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Changes in a cerebellar peduncle lesion in a patient with Dandy-Walker malformation

A diffusion tensor imaging study☆

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Abstract
We report a patient with severe ataxia due to Dandy-Walker malformation, who showed functional recovery over 10 months corresponding to a change in a cerebellar peduncle lesion. A 20-month-old female patient who was diagnosed with Dandy-Walker syndrome and six age- and sex-matched healthy control subjects were enrolled. The superior cerebellar peduncle, the middle cerebellar peduncle, and the inferior cerebellar peduncle were evaluated using fractional anisotropy and the apparent diffusion coefficient. The patients' functional ambulation category was 0 at the initial visit, but improved to 2 at the follow-up evaluation, and Berg's balance scale score also improved from 0 to 7. Initial diffusion tensor tractography revealed that the inferior cerebellar peduncle was not detected, that the fractional anisotropy of the superior cerebellar peduncle and middle cerebellar peduncle decreased by two standard deviations below, and that the apparent diffusion coefficient increased by two standard deviations over normal control values. However, on follow-up diffusion tensor tractography, both inferior cerebellar peduncles could be detected, and the fractional anisotropy of superior cerebellar peduncle increased to within two standard deviations of normal controls. The functional improvement in this patient appeared to correspond to changes in these cerebellar peduncles. We believe that evaluating cerebellar peduncles using diffusion tensor imaging is useful in cases when a cerebellar peduncle lesion is suspected.

Key Words
neural regeneration; neuroimaging; Dandy-Walker malformation; cerebellar peduncle; ataxia; cerebral palsy; functional ambulation category; Berg's balance scale; fractional anisotropy; apparent diffusion coefficient; diffusion tensor tractography; diffusion tensor imaging; grants-supported paper; photographs-containing paper; neuroregeneration

Research Highlights
(1) The Dandy-Walker malformation patient reported in this study presented with severe ataxia.
(2) The patient with ataxic symptoms showed functional recovery.
(3) Clinical improvement of the patient was in accordance with diffusion tensor imaging findings of the cerebellar peduncles.
(4) Diffusion tensor imaging can be used to evaluate recovery of injured cerebellar peduncles in a patient with Dandy-Walker malformation.

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INTRODUCTION

Dandy-Walker malformation is characterized by partial or complete agenesis of the cerebellar vermis, cystic dilation of the fourth ventricle, and an enlarged posterior fossa combined with superior displacement of the cerebellar hemisphere[1]. The cerebellum is an important structure involved with motor control and cognition. The cerebellum communicates with the cerebrum and brainstem through three pairs of cerebellar peduncles[2-3]. Disrupted cerebellar development is associated with neuromotor and cognitive developmental problems, and patients with Dandy-Walker malformation frequently present with symptoms of severe cerebellar ataxia, truncal hypotonia, and various developmental delays[2, 4]. It was previously reported that motor control impairments in patients with Dandy-Walker malformation were related to microstructural abnormalities in the connections from the cerebellum to the brainstem or cerebrum[1, 4]. However, it is difficult to evaluate cerebellar peduncle lesions as they are not wholly isolated from adjacent structures on conventional MRI.

The recent development of diffusion tensor imaging allows evaluation of the integrity and orientation of isolated neural tracts. Diffusion anisotropy has been used to evaluate the extent of fiber damage in diseases that affect the neural tracts. Diffusion tensor tractography, a three-dimensionally visualized version of diffusion tensor imaging, can be used to visualize neural tracts in three-dimensions[5].

In the current study, we report a patient with severe ataxia due to Dandy-Walker malformation, who showed functional recovery associated with changes in the cerebellar peduncles.

CASE REPORT

A 20-month-old female patient and her parents visited our Department of Pediatrics for severe ataxia and developmental delay. The patient was born at 40 weeks of gestation by normal vaginal delivery with a birth weight of 2 980 g. No specific perinatal history or family history of neurological disease or developmental delay was found. The patient showed severe developmental delay and could not sustain a sitting posture by herself with hands on the bottom due to severe ataxia, although she could turn her body over and creep on her belly. On neurological examination, she presented a marked psychomotor delay with severe truncal ataxia and mild axial hypotonia. Conventional MRI of the brain was taken and showed hypoplasia of the cerebellar vermis and enlargement of the fourth ventricle, indicating Dandy-Walker malformation. She had also undergone diffusion tensor MRI to estimate the status of the subcortical neural structure. Other genetic disorder or metabolic disease evaluations showed no specific findings. She was transferred to the pediatric rehabilitation center. The patient received comprehensive rehabilitative therapy for approximately 10 months, and showed considerable improvement in the ataxia and trunk control. At the commencement of rehabilitation, the patient could not sit independently. The functional ambulation category was used to assess the functional level[6]: 0, non-ambulatory; 1, needs continuous support from one person; 2, needs intermittent support from one person; 3, needs only verbal supervision; 4, help is required on stairs and uneven surfaces; 5, can walk independently anywhere. The initial functional ambulation category score before rehabilitative therapy was 0. For measurement of ataxia, Berg's balance scale was also used[7] by estimating the performance of functional tasks. The ability to maintain balance while performing a chain of 14 tasks (sit to stand, stand to sit, stand and sit unsupported, transfer from bed to chair, stand with eyes closed, stand with feet together, reach forward, pick up an object from the floor, single leg stance and tandem standing, turn and look over each shoulder, turn 360°, and stepping) was examined. A 5-point scale ranging from 0 to 4 was used, with a total score of 56. The initial score in the patient was 0. However, at 10 months after rehabilitation therapy, she was able to stand alone with assistance and to walk independently with a walker on an even floor. The functional ambulation category scores and Berg's balance scale scores were re-measured at 10 months after therapy, along with MRI and diffusion tensor imaging (Table 1). The follow-up result of conventional MRI showed no definite interval changes, compared with that of initial conventional MRI (Figure 1).

Table 1 Changes in BBS and FAC in patient and control subjects

		BBS	FAC
Patient	Before rehabilitation therapy	0	0
	Following 10-month rehabilitation therapy	7	2
Control		41.83±2.04	5±0

The higher scores of BBS and FAC indicated the better functions. BBS: Berg's balance scale (0–56); FAC: functional ambulation category (0–5). Values for control subjects are expressed as mean ± SD.

Diffusion tensor imaging was also performed on six healthy, age-matched children (two males and four

females, total: mean age 24.3 months, range 19–33 months; two males: mean age 24 months, range 19–29 months; four females: mean age 24.5 months, range 19–33 months). Control subjects were volunteers whose parents applied for this study. All participants in the control group had no specific pre/perinatal medical history or developmental delay. The developmental state and neurological examination of control subjects were evaluated by a pediatric neurologist. There were no definite abnormal neurologic findings or delayed development state. The Kolmogorov-Smirnov test was used to determine the normalities of variable distributions ($P > 0.05$)[8]. Pearson's correlation analysis was also conducted to estimate the influence of postnatal months on the fractional anisotropy and apparent diffusion coefficient values in each cerebellar peduncle. We found no correlations between various diffusion tensor imaging parameter and postnatal months in the superior cerebellar peduncle, middle cerebellar peduncle, or inferior cerebellar peduncle (correlation coefficient R^2 = 0.14, 0.17, and 0.01, respectively).

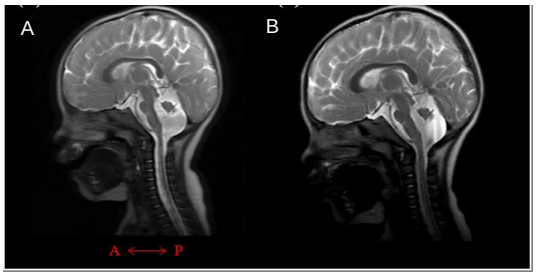

Figure 1 T2-weighted MRI of the patient.

MRI of the sagittal midline section at initial (A) and 10-month follow-up (B) demonstrating cystic enlargement of the fourth ventricle and hypoplasia of the cerebellar vermis. There were no definite interval changes between initial and follow-up on conventional MRI. A: Anterior; P: posterior.

Diffusion tensor imaging protocol

Diffusion tensor imaging data were acquired using a 1.5 T Philips Gyroscan Intera system (Hoffman-LaRoche, Mijdrecht, Netherlands) equipped with a synergy-L sensitivity encoding (SENSE) head coil using a single-shot, spin-echo planar imaging pulse sequence. For each of the 32 non-collinear and non-coplanar diffusion sensitizing gradients, the 67 contiguous slices were acquired parallel to the anterior commissure- posterior commissure line. The imaging parameters were: matrix, 128 × 128; field of view, 221 × 221 mm^2; echo time, 76 ms; repetition time 10 726 ms; sensitivity encoding factor, 2; echo planar imaging factor = 59 and b = 1 000 mm^2/s; number of excitations, 1; and a slice thickness of 2.3 mm. diffusion tensor imaging datasets were preprocessed using the Oxford Center for Functional Magnetic Resonance Imaging of Brain Software Library. Eddy current-induced image distortions and motion artifacts were removed using affine multi-scale two-dimensional registration[9]. Three cerebellar peduncles (superior cerebellar peduncle, middle cerebellar peduncle, inferior cerebellar peduncle) were evaluated using diffusion tensor imaging -Studio software (CMRM, Johns Hopkins Medical Institute, Baltimore, MD, USA)[10].

Fiber tracking was based on the fiber assignment continuous tracking algorithm, a brute-force reconstruction approach, and a multiple regions of interest approach. The cerebellar peduncles were identified by choosing the fibers that passed through both regions of interests on the color map. Region of interest 1 was assigned to the junction of the superior cerebellar peduncle between the upper pons and cerebellum on the coronal view, and region of interest 2 to the area between the lateral wall of the fourth ventricle and the inferior cerebellar peduncle at the fourth ventricle level on the axial view. Region of interest 1 represented the ventral junctional area of the middle cerebellar peduncle between the pons and cerebellum, and the caudal junctional area of the middle cerebellar peduncle on the coronal view. For the inferior cerebellar peduncle, region of interest 1 represented the restiform body (blue), and region of interest 2 represented the caudal part (green) to the superior cerebellar peduncle on the axial view at the upper pons level[11-12]. Fiber tracking was started at the center of the seed voxel with an fractional anisotropy value greater than 0.2 and ended at the voxel with a fiber assignment lower than 0.2 and a tract turning-angle lower than 60°. The fractional anisotropy values and apparent diffusion coefficient of each of the cerebellar peduncles were estimated and defined abnormal as a lesion with fractional anisotropy and apparent diffusion coefficient values deviating more or less than two standard deviations below those of normal control values.

Diffusion tensor imaging data

All three pairs of cerebellar peduncles were well detected in all control subjects as a known anatomical pathway. No significant differences were observed between diffusion tensor imaging parameters of the right and left superior cerebellar peduncle, middle cerebellar peduncle, or inferior cerebellar peduncle in control subjects. The results of the initial diffusion tensor tractography in the patient revealed that the superior cerebellar peduncle and middle cerebellar peduncle were well detected, but that the inferior cerebellar peduncle was not detected in either

hemisphere. No significant differences in fractional anisotropy and apparent diffusion coefficient values were found between the right and left superior cerebellar peduncle and the middle cerebellar peduncles in the patient. As such, we used the mean values of both hemispheres.

Initial diffusion tensor imaging results showed that the fractional anisotropy values of the superior cerebellar peduncle and middle cerebellar peduncle decreased by two standard deviations below that of normal control values, and that the apparent diffusion coefficient values increased by two standard deviations. In the follow-up evaluation, both fractional anisotropy and apparent diffusion coefficient values of the superior cerebellar peduncle were within two standard deviations of control subjects. By contrast, the middle cerebellar peduncle showed increased fractional anisotropy and decreased apparent diffusion coefficient values, but remained below two standard deviations of normal control values. The inferior cerebellar peduncle was not detected by the initial diffusion tensor tractography.

However, at the 10-month follow-up, diffusion tensor tractography revealed both inferior cerebellar peduncles, although the fractional anisotropy had decreased by two standard deviations below normal control values, and the apparent diffusion coefficient had increased by two standard deviations (Figure 2 and Table 2).

DISCUSSION

Herein, we report a patient who showed functional improvement from a cerebellar peduncle lesion due to Dandy-Walker malformation and corresponding changes in the diffusion tensor imaging findings. The patient could not sit independently at the initial evaluation, but could walk with a walker after 10 months. On initial diffusion tensor tractography, the inferior cerebellar peduncle was not detected, the fractional anisotropy of the superior cerebellar peduncle and middle cerebellar peduncle were decreased by two standard deviations below that of normal subjects, and the apparent diffusion coefficient was increased by two standard deviations over normal control values. However, after 10 months follow-up, the inferior cerebellar peduncle was detected, and diffusion parameters improved, with an increase in fractional anisotropy and decrease in apparent diffusion coefficient to within two standard deviations of the normal subjects. A decrease in fractional anisotropy is caused by disruptions in directional structures such as myelin sheaths and axonal microfilaments. An increase in apparent diffusion coefficient values is caused by hindered water motion due to axonal damage. These findings are usually found in injured white matter tracts[5].

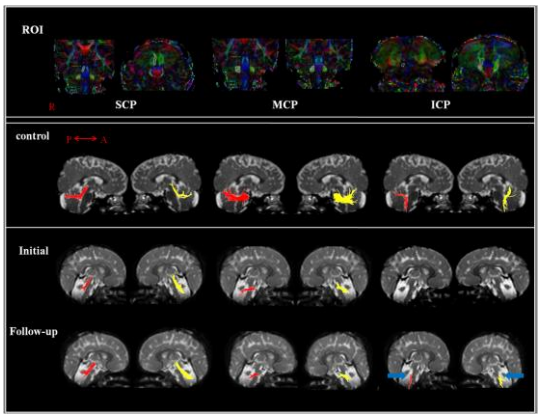

Figure 2 Diffusion tensor tractography in the patient and control subjects.

The ROIs for tractography are marked with white lines. The red tracts indicate right side tracts, and the yellow tracts indicate left side tracts. The blue arrows indicate the inferior cerebellar peduncles, which were not detected at initial diffusion tensor tractography, but appeared at the 10-month follow-up diffusion tensor tractography.

ROI: Region of interest; SCP: superior cerebellar peduncle; MCP: middle cerebellar peduncle; ICP: inferior cerebellar peduncle; R: right; P: posterior; A: anterior.

Table 2 Cerebellar peduncles characteristics in the patient *versus* control subjects.

		FA		ADC	
		Initial	10-month follow-up	Initial	10-month follow-up
Patient	SCP	0.38[a]	0.42	1.09[a]	0.87
	MCP	0.31[a]	0.32[a]	1.52[a]	1.25[a]
	ICP	Unanalyzed	0.35[a]	Unanalyzed	1.05[a]
Control subjects	SCP	0.48±0.04 (0.40–0.56)		0.96±0.06 (0.85–1.07)	
	MCP	0.50±0.03 (0.45–0.55)		0.86±0.05 (0.79–0.97)	
	ICP	0.45±0.03 (0.39–0.51)		0.89±0.06 (0.73–1.00)	

FA: Fractional anisotropy; ADC: apparent diffusion coefficient; SCP: superior cerebellar peduncle; MCP: middle cerebellar peduncle; ICP: inferior cerebellar peduncle. Data in control subjects are expressed as mean ± SD (95% confidence interval). Superscript “a” is decreased or increased by two standard deviations from the control.

Therefore, the decreased fractional anisotropy and increased apparent diffusion coefficient values of the cerebellar peduncles in our patient at initial examination suggest that the neural tract was affected, while the increased fractional anisotropy and decreased apparent diffusion coefficient values at follow-up indicate improvement from the lesions[13]. Moreover, the inferior cerebellar peduncle was not detected at the initial evaluation, but was well detected at the follow-up diffusion tensor tractography.

These diffusion tensor imaging and diffusion tensor tractography results coincided with clinical improvement of the patient, which was not detected by conventional MRI, suggesting that diffusion tensor imaging is useful for assessing cerebellar peduncles in cases of suspected cerebellar peduncle injury. Several studies have identified normal cerebellar peduncles using diffusion tensor imaging [11-12], and a recent study demonstrated that patients with cerebellar peduncle injuries develop diffuse axonal injury or pontine infarcts[14-15].

These results agreed with our findings that the recovery of cerebellar peduncle injury was associated with clinical improvement of ataxia. To the best of our knowledge, this is the first diffusion tensor imaging study examining recovery of injured cerebellar peduncles in a patient with Dandy-Walker malformation. Nevertheless, further complementary studies involving more cases are warranted.

In summary, we report on a patient who showed clinical improvement of ataxia according to the recovery of disrupted cerebellar peduncles using diffusion tensor imaging. diffusion tensor imaging can be performed along with conventional MRI for patients with Dandy-Walker malformation.

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Author contributions: Ah Young Lee perfomed data collection, interpreted the data and wrote the manuscript. Sung Ho Jang interpreted clinical, radiologic data and supported technical, material assistance. Sang Seok Yeo analyzed the data. Ensil Lee performed data collection. Yun Woo Cho performed statistical anlaysis. Su Min Son designed the study, provided critical revision of the manuscript for intellectual content and supervised the article. All authors approved the final version of the paper.

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