Correlation of Diffusion Tensor Imaging with Neuro-chemical Changes in Low Grade Hepatic Encephalopathy

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Introduction: The term hepatic encephalopathy (HE) encompasses a wide spectrum of neurological alterations ranging from subtle changes of personality, sleep disturbances, to confusion and coma (1). Despite the frequent severe impairment of brain function, most episodes of HE in patients with liver failure are reversible and are not associated with structural alteration or neuronal cell loss. In vivo localized one dimensional (1D) and 2D proton MR spectroscopy have described typical alteration of the metabolite alterations in parietal, occipital and frontal lobes, and deep gray matter (2). Similarly diffusion tensor imaging metrics have been shown to correlate with the grade of the encephalopathy and show reversibility following therapy (3). The goal of the present study was to correlate the metabolite changes in right frontal and left occipital regions of the brain with the fractional anisotropy (FA) and mean diffusivity (MD) values from the voxels co-registered with FA and MD maps.

Methods: Ten patients (mean age of 55.9 years, 7/3 males/females) awaiting the liver transplantation were selected for the study and these patients had low grade HE diagnosed on the basis of West Heaven criteria and abnormal neuropsychological tests. The diagnosis in all these patients was cirrhosis with portal hypertension on the basis of typical imaging features and or liver biopsy. In addition, 10 (mean age of 53.2 years, 6/4 males/females) age and education matched volunteers were also selected as controls who had no neurological, neuroimaging or neuropsychological abnormality. In addition to dual echo PD, T2, T1 imaging, 2D Localized correlative spectroscopy (L-COSY) (4) and DTI were performed in all the patients and controls. 2D MRS: A 2-lobe surface coil phased-array assembly was used to receive the signal. One of the surface coils was placed directly on the forehead and the other facing the occipital lobe of the subjects. A 27-ml voxel was placed on two locations: the right prefrontal dorsolateral predominantly white and the left occipital predominantly white matter. Spectra were recorded with the following parameters: TE=30ms, TR=2s and total scans=768. 2D L-COSY spectra were processed using Felix-2000 (MSI, San Diego, CA).
Diffusion tensor imaging (DTI) was performed using a single-shot multi-section spin-echo echo-planar pulse sequence [repetition time (TR) = 10,000 ms; echo-time (TE) = 87 ms; flip angle = 90°; averages = 3] in the axial plane, with a 128×128 matrix size, 230×230 mm^2 field of view (FOV), 2 mm slice thickness, 75 slices and no interslice gap, and a readout bandwidth of 1346 Hz/pixel. For each slice, diffusion gradients were applied along six independent orientations with b = 700 sec/mm2 after the acquisition of b = 0 sec/mm2 (b0) images. An acceleration factor of two was applied using the parallel imaging technique generalized autocalibrating partially parallel acquisition (GRAPPA). We also collected high-resolution T1-weighted images using a magnetization prepared rapid acquisition gradient-echo (MPRAGE) sequence (TR = 1660 ms; TE = 3.87 ms; inversion time = 900 ms; FA = 10°; matrix size = 256×256; FOV = 230×230 mm^2; slice thickness = 1.2 mm; number of slices = 176) for evaluation of brain abnormalities. Brain images of individual subjects, including T1-weighted, PD-weighted, T2-weighted, and b0 images were evaluated by experienced radiologist (RKG) for any major brain lesions before mean diffusivity (MD) and fractional anisotropy (FA) calculation. To ensure that images were acceptable for subsequent processing, b0 images were also examined for motion artifacts. We used the statistical parametric mapping package SPM5 (Wellcome Department of Cognitive Neurology, UK), DTI-Studio (v 2.4, Department of Radiology, John Hopkins University, Baltimore, MD 21205), and Matlab-based (The MathWorks Inc, Natick, MA) custom software to process images.

Results: Summary of the metabolites and DTI metrics from the right frontal and left occipital white matter are summarized in Table 1. FA and MD showed significant changes in the HE patients compared to controls in both regions. There was significant decrease in Cho/Cr, mI/Cr ratios in both right frontal and left occipital white matter. The significant increase was noted in the Glx/Cr ratios in both the regions. The changes in the Glx/Cr and mI/Cr were more significant in the right frontal lobe compared to the left occipital white matter. We looked for the correlation of various metabolites with FA and MD values in the corresponding regions. The FA showed significant direct correlation with PE/Cr (r,p=0.73, 0.016) in the right frontal white matter. In left occipital lobe there was significant correlation between MD and Cho/Cr ratio (r,p= 0.83, 0.003). We did not find any correlation of the remaining metabolite ratios with corresponding lobes white matter FA and MD values.

Discussion and Conclusion: Our study shows that there are individual significant changes in the DTI metrics and Spectroscopy derived metabolite ratios which are consistent with the literature. We expected some correlation with the metabolites like Glx or mI which was not seen in the study. This could be due to the non registration of the DTI images with spectroscopy voxel and contamination of the large voxel with the grey matter how ever it was meant to be kept within the white matter. The significant correlation of PE with FA in the right frontal white matter and significant correlation of Cho in the left occipital white matter are difficult to explain by the biological changes observed in HE. Even though the DTI and neurochemical changes in patients with HE are independent parameters, the DTI changes do not show any correlation with the major metabolites such as Glx and mI.

References

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Table 1. DTI metrics and metabolite ratios (Mean±SD) calculated from the 2D spectra recorded in the right prefrontal and left occipital white matter.

	FA	MD	Ch_d	NAA_d	mICh	Glx	mI	Tau	PCh	GABA	PE
Right Frontal White matter											
Patients	0.31±0.08	1.1±0.2	0.83±0.16	1.5±0.2	0.06±0.02	0.16±0.03	0.01±0.005	0.007±0.002	0.006±0.003	0.007±0.002	0.00±0.0026
Controls	0.37±0.1	0.87±0.2	0.98±0.09	1.7±0.15	0.11±0.01	0.12±0.02	0.02±0.003	0.009±0.003	0.007±0.003	0.006±0.002	0.006±0.003
p	0.2	0.02	0.02	0.07	.000	0.003	0.000	0.07	0.4	0.5	0.9
Left Occipital White matter											
Patients	0.28±0.06	1.07±0.1	0.7±0.14	1.4±0.1	0.05±0.02	0.17±0.05	0.01±0.005	0.007±0.003	0.007±0.003	0.007±0.003	0.004±0.003
Controls	0.4±0.06	0.81±0.06	0.94±0.1	1.6±0.15	0.11±0.02	0.11±0.01	0.02±0.006	0.009±0.003	0.007±0.002	0.007±0.002	0.005±0.001
p	0.000	0.000	0.001	0.010	0.000	0.007	0.014	0.14	0.7	0.8	0.4