Peripheral versus central white matter damage in chronic traumatic brain injury :a quantitative tractography study.

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Introduction: Diffuse traumatic axonal injury has classically been reported in central white matter (WM): the corpus callosum (posterior body and splenium), dorsolateral brainstem, and parasagital WM. However, microscopic lesions may also occur peripherally at gray/white matter interfaces and in subcortical WM. These are difficult to detect, but may contribute substantially to neurocognitive deficits. We have studied the extent of central and peripheral WM damage in patients with chronic traumatic brain injury (TBI), characterized using tractography, fractional anisotropy (FA) and apparent diffusion coefficient (ADC).

Methods: 24 patients (17male, 7 female) were assessed at a median of 11.6 (range 6 to 42) months post-TBI. The mean age was 33 (SD±12.1) years and the median Glasgow Coma Score was 6 (range 3 to 15). 28 age matched healthy volunteers (mean age 33(±7.8) years, 21 male, 7 female) were used as a comparison group. Ethical approval was obtained from the Local Research Ethics Committee and informed consent was obtained in all cases. MR imaging was performed using a 3 Tesla Total Imaging Matrix Siemens Tim Trio, and included a 3D T1-weighted structural sequence (MP-RAGE) as well as spin echo planar diffusion weighted imaging (acquired using 12 non-collinear directions, 5 b values equally spaced from 300 to 1500 s/mm^2 with 4 b = 0 images). The diffusion weighted parameters were: 20 x 20 cm field of view, 100 x 100 matrix size, 63 axial slices, 2 mm slice thickness, TR = 6000ms, TE = 100ms, diffusion sensitizing duration = 23.5ms (δ); with separation (leading edge to leading edge) = 60ms (Δ). All images were visually inspected and subjects (3 patients, 4 controls) who had moved more than 2 voxels (4mm) during the diffusion sequence were removed prior to data analysis. FDT (FMRIB's Diffusion Toolbox) was used to fit a tensor at each voxel and create FA, ADC and eigenvalue maps.[1] DTIquery[2] was used in the subject's native space to create whole brain tractography using the FACT algorithm[3], a variable-step streamline tracking method. Tractography parameters were; a step-size of 2mm, deflection angle of 45^0 and FA termination threshold of 0.15. The b=0 map and the diffusion data, including the tractography maps, were coregistered to MNI152 space using the vtkCISG normalised mutual information algorithm.[4] A whole brain peripheral region of interest (ROI) was manually created in Analyze[5] using Colin27[6] as a template. A whole brain central WM ROI was created by subtracting the peripheral ROI from WM segmented using FSL. Binary masks of these regions were applied to the tractography results to assess WM integrity. To reduce errors due to noise, tracts shorter than three voxels (6mm) were ignored. The mean ADC and FA for each ROI were calculated and histogram analysis performed to assess changes in FA distribution, both in peripheral and central WM. Data were normally distributed and analysed using parametric statistics.

Results: There was a significant decrease in the number (± SD) of fibres counted in both peripheral WM (TBI 7344(±924), controls 8159(±811), p<0.001) and central WM (TBI 11754(±1384), controls (12954(±1185), p<0.001)) (Figure 1). This corresponded to a significant decrease in the mean FA in peripheral WM (TBI 0.28(±0.02) Vs controls 0.29(±0.01), p=0.024) and central WM (TBI 0.45(±0.03) vs controls (049(±0.01), p<0.001). Histograms revealed distinct differences in distribution (Figure 2). The central white matter had a more marked leftward shift of the patient histograms when compared with controls than the peripheral white matter. There was also a significant increase in mean ADC (±SD(x10^{-3}mm^2/s)) in the peripheral ((TBI (0.78(±0.04), controls 0.72(±0.02), p<0.001) and central ((TBI(0.75(±0.06) controls (0.68(±0.01) P<0.001) white matter regions.

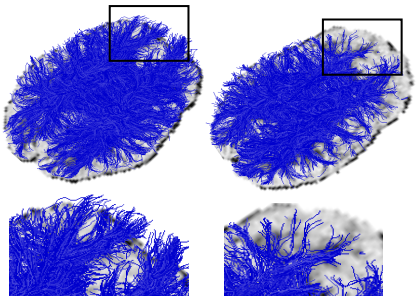

Figure 1: Tractography for a control (left) and a patient approximately 7 months post TBI (right). The frontal WM is markedly decreased in the patient.

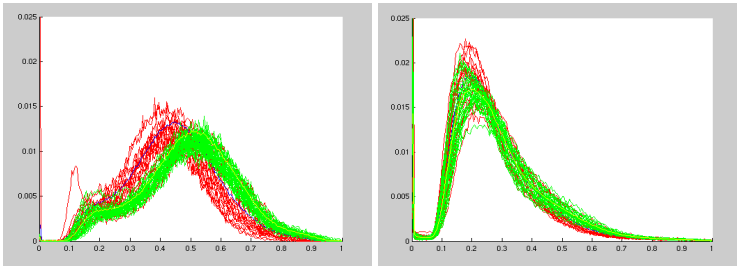

Figure 2: FA histograms for the central (A) and peripheral (B) WM from controls (green) and patients (red). Note the marked leftward shift in central WM histograms in patients.

Discussion: There is evidence of damage to both the central and peripheral WM in patients with chronic TBI, which appears to be more dominant in the central or deep WM. This tractographic approach, while not a true reflection of a white matter tract size or function, provides a useful surrogate measure of the structural integrity of WM and maps changes in connectivity with disease.

Conclusions: Quantitative tractography may provide a useful way to detect microscopic damage to physical connectivity. Further work needs to correlate these structural data with neuropsychological parameters and functional outcome.

References:

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