

● IMAGING IN NEURAL REGENERATION

## Recovery of cerebellar peduncle injury in a patient with a cerebellar tumor: validation by diffusion tensor tractography

The cerebellum has a complex network and relates to various clinical functions including ataxia, gait disturbance, hearing and vision, cognition and affective control. Cerebellar peduncles are the structure connecting the cerebellum to the brain stem and the cerebrum. There exist three cerebellar peduncles. The superior cerebellar peduncle (SCP) involves vestibular sense and proprioception connecting to the thalamocortical pathway. The middle cerebellar peduncle (MCP) is the largest structure among the three cerebellar peduncles conveying impulses from the cerebral cortex to the cerebellum through corticopontocerebellar tract. The main function of the inferior cerebellar peduncle (ICP) is to integrate proprioceptive sensory input and postural maintenance connecting the cerebellum with the spinal cord. Therefore, these three cerebellar peduncles were known as useful indicators of neurological ataxia in several kinds of diseases including cerebellar tumor, cerebellar infarct and traumatic brain injury (Kashimura et al., 2003; Ying et al., 2009; Hong and Jang, 2010). However, because conventional MRI is limited in delineating structural abnormalities of cerebellar peduncle, accurate estimation of the cerebellar peduncle is difficult (Lee et al., 2013). Recent development of diffusion tensor imaging (DTI) has enabled detailed assessment of the state of neural tracts *in vivo* using its ability to visualize characteristics of water diffusion (Lee et al., 2013).

In the current study, we attempted to investigate the state of the cerebellar peduncle using diffusion tensor tractography (DTT) in a pediatric patient with suspected cerebellar peduncle injury due to a cerebellar tumor but recovered over time.

One 6-year-old female patient with a cerebellar tumor and eleven normal control subjects (five males; mean age: 6.18 years, range: 5–7 years) participated in this study. Control subjects were volunteers whose parents were also included in this study and they had no history of neurologic or psychological diseases. At initial evaluation, she was unable to sit up independently because of ataxia although she showed more than good grade of strength in both extremities. Her ataxia was severe, with a score of 0 separately on the Berg's Balance Scales (BBS) (Berg et al., 1992) and Functional Ambulation Category (FAC) (Cunha et al., 2002). T2-weighted MR images showed a brain tumor mainly involved in the left cerebellar hemisphere (**Figure 1A**) and the result of pathologic evaluation indicated astrocytoma.

MRI revealed a left cerebellar hemispheric cystic mass with a heterogeneous enhanced mural nodule in the gadolinium-enhanced T1-weighted image. Retrosigmoid suboccipital craniotomy was performed under general anesthesia. The tumor was located on the superficial petrosal surface of the cerebellum. The lateral portion of the tumor was grayish, solid, and easily distinguishable from the normal tissue. The cyst contained xanthochromic fluid. Radical resection of the enhanced tumor on the superficial petrosal surface of the cerebellum was performed easily without retraction of surrounding normal tissue. Histological examination of the specimens revealed typical pilocytic astrocytoma. At 3 weeks after surgery, mild improvement of ataxic symptoms was observed and the patient was able to maintain the position of sitting alone (FAC: 1; BBS: 0). However, her ataxic symptom sustained and she easily fell down without holding side bar intermittently. After 6 weeks,

she was able to maintain standing position, but she still showed difficulty in postural control. She could take a few steps from sustained ataxia, but she could not walk independently without continuing assistance (FAC: 2; BBS: 8). However, after 3 months, she showed considerable improvement and she was able to walk independently, with a score of 30 on the BBS and 5 on the FAC.

Initial DTI evaluation was performed at 3 weeks after surgery and the patient was followed up at 3 months after surgery. Preoperative DTI data were not obtained because both parents of the patient refused to perform additional DTI evaluation. DTI data were acquired using a 1.5-T Philips GyroscanIntera system (Philips, Ltd., Best, the Netherlands) equipped with a synergy-L sensitivity encoding (SENSE) head coil utilizing a single-shot, spin-echo planar imaging pulse sequence. For each of the 32 non-collinear and non-coplanar diffusion sensitizing gradients, we acquired 67 contiguous slices parallel to the anterior commissure-posterior commissure line. The imaging parameters were: matrix =  $128 \times 128$  matrix, field of view =  $221 \times 221$  mm<sup>2</sup>, TE = 76 ms, TR = 10,726 ms, SENSE factor = 2, EPI factor = 67,  $b = 600$  mm<sup>2</sup>/s, NEX = 1, and a slice thickness of 2.3 mm.

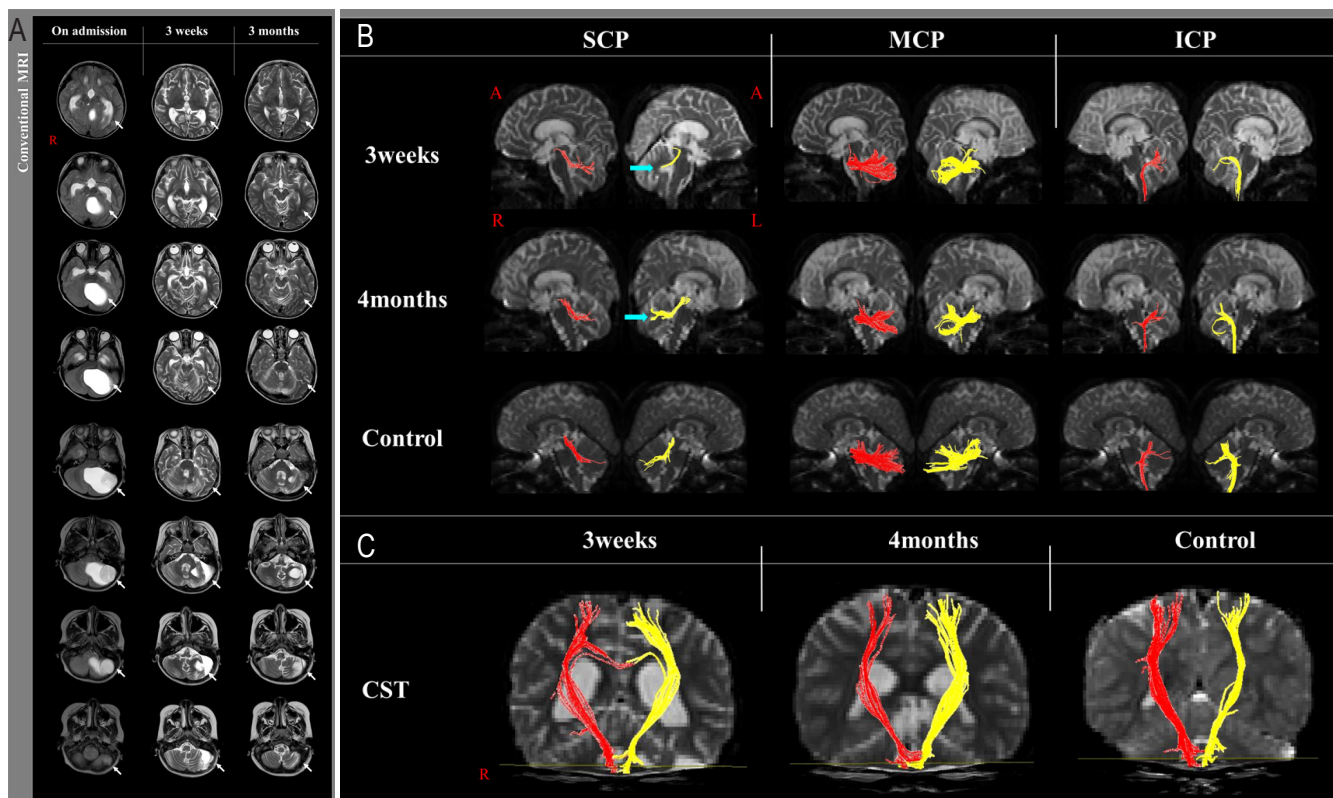
Preprocessing of DTI datasets was performed using the Oxford Centre for Functional Magnetic Resonance Imaging of Brain (FMRIB) Software Library (FSL; [www.fmrib.ox.ac.uk/fsl](http://www.fmrib.ox.ac.uk/fsl)) (Analysis Group, Oxford University, UK). Eddy current-induced image distortions and motion artifacts were removed using affine multi-scale two-dimensional registration. Using DTI-Studio software (CMRM, Johns Hopkins Medical Institute, Baltimore, MD, USA), three cerebellar peduncles (SCP, MCP, and ICP) and the corticospinal tract (CST) were evaluated (Jiang et al., 2006).

The cerebellar peduncles were determined by selection of fibers passing through both regions of interest (ROIs) on the color map (**Figure 2**). Fiber tracking was started at the center of the seed voxel with a fractional anisotropy (FA) > 0.2 and ended at the voxel having a fiber assignment < 0.2 and a tract turning angle < 60°. FA, apparent diffusion coefficient (ADC), tract volume and tract length were measured across entire bundle volumes in each peduncle.

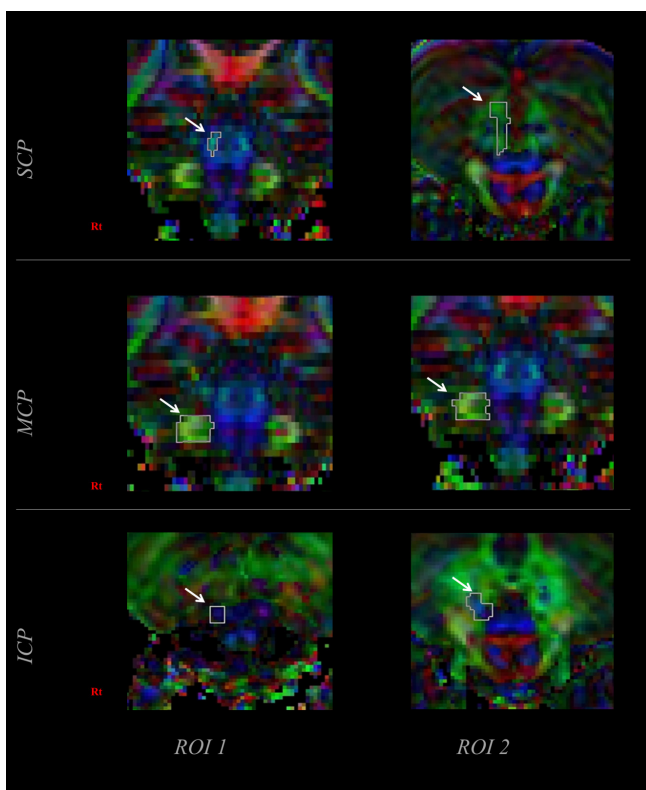
The results of DTI taken at 3 weeks after surgery revealed involvement of both SCPs and left MCP. Compared to the control subjects, the patient showed decreased FA, tract volume and tract length values to two standard deviations (2SD) below, and increased ADC values 2SD over, the control values in both SCPs. The left MCP showed decreased FA, tract volume and tract length values 2SD below the control values, however, ADC value was within 2SD of the controls. The FA and ADC values of both ICPs and right MCP showed no definite differences from those of controls (**Figure 3**). The results of DTI at 3 months after surgery showed increased FA values of both SCPs and left MCP. Those FA values were within 2SD of the controls, however, the tract volume and tract length of the left SCP showed decreased values to 2SD below the control values. ADC value of the left SCP was also increased to 2SD over the control values.

Initial DTT revealed that the posterior portion of the left SCP was shortened; however, interrupted SCP showed intact continuity at follow up. For the CST, there was no definite evidence of disruption (**Figure 1B, C**).

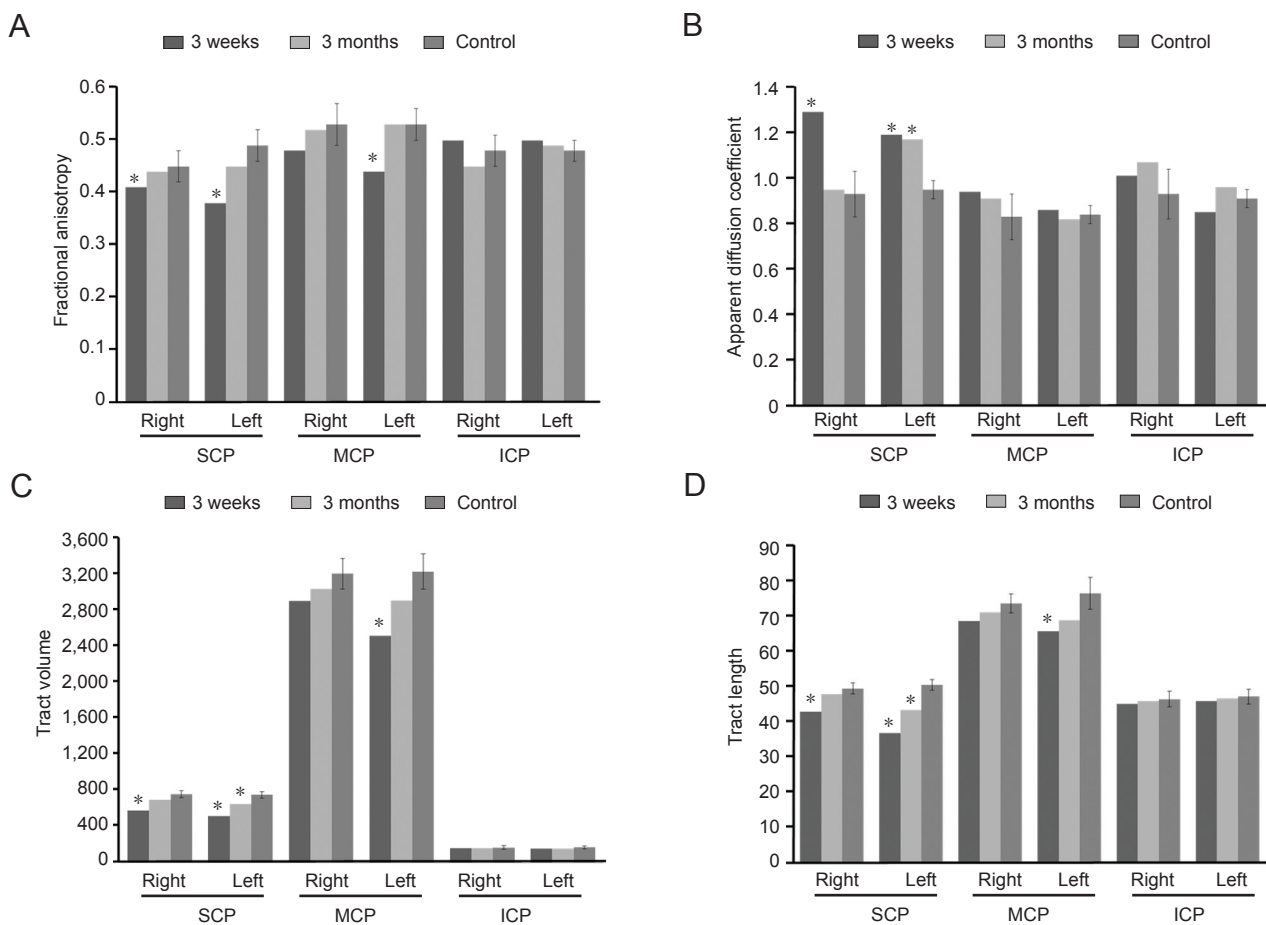
In this study, we included a patient with a cerebellar tumor who showed functional recovery and significant change of DTI parameters. For the following reasons, we believe that the functional recovery in this patient is related to the recovery of interrupted cerebellar peduncles. Initial results of both SCPs showed decreased FA, tract volume and tract length values and increased ADC values compared to the control group. The left MCP also showed decreased FA, tract volume and tract length values. Decreases in FA values are caused by the disruptions of directional structures, such as, myelin sheaths and axonal microfilaments. In contrast, increas-



**Figure 1** Conventional MRI and diffusion tensor tractography (DTT) images of a 6-year-old female patient with cerebellar tumor. (A) Initial T2-weighted images on admission show a solid and cystic mass involved mainly in the left cerebellum. After retrosigmoid suboccipital craniotomy, the size of the lesion was reduced. Follow up images taken at 3 weeks after surgery show focal encephalomalacia in the left cerebellum and subdural hygroma in the left posterior fossa. Follow up images taken at 3 months after surgery show much reduced encephalomalatic signal changes and subdural hygroma in the left posterior fossa. The lesion is indicated by arrows. (B) DTT (right: red; left: yellow) taken at 3 weeks after surgery shows a shortened posterior portion of the left superior cerebellar peduncle (blue arrow). However, 3-month results demonstrate intact integrity of the left superior cerebellar peduncle. (C) Corticospinal tracts (right: red; left: yellow) show preserved integrity in both patient and control groups.



**Figure 2** Location of regions of interest (ROI) in the superior cerebellar peduncle (SCP), middle cerebellar peduncle (MCP) and inferior cerebellar peduncle (ICP) on diffusion tensor imaging (DTI) images. For SCP, we placed ROI1 at the junction of SCP between the upper pons and cerebellum on the coronal view, and ROI2 at the area between the lateral wall of the fourth ventricle and ICP at the fourth ventricle level on the axial view. For MCP, ROI1 represented the ventral junctional area of the MCP between the pons and cerebellum, the caudal junctional area of the MCP on the coronal view. For ICP, ROI1 represented the restiform body and ROI2 represented the caudal part to the SCP on the axial view at the upper pons level. For CST, ROI1 was drawn in the blue portion of the anterior pons on two-dimensional fractional anisotropy color maps, and ROI2 was drawn in the midportion of the cerebral peduncle (Lee et al., 2013). Arrow indicates ROI.



**Figure 3** The diffusion parameters determined by diffusion tensor imaging (DTI) in a patient with cerebellar tumor.

Fractional anisotropy (FA), tract volume and tract length of both superior cerebellar peduncle (SCP) and the left middle cerebellar peduncle (MCP) at 3 weeks after surgery, showing values to 2 standard deviations (SD) below those of control subjects. Apparent diffusion coefficient (ADC) at 3 weeks after surgery shows values 2 standard deviations (SD) over that of control subjects. The only result at 3 months after surgery which shows beyond 2 SD of the control values is the left SCP. The left SCP shows the FA, tract volume and tract length values 2SD over those of the control subjects. \* Indicates values 2 standard deviations below or over the values of the control subjects.

es in ADC values are more likely to be caused by hindered water motion due to axonal damage. Using these characteristics, DTI can be used to distinguish a primary lesion from associated Wallerian degeneration. That is, decreased FA with increased ADC indicates a primary lesion, and decreased FA with preserved ADC indicates the presence in the degenerated tract (Jang et al., 2006). The decreased FA and increased ADC values of cerebellar peduncles in this study signified that those were primary lesions rather than the degenerated tract. This result was more prominent in the left SCP than in other cerebellar peduncles, although it was possible that the right SCP and the left MCP were also involved in the tumor. DTT showed similar result that the left SCP was disrupted on initial DTT and recovered on follow up image. In addition, even at 3 months, tract volume, tract length and ADC values of the left SCP were still beyond the range of control values. The consistent results of DTI and DTT suggest that the left SCP was mainly affected and recovered; however, the right SCP and the left MCP were invaded by the tumor, but not disrupted. Moreover, it cannot exclude the possible effect of edema shown in the conventional MRI of the right MCP or both ICPs as well as the right SCPs and the left MCP.

The clinical course apparently corresponded to the radiologic results for cerebellar peduncles. The patient could maintain a sitting position with intermittent holding side bar at 3 weeks after surgery, and she could maintain a standing position and take a few steps with assistance at 6 weeks after surgery. However, she

had difficulty in postural control for a long time period, and she could not walk without continuing assistance until 3 months after surgery. In the previous studies, SCP is known to be important in proprioceptive weighting for postural control. Therefore, disruption of SCP can cause dysfunction of postural control or gait, corresponding to our patient (Hong et al., 2009; Pijnenburg et al., 2014). This gradual recovery of ataxic symptoms and equivalent change of DTI suggest that functional deterioration and ataxia in this patient were related to cerebellar peduncle lesion. Besides, DTT showed no definite evidence of CST injury and the patient showed a good grade of strength, even on admission.

Several previous studies have reported on the usefulness of DTI for evaluation of cerebellar peduncle lesion in neurodegenerative disease (Ying et al., 2009), diffuse axonal injury (Hong et al., 2009), cerebral infarct (Hong and Jang, 2010), and Dandy-Walker malformation (Lee et al., 2013). DTI is an additional helpful tool for assessment of patients with suspected cerebellar peduncle injury due to a cerebellar tumor. To the best of our knowledge, there has been no study reported on use of DTI in pediatric patients with cerebellar peduncle injury due to a cerebellar tumor. However, this study is limited because it is a case report which cannot demonstrate statistical significance between radiographic and clinical data. Another limitation is lack of preoperative DTI data. It cannot exclude the possible effect of the surgery as well as tumor itself. Further complementary studies involving larger case numbers are needed.



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## References

- Berg KO, Wood-Dauphinee SL, Williams JJ, Maki B (1992) Measuring balance in the elderly: validation of an instrument. *Can J Public Health* 83 Suppl 2:S7-11.
- Cunha IT, Lim PA, Henson H, Monga T, Qureshy H, Protas EJ (2002) Performance-based gait tests for acute stroke patients. *Am J Phys Med Rehabil* 81:848-856.
- Hong JH, Jang SH (2010) The usefulness of DTI for estimating the state of cerebellar peduncles in cerebral infarct. *NeuroRehabilitation* 26:299-305.
- Hong JH, Kim OL, Kim SH, Lee MY, Jang SH (2009) Cerebellar peduncle injury in patients with ataxia following diffuse axonal injury. *Brain Res Bull* 80:30-35.
- Jang SH, Byun WM, Han BS, Park HJ, Bai D, Ahn YH, Kwon YH, Lee MY (2006) Recovery of a partially damaged corticospinal tract in a patient with intracerebral hemorrhage: a diffusion tensor image study. *Restor Neurol Neurosci* 24:25-29.
- Jiang H, van Zijl PC, Kim J, Pearlson GD, Mori S (2006) DtiStudio: resource program for diffusion tensor computation and fiber bundle tracking. *Comput Methods Programs Biomed* 81:106-116.
- Kashimura H, Inoue T, Ogasawara K, Ogawa A (2003) Preoperative evaluation of neural tracts by use of three-dimensional anisotropy contrast imaging in a patient with brainstem cavernous angioma: technical case report. *Neurosurgery* 52:1226-1229.
- Lee AY, Jang SH, Yeo SS, Lee E, Cho YW, Son SM (2013) Changes in a cerebellar peduncle lesion in a patient with Dandy-Walker malformation: A diffusion tensor imaging study. *Neural Regen Res* 8:474-478.
- Pijnenburg M, Caeyenberghs K, Janssens L, Goossens N, Swinnen SP, Snaert S, Brumagne S (2014) Microstructural integrity of the superior cerebellar peduncle is associated with an impaired proprioceptive weighting capacity in individuals with non-specific low back pain. *PLoS One* 9:e100666.
- Ying SH, Landman BA, Chowdhury S, Sinofsky AH, Gambini A, Mori S, Zee DS, Prince JL (2009) Orthogonal diffusion-weighted MRI measures distinguish region-specific degeneration in cerebellar ataxia subtypes. *J Neurol* 256:1939-1942.

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