Aggravation of an injured dentato-rubro-thalamic tract in a patient with mild traumatic brain injury
A case report

Sung Ho Jang, MDa, Hyeok Gyu Kwon, PhDb,∗

Abstract
Rationale: We report on a patient with mild traumatic brain injury (TBI) by follow-up diffusion tensor tractography (DTT), and observed for approximately nine months by serial diffusion tensor tractography (DTT).

Patient concerns: A 66-year-old male patient was injured in a car crash. Approximately four weeks after the crash, he developed a tremor in the right hand and leg. His symptoms worsened over time.

Diagnoses: Approximately six months after the crash, he developed a mild tremor in the left hand. Nine months after the crash, he manifested severe tremor in his right hand, mild resting and intentional tremor in his left hand and both legs, and mild truncal ataxia.

Interventions: N/A.

Outcomes: On 3-week DTT, well reconstructed DRTTs were observed in both hemispheres, except for the thinned lower portion of the right DRTT. On 9-month DTT, the right lower DRTT had thinned compared with the 3-week DTT and showed a disruption at the upper portion. The left DRTT showed thinning in the lower portion and tearing in the upper portion compared with 3-week DTT.

Lessons: Aggravation of an injured DRTT was demonstrated in a patient with mild TBI, using serial DTT examination.

Abbreviations: DRTT = dentato-rubro-thalamic tract, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, ROI = region of interest, SARA = Scale for Assessment and Rating of Ataxia, TBI = traumatic brain injury.

Keywords: ataxia, dentato-rubro-thalamic tract, diffusion tensor tractography, mild traumatic brain injury, tremor

1. Introduction

Tremor, an unintentional and uncontrollable rhythmic movement, is a major clinical manifestation of movement disorders. It is the most frequent movement disorder in patients with traumatic brain injury (TBI). Injury of the dentato-rubrothalamic tract (DRTT), a major efferent pathway from the deep cerebellar nuclei to the brainstem and thalamus, is suggested as a major pathogenetic mechanism of tremor. Several studies reported injury of the DRTT in patients with tremor following various brain pathologies including TBI. However, little is known about aggravation of an injured DRTT.

Most studies of the DRTT in the human brain used conventional brain MRI and precise evaluation has been limited because of its long, narrow shape, multisynapse, low discrimination with adjacent neural structures, and decussation to the opposite hemisphere in the midbrain. Introduction of diffusion tensor tractography (DTT), derived from diffusion tensor imaging (DTI), enabled 3-dimensional reconstruction and evaluation of the DRTT in the live human brain. A patient with injury of the DRTT following mild TBI was recently reported, however, it has not been clearly elucidated so far.

To demonstrate aggravation of injured DRTT over approximately 9 months, we report on a patient with mild TBI using serial DTT.

2. Case report

A 66-year-old male patient was injured in a car crash. While driving on a congested highway, his car was struck by a tow truck from behind. The patient lost consciousness for approximately 1 minute and experienced post-traumatic amnesia approximately 5 minutes from the time of the accident. The patient’s Glasgow Coma Scale score was 15. No specific lesion was observed on the conventional brain MRI performed at 3 weeks after onset (Fig. 1A). Three weeks after the crash, he was admitted to the rehabilitation department of a university hospital. At the beginning of rehabilitation, Mini-Mental State Examination was 29 (full score: 30; cutoff score: 25). Neurological examination revealed mild motor weakness without spasticity and flaccidity and somatosensory impairment of the right upper and lower extremities (Manual Muscle Test; right upper extremity [good grade: movement against a resistance lower

Editor: Song Liu.

This research is supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2015R1A1A4A01020385).

The authors have no conflicts of interest to disclose.

∗Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University, Daegu, †Department of Physical Therapy, College of Health Sciences, Catholic University of Pusan, Republic of Korea.

Correspondence: Hyeok Gyu Kwon, Department of Physical Therapy, College of Health Sciences, Catholic University of Pusan, 57 Oryundae-ro, Geumjeong-gu, Pusan 46252, Republic of Korea (e-mail: kg0715@hanmail.net).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-NDD), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medicine (2017) 96(43):e8253

Received: 19 August 2016 / Received in final form: 6 July 2017 / Accepted: 28 August 2017
http://dx.doi.org/10.1097/MD.0000000000008253
than resistance overcome by the healthy side and right lower extremity [fair grade: movement against gravity], Nottingham Sensory Assessment; tactile sensation—right upper extremity [6; full score, 10], right lower extremity [4; full score, 10]; kinesthetic sensation—the right upper extremity [8; full score, 12], right lower extremity [8; full score, 12]). He reported central pain in the right upper and lower extremities (tingling sensation with allodynia), visual analogue scale score (6; full score, 10), memory impairment (Memory Assessment Scale; global memory: 68 [2 percentile], short-term memory: 53 [1 percentile], verbal memory: 53 [1 percentile], and visual memory: 98 [45 percentile]), and visual disturbance. He received comprehensive rehabilitative therapy including movement therapy and neuro-muscular electrical stimulation on the right finger and knee extensor muscles. Movement therapy was conducted for 30 minutes, 5 times per week in our physical and occupational therapy department. Although we tried medications for weakness and central pain, his severe drug allergies prevented this treatment. Approximately 4 weeks after the crash, he began to show a resting and intentional tremor in the right hand and leg, and developed a mild truncal ataxia. His symptoms worsened with time. Approximately 6 months after the crash, he developed mild resting and intentional tremor in the left hand. Nine months after the crash, he manifested severe resting and intentional tremor on his right hand, mild resting and intentional tremor in his left hand and both legs, and mild truncal ataxia. The Scale for Assessment and Rating of Ataxia (SARA, full mark: 40 points) indicated aggravation from 2 points at 3 weeks after onset to 26 points at 9 months after onset. Eight age- and sex-matched normal control subjects (mean age: 62.9 ± 5.0 years, range: 60–71 years) with no history of neurological disease were recruited for this study. The patient provided written informed consent, and the study protocol including data deposition was approved by the Yeungnam University Hospital Institutional Research Board.

2.1. Diffusion tensor tractography

DTI was acquired twice (at 3 weeks and 9 months) 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 non-collinear 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; parallel imaging reduction factor = 2; echo-planar imaging factor = 59; b = 1000 s/mm²; and a slice thickness of 2.5 mm. Prior to the fiber tracking, eddy current correction was applied to correct the head motion effect and image distortion using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRI) Diffusion Software. Fiber tracking used probabilistic tractography with default tractography option in the FMRIB Diffusion Software (5000 streamline samples, 0.5 mm step lengths, curvature thresholds = 0.2). For reconstruction of the DRTT, the seed
region of interest (ROI) was placed at the dentate nucleus beyond the floor of the fourth ventricle on the coronal image.\[^{11}\] Two target ROIs were placed on the portion of the superior cerebellar peduncle on the color map with the corona 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. The tract volume of the DRTT was measured by counting voxels. Tract volume in DTT parameter value showing a deviation of more than 2 standard deviations from normal control values were defined as injury.

On 3-week DTT, well-reconstructed DRTTs were observed in both hemispheres, except for the thinned lower portion of the right DRTT. On 9-month DTT, the right DRTT had become thinner in the lower portion compared with 3-week DTT, and a disruption was observed at the upper portion. Thinning of the left DRTT in the lower portion and tearing in the upper portion were observed compared with 3-week DTT (Fig. 1B and C). Compared with normal controls (652.8 ± 76.5 voxels), the right DRTT (465 voxels) tract volume on 3-week DTT was significantly less. On the 9-month DTT, the DRTT in both hemispheres (right: 52 voxels and left: 476 voxels) revealed significantly less tract volume compared with normal controls. Tract volume decreased in both DRTTs on 9-month DTT (right: 52 voxels and left: 476 voxels) compared with the 3-week DTT (right: 465 voxels and left: 639 voxels).

3. Discussion

In this study, the DRTT was observed over time in both hemispheres in a patient with mild TBI using serial DTT. On 3-week DTT, DRTTs were well reconstructed, except for the thinned lower portion of the right DRTT. However, on 9-month DTT, both lower portions of the DRTTs had become thinner and the upper portions of the DRTT showed abnormalities: disruption (the right DRTT) and tearing (the left DRTT). Mild injury of the right DRTT was observed on 3-week DTT and injuries of both DRTTs (more severe injury in the right DRTT) were observed on 9-month DTT. These changes suggest that the aggravation of both injured DRTTs developed during the period from 3 weeks to 9 months after onset. However, clinical symptoms related to the DRTT (tremor) began on the right side at 4 weeks after the crash, worsened and spread to the left side over time. The tremor in this patient can be partially ascribed to injury of the DRTT caused by traumatic axonal injury because the conventional brain MRI did not show any specific lesion.\[^{13}\] In addition, the delayed onset (4 weeks after head trauma) and gradual aggravation of the tremor in this patient suggests that the traumatic axonal injury might be mainly ascribed to secondary injury. In this condition axons were not damaged by direct shear/strain injury at the time of head trauma, but axonal injury developed by progressively impaired axoplasmic transport, continued axonal swelling, and disconnection.\[^{14}\] No specific causes for the neurological manifestations, including Parkinson disease were observed by a neurologist and a neurosurgeon. Furthermore, the patient presented with only tremor and ataxia, but without rigidity and bradykinesia which are main symptoms of Parkinson disease.\[^{15,16}\]

Several studies using DTT have described injured DRTT with movement disorder in patients with stroke, brain tumor, and TBI.\[^{3-9}\] Only 1 study has reported injury of the DRTT from TBI.\[^{9}\] In 2015, Kwon and Jang demonstrated injury of the DRTT (thinning) on DTT in a patient who showed delayed onset (2 weeks after head trauma) and aggravation of tremor and ataxia following mild TBI. To the best of our knowledge, this is the first study to demonstrate aggravation of an injured DRTT in a patient with TBI using serial DTT. Limitations of this study should be considered. First, because it is based on a case report, this study is limited. Second, DTT can show both false positive and negative results throughout the white matter of brain due to the crossing fiber and partial volume effects.\[^{17}\] Third, the patient was managed only at the department of rehabilitation, so more comprehensive assessment of the patient’s neurological state following TBI could have been obtained by collaborating with the neurology staff.

In conclusion, aggravation of an injured DRTT was demonstrated in a patient with mild TBI, using serial DTT. Our results suggest the need to evaluate the DRTT in patients who develop delayed onset of a movement disorder after TBI, even though no definite brain lesion is observed on conventional brain MRI. Further studies involving large numbers of subjects on the anterograde axonal degeneration of injured DRTTs following the initial injury should be encouraged.

References

\[^{1}\] Adler CH, Ahlskog JE. Parkinson’s Disease and Movement Disorders: Diagnosis and Treatment Guidelines for the Practicing Physician. Humana Press, New Jersey:2000.
\[^{2}\] McNtosh GC. Medical management of noncognitive sequelae of minor traumatic brain injury. Appl Neuropsychol 1997;4:62–8.
\[^{3}\] Alfii AK, Bergman RA. Functional Neuroanatomy: Text and Atlas. 2nd ed. New York, NY: Lange Medical Books/McGraw-Hill; 2005.
\[^{4}\] Marx JJ, Iannetti GD, Thonke F, et al. Topodiagnostic implications of hemiataxia: an MRI-based brainstem mapping analysis. Neuroimage 2008;39:1625–32.
\[^{5}\] Coenen VA, Allert N, Madler B. A role of diffusion tensor imaging fiber tracking in deep brain stimulation surgery: DBS of the dentato-rubro-thalamic tract (DRT) for the treatment of therapy-refractory tremor. Acta Neurochir (Wien) 2011;153:1579–85.
\[^{6}\] Coenen VA, Allert N, Paas S, et al. Modulation of the cerebello-thalamo-cortical network in thalamic deep brain stimulation for tremor: a diffusion tensor imaging study. Neurosurgery 2014;73:657–69.
\[^{7}\] Marek M, Paas S, Allert N, et al. Ataxia and tremor due to lesions involving cerebellar projection pathways: a DTT tractographic study in six patients. J Neurol 2015;262:54–8.
\[^{8}\] Schläfer J, Anthofer J, Steib K, et al. Deep brain stimulation for essential tremor: targeting the dentato-rubro-thalamic tract? Neuromodulation 2015;18:105–12.
\[^{9}\] 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.
\[^{10}\] Lehircy S, Grand S, Pollak P, et al. Clinical characteristics and topography of lesions in movement disorders due to thalamic lesions. Neurology 2001;57:1055–66.
\[^{11}\] Kwon HG, Hong JH, Hong CP, et al. Dentatorubrothalamic tract in human brain: diffusion tensor tractography study. Neuroradiology 2011;53:787–91.
\[^{12}\] Mori S, Crain BJ, Chacko VP, et al. Three-dimensional tracking of axonal projections in the brain by magnetic resonance imaging. Ann Neurol 1999;45:265–9.
\[^{13}\] Alexander MP. Mild traumatic brain injury: pathophysiology, natural history, and clinical management. Neurology 1995;45:1253–60.
\[^{14}\] Pavlovshock JT. Traumatically induced axonal injury: pathogenesis and pathological implications. Brain Pathol 1992;2:1–2.
\[^{15}\] Samii A, Nutt JG, Ransom BR. Parkinson’s disease. Lancet 2004;363:1783–93.
\[^{16}\] Jankovic J. Parkinson’s disease; clinical features and diagnosis. J Neurol Neurosurg Psychiatry 2008;79:368–76.
\[^{17}\] Yamada K. Diffusion tensor tractography should be used with caution. Proc Natl Acad Sci U S A 2009;106:E14.