Clinical Case Report

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Severe disinhibition due to injuries of neural tracts related to emotion circuit in a patient with traumatic brain injury

A case report

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Abstract

Rationale: Approximately 30% of patients with traumatic brain injury (TBI) develop disinhibition, a condition that involves several brain structures, including the amygdala, orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC). Using diffusion tensor tractography (DTT), we report on a patient with severe disinhibition and injuries of the amygdala, OFC, and ACC following TBI.

Patient concerns: A 27-year-old male patient suffered an in-car accident.

Diagnoses: Since the onset of the TBI, the patient showed severe disinhibition including violence, as follows: 1) he sometimes attacked therapists and nurses with no provocation, 2) while he was laying on a bed, he shouted and kicked the bed when asked questions, and 3) during therapy with a difficult task, he behaved violently to a therapist. The subscale of disinhibition in Neuropsychiatric Inventory scored three points for severity and for distress.

Interventions: N/A.

Outcomes: On 10-month DTT, the connectivity of amygdala to the prefrontal cortex including the medial prefrontal cortex and OFC had decreased in both hemispheres. In the prefronto-thalamic tracts, the orbitofronto-thalamic tractshad narrowed (the right hemisphere), and were non-reconstructed (the left hemisphere). Discontinuations of both anterior cingulums were observed in both hemispheres.

Lessons: Using DTT, concurrent injuries of the amygdala, OFC, and ACC were demonstrated in a patient with severe disinhibition following TBI. Our result suggests the need to assess these neural structures in patients with disinhibition after brain injury.

Abbreviations: ACC = anterior cingulate cortex, BA = Brodmann area, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, OFC = orbitofrontal cortex, PFC = prefrontal cortex, ROI = region of interest, TBI = traumatic brain injury.

Keywords: amygdala, anterior cingulate cortex, diffusion tensor tractography, disinhibition, orbitofrontal cortex, traumatic brain injury, violence

1. Introduction

Disinhibition is an inability to suppress behavior or verbalization. It is a common sequela of traumatic brain injury (TBI) and approximately 30% of patients with TBI develop disinhibition.[1–5] It is usually results in caregiver distress, poor family functioning, and legal problems.[2,3,5] Disinhibition involves several brain structures, including the amygdala, orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC).[6–8] Several studies have reported on injuries of these brain structures in patients with disinhibition using neuroimaging and electrophysiological techniques.[7,9–14]

Recently developed diffusion tensor tractography (DTT), derived from diffusion tensor imaging (DTI), enables evaluation of the brain structures in the live human brain.[15] The neural connectivity between amygdala and thalamus, the OFC, and 3-dimensional reconstruction of the cingulum were reconstructed to evaluate patients with neurobehavioral problems, including depression, demotivation, and memory deficit after brain injury.[16–19] However, no study of concurrent injuries of the amygdala, OFC, and ACC in patients with disinhibition following TBI has been reported.

In this study, using DTT, we demonstrated injuries of the amygdala, OFC, and ACC in a patient with severe disinhibition following TBI.

2. Case report

A 27-year-old male patient suffered an in-car accident: while sitting in the seat next to the driver of a vehicle; his head struck the front window when the car hit a guardrail. The patient lost consciousness for approximately 30 days and experienced

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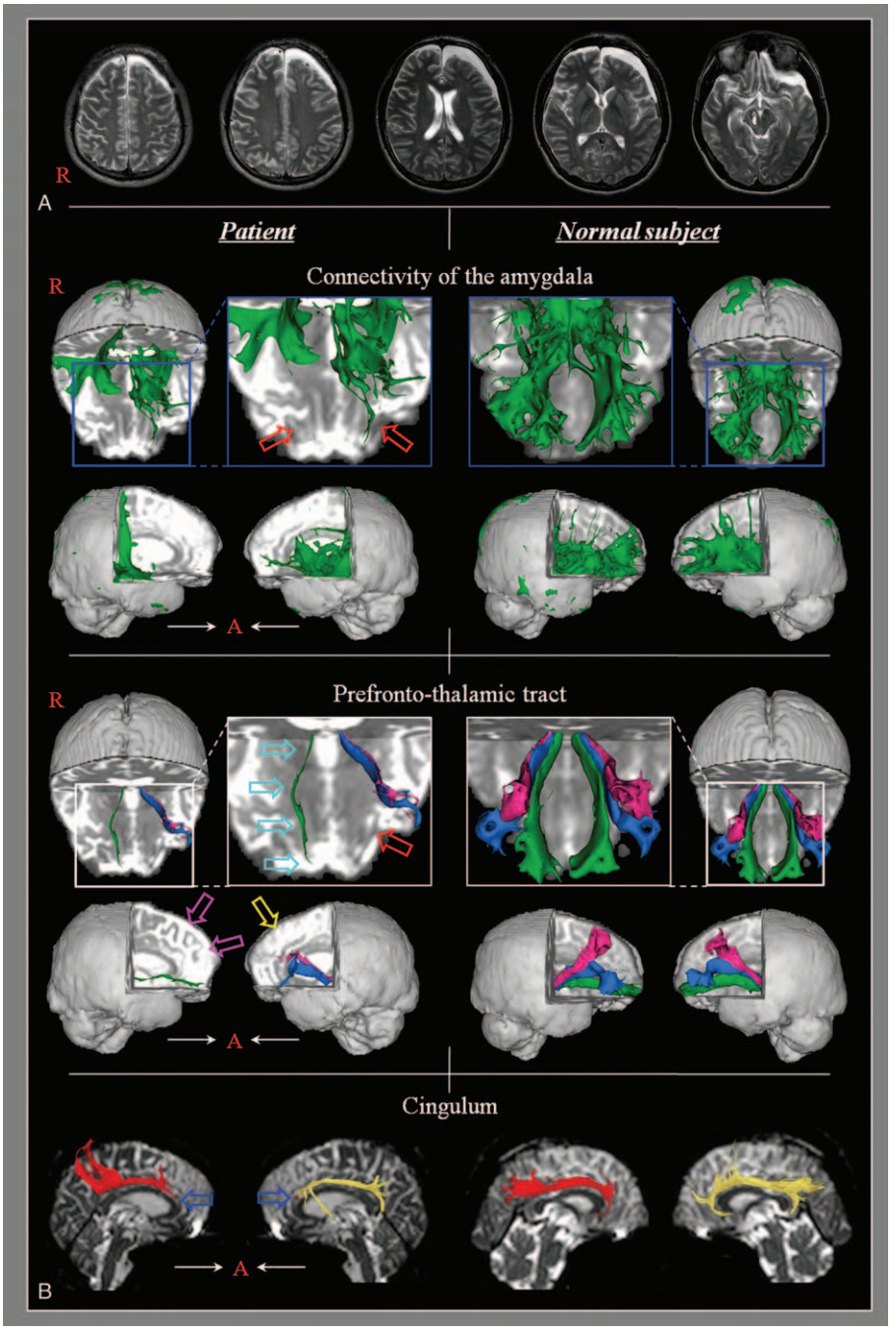

Figure 1. (A) Brain MR images subdural hemorrhage on right temporo-parieto-occipital lobe and multiple hemorrhage in the right midbrain and both frontal and temporal lobes at 10 months after onset are observed. (B) On 10-month diffusion tensor tractography, the neural connectivity of amygdala to the prefrontal cortex including orbitofrontal cortex is decreased in both hemispheres (red arrows). Regarding the prefronto-thalamic tracts, orbitofrontothalamic tracts present narrowing (right side, sky blue arrows) and nonreconstruction (left side, red arrow). In addition, nonreconstruction of the ventrolateral and dorsolateral prefronto-thalamic tracts in the right hemisphere (purple arrows) and narrowing of the dorsolateral prefronto-thalamic tract in the left hemisphere (yellow arrow) are revealed. In the anterior cingulate cortex, discontinuations of both anterior cingulums are observed in both hemispheres (blue arrows).

post-traumatic amnesia continuously from the time of the accident. His Glasgow Coma Scale score was 3. Brain computer tomography at time of injury showed a subdural hemorrhage on the right temporo-parieto-occipital lobe, and multiple hemorrhages in the right midbrain and both frontal and temporal lobes. Since the TBI, the patient showed severe disinhibition including violence: he sometimes attacked therapists and nurses with no provocation, while he was laying on a bed, he shouted and kicked the bed when asked questions, and during therapy with a difficult task, he behaved violently to a therapist. The subscale of disinhibition in Neuropsychiatric Inventory was 3 points for severity (full score: 3, a higher score indicates a worse state) and for distress (full score: 5, a higher score indicates a worse state).[20] The patient's mother provided signed, informed consent, and the Yeungnam University hospital institutional review board approved the study protocol.

DTI data were acquired at 10 months after the TBI using a 6 channel head coil on a 1.5 T (Philips Ltd., Best, the Netherlands) with 32 gradients. Imaging parameters were as follows: acquisition matrix = 96 × 96; reconstructed to matrix = 192 × 192; field of view = 240 × 240 mm^2; repetition time = 10,398 ms; echo time = 72 ms; echo-planar imaging factor = 59; b = 1000 s/mm^2; and a slice thickness of 2.5 mm. Eddy current correction and fiber tracking were performed using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain Diffusion Software with default option. For the neural connectivity of the amygdala, the known anatomical location of the amygdala on the axial image was used as a seed region of interest (ROI).[17] Regarding the reconstruction of prefronto-thalamic tracts,[18] a seed ROI was placed on the known anatomical location of the mediodorsal nucleus of the thalamus on the coronal image and each target ROI was as follows: OFC as Brodmann areas (BAs) 11 and 13 on the axial image, ventrolateral prefrontal cortex (PFC) as BAs 44, 45, and 47 on the coronal image, and dorsolateral PFC as BAs 8, 9, and 46 on the coronal image. For evaluation of the ACC, we reconstructed the cingulum using 2 ROIs (middle and posterior green portions of the cingulum on the coronal images) by a Philips Extended magnetic resonance Work Space 2.6.3 (Philips Healthcare, Best, The Netherlands).[16]

On 10-month DTT, the neural connectivity of amygdala to the PFC including the medial PFC and OFC was decreased in both hemispheres (Fig. 1B). In the prefronto-thalamic tracts, the orbitofrontothalamic tracts were narrowed (the right hemisphere) and nonreconstructed (the left hemisphere). In addition, the nonreconstruction of the ventrolateral and dorsolateral prefronto-thalamic tracts in right hemisphere and the narrowing of the dorsolateral prefronto-thalamic tract in left hemisphere were revealed. In the ACC, discontinuations of both anterior cingulums were observed in both hemispheres.

3. Discussion

In this study, the patient showed severe disinhibition, including violence, after TBI. We evaluated the connectivity of the amygdala, prefronto-thalamic tract for the OFC, and cingulum for the ACC that are associated with disinhibition using DTT. The results can be summarized as follows: injuries of the connectivity of the amygdala to OFC and the prefronto-thalamic tracts, particularly the OFC, were observed in both hemispheres, both anterior cingulums related to the ACC were injured. It appears that the severe disinhibition including the violence in this patient was as least in part ascribed to injuries of the amygdala, OFC, and ACC.

Several studies have reported that injuries of the amygdala, OFC, and ACC are involved in disinhibition in patients with brain injury using neuroimaging and electrophysiological studies.[7,9–14] Yudofsky et al[12] described damage of the diffuse bilateral PFC including the OFC in a patient with TBI led to violent behavior. In 1996, Grafman et al[14] investigated 279 veterans with aggression and violence after TBI during the Vietnam War, and found injury of the ventromedial PFC including the OFC. In 1999, Siever et al[21] reported that increased glucose metabolism in PFC and ACC were revealed in 6 impulsive-aggressive patients using positron emission tomography (PET). Furthermore, Blair and Cipolotti[11] reported injury of the bilateral OFC and left amygdala in a patient with aggressive, violent behavior after TBI. During the same year, Davidson et al[8] review study suggested that injuries of the OFC, the amygdala connected to the OFC, and the ACC were associated with disinhibition including violence. Regarding the normal study, Blair et al[9] reported the OFC and ACC were increasingly activated by increasing intensity of angry facial expressions in 13 healthy study participants using PET. In addition, other 2 neuroimaging studies demonstrated that the OFC and ACC are associated with anger emotion.[22,23] Our results were coincided with previous studies. As far as we are aware, using DTT, this is the 1st study to demonstrate concurrent injuries of the amygdala, OFC, and ACC in a patient with disinhibition following TBI.

In conclusion, using DTT, concurrent injuries of the amygdala, OFC, and ACC were demonstrated in a patient with severe disinhibition following TBI. Our result suggests the necessity of assessment of these neural structures in patients with disinhibition after brain injury. However, several limitations of this study should be considered. First, because it is a single case report, this study is limited. Second, because of severe disinhibition, we could not perform neuropsychological assessment such as executive functions and social cognition which are necessary after TBI.[24] Third, use of DTT could lead to both false positive and negative results because of multiple fiber orientations in a voxel.[25] Therefore, we suggest that further studies including large numbers of patients, various neuropsychological assessment, and overcoming limitations of DTT should be encouraged.

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