Temporal changes in moderate-to-severe traumatic brain injury: a tract-based spatial statistical analysis

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Introduction:

Traumatic axonal injury (TAI) plays an important role in the pathophysiology of traumatic brain injury (TBI), and contributes substantially to morbidity and mortality.[1] Conventional imaging methods poorly describe the extent of the damage. Diffusion tensor imaging (DTI) may provide insight into its extent and severity. Tract-based spatial statistics (TBSS) was used to investigate temporal changes in diffusivity parameters post TBI in the areas of maximal anisotropy in the white matter tracts.

Methods:

9 patients (4 male, 5 female) with TBI, who required sedation and mechanical ventilation for intracranial pressure (ICP) control, underwent magnetic resonance (MR) imaging at a median of 28 hours (range 7 to 109 hours) post injury (scan 1) and again at follow up (median 274 days post injury, range 154 to 380 days) (scan 2). The mean age was 37.9 (SD ± 17.0) years, and the median Glasgow Coma Score (GSC) was 6 (range 3 to 11). Median Glasgow Outcome Score (GOS) at follow-up was 4 (range 3 to 5). All values were compared to data collected from 10 controls (healthy volunteers) (mean age (SD 32.7± 9.9), 5 male, 5 female). The imaging protocol included spin echo planar diffusion weighted imaging (12 non-collinear directions, 5 b values equally spaced from 300 to 1500mm^2/sec, 4 b = 0 images were also acquired). Mean fractional anisotropy (FA), the apparent diffusion coefficient (ADC) and eigenvalues ($\lambda1>\lambda2>\lambda3$) were calculated using in-house software based on the method proposed by Basser and Pierperoli.[2] Brain tissue was extracted from the non-weighted (b=0) image using BET[3] and a binary mask created, which was then applied to the FA image. Any excess noise was removed manually using Analyze 7.0.[4] Voxelwise statistical analysis of the FA data was then carried out using TBSS[5] part of FSL.[6] TBSS projects all subjects' FA data onto a mean FA tract skeleton, before applying voxelwise cross-subject statistics. A threshold of 2500 was used in this analysis**.** Due to concerns that firstly, patients may have their normal architecture distorted and secondly, that lesions in their WM tracts with FA <0.25 (below the threshold) it was decided to use a target image for registration. The target image was chosen to be the "most typical" from a group of 10 controls, different to those used in the TBSS analysis. Unpaired t-tests were applied to the patient-control data using permutation based inference on cluster size ($t>3$, $p < 0.05$, fully corrected for multiple comparisons).[5] Changes in ADC and the eigenvalues were also assessed.

Results:

In the acute scans regions of decreased FA were observed in the posterior corpus callosum, internal capsule and brainstem (Figure 1). There were also small clusters of increased ADC and the radial eigenvalues in the splenium. The follow-up scans illustrated larger clusters and more widespread changes than the acute scans. Clusters of decreased FA were apparent in the splenium, corticospinal tracts and the brainstem. In addition, clusters of decreased FA were also observed in the genu and body of the corpus callosum, the external capsule, frontal and posterior white matter tracts. A corresponding widespread increase in ADC was also observed. Multiple areas of increased radial diffusivity ($\lambda2$, $\lambda3$) were seen, particularly in the genu and splenium of the corpus callosum. Increased axial diffusivity ($\lambda1$) was also observed in the corpus callosum as well as the left corticospinal tract.

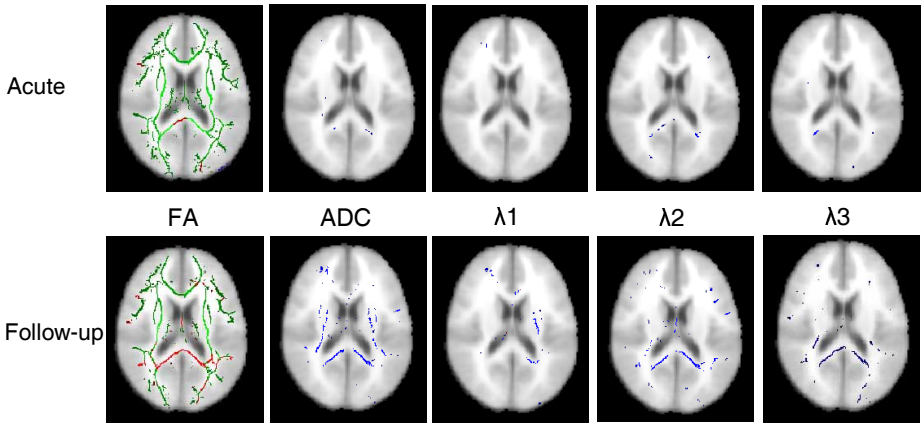

Figure 1: TBSS results from 9 patients, imaged in both the acute and chronic stage post TBI, compared to 10 controls. Differences compared to controls in FA, ADC, and the eigenvalues are overlaid on the MNI152 image. The mean FA skeleton is shown in green. Red voxels show significantly lower values and blue significantly higher in patients compared with controls corrected for multiple comparisons

Discussion:

Damage to the centres of the tracts was more widespread in the chronic phase of injury, indicating that the damage in the centre of the tracts evolves overtime. Acutely, the decrease in FA may be secondary to axonal swelling. The radial diffusivities ($\lambda2$ and $\lambda3$) were increased in areas corresponding to decreased FA in the follow-up scans, consistent with demyelination. These results are in agreement with clinical and histopathological studies. Further studies with larger numbers are required.

References:

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