Quantitative diffusion tensor tractography of the cingulum: reproducibility, normal values and findings in traumatic brain injury

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Purpose

Cingulum is a major part of the limbic system responsible for connections essential for memory, emotions and attention. The trajectory can be divided anatomically to anterior-dorsal component with frontal and parietal connections and posterior-ventral component with temporal, occipital and precuneal fibres [1]. The corresponding division can be made by means of tractography [2]. Degradation of cingulum has been found in several conditions with cognitive symptoms including traumatic injury.

Although quantitative diffusion tensor (DT) tractography is sensitive to the integrity of cingulum, the clinical utility can be constrained by structural variability and volume changes in injuries [2,3]. These pitfalls can possibly be eliminated by performing tractography-based core analysis (TBCA) instead of tractography with fixed FA values (TF) [2,3]. The aim was to investigate the reliability of these methods and findings in TBI by using DT sequences suitable for clinical studies.
Methods and Materials

Patients with persisting symptoms after TBI without findings in conventional MRI were studied. The inclusion criteria were: 1) traumatic injury leading to loss of consciousness and/or posttraumatic amnesia; 2) no other neurological or vascular disease, chronic hypertension or chronic alcoholism; 3) no signs of other brain diseases in routine MRI; 4) age 18-54 years, 5) time from injury ≤ 3 months, 6) detailed clinical background information available. 80 randomly selected patients were included (age 18-53 years, mean 37.1 ± 9.1 years, 40 men and 40 women) and compared with 78 demographically matched normal controls (age 18-54 years, mean 37.1 ± 9.8 years; 39 men and 39 women).

MRI was performed at 3 tesla using a sensitivity encoding (SENSE) 8-channel transmit-receive head coil. The imaging protocol consisted of routine T2-weighted TSE, FLAIR, 3DT1 and SWI images. DT imaging was performed by using diffusion-weighted turbo spin echo EPI images (TR/TE 6367/62, 65 slices with 2.0 mm thickness, 112 x 128 matrix, number of excitations 2, imaging time 4 min 12 s); b values of 0 and 800 sec/mm² and 15 different gradient encoding directions were used, images with 2.0 x 2.0 x 2.0 mm voxel size, reconstructed to 2.0 x 1.75 x 1.75 mm voxel size were obtained.

To determine the inter-scan reproducibility 15 subjects were scanned twice. Tractography of superior (SC) and inferior (IC) cingulum was performed separately with FA thresholds 0.15 and 0.30, the angle threshold was 27 degrees. Core FA was measured from several predetermined volumes (3 cm³, 2 cm³, 1.5 cm³ and 1 cm³ for SC and 2 cm³, 1.5 cm³, 1 cm³ and 0.5 cm³ for IC) defined by tractography with gradually changed FA thresholds (3). Tractography was performed by using two inclusion ROIs in standard anatomical positions on coronal slices around cingulum for both SC and IC and an exclusion ROI in the midsagittal slice.
Results

The lowest coefficient of variation was obtained by the threshold 0.30 (1.6%/2.0% for SC and 3.5%/2.7% for IC) but compared with standard deviations (sd) of normal controls TBCA had the best coefficient of variation (0.34 sd/0.41 sd for SC 3cm$^3$; 0.56 sd/0.59 sd for IC 1.5 cm$^3$).

The normal values are represented in Table 1. In normal controls, there was marked volume variability (standard deviation 17-30% from the mean value), whereas the variability of FA and MD values was relatively small (Table 1, Figures). In patients, FA reduction (>2 sd) was relatively common by both FA thresholds (5-9% of the tracts). In patients, marked volume reduction with total or partial absence of the peripheral parts of tract was common especially by the FA threshold 0.30 (6-16% of the tracts). In these tracts mean FA values were mostly normal (in 39 of the 47 measurements of the tracts with volume reduction >2sd). There were several cases with increased volume or FA value in SC but only normal statistical number in IC.

A uniform central volume could be delimited for TBCA in all cases. There was minor variability in the shape and position of the measurement volumes for TBCA (Figure). TBCA showed more abnormalities than TF; FA reduction was present in 10-15% of the tracts (Table 2). Increased core FA value (>2 sd) was present in some cases in SC.

TABLE 1. Volumes (vol, mL), mean FA and mean MD values of normal controls, results in mean values (standard deviations).

<table>
<thead>
<tr>
<th></th>
<th>vol$_{0.15}$</th>
<th>vol$_{0.30}$</th>
<th>FA$_{0.15}$</th>
<th>FA$_{0.30}$</th>
<th>MD$_{0.15}$</th>
<th>MD$_{0.30}$</th>
<th>FA$_{core}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC right, women</td>
<td>8.42(1.54)</td>
<td>5.45(1.10)</td>
<td>0.408(.017)</td>
<td>0.461(.013)</td>
<td>0.798(.021)</td>
<td>0.787(.021)</td>
<td>0.510(.027)</td>
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<tr>
<td>SC right, men</td>
<td>10.20(1.97)</td>
<td>6.69(1.47)</td>
<td>0.418(.015)</td>
<td>0.470(.012)</td>
<td>0.801(.023)</td>
<td>0.789(.025)</td>
<td>0.539(.027)</td>
</tr>
<tr>
<td>SC left, women</td>
<td>9.34(1.62)</td>
<td>6.39(1.07)</td>
<td>0.421(.017)</td>
<td>0.473(.011)</td>
<td>0.793(.019)</td>
<td>0.784(.019)</td>
<td>0.549(.026)</td>
</tr>
<tr>
<td>SC left, men</td>
<td>10.90(2.45)</td>
<td>7.60(1.94)</td>
<td>0.428(.017)</td>
<td>0.481(.014)</td>
<td>0.791(.019)</td>
<td>0.782(.021)</td>
<td>0.574(.034)</td>
</tr>
<tr>
<td>IC right, women</td>
<td>4.40(0.98)</td>
<td>2.28(0.61)</td>
<td>0.374(.022)</td>
<td>0.439(.019)</td>
<td>0.872(.037)</td>
<td>0.816(.024)</td>
<td>0.466(.029)</td>
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<tr>
<td>IC right,</td>
<td>4.84(1.04)</td>
<td>2.47(0.70)</td>
<td>0.385(.02)</td>
<td>0.446(.015)</td>
<td>0.871(.042)</td>
<td>0.817(.026)</td>
<td>0.475(.030)</td>
</tr>
<tr>
<td>men</td>
<td></td>
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<tr>
<td>IC left,</td>
<td>4.60(1.13)</td>
<td>2.24(0.68)</td>
<td>0.373(.020)</td>
<td>0.431(.016)</td>
<td>0.890(.037)</td>
<td>0.835(.027)</td>
<td>0.453(.027)</td>
</tr>
<tr>
<td>women</td>
<td></td>
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<tr>
<td>IC left,</td>
<td>5.00(1.17)</td>
<td>2.44(0.72)</td>
<td>0.381(.021)</td>
<td>0.443(.020)</td>
<td>0.891(.038)</td>
<td>0.846(.033)</td>
<td>0.471(.032)</td>
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<tr>
<td>men</td>
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</table>
**Fig. 1:** Figure 1. SC of normal controls. Tractograms of the left SC by FA thresholds 0.15 (blue), 0.30 (green) and in TBCA by volumes 3.0 cm³ (violet).

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**Fig. 2:** Figure 2. SC of patients with TBI. Tractograms of the left SC by FA thresholds 0.15 (blue), 0.30 (green) and in TBCA by volumes of 3.0 cm³ (violet).

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**Fig. 3:** Figure 3. IC of normal controls. Tractograms of the left IC by FA thresholds 0.15 (blue), 0.30 (green) and in TBCA by volumes 1.5 cm3 (violet).

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**Fig. 4:** Figure 4. IC of patients with TBI. Tractograms of the left IC by FA thresholds 0.15 (blue), 0.30 (green) and in TBCA by volumes of 1.5 cm3 (violet).

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Conclusion

Although there is considerable variability in the results of tractography-based analysis, the reproducibility is sufficient for demonstration of severe abnormalities. SC can be measured more accurately than IC, which can be related to the size difference of the trajectories.

Injury of cingulum can lead in tractography to a marked volume reduction with total or partial absence of peripheral parts with relatively low FA values and to misleading mean FA values representing only the central parts. By using TBCA corresponding areas are measured in patients and controls, and inaccuracies due to traumatic volume changes can be avoided. The method showed abnormalities in symptomatic patients with TBI with normal routine MRI in 10-15% of measurements.

Cases with increased FA were observed in SC more often than in IC. The increased anisotropy can be due to injury of crossing tracts, most probably of callosal fibres, which have relatively perpendicular course to SC but parallel course to IC.
References