Recovery of gait and injured corticoreticulospinal tracts in a patient with diffuse axonal injury

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Diffuse axonal injury (DAI) is defined as the presence of microscopic axonal damage in the white matter of the brain produced by mechanical forces and is characterized histologically by widespread damage to axons (Maxwell et al., 1997). Diffusion tensor imaging (DTI) allows evaluation of the integrity of the white matter of brain to be determined by virtue of its ability to image water diffusion characteristics (Basser et al., 1994). Therefore, DTI has a unique advantage to detect DAI and many studies using DTI have investigated DAI (Wang et al., 2008). Furthermore, previous studies using DTI have demonstrated the recovery of DAI in the corticospinal tract, cingulum, and white matter (Kim et al., 2009; Edlow et al., 2016; Jang and Seo, 2016). There is no study on the recovery of DAI in the corticoreticulospinal tract (CRT) which is involved in gait function by innervating axial and leg muscles (Matsuyama et al., 2004).

In this study, we reported a patient with DAI who showed the recovery of injured CRT with gait recovery, which was demonstrated on serial diffusion tensor tractographies (DTTs) which are derived from DTI data.

A 23-year-old male with no history of illness suffered from head trauma in a pedestrian-car crash: he was struck by a truck. Following the head trauma he lost consciousness, remained unconscious for approximately 2 months, and suffered post-traumatic amnesia for about 3 months. His Glasgow Coma Scale score was 6 and he was diagnosed with DAI. After 3 months, he presented quadriparesis and could not even stand (Manual muscle test (Yang and Kim, 2015): hip flexor; 0/3, knee extensor; 1/3 and ankle dorsiflexor; 0/3). He underwent rehabilitative therapy including neurotropic drugs (methylphenidate, pramipexole, ropinirole, and amantadine), movement therapy at sections of the physical and occupational therapy: motor strengthening of the trunk and both legs, and exercises for trunk stability and control, static and dynamic balance training on sitting and standing positions, and neuromuscular electrical stimulation of the right knee extensor and ankle dorsiflexor muscles. The leg weakness slowly recovered over 15 months, until 18 months after the initial injury (Manual muscle test: hip flexor; 4/5, knee extensor; 4/5 and ankle dorsiflexor; 3/5). He was able to walk independently on an even floor at 18 months after trauma. This study was conducted retrospectively, and approval for the study was obtained from the Institutional Review Board of Yeungnam University Hospital (approval No. YUMC-2019-06-032) on June 28, 2019. The participants signed informed consent.

Diffusion tensor imaging data were acquired at three different time points (3, 10, and 18 months after trauma) using a sensitivity-encoding head coil on a 1.5-T Philips Gyroscan Intera (Hoffman-LaRoche Ltd, Best, the Netherlands). Imaging parameters were as follows: *b* value = 1000 s/mm^2, direction = 32, acquisition matrix = 96 × 96, reconstructed to matrix = 192 × 192, field of view = 240 × 240 mm^2, repetition time = 10,726 ms, echo time = 76 ms, parallel imaging reduction factor (SENSE factor) = 2, echo planar imaging factor = 49, number of excitations = 1, and slice thickness = 2.5 mm (acquired isotropic voxel size 2.5 × 2.5 × 2.5 mm^3). The fiber assignment continuous tracking algorithm was used for fiber tracking. For reconstruction of the CRT, fibers passing through two regions of interest on the color map were adopted: the first region of interest, the medullary reticular formation, and the second region of interest, the midbrain tegmentum. The termination criteria for fiber tracking were fractional anisotropy < 0.1, angle < 27° (Jang et al., 2018). Tract volumes of both CRTs of the patient were as follow: 3 months (right: 0, left: 279), 10 months (1442, 1739), and 18 months (1442, 1739) after trauma, and CRTs of age-sex matched normal subject are as follows (right: 2118, left: 2243).

The 3-month DTT showed severe narrowing of the left CRT, while the right CRT was not reconstructed. In contrast, the left CRT became thicker and the right CRT was discontinued at the subcortical white matter although it was reconstructed on 10-month DTT. Both CRTs became thicker on the 18-month DTT, although these revealed partial tearing at the subcortical white matter (**Figure 1**).

In this study, we observed the changes of the injured CRTs on DTT over 15 months in a patient with DAI. On the 3-month DTT, both CRTs showed severe injuries (right: discontinuation, left: severe narrowing) and these injured CRTs slowly recovered over 15 months. Both CRTs revealed mild injuries (partial tearing at the subcortical white matter) on 18-month DTT. In addition, tract volume of both CRTs increased with time. Among DTT parameters, tract volume is the sensitive parameter for the recovery of an injured neural tract because tract volume indicates the number of neural fibers in a neural tract (Assaf and Pasternak, 2008). These changes of the CRTs on serial DTTs appeared to coincide with changes of the gait function and leg weakness: although he could not even stand independently at 3 months after trauma, he could walk independently at 18 months. Therefore, we believe, the regaining of gait function in this patient was at least partly attributed to the recovery of injured CRTs (Jang and Lee, 2017; Jang et al., 2018).

In summary, using serial DTTs which is a non-invasive image technique, the recovery of injured CRTs was presented in a patient with DAI who revealed gait recovery. Our results suggest the usefulness of DTT to reveal the recovery of injured CRT in patients with gait disturbance. In addition, this study gives us an important message in the recovery of injured CRTs facilitated by the long-term rehabilitation. Since the introduction of reconstruction method of the CRT using DTT, several studies

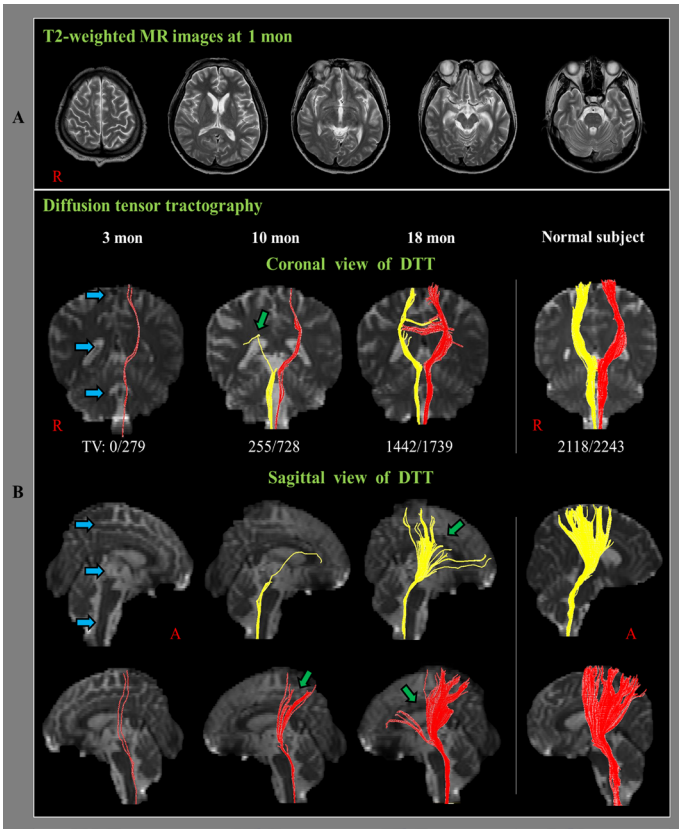

Figure 1 | **Diffusion tensor tractography for the CRT in a 23-year-old male patient with diffuse axonal injury.**
(A) T2-weighted MR images at 1 month shows no abnormality. (B) The DTT for the CRT. On 3-month DTT for the CRT, the left CRT shows severe narrowing whereas the right CRT is not reconstructed (blue arrows). In contrast, the left CRT becomes thicker with the partial tearing at the subcortical white matter (green arrow) and the right CRT is discontinued at the subcortical white matter (green arrow) although it is reconstructed on 10-month DTT. On 18-month DTT, both CRTs become thicker although these show partial tearing (green arrows) at the subcortical white matter compared with those of a normal subject (24-year-old male) who were recruited from the same university hospital. CRT: Corticoreticulospinal tract; DTT: diffusion tensor tractography; R: right; TV: tract volume.

reported the recovery monitoring of injured CRT in patients with stroke or traumatic subdural hematoma (Jang et al., 2015; Jang and Chang, 2016). As far as we know, this is the first study to demonstrate the recovery monitoring of injured CRT after DAI. However, because it is a case report, this study is limited.

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