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Cingulum injury in patients with diffuse axonal injury: A diffusion tensor imaging study

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HIGHLIGHTS

- We investigate changes in cingulum after diffusion axonal injury.
- We divided the cingulum into five parts.
- Diffusion tensor tractography was used for this research.
- The anterior portion of the superior cingulum was the most severely injured.

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ABSTRACT

Accurate assessment of the cingulum is difficult, because it is a long neural tract that extends from the orbitofrontal cortex to the medial temporal lobe. We divided the cingulum into five parts and investigated changes caused by injury in these regions in patients with diffuse axonal injury (DAI) using diffusion tensor tractography (DTT). Twenty-one patients with DAI and 21 control subjects were recruited. The cingulum was divided into; the anterior, superior (the anterior and posterior portions), posterior, and inferior regions. Fractional anisotropy (FA), apparent diffusion coefficient (ADC), and tract number were measured in each region. FA values and tract numbers in the patient group were lower in the anterior superior cingulum than in controls ($p < 0.05$); whereas the ADC values in the patient group were higher in the anterior and posterior superior cingulum than in controls ($p < 0.05$). In the superior cingulum, increases in the ADC values of the anterior portion (Δ8.1%) were higher than those of the posterior portion (Δ5.5%). We found that the superior cingulum was injured in patients with DAI, and that the anterior portion of the superior cingulum was more injured than the posterior portion. Consequently, the superior cingulum appears to be a vulnerable area and the anterior superior cingulum appears more vulnerable than the posterior superior cingulum in DAI.

1. Introduction

Traumatic brain injury (TBI) is one of the main neurologic causes of disabling sequelae, and diffuse axonal injury (DAI) is one of the most predominant and devastating mechanisms of TBI [14]. DAI typically shows widespread focal white-matter lesions due to shearing forces induced by rapid acceleration–deceleration and rotation of the brain [14]. However, conventional MRI is not sensitive enough to detect DAI lesions because many of these are microscopic [8]. During brain rehabilitation, a thorough estimation of DAI lesions is important because this enables clinicians to predict outcomes and to establish rehabilitation strategies [5,10,26].

The cingulum is a well-marked collection of neural fiber tracts longitudinally in the white matter of the cingulate gyrus, composed largely of fibers from the orbitofrontal cortex to the medial temporal lobe [1]. Furthermore, it is a major structure in the limbic system, and is likely to play an important role in diverse processes, such as, attention, memory, learning, motivation, emotion, and pain perception [7,19]. In the past, assessment of the cingulum was difficult due to its long shape and location deep within the brain. However, recent advancements in diffusion tensor tractography (DTT), which was derived from DTI, now allow the cingulum to be visualized three-dimensionally [6,9,23,24,26]. This brain structure has the potential to be vulnerable to DAI because of its location

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Table 1
Demographic data of the patient and control groups.

	Patient group (n = 21)	Control group (n = 21)
Age (year)	32.3 ± 9.9 (20–54)	32.5 ± 10.0 (20–54)
Sex	16 males, 5 females	16 males, 5 females
Education (year)	13.4 ± 1.4 (12–16)	14.4 ± 1.9 (12–16)
Duration of LOC (day)	22.3 ± 38.7 (1–180)	
Duration after onset (month)	7.8 ± 7.9 (1–29)	
DAI grading	Grade[a] 1:2:3 (7:9:5)	

DAI: diffuse axonal injury, LOC: loss of consciousness. Values are mean ± standard deviations (range).

[a] Grade 1: histological evidence of axonal injury in white matter of the cerebral hemispheres, the corpus callosum, the brain stem, and the cerebellum, Grade 2: focal lesions in the corpus callosum, and Grade 3: additional focal lesions in the dorsolateral quadrant or quadrants of the rostral brain stem.

adjacent to the corpus callosum (CC), which is one of the most commonly injured structures by DAI [14]. Among the CC, the isthmus and its adjacent areas are known to be the most vulnerable areas by DAI [4]. Thus, we hypothesized that cingulum injury also can be different according to its location along the long structure in DAI [16,18]. To date, no study has addressed this topic, although several DTT studies have reported on cingulum injury in cases of DAI [9,23,24,26].

In the current study, we divided the cingulum into five parts and investigated the differences of the presence and severity of injury according to these five parts of cingulum, using DTT.

2. Methods

2.1. Subjects

Twenty-one consecutive patients (16 males, 5 females; mean age, 32.3 years; range, 20–54) and 21 age-and sex-matched control subjects (16 males, 5 females; mean age, 32.5 years; range, 20–54) with no history of neurological or psychiatric disease were recruited (Table 1). These patients were recruited retrospectively from patients admitted for rehabilitation at a department of rehabilitation in a university hospital according to the following criteria [8]: (1) a mechanism of injury associated with significant acceleration/deceleration force, (2) any loss of consciousness at the time of injury without a lucid interval, (3) conventional brain MRI showing no specific lesion other than a DAI lesion, (4) at least a twelfth grade education level, (5) age 20–59 years, and (6) more than 30 days after TBI onset. All patients signed an informed consent statement. This study was conducted in compliance with the international "Declaration of Helsinki". The Institutional Review Board of our university hospital approved the study protocol.

2.2. DTI acquisition

Mean duration from onset to DTI scanning was 7.8 ± 7.9 months (range: 1–29 months). DTI was performed using a sensitivity-encoding head coil on a 1.5-T Philips Gyroscan Intera unit (Hoffman-LaRoche, Ltd., Best, the Netherlands) using single-shot echo-planar imaging and navigator echo. Sixty contiguous slices (matrix = 128 × 128, field of view = 221 × 221 mm^2, TE = 76 ms, TR = 10,726 ms, SENSE factor = 2; EPI factor = 67, b = 1000 s/mm^2, and NEX = 1 with a 2.3 mm slice thickness) were acquired for each of the 32 noncollinear diffusion-sensitizing gradients. Eddy current image distortions and motion artifacts were removed using affine multi-scale two-dimensional registration, which was performed using the FMRIB Software Library (FSL, http://www.fmrib.ox.ac.uk/fsl).

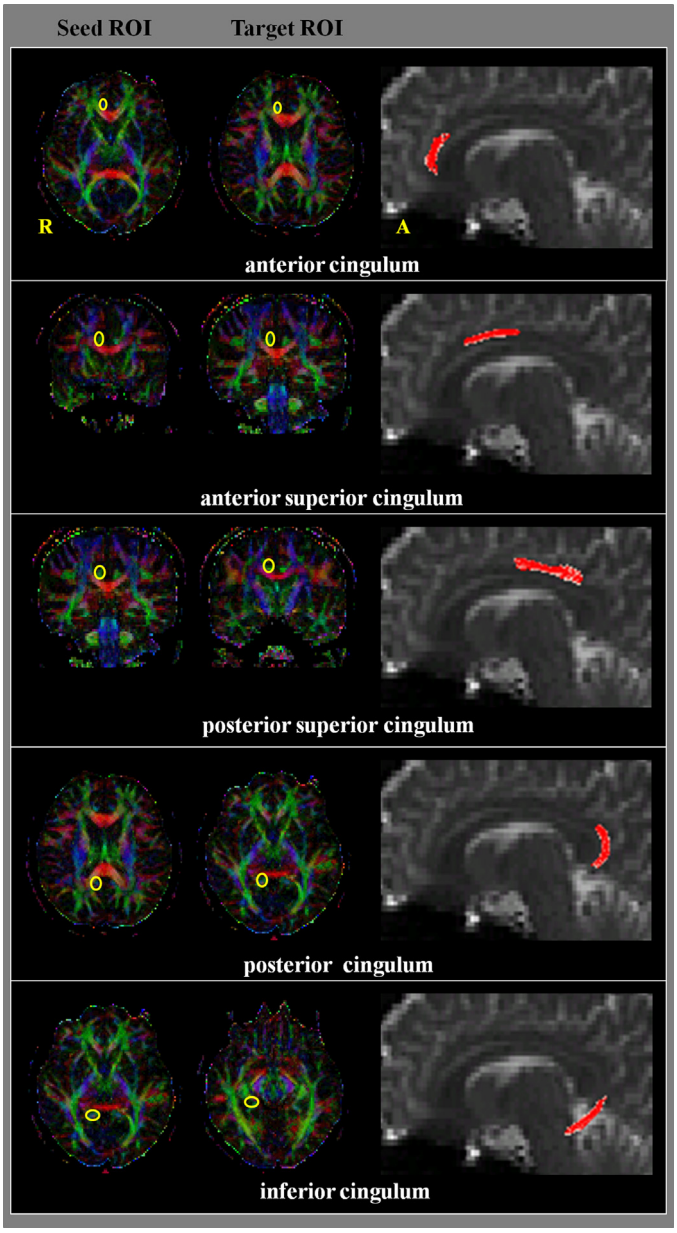

Fig. 1. Regions of interest and tractography for each part of the cingulum. ROI: region of interest.

2.3. DTI analysis

We evaluated the cingulum using DTI-Studio software (CMRM, Johns Hopkins Medical Institute, USA). The cingulum was divided into five parts with based on Concha's study [6], that is, into the anterior, superior (divided into two portions: the anterior and posterior superior cingulum), posterior, and inferior cingulum (Fig. 1). Regions of interest (ROIs) were placed on DTI-based color-coded maps (Fig. 1), as follows: anterior cingulum-a seed ROI was placed on the blue portion in front of the CC on axial images showing the lowest level of the genu of the CC, a target ROI was placed on the cingulum in axial images showing the fornix body; anterior superior cingulum-a seed ROI was placed on the green portion above the CC at the coronal slice level at the posterior border of the genu of the CC, a target ROI was placed on the mid-point of the superior cingulum on coronal images; Posterior superior cingulum-a seed ROI was placed on the mid-point of the superior cingulum in coronal images, and a target ROI was placed on the green portion above the