Clinical Case Report

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Neural reorganization between injured cingula and the brainstem cholinergic nuclei in a patient with cerebral concussion

A case report

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Abstract

Rationale: We report on a patient who showed neural reorganization between injured cingula and the brainstem cholinergic nuclei following cerebral concussion.

Patient Concerns: The main concern of the patient is memory impairment.

Diagnoses: Cerebral concussion.

Outcomes: When she visited our hospital at 2 years after onset, cognitive function was evaluated using 2 scales; the Wechsler Intelligence Scale, and the Seoul neuropsychological screening battery: total IQ 97, verbal immediate recall 5.70 percentile, visual immediate recall 30.75 percentile, verbal delayed recall 3.13 percentile, visual delayed recall 11.00 percentile, verbal recognition <0.01 percentile, and visual recognition 13.70 percentile. Conventional brain magnetic resonance imaging did not show any abnormality. On 2-year diffusion tensor tractography for the cingulum, both anterior cingula were discontinued over the genu of the corpus callosum. One neural fiber bundle originating from the middle portion of the left cingulum descended through the left subcortical white matter, and connected to the left pedunculopontine nucleus (Ch 5) in the midbrain and the left laterodorsal tegmental nucleus (Ch 6) in the upper pons.

Lessons: Reorganization of cholinergic innervations between cholinergic nuclei in the basal forebrain and brainstem following injury of the anterior cingulum was demonstrated in a patient with cerebral concussion.

Abbreviations: DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, SNSB = Seoul neuropsychological screening battery, TBI = traumatic brain injury, WAIS = Wechsler Adult Intelligence Scale.

Keywords: cerebral concussion, cingulum, diffusion tensor imaging, head trauma, traumatic axonal injury

1. Introduction

Human brain has several cholinergic nuclei: the basal forebrain and septal region; the medial septal nucleus (Ch 1), the vertical nucleus of the diagonal band (Ch 2), the horizontal limb of the diagonal band (Ch 3), the nucleus basalis of Meynert (Ch 4), and the brainstem; the pedunculopontine nucleus (Ch 5) and the laterodorsal tegmental nucleus (Ch 6).[1–3]

Introduction of diffusion tensor tractography (DTT) is derived from diffusion tensor imaging (DTI) allows 3-dimensional visualization and estimation of the cingulum which contains the medial cholinergic pathway, which originates from Ch 4 and the cholinergic nuclei in the septal region.[4,5] Therefore, using DTT for the cingulum, reorganization of cholinergic innervation between cholinergic nuclei has been reported in various brain pathologies including stroke and traumatic brain injury (TBI, moderate and severe).[6,9] However, very little is known about cerebral concussion.

In the present study, we reported on a patient who showed neural reorganization between injured cingula and the brainstem cholinergic nuclei following cerebral concussion.

2. Case report

A 41-year-old female patient suffered head trauma resulting from a car accident and she had no history of head trauma, neurologic or psychiatric disease. Her family did not have neurologic or psychiatric disease history. She graduated from a junior college 19 years ago and had worked as a hairdresser. While she was riding in the passenger seat in a running car, a car collided with her car from the right side. Her head hit the driver's seat, resulting in a whiplash injury and concussion. The patient mentioned that she lost consciousness for approximately 5 min and experienced

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post-traumatic amnesia for approximately 10 min. The patient's Glasgow Coma Scale score was 15. She felt memory impairment after the head trauma. Although she had visited a few hospitals, her brain function was considered normal because her brain computed tomography and conventional magnetic resonance imaging (MRI) did not reveal any abnormality. However, she could not work as a hairdresser after the head trauma. When she visited our hospital at 2 years after onset, she complained of memory impairment. Her cognitive function was evaluated using 2 scales; the Wechsler Adult Intelligence Scale (WAIS) and the Seoul neuropsychological screening battery (SNSB). The WAIS is the most standardized intelligence test.[10] Full Scale Intelligence

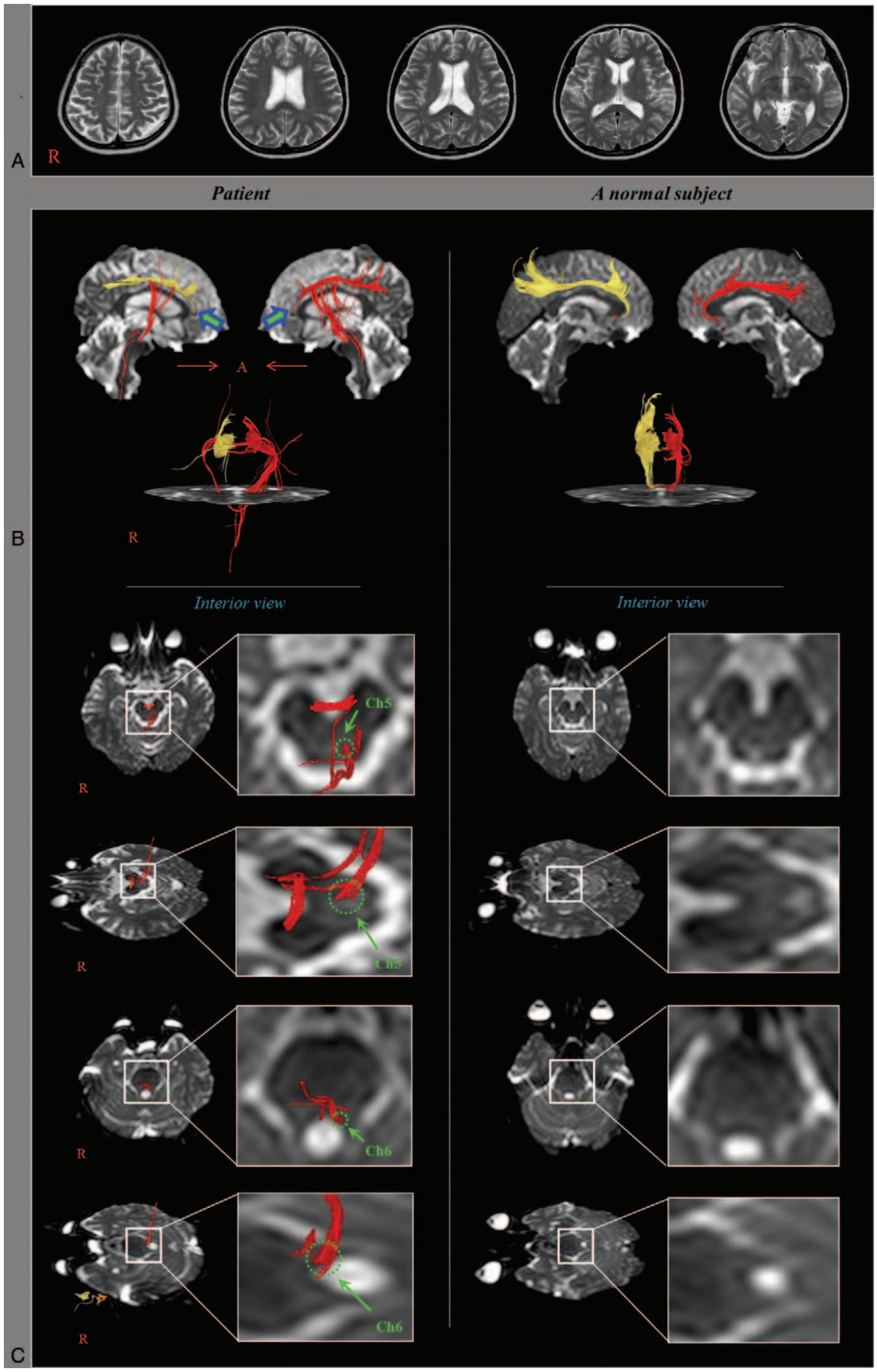

Figure 1. (A) Brain magnetic resonance images at 2 years after onset show no abnormality. (B) Diffusion tensor tractography (DTT) of the cingula of the patient and a normal subject (43-year-old female). On 2-year DTT, both anterior cingula are discontinued over the genu of the corpus callosum (arrows). (C) One neural fiber bundle originating from the middle portion of the left cingulum descends through the left subcortical white matter, and connects to the left pedunculopontine nucleus (Ch 5) in the midbrain and the left laterodorsal tegmental nucleus (Ch 6) in the upper pons. The other neural fiber bundles originated from the middle portion of the left cingulum connects to the right cingulum, descends through the right subcortical white matter, and then interconnects with the left neural fiber bundles at the midbrain.

Index (IQ) derived from verbal and performance intelligence indices was obtained: total IQ 97.[10] The SNSB is a comprehensive neuropsychological test.[11] She showed abnormality in retrieval of the verbal memory, and borderline in the verbal short- and long-term memories (verbal immediate recall 5.70 percentile, visual immediate recall 30.75 percentile, verbal delayed recall 3.13 percentile, visual delayed recall 11.00 percentile, verbal recognition <0.01 percentile, and visual recognition 13.70 percentile). She also revealed mild dysarthria, hypersomnia (Epworth sleepiness scale: 22 out of 24, cut-off value: 10 points), fatigue (fatigue severity scale: 62 out of 63, cut-off value: 36), and pain in all 4 extremities and trunk (visual analog scale: 7 out of 10).[12–15] Conventional brain MRI did not show any abnormality (Fig. 1A). The patient provided signed informed consent, and the study protocol was approved by our Institutional Review Board.

At 2 years after onset, DTI was performed using a 6-channel head coil on a 1.5 T Philips Gyroscan Intera (Philips Inc, Amsterdam, Nederland). For each of the 32 noncollinear diffusion-sensitizing gradients, we acquired 67 contiguous slices parallel to the anterior commissure–posterior commissure line. Imaging parameters used were as follows: acquisition matrix = 96×96, reconstructed to matrix = 128×128 matrix, field of view (c) = 221×221 mm^2, Repetition time = 10,726 ms, echo time = 76 ms, Sensitivity encoding factor = 2, Echo planar imaging factor = 49 and b = 1000 s/mm^2, Number of excitations = 1, and a slice thickness of 2.3 mm. Eddy current image distortions and motion artifacts were corrected using affine multiscale 2-dimensional registration, performed using the FMRIB Software Library (FSL, http://www.fmrib.ox. ac.uk/fsl, Oxford). DTI-Studio software (CMRM, Johns Hopkins Medical Institute, Baltimore) was used for evaluation of the cingulum. To analyze the cingulum, the seed and target region of interest were placed on the middle and posterior portion of the cingulum on the color map of coronal images, respectively (termination criteria: fractional anisotropy < 0.15, angle change $> 27°$).[8]

On 2-year DTT for the cingulum, both anterior cingula were discontinued over the genu of the corpus callosum. One neural fiber bundle originating from the middle portion of the left cingulum descended through the left subcortical white matter, and connected to the left Ch 5 in the midbrain and the left Ch 6 in the upper pons (Fig. 1B).[6,7,16] The other neural fiber bundle originating from the middle portion of the left cingulum connected to the right cingulum and descended through the right subcortical white matter, then interconnected with the left neural fiber bundles at the midbrain.

3. Discussion

In this patient, discontinuation of both anterior cingula appeared to be ascribed to a traumatic axonal injury, because conventional MRI did not show an abnormality.[17–21] We observed abnormal neural connections between the anteriorly discontinued cingula and the left Ch 5 and 6. The cingulum receives cholinergic innervation from 3 cholinergic nuclei in the basal forebrain (the medial septal nucleus [Ch 1], the vertical nucleus of the diagonal band [Ch 2], and the nucleus basalis of Meynert [Ch 4]).[6,7,16] Therefore, the unusual neural connection between both anteriorly injured cingula and the left Ch 5 and 6 apparently resulted from a compensatory phenomenon to obtain cholinergic innervation from the cholinergic nuclei in the brainstem instead of from the cholinergic nuclei in the basal forebrain. [6,7,16] This finding suggests a reorganization of cholinergic innervations between cholinergic nuclei in the basal forebrain and brainstem following injury of the anterior cingulum.

Regarding TBI, a few studies have demonstrated on the neural reorganization of cholinergic nuclei following injury of the cingulum.[6–8] In 2012, Yeo reported on a patient who showed a neural connection between an injured cingulum and the ipsilateral Ch 5 via thalamus following traumatic subarachnoid hemorrhage.[6] Subsequently, Yoo et al[7] found that the patients with neural connection between injured cingulum and brainstem cholinergic nuclei had better short-term memory than the patients without neural connection among 20 chronic patients with moderate and severe TBI who showed discontinuations of both anterior cingula from the basal forebrain. In 2015, Lee and Jang[8] reported on a pediatric patient who revealed appearance of neural connections between an injured cingulum, and Ch 6 and 8 concurrent recovery of short-term memory impairment following traumatic IVH and diffuse axonal injury. Therefore, to the best of our knowledge, this is the first case study to demonstrate reorganization of cholinergic innervations between cholinergic nuclei in the basal forebrain and brainstem in patient with cerebral concussion. However, although DTT is a powerful anatomic imaging tool, it can produce both false positive and negative results throughout the white matter of the brain due to crossing fiber or partial volume effect.[22]

In conclusion, reorganization of cholinergic innervations between cholinergic nuclei in the basal forebrain and brainstem following injury of the anterior cingulum was demonstrated in a patient with cerebral concussion. However, this study is limited because it is a case report, and lack of DTT at early stage of concussion. Therefore, further studies involving large number of patients and including follow-up DTT data with cerebral concussion should be encouraged.

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