

Proton Metabolite Changes in the Corpus Callosum, Thalamus and Brainstem Following Traumatic Brain Injury

V. Govind¹, K. Kaliannan¹, G. Saigal¹, S. Gold², J. Jagid³, L. Harris¹, and A. A. Maudsley¹

¹Radiology, University of Miami, Miami, Florida, United States, ²Jackson Memorial Hospital, Miami, Florida, United States, ³Neurosurgery, University of Miami, Miami, Florida, United States

INTRODUCTION: Conventional neuroimaging methods are not helpful in identifying imaging correlates for the cognitive deficits commonly observed in a small percentage of subjects with mild traumatic brain injury (TBI). Our previous whole-brain MRSI study indicated widespread and diffuse proton metabolite alterations [1, 2] in subjects with mild-to-moderate TBI. It has been reported recently [3, 4] that volume loss (atrophy) occurs in individual structures such as the corpus callosum, thalamus and brainstem following TBI that correlates with the processing speed on a working memory task [4]. In this study, metabolite data from the corpus callosum (CC), thalamus and brainstem were extracted from whole-brain MRSI data, acquired from controls and subjects with TBI, to evaluate alterations in N-acetyl aspartate (NAA), total-choline (Cho) and total-creatine (Cr), and their associations with neuropsychological (NP) test scores.

METHODS: MRI and MRSI data were obtained at 3T from 26 subjects with mild-to-moderate TBI (Glasgow coma scale score: 8-15, mean age: 26 years, scanned between 1 and 14 weeks after injury) and 20 age-matched controls (mean age: 26 years). The MRSI data were obtained from the whole-brain using a volumetric EPSI sequence (TR/TE=1710/70 ms, 135 mm slab, Tacq= 26 min.). Data were processed using the MIDAS package [5], and included calculation of voxel tissue content, signal normalization and spatial registration. Data from the whole-corpus-callosum, midbrain and thalamus regions-of-interest (ROIs) were obtained by identifying these anatomical structures on co-registered T1-weighted MRIs. In each ROI, spectral quality was controlled by including only spectra with fitted linewidths of ≤ 13 Hz (for the ROIs from the corpus callosum and thalamus) or ≤ 16 Hz (the midbrain ROI). An hour-long battery of NP tests was administered on all subjects with TBI on the same day of the scan and the standard scores of these tests were converted to z-scores using the population mean and SD. The metabolite values ([NAA] and [Cho]; in institutional units) and their ratios (NAA/Cho and Cho/Cr) were compared between the groups using the 2-tailed t-test, and the metabolite values and their ratios from the subjects with TBI group and the NP z-scores were correlated using a linear correlation method and the Pearson correlation coefficients (r) were obtained. A p-value of <0.05 was considered significant for both the tests.

RESULTS AND CONCLUSIONS: In the table, the mean metabolite values or their ratios in all the ROIs from the control and TBI groups are listed. The observations from the table, in the TBI group as compared to similar values in the control group, are: 1) [NAA] decreased in all the ROIs in the TBI group with a significant reduction (-13.3 %) from the

Table: Metabolite values (in inst. units) and ratios in the corpus callosum, midbrain and thalamus for the control and TBI groups. Mean \pm SD and p-values for the blue- and red-colored numbers are provided.

Metabolite or ratio	Corpus Callosum		Midbrain		Thalamus	
	Control	TBI	Control	TBI	Control	TBI
NAA	2121 \pm 213	1839 \pm 296	2376 \pm 276	2310 \pm 473	2335 \pm 167	2292 \pm 309
Cho	359 \pm 63	388 \pm 77	564 \pm 111	586 \pm 134	468 \pm 58	503 \pm 95
NAA/Cho	5.87 \pm 0.67	4.99 \pm 0.87	4.08 \pm 0.81	3.94 \pm 0.98	5.08 \pm 0.43	4.71 \pm 0.67
Cho/Cr	0.25 \pm 0.03	0.32 \pm 0.05	0.35 \pm 0.05	0.4 \pm 0.08	0.3 \pm 0.02	0.32 \pm 0.03
	p=0.069	p<0.05				

CC, 2) [Cho] increased from all the ROIs but only [Cho] from the CC showed significance (+8.1%), 3) decreased NAA/Cho in all the ROIs, with significant reductions from the CC (-15%) and the thalamus (-7.3%), and 4) increased Cho/Cr in all the ROIs, with values reaching significance only for the CC and midbrain; however, the p-value (~ 0.07) for the thalamus approaches towards significance. Associations between the metabolite measures (values and ratios) and NP scores indicated (not shown) that there was no strong and significant correlation for any of the metabolite measures ($r = 0.01-0.32$). The results of this study indicate that significant metabolite changes observed in the CC, midbrain and thalamus prove that there were microscopic injuries in these structures undetectable on conventional MRI. But these metabolite changes cannot be specifically associated with cognitive deficits as determined from the neuropsychological testing. Our previous MRSI analyses by tissue-type indicated significant correlations between the whole-brain metabolite changes and NP test scores [2]. Therefore, the use of whole-brain metabolite measures may provide greater sensitivity of detecting metabolite changes predictive of cognitive impairments seen in subjects with TBI.

ACKNOWLEDGEMENTS: This work is supported by NIH grants R01NS055107 and R01EB000822.

REFERENCES: 1) V. Govindaraju, J. Jagid, S. Falcone, A.A. Maudsley. Proceedings ISMRM, Toronto, 2008, p2274. 2) J. Jagid et al., Neurotrauma Symposium, July 27-30, Orlando, Florida, poster 197 (2008). 3) J. Kim, et al. NeuroImage 39: 1014-1026 (2008). 4) MA Fearing et al., J. Child Neurol. 23: 729-737 (2008). 5) A.A. Maudsley, et al., NMR Biomed, 19: 492-503 (2006).