Volumetric MRSI of Metabolic Alterations with Traumatic Brain Injury

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INTRODUCTION:

The detrimental cognitive consequences of mild traumatic brain injury (TBI) commonly remain uncorroborated by clinical or neuroimaging findings, and it is hypothesized that diffuse injury may occur that is not manifested in structural alterations visible by common neuroimaging methods. It has previously been demonstrated that alterations of 1H-MRS-observed tissue metabolites can be detected following TBI. In this study a volumetric MRSI acquisition method is being evaluated to test the hypothesis that this imaging method is sensitive to detection of widespread and diffuse metabolic dysfunction occurring as a consequence of mild closed head injury.

METHODS:

MRI and MRSI data was obtained from 13 subjects admitted to the trauma center with mild to moderate TBI, GCS score between 10 and 15, within 1 to 3 weeks after injury. Of these, 1 was considered to be of inadequate quality for further analysis. Corresponding data from 52 control subjects matching the subject age range of 19 to 40 y.o. was obtained from an existing database[1]. The 1H MRS data was obtained using a volumetric EPSI sequence at 3 T, with TE=70 ms, voxel volume of 0.6 ml, and selection of a 14 cm slab covering the cerebrum. Reconstruction of the metabolite images for N-Acetylaspartate (NAA), Creatine (Cr), and Choline (Cho) was carried out using the MIDAS package[1], which included signal intensity normalization relative to brain tissue water and spatial normalization. In addition, tissue content at each image voxel was obtained using segmentation of coregistered MRI.

To evaluate the presence of diffuse metabolic alterations the relative values of the metabolite ratios was obtained for each of the grey- and white-matter regions in each brain lobe, and results averaged over all subjects. This regression analysis was carried out automatically after coregistration to a standard spatial reference for which a brain atlas was defined. Voxel selection was limited to spectra fitted with a linewidth of less than 10 Hz and at least 50% of tissue content in the voxel. The significance of differences between the TBI and Control group was evaluated using a 2-tailed unpaired t-test.

RESULTS AND CONCLUSIONS:

Images of individual normalized metabolite values show a general reduction throughout the brain that may possibly be attributed to alterations of brain water content and/or T1, and remains under further investigation, therefore further analysis was limited to metabolite ratios. The images generated from the metabolite ratio values most notably showed a general trend to increased Cho/NAA in white matter regions, although with an unstructured and patchy spatial distribution.

The following table lists the values of the regression analysis for each metabolite ratio, tissue type, and brain region:

Brain Region	NAA/Cr				Cho/Cr				Cho/NAA			
	Control		TBI		Control		TBI		Control		TBI	
	GM (sd)	WM (sd)	GM	WM	GM	WM	GM	WM	GM	WM	GM	WM
L Frontal Lobe	1.42 (0.10)	1.73 (0.15)	**1.33**	**1.58**	0.22	0.29	0.21	0.31	0.15	0.17	0.16	**0.20**
R Frontal Lobe	1.43 (0.10)	1.72 (0.14)	1.35	**1.57**	0.21	0.28	0.21	**0.31**	0.15	0.17	0.16	**0.20**
L Temporal Lobe	1.43 (0.13)	1.85 (0.15)	1.32	**1.67**	0.19	0.30	0.18	0.33	0.13	0.17	0.15	**0.21**
R Temporal Lobe	1.43 (0.13)	1.86 (0.17)	**1.24**	1.72	0.18	0.30	0.17	**0.35**	0.13	0.16	0.15	**0.21**
L Parietal Lobe	1.43 (0.09)	1.80 (0.15)	1.41	**1.64**	0.15	0.28	0.15	**0.32**	0.11	0.16	0.11	**0.20**
R Parietal Lobe	1.41 (0.10)	1.79 (0.15)	1.38	**1.66**	0.15	0.28	0.15	**0.33**	0.11	0.16	0.11	**0.20**
L Occipital Lobe	1.45 (0.14)	1.80 (0.16)	**1.27**	**1.66**	0.15	0.23	0.15	0.25	0.11	0.13	**0.13**	**0.15**
R Occipital Lobe	1.42 (0.14)	1.77 (0.17)	**1.25**	**1.61**	0.15	0.22	0.16	0.24	0.11	0.13	0.13	**0.15**
Cerebellum	0.99 (0.16)	1.08 (0.61)	0.88	1.12	0.25	0.25	0.21	0.30	0.20	0.23	0.25	0.26

Significant alterations are indicated for the TBI group, for $p<0.05$ by the background shading, and values with $p<0.01$ in bold font. Standard deviations are only shown for the initial columns for brevity, but values are similar for all results.

Results indicate widespread metabolic alterations in all brain regions, with decreased NAA/Cr and increased Choline/NAA, most strongly occurring in white matter. Additional analysis indicated no relationship between GCS injury measures and metabolite analysis results from individual subjects.

Despite the considerable heterogeneity of the types of injury among the TBI subject group used for this study, this study demonstrates the potential for volumetric MRSI analysis for detection of diffuse metabolic alterations. Further analysis will evaluate these metabolic findings with clinical measures of injury and outcome.

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REFERENCES: 1) A.A. Maudsley, et al., *NMR Biomed*, 19: 492-503 (2006).