OPEN

Relationship between ataxia and inferior cerebellar peduncle injury in patients with cerebral infarct

Sung Ho Jang, MD[a], Han Do Lee, PhD[b],*

Abstract

Introduction: The inferior cerebellar peduncle (ICP) is a major neural tract in the cerebellum and is involved in coordination of movement and proprioceptive; therefore, ICP injury can be accompanied by poor coordination of movement, including ataxia. In this study, using diffusion tensor tractography (DTT), we investigated the relationship between ataxia and ICP injury in patients with cerebral infarct.

Methods: We recruited 14 stroke patients with ataxia after the onset of stroke and 12 normal subjects. The Score of Assessment and Rating of Ataxia (SARA) was used to evaluate ataxia. The values of fractional anisotropy (FA), apparent diffusion coefficient, and fiber number (FN) of the ICP were measured for the diffusion tensor imaging parameters.

Results: Significant differences were observed in the FA and FN values of the ICP in the affected hemisphere between the patient and control groups ($P < .05$). In addition, the FN value of the ICP in the affected hemisphere showed a negative correlation with SARA ($r = -0.538$, $P < .05$). However, parameters of the ICP in the unaffected hemisphere or the FN value in the unaffected hemisphere showed no correlation with SARA ($P > .05$).

Conclusion: We found that the ataxia severity was closely related to the severity of ICP injury in patients with cerebral infarct. Our results suggest that evaluation of the ICP using DTT would be useful for patients with ataxia after cerebral infarct.

Abbreviations: ADC = apparent diffusion coefficient, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, FA = fractional anisotropy, FN = fiber number, ICP = inferior cerebellar peduncle, ROI = region of interest, SARA = Score of Assessment and Rating of Ataxia.

Keywords: ataxia, diffusion tensor imaging, diffusion tensor tractography, inferior cerebellar peduncle, stroke

1. Introduction

The cerebellum has a complex network and relates to various clinical dysfunctions including ataxia, gait disturbance, problems of hearing and vision, and problems of cognition and affective control.[1] Cerebellar peduncles are the structures connecting the cerebellum to the brain stem and the cerebrum.[2,3] Therefore, cerebellar peduncles are useful indicators of neurological ataxia in cerebellar pathology.[4–6] Among the three cerebellar peduncles (superior, middle, and inferior cerebellar peduncle), the inferior cerebellar peduncle (ICP) consists of fibers of the olivocerebellar and dorsal spinocerebellar tracts. The olivocerebellar tract is mainly involved in coordination of movement, and the spinocerebellar tract is mainly involved in rapidly conducting the accompanying proprioceptive information.[7] Because of its involvement in the coordination of movement and proprioceptive information, ICP injury can be accompanied by ataxia, which means lack of voluntary coordination of muscle movements and loss of sensitivity to the positions of joints and body parts.[5,7–9] Therefore, elucidating the relationship between ataxia and ICP injury following brain injury would be important in terms of rehabilitation in patients with ataxia. However, no study on this topic has been reported so far.

The ICP is a major neural tract in the cerebellum involved in coordination of movement and proprioceptive information with other cerebellar peduncles. Therefore, ICP injury can be accompanied by poor coordination of movement, including ataxia and balance problems.[5,9] Use of diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), has enabled 3-dimensional reconstruction of the ICP.[10] Several studies have demonstrated injury of the ICP after brain injury using DTT.[5,7–9,11,12]. However, only a few case studies have demonstrated ICP injury in cerebral infarct.[5,7] In the current study, using DTT, we investigated the relationship between ataxia and ICP injury in patients with cerebral infarct.

2. Methods

2.1. Subjects

Fourteen stroke patients (10 males, 4 females, mean age 62.28 years, range 43–78), and 12 age and sex-matched control subjects (8 males, 4 females, mean age 65.81 years, range 45–75) with no history of neurological or psychiatric disease were recruited for this study.

Stroke patients were recruited according to the following inclusion criteria: first-ever stroke; age 20 to 80 years; an available DTI scan and clinical data collected during the early stage after onset (1–5 weeks after onset); infarction confined to the brainstem (pons and medulla) and cerebellum in T2-weighted brain MRI (Fig. 1A); and patients who showed ataxia after the onset of stroke. Patients with apraxia, somatosensory problems, and severe cognitive problems (Mini-Mental State Examination <25) were excluded. The study protocol was approved by the institutional review board of the Yeugnam University Hospital, and written informed consent was obtained from the participants of study.

2.2. Clinical evaluation

The Score of Assessment and Rating of Ataxia (SARA) was used to evaluate ataxia in the patient group. This scale consists of 8 items related to gait (0–8 points), stance (0–6 points), sitting (0–4 points), speech disturbance (0–6 points), finger-chase test (0–4 points), nose-finger test (0–4 points), fast alternating hand
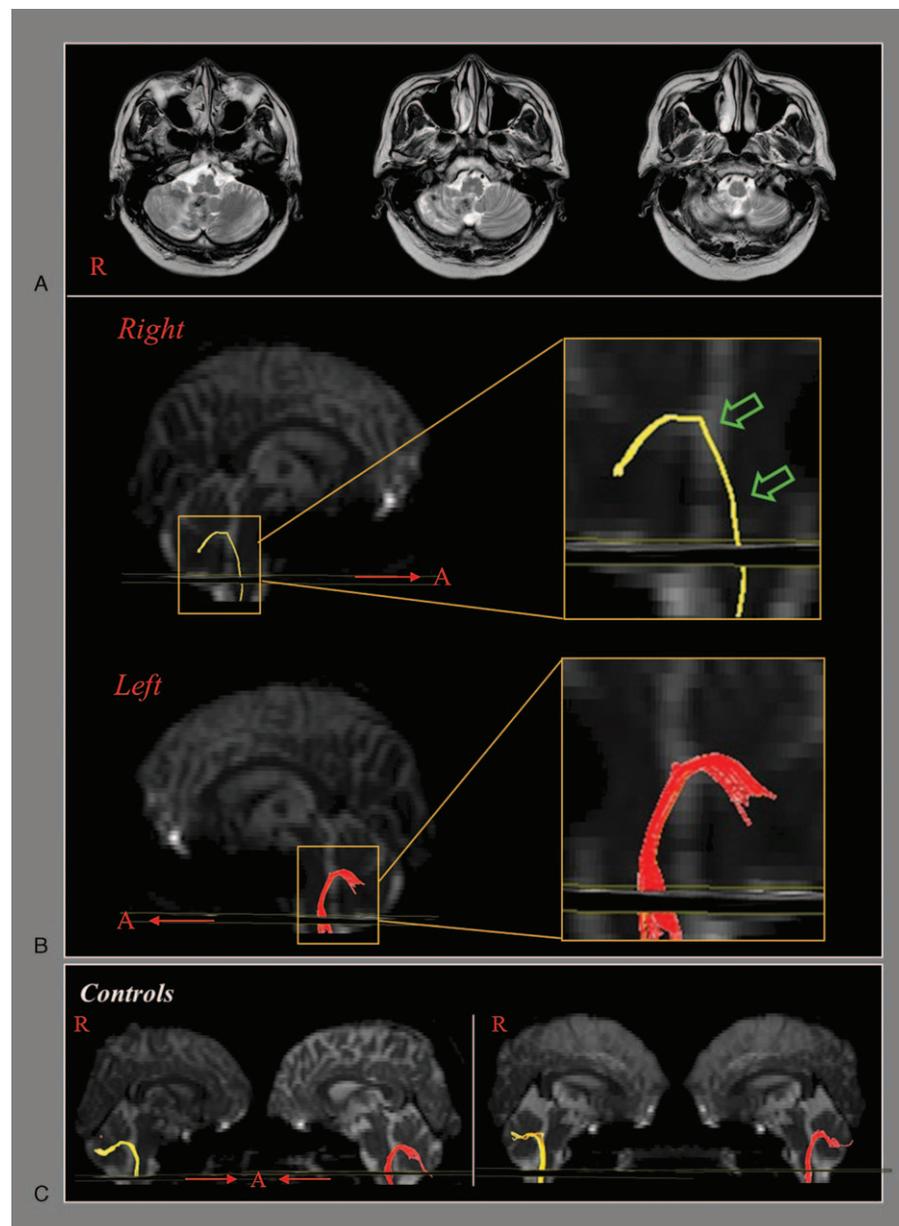
Figure 1. (A) T2-weighted brain magnetic resonance images show an infarct in the right cerebellum in a representative patient (61-year-old female). (B) Diffusion tensor tractography (DTT) results of the inferior cerebellar peduncle (ICP) in the above patient showed narrowing (green arrows) on the right side compared with the left side and compared with control subjects. (C) DTT results for the ICP in 2 representative control subjects (58-year-old female and 60-year-old female).

movement (0–4 points), and heel-shin test (0–4 points).[13] Once each of the 8 categories was assessed, the total was calculated to determine the severity of ataxia. The cumulative score of these 8 categories can range from 0 (no ataxia) to 40 (most severe ataxia). Both the reliability and validity of SARA are well established.[14,15]

2.3. Diffusion tensor imaging

The DTI data were acquired an average of 4.13 ± 1.84 weeks after onset, using a 1.5-T Philips Gyroscan Intera system (Philips Ltd, Best, Netherlands) equipped with a Synergy-L Sensitivity Encoding (SENSE) head coil and using a single-shot, spin-echo planar imaging pulse sequence. For each of the 32 noncollinear diffusion sensitizing gradients, 60 contiguous slices were acquired parallel to the anterior commissure-posterior commissure line. Imaging parameters were as follows: acquisition matrix $= 96 \times 96$, reconstructed to matrix $= 192 \times 192$, field of view $= 240$ mm $\times 240$ mm, TR $= 10,398$ ms, TE $= 72$ ms, parallel imaging reduction factor (SENSE factor) $= 2$, EPI factor $= 59$, and $b = 1000$ s/mm^2, NEX $= 1$, thickness $= 2.5$ mm. Before the fiber tracking, eddy current correction was applied using the FMRIB Software Library to correct the head motion effect and image distortion. DTI-Studio software (CMRM, Johns Hopkins Medical Institute, Baltimore, MD) based on deterministic tracking was used for fiber tracking.[16] For reconstruction of the ICP, 2 regions of interest (ROIs) were used on the axial image with a color map (blue: superioinferior orientation; red: mediolateral orientation; green: anteroposterior orientation). The first ROI was placed on the restiform body (blue portion) of the medulla and the second ROI was on the caudal portion of the superior cerebellar peduncle (green portion) with the option of "AND" operation.[9] The fiber tracking started at the center of a seed voxel with a fractional anisotropy (FA) of <0.2 and a tract turning-angle of $<60°$. DTT parameters including the FA, apparent diffusion coefficient (ADC), and fiber number (FN) of the ICP were measured using DTI-Studio software.

2.4. Statistical analysis

Statistical analyses were performed using SPSS software (v. 20.0; SPSS, Chicago, IL). The Mann–Whitney test was used for comparison of each DTT parameter (values of FA, ADC, and FN) between hemispheres of the patient group (affected and unaffected) and the control group. Relationships between SARA

and DTT parameters of the ICP were determined using the Pearson correlation test. The level of statistical significance was set at P value $<.05$.

3. Result

A summary of results for DTT parameters of the patient (Fig. 1B) and control groups (Fig. 1C), and correlation of the patient affected hemisphere of the ICP and SARA score are shown in Table 1. Significant differences were observed in the values of the FA and FN of the ICP between the affected hemisphere and the control groups ($P < .05$). However, no significant differences were observed in the values of FA and FN of the ICP in the unaffected hemisphere and the control groups ($P > .05$). In addition, no significant difference was observed in the ADC value of the ICP between the patient and control groups ($P > .05$).

In correlation analysis between the SARA and DTT parameters of the ICP in the affected hemisphere, negative correlation was observed between the SARA and the FN value of the ICP in the affected hemisphere ($r = -0.538$, $P < .05$). However, no significant correlations were observed between the SARA and the FA and ADC values in both hemispheres or the FN value in the unaffected hemisphere ($P > .05$).

4. Discussion

In the current study, we investigated the relationship between the SARA and ICP injury in patients with cerebral infarct. Our results can be summarized as follows: in the DTT parameters, the FA and FN values of the ICP in the affected hemisphere in the patient group were lower than those of the control group; in the correlation analysis, the FN value of the ICP in the affected hemisphere showed moderate negative correlation with the SARA. The FA value indicates the degree of directionality of water diffusion; thus, representing the degree of directionality and integrity of white matter microstructures, such as axons, myelin, and microtubules, while the ADC value indicates the magnitude of water diffusion.[17,18] In contrast, the FN value indicates the existing number of voxels within a neural tract.[17–19] Therefore, a decrease in the value of FA or FN indicates an injury to the neural tract. Consequently, our results show that the values of FA and FN in the affected hemisphere of the patient group were significantly lower than those of the control group, indicating an injury of the ICP in the affected hemisphere of the patient group. Regarding the correlation

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Table 1

Diffusion tensor tractography parameters of the inferior cerebellar peduncle in the patient and control groups.

DTT parameters

Group	Hemisphere	FA	ADC	FN
Patient	Affected	0.39 (0.03)*	0.94 (0.10)	182.28 (69.09)*
	Unaffected	0.43 (0.04)	0.98 (0.16)	230.64 (49.05)
Control	Both	0.44 (0.04)	0.92 (0.08)	241.35 (53.50)

Correlation between SARA and DTT parameters

Affected hemisphere	FA	ADC	FN
SARA	0.448	0.817	−0.538†

Values represent mean (±standard deviation).

ADC = apparent diffusion coefficient, DTT = diffusion tensor tractography, FA = fractional anisotropy, FN = fiber number, SARA = Score of Assessment and Rating of Ataxia.

* Significant differences between the affected and unaffected hemisphere in the patient group and between the affected hemisphere of the patient group and both hemispheres of the control group ($P < .05$).

† Significant differences between SARA and unaffected hemisphere in the patient group ($P < .05$).

between ICP injury in the affected hemisphere and SARA, the SARA showed a moderate negative correlation with the FN value of the ICP in the affected hemisphere. These results indicate that the severity of ataxia correlated to the decreased FN of the ICP in the affected hemishpere and conversely that the degree of ICP injury correlated to the severity of ataxia.

Since the introduction of DTT, several studies have reported on ICP injury after various brain pathologies.[5,7–9,11,12]. However, only 2 case studies have reported on ICP injury in patients with cerebral infarct.[5,7] In 2003, Yamada et al[7] reported Wallerian degeneration of the ICP in a patient with forward leaning posture and inability to walk after left lateral medulla infarct. In 2009, Hong et al[5] reported a case study including six patients with cerebellar infarct who showed poor balance due to ICP injury and injuries of the superior and middle cerebellar peduncles. As a result, to the best of our knowledge, the current study is the first to demonstrate a relationship between the severity of ataxia and ICP injury in patients with cerebral infarct. However, the limitations of this study should be considered. First, although ataxia might be related to various neural tracts, such as the superior cerebellar peduncle, middle cerebellar peduncle, dentate-rubro-thalamic tract, cortico-ponto-cerebellar tract, and medial lemniscus, these tracts were not examined because the main purpose of this study was to describe ICP injury in cerebral infarct. Therefore, further studies involving the above neural tracts would be necessary. Furthermore, further prospective studies on the clinical differences of ataxia according to injury of the neural tracts which are related to ataxia should be elucidated. Second, DTT could lead to both false positives and false negatives throughout the white matter of the brain due to multiple fiber directions in a voxel or partial volume effects.[20] Last, as this study was conducted retrospectively, we were not able to evaluate detailed clinical data for the ICP injury.

In conclusion, we found that the ataxia severity was closely related to the injury severity to the ICP in patients with cerebral infarct. Our results suggest that the evaluation of the ICP using DTT would be useful for patients with ataxia following cerebral infarct.

Author contributions

Sung Ho Jang: Study concept and design, Manuscript development and writing, Han Do Lee: Acquisition and analysis of data, Manuscript authorization and writing

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