Demonstration of Differentially Degenerated Corpus Callosum in Patients with Moderate Traumatic Brain Injury: With a Premise of Cortical-callosal Relationship

Kavita Singh1, Richa Trivedi1, Maria M D’souza1, Ajay Chaudhary2, Pawan Kumar1, Ram KS Rathore2, Rajendra P Tripathi1, and Subash Khushu1

1Institute of Nuclear Medicine & Allied Sciences, Delhi, Delhi, India; 2Dr. Ram Manohar Lohia Hospital, Delhi, Delhi, India, 3Indian Institute of Technology, Kanpur, Kanpur, Uttar Pradesh, India

Target Audiences: Researchers and clinicians working in the field of traumatic brain injury and tractography

Introduction: Traumatic brain injury (TBI) has been defined as an alteration in brain function or other evidence of brain pathology caused by an external force. Injury to CC has been documented in axonal injury resulting from sheer strain forces of TBI owing to its long coursing nature and the midline location adjacent to the flux cerebri. Based on Witelson’s classification, CC has been divided into 7 segments viz rostrum, genu, rostral body (RB), anterior mid body (AMB), posterior mid body (PMB), splenium and isthmus. Studies have also been conducted showing involvement of CC in severity specific TBI but to our knowledge no study till date has shown cortical region specific disruption of the corresponding subdivisical fibres of CC. Based on the established cortico-callosal connections and studies of persistent cognitive impairment and continued WM degeneracy in post TBI patients, we hypothesised that extent of damage to a subdivision of CC due to TBI is in a way related to the corresponding cortical area primarily injured. To verify the aforementioned hypothesis patients with moderate TBI have been divided into three groups based on the cortical regions primarily injured.

Materials and methods: 18 moderate TBI patients (13 male and 5 female; age=25.3±9.1years) and 11 age and gender matched neurologically healthy control subjects were included in this study. Severity of TBI was assessed based on Glasgow coma scale. DTI scans were performed from 2 to 6 months of initiating traumatic insult. Control subjects with history of head trauma, substance abuse and other neurological or psychiatric illness were excluded. Written informed consent was taken from all the participants of the study. This study was approved by the institutional ethics committee.

The imaging study was performed using 3-Tesla MRI scanner (Magnetom, Skyra, Siemens) with a 20 channel head coil. The conventional MR imaging was done prior to DTI to rule out any structural abnormality. Diffusion MR imaging was done using a single-shot echo-planar dual SE sequence in 30 directions with ramp sampling. Diffusion-weighted acquisition parameters were: b-factor= 0 and 1000 s/mm², slice thickness=3 mm with no interslice space, number of slices=45, FOV=230 mm×230 mm, matrix size = 128×128, flip angle 90°, TR = 8800 ms, TE = 95 ms and NEX=2.

Different fiber bundles were reconstructed using fiber assignment by continuous tracking algorithm. Fibres with FA values more than 0.15 were considered for tractography. The ROI on mid-sagittal slice was selected for generating CC tracts. It was further subdivided based on Witelson scheme into seven sub-divisions viz rostrum, genu, RB, AMB, PMB, isthmus and splenium that approximately represented the CC connections hypothesised across cortical brain regions.

Statistical analysis: One way analysis of variance (ANOVA) with post-hoc and boneferroni correction was performed to study the difference in DTI measures among patient groups and controls. p-value of ≤0.05 was considered to be significant.

Results: Based on the findings of conventional imaging, all the patients were classified into 3 groups as: frontal lobe injury patients (Group A, n=6); occipito-temporal lobe injury patients (Group B, n=5); and fronto-parieto-temporal lobe injury patients (Group C, n=7). None of the patient showed any injury in CC on conventional imaging.

Group A versus Control: Comparing the callosal fibers of Group A patients with controls, Group A showed significantly decreased FA values in rostrum, genu, splenium and whole CC. MD values of rostrum and genu showed significant increase in Group A as compared to controls while increases in MD values of splenium did not reach at the level of statistical significance.

Group B versus Control: Group B patients showed decreased FA values in PMB, isthmus, splenium and whole CC fibres compared with control participants, however significant difference was observed in isthmus and whole CC. Increased MD values were observed in isthmus, splenium and whole CC fibres in group B patients compared to controls.

Group C versus Control: The FA values of callosal fibres were significantly decreased in Group C as compared to controls in whole CC and its all subdivisions. However, MD values showed significant increase in genu, splenium and whole CC in Group C as compared to controls.

Discussion: Here, we demonstrate the degenerative changes, secondary to TBI, in the sub divisional fibres of CC which showed a direct association to the corresponding cortical lobes primarily involved in injury. As compared to controls, we observed microstructural damage to CC in patients with moderate TBI during chronic phase of insult when no damage was visible on conventional MRI. Trauma induced atrophy of CC may be due to direct effect of trauma to CC or Wallerian type secondary degeneration occurring due to diffuse brain damage disrupting the integrity of white matter fibres. Significantly decreased FA with increased MD values in rostrum and genu compared with controls in group A patients can be attributed to microstructural changes secondary to injury in frontal lobe. Decreased FA along with increased MD in both isthmus and splenium of Group B patients can be explained on the basis of circumscribed lesions in occipito-temporal lobes as callosal fibers originating from occipital and temporal lobes constitute the isthmus and splenium of CC. Group C patients, had circumscribed lesions in frontal, parietal and temporal lobes, showed decreased FA along with increased MD in all the subdivisions of CC. In contrast to group A and B patients, group C patients also showed microstructural damage in RB, AMB, and PMB subdivision of CC. It has been documented that fibres from the RB and AMB course through the premotor/supplementary motor areas and motor somesthetic areas, respectively. Fibres from the posterior parietal regions constitute the PMB. We speculate that the microstructural damage in anterior callosal subdivisions (rostrum, genu and RB), AMB and PMB is a consequence of the primary lesions in fronto-parietal lobes in group C patients. In conclusion, this study demonstrates cortico-callosal topographical relationship in patients with TBI. A decline in observed FA and increase in MD values appears to represent regional WD. This may contribute to the understanding why patients with same severity of TBI present with a wide variation in cognitive functions.

References:

Fig1: Figure shows the methodology used for reconstruction and segmentation of corpus callosum (CC) into seven subdivision [Rostrum: grey, genu: green, RB: blue, AMB: yellow, PMB: turquoise, isthmus: pink, splenium: white] Fig 2: Figure shows the reconstructed subdivisions callosal fibres in controls, group A, group B and group C. In group A, thinning in CC (yellow arrow) is apparent in rostrum, genu and splenium compared with control. In comparison to control, group B patient shows thinning of CC in both isthmus and splenium. In group C patients, all the CC subdivisions shows thinning compared to control.