Comparative Evaluation of Corpus Callosum Diffusion Tensor Imaging Metrics in Acute Mild and Moderate Traumatic Brain Injury (TBI): It's Correlation with Neuropsychometric Tests (NPT)

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Introduction: Diffuse axonal injury (DAI) contributes largely to mortality and morbidity following traumatic brain injury (TBI). Diffuse changes that result from DAI following stretching and shearing of white matter fibers consequent to rotational forces are believed to play an important role in the neurologic outcome in TBI[1]. TBI patients are impaired in attention and executive functions that include learning, working memory and executive control[2]. Corpus callosum (CC), the largest commissural fibers in the brain, has been considered especially vulnerable to TBI due to its unique location and composition[3]. Injury to CC is of serious concern in TBI because of its structural's role in the interhemisperic transfer of auditory, visual, sensory and motor information relevant to multiple cognitive processes[3].

Accurate identification of the extent of axonal injury early on is a major diagnostic challenge, since computed tomography (CT) or conventional T1- and T2-weighted MRI are poor at characterizing this injury. Diffusion tensor imaging (DTI) may provide better detection as well as insights into the mechanism of white matter injury. The aim of this study was to see the difference in vulnerability of CC between patients of mild and moderate TBI in the acute stage through DTI and to correlate these changes with neuropsychometric tests (NPT) done at 6 months of injury.

Materials and Methods: ***Subjects:*** Our study included 33 age/sex matched healthy controls and 83 patients with TBI (moderate TBI, n=57; mild TBI, n=26; mean±SD=34.25±10.28 years). These patients sustained mild and moderate TBI with demonstrable CT findings at the time of injury. The mean Glasgow Coma Score (GCS) was 10.6 with a range of 9 to 13 in moderate TBI and 14 to 15 in mild TBI with the mean GCS of 14.5. Patients underwent MRI within a mean interval of 8.9 days (range 5-14 days) after the traumatic incident. ***Imaging protocol:*** Whole-brain conventional MRI and DTI data were acquired on a 1.5 Tesla GE MRI scanner using a quadrature birdcage receive and transmit head coil. DTI data were acquired by using a single-shot echo planar dual spin echo sequence with ramp sampling. The diffusion weighting b-factor was set to 0 sec mm^{-2}, 1000 sec mm^{-2}. The other acquisition parameters were TR=8 sec, TE=100 msec, number of axial sections=36, slice thickness of 3 mm with no gap, field-of-view=240 mm^2, image matrix of 256 × 256 (following zero-filling) and NEX=8. The DTI data was processed and evaluated using JAVA based program. The DTI-derived maps were displayed and overlaid on images with different contrasts to facilitate the region-of-interest(s) (ROIs) placement for quantification of different DTI metrics. The rectangular ROIs of size ranging from 5×5 to 7×7 pixels were placed according to Witelson method[4] on 7 segments of CC [i.e. genu, midbody, and splenium] at the level of massa intermedia in mid saggital image.

NP Tests: NPT were performed in healthy controls and patients with TBI. NPT were performed only at six months and not at the time of first study as the pain associated with trauma in the initial phase of mild to moderate TBI is known to influence the NPT results The test included number connection tests (NCT A and B), figure connection tests (FCT A and B), and performance subset of modified Wechsler Adult Intelligence Scale (WAIS-P, modified for Indian population).

Multiple comparisons using Bonferroni, Post Hoc test was performed to determine the changes in fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), radial diffusivity (RD) values and NPT scores among these study groups. To study the relationship between NPT and FA, MD, AD and RD values, Pearson's Correlation coefficient was computed. A p value ≤ 0.05 was considered to be significant.

Results: The mean FA, MD, AD and RD values in different regions of the CC in healthy controls as well as patients with mild and moderate TBI are reported in Table. We observed significantly decreased FA in genu ($p<0.001$) and splenium ($p<0.001$), significantly increased RD values in genu ($p<0.001$), midbody ($p=0.007$) and splenium ($p<0.001$) along with significant increase in MD and decrease in AD only in genu ($p=0.004$; $p=0.034$) respectively in patients with moderate TBI compared to healthy controls. However, in moderate TBI significantly decreased FA was found only in genu ($p=0.002$) compared to mild TBI. NPT were found to be impaired in patients with mild and moderate TBI compared to healthy controls at six months and showed significant correlation with different DTI metrics in the regions of the CC. The moderate TBI showed poor NPT scores than mild TBI but did not reach the level of statistical significance.

Table. Summary of mean FA, MD, AD, and RD values in different regions of corpus callosum in healthy controls and patients with moderate and mild TBI.

DTI metrics	Groups	(Mean±SD)		
		Genu	Midbody	Splenium
FA	Controls	0.56±0.03	0.45±0.03	0.62±0.02
	Mild	0.50±0.05	0.44±0.02	0.61±0.02
	Moderate	0.47±0.03	0.43±0.03	0.60±0.03
MD×10^{-3} mm^2/s	Controls	0.78±0.05	0.80±0.07	0.76±0.07
	Mild	0.80±0.05	0.83±0.09	0.78±0.08
	Moderate	0.82±0.05	0.84±0.07	0.80±0.07
AD×10^{-3} mm^2/s	Controls	1.92±0.13	1.74±0.13	1.93±0.12
	Mild	1.87±0.12	1.73±0.14	1.86±0.14
	Moderate	1.84±0.14	1.72±0.13	1.87 ±0.13
RD×10^{-3} mm^2/s	Controls	0.69±0.07	0.81±0.12	0.62±0.09
	Mild	0.78±0.07	0.84±0.11	0.71±0.10
	Moderate	0.79±0.07	0.89±0.10	0.75±0.11

Discussion: In the present study, the observed decreased FA in genu and splenium along with increased RD in genu, splenium, midbody and decreased AD values in genu in moderate TBI can be explained on the basis of axonopathy occurring simultaneously with degradation of myelin within 5-14 days of TBI. The myelin breakdown at this time point reflects progressive structural degeneration changes which correspond well to the findings from histopathological and DTI studies of WD in acute ischemic stroke[5,6]. This indicates that RD may be a more sensitive index than FA in detecting the microstructural damage during 5-14 days of injury and probably represent myelin breakdown along with axonopathy. We observed higher MD values in genu of the CC in patients with moderate TBI, indicating a reduction in the hindrance of water molecules rather than an increase. Our findings are different from those of Arfanakis et al. who found no significant difference in MD values in patients with mild TBI[7]. This is likely to depend on the elapsed time of trauma, which was within 24 hours in a study reported by Arfanakis and colleagues[7] and within 8.9 days (5-14 days) in our study. An expansion of the extracellular space associated with neuronal or glial loss may explain the increase in MD values at late post injury time point[8]. In the current study, patients with moderate and mild TBI showed impaired neurocognitive function, even when changes in the DTI metrics were localized to a few regions within the CC. The neuropsychological changes were found to be more in patients with moderate TBI compared to mild TBI but did not reach the level of statistical significance suggesting that patients with moderate TBI have more neurocognitive deficits. We conclude that DTI abnormalities in the regions of CC was more in patients with moderate TBI compared to mild TBI and was associated with relatively poor neuropsychological outcome.

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