP-R**	**FWM-R**	**OWM-L**
MHE	440.34±30.48	447.66±32.69	91.85±4.88	95.47±4.81	105.87±9.87	117.45±12.33
Healthy	361.17±17.66	361.66±19.44	91.12±3.13	95.33±3.88	102.09±3.86	114.09±5.45

Table 2. Metabolite ratios (Mean±SD) calculated from the 2D spectra recorded in the frontal and occipital white matter regions.

Metabolites	**MHE (n=15)**	**Healthy (n=16)**	**t**	**p**
Frontal White				
Ch/Cr	0.856±0.176	0.995±0.117	2.33	0.04
mI/Cr	0.013±0.007	0.023±0.005	4.49	0.001
mICh/Cr	0.072±0.025	0.117±0.011	7.88	0.0001
Glx/Cr	0.150±0.024	0.119±0.017	-4.23	0.001
Tau/Cr	0.008±0.003	0.010±0.003	1.9	0.078
NAA/Cr	1.552±0.211	1.60±0.236	0.51	0.62
PE/Cr	0.005±0.002	0.006±0.002	1.38	0.19
Occipital White				
Ch/Cr	0.805±0.174	0.951±0.105	2.65	0.02
mI/Cr	0.0117±0.007	0.020±0.005	1.31	0.22
mICh/Cr	0.073±0.027	0.114±0.019	4.57	0.001
Glx/Cr	0.152±0.044	0.115±0.016	-2.72	0.02
Tau/Cr	0.008±0.003	0.008±0.003	0.22	0.83
NAA/Cr	1.597±0.177	1.614±0.126	0.27	0.79
PE/Cr	0.006±0.004	0.004±0.001	-1.38	0.19

Discussion and Conclusion: Our preliminary data confirm the previous findings of increased global pallidal hyperintensities using T_1-weighted MRI as well as increased T_2 in the frontal and occipital white matter of minimal HE patients compared to healthy subjects. Also, the 2D MRS data is able to identify more metabolite changes than what was reported using conventional 1D MRS (3).

References

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