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CASE REPORT

DEGENERATION OF CINGULUM AND FORNIX IN A PATIENT WITH TRAUMATIC BRAIN INJURY: DIFFUSE TENSOR TRACTOGRAPHY STUDY

Ji Heon Hong, PT and Sung Ho Jang, MD

From the Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University, Republic of Korea

Objectives: **The cingulum and fornix are important structures for memory function. Using follow-up diffusion tensor tractography in a patient with traumatic brain injury we found degeneration of the cingulum and fornix.**

Case report: **An 18-year-old male who had had a traffic accident underwent conservative management for diffuse axonal injury. Brain magnetic resonance imaging showed an encephalomalactic lesion in the posterior portion of the corpus callosum. The patient had severe cognitive problems at 3 months after onset. However, while his intelligence had improved, his memory impairment had been aggravated at 14 months from onset.**

Results: **On the first diffusion tensor tractographies, the integrity of both corticospinal tracts, right cingulum, and left fornix were preserved; however, compared with controls, there were disruptions in both ends of the left cingulum and right fornical crus. On the second diffusion tensor tractographies, both the cingulum and fornix showed severe degeneration, although the integrities of both corticospinal tracts were well preserved.**

Conclusion: **We conclude that patients with memory impairment following traumatic brain injury should be evaluated using diffusion tensor imaging. In addition, follow-up diffusion tensor imaging may be necessary in patients with sustained memory impairment.**

Key words: cingulum; fornix; trauma; brain injury; memory; diffusion tensor image.

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Correspondence address: Sung Ho Jung, Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University 317-1, Daemyungdong, Namku, Taegu, 705-717, Republic of Korea. E-mail: strokerehab@hanmail.net, belado@med.yu.ac.kr

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INTRODUCTION

During rehabilitation of patients with traumatic brain injury (TBI), neuronal degeneration is just as important as neuronal regeneration. Several neuroimaging studies have reported neuronal degeneration following TBI (1–3). These studies were mainly conducted using brain magnetic resonance imaging (MRI); therefore, they usually reported changes in volume in the involved brain region without reporting detailed changes in neural tracts (1–3). Recent development of diffusion tensor imaging (DTI) allows us to evaluate the status of, and changes in, neural tracts at the subcortical level (4). Many DTI studies have reported injury of the cingulum and fornix after TBI; however, little is known about DTI changes associated with neuronal degeneration following TBI (5–13).

The cingulum and fornix are important components of the Papez circuit and limbic system. The cingulum is a part of the medial cholinergic pathway, which originates from the nucleus basalis of Meynert in the basal forebrain, whereas the fornix connects the hippocampus and mammillary body (14). Therefore, these two structures are important with respect to memory function (14). In the past, due to their long, thin shape and location deep within the brain, assessment of these structures has been difficult. Diffusion tensor tractography (DTT), derived from DTI, now allows 3-dimensional visualization of the cingulum and fornix (15, 16).

The current study used follow-up DTT to examine a patient with degeneration of the cingulum and fornix following TBI.

CASE REPORT

One patient and 6 right-handed sex-matched control subjects (6 males; mean age 21.5 years, age range 19–24 years) with no history of neurological disease participated in this study. Prior to commencement of the study, all subjects provided signed, informed consent; and our institutional review board approved the study protocol.

An 18-year-old, right-handed male who had had a traffic accident underwent conservative management for diffuse axonal injury (DAI) and subarachnoid haemorrhage in the occipital area at the department of neurosurgery in a university hospital. The patient lost consciousness for 7 days from the time of onset. Brain MRI, including DTI, was performed at 3 months from onset. T1- and T2-weighted images showed an encephalomalactic lesion in the posterior portion of the corpus callosum (Fig. 1). The patient showed mild hemiparesis of the right upper and lower extremities; however, his weakness had recovered completely at 12 months from onset. He showed cognitive problems (3 months after onset: total intelligence quotient (IQ) on the Wechsler adult intelligence scale: 75, total score on the Memory Assessment Scale: 95 (37^{th} percentile). However, while his total IQ had improved to 105, his memory impairment had been aggravated (total score on Memory Assessment Scale: 81 (10^{th} percentile) at 14 months from onset (17, 18).

DTIs were acquired twice (3 and 19 months after onset) using a sensitivity encoding head coil on a 1.5-T Philips

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Gyroscan Intera (Philips, Ltd, Best, the Netherlands) with single-shot echo-planar imaging. Sixty contiguous slices (matrix = 128 × 128, field of view = 221 × 221 mm^2, repetition time/echo time = 10726/76 ms, b = 1000 mm^2s^{-1}, NEX = 1, thickness = 2.3 mm) were acquired for each of the 32 non-collinear diffusion-sensitizing gradients. Eddy current image distortions and motion artefacts were removed using affine multi-scale 2-dimensional registration, which was performed using the FMRIB Software Library (FSL, http://www.fmrib.ox.ac.uk/fsl). Fibre tracking was identified using fibres passing through two regions of interest (ROIs) on the colour map on DTI-studio software (CMRM, Johns Hopkins Medical Institute, Baltimore, MD, USA). The seed ROI was located on the blue portion of the anterior ponto-medullary junction on the axial slice for the corticospinal tract (CST), the junction between the column and body of the fornix on the axial slice for the fornix, and the green portion of the anterior cingulum areas on the coronal slice level as the genu of the corpus callosum for the cingulum. The target ROI was defined as the blue portion of the anterior pons on the axial slice for the CST, the junction between the body and crus of the fornix on the coronal slice for the fornix, and the green portion of the posterior cingulum areas on the coronal slice level as the splenium of the corpus callosum for the cingulum (15, 16, 19, 20). Fibre tracking was initiated at the centre of a seed voxel with a fractional anisotropy (FA) > 0.2 for the CST and FA > 0.15 for the fornix and cingulum that ended at a voxel with a fibre assignment of FA < 0.2 for the CST and < 0.15 for the fornix and cingulum. Limits of angular deviation were defined the path trajectory of < 60 degrees.

On the first DTTs, integrities of both CSTs, right cingulum, and left fornix were preserved; however, compared with controls, there were interruptions in both ends of the left cingulum and right fornical crus. On the second DTTs, both the cingulum and fornix showed severe degeneration, although integrities of both CST was well preserved (Fig. 1B).

DISCUSSION

In the current study, we observed changes in DTT along with clinical changes in a patient with TBI. At the time of the first DTI scan, this patient showed cognitive impairment and mild hemiparesis. Total intelligence and hemiparesis had recovered well until the time of the second DTI scan; however, his memory function had been aggravated. These clinical changes are well correlated with DTT changes. Although the integrities of both CSTs were preserved on the first and second DTTs, both the cingulum and fornix showed severe degeneration on the second DTT. Several studies reported that intra- and inter-rater reliability of the diffusion tensor tractography were high (21–23). In particular, Malykhin et al. (23) demonstrated that the DTI protocol provided a reliable method to analyse limbic and paralimbic white matter tracts relevant to psychiatric disorders (22). As for longitudinal reliability, Danielian et al. (24) reported that fibre tracking provides a reliable tool for the longitudinal evaluation of white matter diffusion properties. Considering that the patient satisfied the diagnostic criteria of DAI: (*i*) a mechanism of injury associated with significant acceleration/deceleration force; (*ii*) any loss of consciousness at the time of injury without a lucid interval; and (*iii*) brain T1- and T2-weighted MRI showing no specific lesion, except for the corpus callosum lesion (25), it appears that DAI in this patient occurred at the onset of the traffic accident. Because the right fornix and left cingulum showed disruption on the first DTT, degeneration of the cingulum and fornix was already in progress at the time of the first DTT scan. Subsequent degeneration appeared to result in disruption of both the cingulum and fornix on the second DTT.

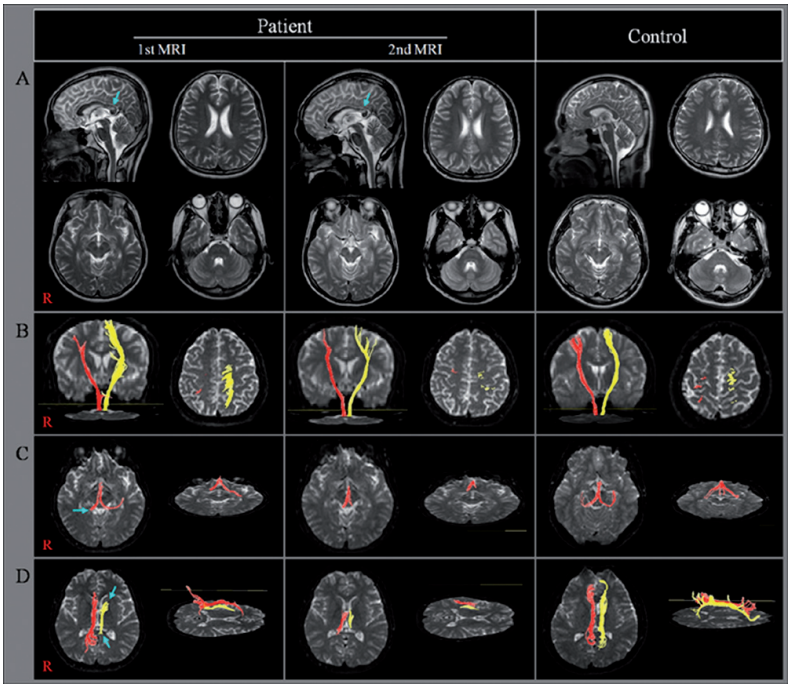

Fig. 1. T2-weighted magnetic resonance images taken 3 months after onset showed an encephalomalactic lesion (*arrow*) in the posterior portion of the corpus callosum (A). The integrity of (B) both corticospinal tracts (CST), (C) left fornix, and (D) right cingulum were preserved on the first diffusion tensor tractography (DTT); however, compared with controls, there were interruptions in both ends of the left cingulum (*arrow*) and right fornical crus (*arrow*). On the second DTTs, both the cingulum and fornix showed severe degeneration, although the integrities of both CST were well preserved.

The reason that the cingulum and fornix showed degeneration while the CST showed no degeneration appeared to be associated with frequent injury to the area of DAI. It is well-known that DAI involves 3 common areas: the corpus callosum (particularly the posterior portion), the brainstem (particularly the dorsolateral region and the cerebral peduncle), and the lobar white matter (25–27). Because the cingulum and fornix are located adjacent to the corpus callosum, these areas appeared to be more vulnerable than the CSTs.

Some studies have reported on DTI changes in neuronal degeneration following TBI (11–13). In 2008, Sidaros et al. scanned DTIs twice, at 8 weeks and 12 months following TBI, and discovered that patients with DTI parameters in the internal capsule and in the centrum semiovale showed improvement, with a favourable outcome; by contrast, patients who did not show improvement in the cerebral peduncle and corpus callosum had an unfavourable outcome (13). Subsequently, Bendlin et al. investigated DTI changes (between 2 and 12.7 months) in patients with TBI. They found that DTI parameters were aggravated, although neuropsychological function was improved (11). Kumar et al. recently reported on DTI changes between 5–14 days and 6 months following DAI (12). They discovered that even patients who showed no abnormality on conventional MRI and DTI at the first DTI had aggravated DTI findings, which suggested demyelination/gliosis, on the subsequent DTI. The current study described a patient who showed degeneration of the cingulum and fornix and aggravated memory function on follow-up evaluation after TBI. We reported on the visual finding of DTTs without DTI parameters because the degeneration was visually definite. We conclude that patients with memory impairment following TBI should be evaluated using DTI. In addition, follow-up DTI appears to be necessary in patients who showed sustained memory impairment. However, this study is limited to a case report. Further complementary studies involving larger case numbers are warranted.

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