Long-term diffusion changes in the corpus callosum of patients with severe traumatic brain injury

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Introduction:
Diffuse axonal injury (DAI) is the dominating type of primary neuronal injury in patients with severe blunt head trauma. DAI is produced by sudden acceleration/deceleration/rotation that causes shear of the axons and immediate or delayed axonal disruption. The predominant sites of DAI are the subcortical gray-white matter junction, the corpus callosum and the dorsolateral upper brain stem. Structural MRI is known to underestimate the extent of DAI. Diffusion tensor imaging (DTI) allows for quantitative measurements of the degree and directionality (anisotropy) of water diffusion that reflect white matter architecture. Previous studies of DTI in patients with DAI have found decreased fractional anisotropy (FA) in the corpus callosum [1,2], but no long-term follow-up studies are presently available. We performed a longitudinal follow-up study on patients with severe head injury, aiming to investigate the long-term changes of diffusion parameters following DAI.

Methods:
Fourteen adult patients (age, mean +/- SD; 31.9 +/- 15.0 yrs; 10 male, 4 female) admitted for neurorehabilitation were included. All patients had sustained severe (initial Glasgow Coma Score < 9) non-missile head injury requiring admission to neuro-intensive care unit. Trauma was due to either traffic accident (n=10), fall (n=3) or violence (n=1). MRI was performed 5-11 weeks after trauma (mean 54 days), in all patients followed up by a second scan 32-60 weeks later (mean 49 weeks). Fourteen healthy subjects with similar age (mean 33.2 +/- 8.0 yrs; 3 male, 11 female) served as controls and were scanned with a time interval similar to that of the patients. All scans were performed on a 1.5T Siemens Vision scanner. Anaesthesia was necessary in 11 patients for first scan and in 3 patients for second scan. The protocol for patients and controls included at each session DTI and a 3D T1-weighted structural sequence (MPRAGE; voxel dimensions approximately 1 mm3). Diffusion weighted SE-EPI (TE=60 ms) was acquired with 6 directions and 6 repetitions (axial, 30 slices, 5 mm thickness; b values 0 and 724 s/mm²). MPRAGE volumes were spatially normalised to Talairach space using SPM. An anatomical ROI was manually drawn delineating the posterior part of corpus callosum on the midsagittal slice plus 4 slices to each side. The anterior part was omitted due to frequent susceptibility artifacts in this region, and the border was defined arbitrarily as a line perpendicular to the AC-PC line, crossing it at the midpoint. A separate ROI was made for each scan, to minimise partial volume effects due to between-scan structural changes. The DTI parameters: FA, ADC trace, and the eigenvalues were calculated according to [3]. The parameter maps were resliced to Talairach space, and values for FA, ADC trace and eigenvalues were averaged over the ROIs.

Results:
Group comparisons of patients and controls: In patients, FA was slightly lower at first scan (0.57 +/- 0.05; p=0.04) and much lower at follow-up (0.46 +/- 0.06; p<0.001) as compared to controls (0.61 +/- 0.06 first scan; 0.61 +/- 0.04 follow-up). ADC in patients was not significantly different from controls at the first scan, but higher than for controls at follow-up (1.29x10⁻³ +/- 0.10 vs. 1.06x10⁻³ +/- 0.09x10⁻³ mm²/s; p<0.001). Paired analysis between first scan and follow-up: Patients showed a decrease in FA (18.4%, p=0.001) and an increase in ADC (24.8%, p=0.012) between scans. Separate analysis of the eigenvalues showed increased diffusion perpendicular to the long axis of fibers (mean of λ2 and λ3 increased by 23.4%, p<0.001) with no significant change of diffusion parallel to the fibers (λ1). In patients, ROI volume was generally smaller at follow-up compared to first scan, due to atrophy as a consequence of DAI. Controls showed no significant temporal changes of the measured diffusion parameters or of ROI volume. The variance of diffusion parameters within each ROI was similar between groups and between first and second scans. There were no trends towards any influence on diffusion parameters by age, gender, cause of trauma or by anaesthesia, although sample size did not allow appropriate statistical testing for these potential confounders.

Conclusions:
In this follow-up study of patients with diffuse traumatic white matter injury, we showed significant decrease in FA and increase in ADC in the corpus callosum. Evaluating the underlying changes of the eigenvalues, we found a significant increase of diffusion perpendicular to the long axis of fibers (mean of λ2 and λ3). These findings suggest ongoing degeneration several months following DAI, which is in agreement with morphometric and pathological studies.

References:

Figure 1. MPRAGE, mid-sagittal slice, showing the positioning of the ROI outlining the posterior part of corpus callosum (AC-PC line also shown).

Figure 2. FA in patients and controls, at first scan (time point 1, sub-acute phase) and at follow-up (time point 2, mean 49 weeks after first scan). Paired t-test: patients p<0.001; controls NS.

Figure 3. ADC trace in patients and controls, displayed similar to Figure 2. Paired t-test: patients p<0.012; controls NS.