Injury of the dentato-rubro-thalamic tract in patients with cerebellar infarct

Case report

Sung Ho Jang, MD, Hyeok Gyu Kwon, PhD

Abstract

Rationale: Several studies using diffusion tensor tractography (DTT) have reported on injury in the dentato-rubro-thalamic tract (DRTT) in patients with brain injury. However, there is no study of injury in the DRTT following cerebellar infarct. We report on patients with injury in the DRTT following cerebellar infarct, demonstrated on DTT.

Patient concerns: Three patients with cerebellar infarct were enrolled in this study. Diffusion tensor imaging data were acquired at 3 weeks (patient 1) and 2 weeks (patients 2 and 3) after onset and the DRTT was reconstructed. The Scale for Assessment and Rating of Ataxia and the Functional Ambulation Category were used for evaluation of ataxia and gait function.

Diagnoses and Outcomes: With clinical evaluation, patient 1 scored 18, patient 2 scored 22, and patient 3 scored 28 points on the Scale for Assessment and Rating of Ataxia. On the Functional Ambulation Category patient 1 scored 2, patient 2 scored 2, and patient 3 scored 1 point. DRTT abnormalities were as follows: discontinuation (the upper portion of the left DRTT in the patient 1), narrowing (the lower portion of the left DRTT in patient 2, and the whole right DRTT in the patient 3), and nonreconstruction (the left DRTT in the patient 3).

Lessons: Using DTT, we demonstrated injury in the DRTT in 3 patients with severe ataxia following cerebellar infarct. We believe that evaluation of the DRTT would be helpful in patients who develop ataxia following cerebellar infarct.

Abbreviations: DRTT = dentato-rubro-thalamic tract, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, FAC = Functional Ambulation Category, ROI = region of interest, SARA = Scale for Assessment and Rating of Ataxia.

Keywords: ataxia, cerebellar infarct, dentato-rubro-thalamic tract, diffusion tensor imaging

1. Introduction

Cerebellar infarct is uncommon, approximately 2% to 3% in stroke patients. It can cause movement disorders, including tremor, ataxia, and incoordination, because the main role of the cerebellum is movement control by communicating between the cerebrum and cerebellum via the dentato-rubro-thalamic tract (DRTT) and cortico-ponto-cerebellar tract.[1–5] In particular, ataxia is typically defined as a lack of voluntary coordinated movements on hand, leg, and trunk, and it usually occurs after cerebellar injury; however, precise cause of the ataxia is not fully understood. Among causes of the ataxia, injury in the DRTT, a major efferent pathway from the deep cerebellar nuclei to the brainstem and thalamus, is suggested as a major pathogenetic mechanism of ataxia.[6–9] Therefore, in terms of the diagnosis, examination of the DRTT would be important in patients with ataxia following cerebellar infarct. However, research on the DRTT has been limited in the live human brain due to anatomical features of a long, multisynapse, low discrimination with adjacent neural tracts that cross to the opposite side.[7,9]

Recently developed diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), has enabled three-dimensional reconstruction and estimation of the microstructural integrity of white matter including the DRTT.[10,11] Several studies using DTI have reported that injury in the DRTT commonly accompanies ataxia in patients with brain injury.[12–15] However, there is limited understanding on study on injury in the DRTT following cerebellar infarct.

In this study, we report 3 patients with injury in the DRTT following cerebellar infarct, demonstrated on DTT.

2. Methods

2.1. Subjects

We recruited 3 patients (male: 1, female: 2, mean age: 64.7±10.7 years, range: 50–75 years) with cerebellar infarct who were admitted to the rehabilitation department of a university hospital. Inclusion criteria for patients were as follows: first ever stroke; an
infarct is located in the cerebellum, as confirmed by a neuroradiologist; DTI scanning was performed at an early stage (between 2 and 3 weeks) after the stroke showed ataxia and gait disturbance after the stroke; and no severe apraxia and somatosensory problems (<22 points [full mark: 24] on the subscale for kinesthetic sensation of the Nottingham Sensory Assessment). The patients provided signed, informed consent, and the study protocol was approved by Yeungnam University Hospital institutional review board.

2.2. Clinical evaluation
The Scale for Assessment and Rating of Ataxia (SARA, 0–40 points; a higher score indicates a worse state) and the Functional Ambulation Category (FAC, 0–5 points: a lower score indicates a worse state) were administered to assess ataxia and gait function, respectively.[16,17]

2.3. Diffusion tensor imaging
DTI data were acquired at 3 weeks (patient 1) and 2 weeks (patients 2 and 3) after their strokes using a 6-channel head coil on a 1.5T Philips Gyroscan Intera (Philips, Ltd, Best, the Netherlands) with single-shot echo-planar imaging. For each of the 32 noncollinear diffusion sensitizing gradients, 70 contiguous slices were acquired parallel to the anterior commissure–posterior commissure line. Imaging parameters were as follows: acquisition matrix = 96 × 96; reconstructed to matrix = 192 × 192; field of view = 240 × 240 mm²; repetition time = 10,398 ms; echo time = 72 ms; b = 1000s/mm²; and a slice thickness of 2.5 mm. Affine multiscale two-dimensional registration at the Oxford Centre for Functional Magnetic Resonance Imaging of Brain (FMRIB) Software Library was used for correction of head motion effect and image distortion.[10,18] Fiber tracking was performed using a probabilistic tractography method based on a multfiber model, and applied in the present study utilizing tractography routines implemented in FMRIB Diffusion (5000 streamline samples, 0.5 mm step lengths, curvature thresholds = 0.2). For the reconstruction of the DRTT, the seed region of interest (ROI) was placed on the dentate nucleus behind the floor of the fourth ventricle on the coronal image.[11]

Two target ROIs were given at the junction of the superior cerebellar peduncle between the upper pons and cerebellum on the coronal image and the contralateral red nucleus of the upper midbrain on the axial image.[11] A threshold of 2 streamlines was applied for the results of fiber tracking.

3. Results
The demographic and clinical data for 3 patients are summarized in Table 1. With clinical evaluation, patient 1 scored 18, patient 2 scored 22, and patient 3 scored 28 points on the SARA. On the FAC patient 1 scored 2, patient 2 scored 2, and patient 3 scored 1 point. DRTT abnormalities were discontinuation (the upper portion of the left DRTT in the patient 1), narrowing (the lower portion of the left DRTT in patient 2, and the entire right DRTT in the patient 3), and nonreconstruction (the left DRTT in the patient 3) (see Fig. 1).

4. Discussion
In this study, we demonstrated injury in the DRTT in 3 patients with severe ataxia following the cerebellar infarct. DRTT injuries

Table 1
Demographic and clinical characteristics.

| Patient    | Age/sex  | Duration to DTT from onset (wk) | Lesion side | Functional Ambulation Category | Scale for Assessment and Rating of Ataxia |
|------------|----------|---------------------------------|-------------|--------------------------------|------------------------------------------|
| Patient 1  | 69/female| 3                               | Left        | 2                              | Gait 5, Stance 4, Speech disturbance 0, Nose-finger test 3, Finger chase 2, Fast alternating hand movements 3, Heel-shin slide 3, Total 22 |
| Patient 2  | 75/female| 2                               | Left        | 2                              | Gait 5, Stance 4, Speech disturbance 0, Nose-finger test 3, Finger chase 2, Fast alternating hand movements 3, Heel-shin slide 3, Total 22 |
| Patient 3  | 50/male  | 2                               | Both        | 2                              | Gait 5, Stance 4, Speech disturbance 0, Nose-finger test 3, Finger chase 2, Fast alternating hand movements 3, Heel-shin slide 3, Total 22 |

DTT = diffusion tensor tractography.

![Figure 1](image-url)
were discontinuation (the upper portion of the left DRTT in the patient 1), narrowing (the lower portion of the left DRTT in patient 2, and the whole right DRTT in the patient 3), and nonreconstruction (the left DRTT in the patient 3). Therefore, it appears that ataxia in 3 patients was at least in part attributable to injury in the DRTT. We believe that our results suggest the necessity of evaluation of the DRTT in patients with ataxia after cerebellar infarct.

Several studies using DTI reported on injury in the DRTT in patients following cerebellar infarct. In 2014, Akhlaghi et al\[12\] described an injured DRTT by abnormal DTT parameters, including lower fractional anisotropy and higher mean diffusivity in 12 patients with Friedreich ataxia compared with 14 normal controls. During the next year, Marek et al\[13\] described 6 patients with ataxia and tremor who had injuries of the cerebello-thalamic portion of the DRTT.\[13\] Jang and Kwon\[14\] ascribed thinning of the DRTT in the right hemisphere to a patient’s ataxia and tremor [SARA: 12 points] following mild traumatic brain injury. In 2015, Schulz et al\[15\] reported concurrent injuries of the cortico-ponto-cerebellar tract and DRTT related to residual motor function in 26 patients with chronic ischemic stroke.\[15\] To the best of our knowledge, this is the first study to demonstrate injury in the DRTT in patients with cerebellar infarct and suggest injured DRTT is one of the causes of the ataxia. Therefore, clinicians should consider injury of the DRTT in patients with ataxia following various brain injuries, particularly lesions on the pathways of the DRTT such as thalamus and pontine. However, several limitations should be considered. First, this study is a case report. Second, we could not investigate the degree of ataxia by several limitations should be considered. First, this study is a case report. Second, we could not investigate the degree of ataxia by

5. Conclusions

Using DTT, we demonstrated injury in the DRTT in 3 patients with severe ataxia following cerebellar infarct. We believe that evaluation of the DRTT would be helpful in patients with ataxia following cerebellar infarct.

References

[1] Sypert GW, Alvord EC Jr. Cerebellar infarction. A clinicopathological study. Arch Neurol 1975;32:357–63.
[2] Macdonell RA, Kalnins RM, Donnan GA. Cerebellar infarction: natural history, prognosis, and pathology. Stroke 1987;18:849–55.
[3] Kase CS, Norrving B, Levine SR, et al. Cerebellar infarction. Clinical and anatomic observations in 66 cases. Stroke 1993;24:76–83.
[4] Javalkar V, Khan M, Davis DE. Clinical manifestations of cerebellar disease. Neurol Clin 2014;32:871–9.
[5] Dutar S, Rabstein AA. Cerebellar infarction. Neurol Clin 2014;32:979–91.
[6] Lehericy S, Grand S, Pollak P, et al. Clinical characteristics and topography of lesions in movement disorders due to thalamic lesions. Neurology 2001;57:1053–66.
[7] Afiş AK, Bergman RA. Functional Neuroanatomy: Text and Atlas. 2nd ed. Lange Medical Books/McGraw-Hill, New York, NY:2005.
[8] Marx JJ, Iannetti GD, Thomek F, et al. Topodiagnostic implications of hemiataxia: an MRI-based brainstorm mapping analysis. Neuroimage 2008;39:1625–32.
[9] Mendoza JE, Foundas AL. Clinical Neuroanatomy: A Neurobehavioral Approach. Springer, New York/London:2007.
[10] Behrens TE, Berg HJ, Jbabdi S, et al. Probabilistic diffusion tractography with multiple fibre orientations: what can we gain? Neuroimage 2007;34:144–55.
[11] Kwon HG, Hong JH, Hong CP, et al. Dentatorubrothalamic tract in human brain: diffusion tensor tractography study. Neuroradiology 2011;53:787–91.
[12] Akhlaghi H, Yu J, Corben L, et al. Cognitive deficits in Friedreich ataxia correlate with micro-structural changes in dentatorubral tract. Cerebellum 2014;13:187–98.
[13] Marek M, Paus S, Allert N, et al. Ataxia and tremor due to lesions involving cerebellar projection pathways: a DTI tractographic study in six patients. J Neurol 2015;262:54–8.
[14] Jang SH, Kwon HG. Injury of the dentato-rubro-thalamic tract in a patient with mild traumatic brain injury. Brain Inj 2015;29:1725–8.
[15] Schulz R, Frey BM, Koch P, et al. Cortico-cerebellar structural connectivity is related to residual motor output in chronic stroke. Cereb Cortex 2017;27:635–45.
[16] Cunha IT, Lim PA, Henson H, et al. Performance-based gait tests for acute stroke patients. Am J Phys Med Rehabil 2002;81:848–56.
[17] Weyer A, Abele M, Schmitz-Hubsch T, et al. Reliability and validity of the scale for the assessment and rating of ataxia: a study in 64 ataxia patients. Mov Disord 2007;22:1633–7.
[18] Smith SM, Jenkinson M, Woolrich MW, et al. Advances in functional and structural MR image analysis and implementation as FSL. Neuroimage 2004;23(Suppl. 1):S208–19.
[19] Fillard P, Descoteaux M, Goh A, et al. Quantitative evaluation of 10 tractography algorithms on a realistic diffusion MR phantom. NeuroImage 2011;56:220–34.
[20] Yamada K, Sakai K, Akazawa K, et al. MR tractography: a review of its clinical applications. Magn Reson Med Sci 2009;8:165–74.