Neuroscience Letters 665 (2018) 147–151

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Research article

Lateral medullary syndrome following injury of the vestibular pathway to the core vestibular cortex: Diffusion tensor imaging study

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ARTICLE INFO

Keywords:
Lateral medullary syndrome
Wallenberg syndrome
Parieto-insular vestibular cortex
Central vestibular disorder
Diffusion tensor imaging

ABSTRACT

Objective: The parieto-insular vestibular cortex (PIVC) is a core region of vestibular input into regions of the cortex. The vestibular nuclei have reciprocal connections with the PIVC. However, little is known about injury of the core vestibular pathway to the PIVC in patients with dorsolateral medullary infarctions. In this study, using diffusion tensor tractography (DTT), we investigated injury of the neural connections between the vestibular nuclei and the PIVC in patients with typical central vestibular disorder.

Methods: Eight consecutive patients with lateral medullary syndrome and 10 control subjects were recruited for this study. To reconstruct the core vestibular pathway to the PIVC, we defined the seed region of interest (ROI) as the vestibular nuclei of the pons and the target ROI as the PIVC. Fractional anisotropy (FA), mean diffusivity (MD), and tract volume were measured.

Result: The core vestibular pathway to the PIVC showed significantly lower tract volume in patients compared with the control group ($p < 0.05$). By contrast, other DTI parameters did not show significant differences between the patient and control groups ($p > 0.05$).

Conclusion: In conclusion, injury of the core vestibular pathway to the PIVC was demonstrated in patients with lateral vestibular syndrome following dorsolateral medullary infarcts. We believe that analysis of the core vestibular pathway to the PIVC using DTT would be helpful in evaluating patients with lateral medullary syndrome.

1. Introduction

The human vestibular system plays a key role in motion perception, eye movements, and posture control, and provides the brain with sensory signals concerning three-dimensional head rotations and translations [4]. These complex functions require integration of vestibular inputs with signals from other sensory modalities, such as vision and somatosensation [19]. The central vestibular system has three major connections: between (1) the vestibular nerve and the vestibular nucleus in the brainstem, (2) the vestibular nucleus in the brainstem and the thalamic nuclei, and (3) the thalamic radiation to the core vestibular cortex [10,19].

In previous studies, researchers identified major regions of the vestibular cortex in the human brain [8,13,26]. These areas are found in the Sylvian fissure, cingulate cortex, superior temporal gyrus, precuneus, prefrontal cortex, and frontal eye field. In addition, the parieto-insular vestibular cortex (PIVC) is known to be a core region of vestibular input into cortical regions; it is located in the posterior parietal operculum/retroinsular region and extends into posterior sections of the insular lobe [9,12]. The PIVC is involved in processing of self-motion perception, estimation of verticality, and processing of visual motion, particularly motion coherent with gravitational vector [14,19,22]. Hence, the human vestibular system has an important reciprocal connection with the PIVC; the PIVC has ipsilateral connection with vestibular nuclei through the posterolateral thalamus and paramedian thalamus, and also has contralateral connection though the brain stem structure [17]. Recent developments in diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), allow visualization and localization of neural tracts at the subcortical level in three dimensions. Many DTT studies have identified and visualized the human vestibular system at subcortical levels, such as the level of the vestibulospinal tract and neural connections of the vestibular nuclei [1,16,17]. However, no study has yet reported on injuries to the core vestibular pathway to the PIVC in patients with lateral medullary infarctions. In this study, using DTT, we attempted to investigate the neural connectivity of the PIVC in patients with lateral

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https://doi.org/10.1016/j.neulet.2017.12.010
Received 11 January 2017; Received in revised form 30 November 2017; Accepted 4 December 2017
Available online 05 December 2017
0304-3940/

Table 1
Demographic and clinical characteristics of the patients with lateral medullary syndrome.

Patient	Sex/Age	Duration to DTI (days)	Location of lesion	Central vestibular disorder			
				Vertigo	Ataxia	Dysarthria	Dysphagia
1	M/47	15	Left dorsal medulla	+	−	+	+
2	F/70	21	Left dorsolateral medulla	+	−	−	−
3	F/76	11	Right dorsolateral medulla	+	+	−	+
4	M/73	10	Right dorsal medulla	+	+	+	+
5	F/54	13	Left dorsolateral medulla	+	+	−	+
6	M/77	21	Left dorsolateral medulla	+	+	+	+
7	M/63	17	Right dorsolateral medulla	−	−	−	+
8	F/54	17	Right dorsolateral medulla	+	+	−	−

DTI: diffusion tensor imaging.

medullary syndrome.

2. Subjects and methods

2.1. Subjects

Eight patients with lateral medullary syndrome (4 males, 4 females; mean age, 63.4 years; range, 47–77 years) and 10 age-and sex-matched control subjects (5 males, 5 females; mean age, 58.3 years; range, 41–77 years) with no history of neurological or psychiatric disease were enrolled in this study. Stroke patients were consecutively enrolled from 26 patients with medullary infarcts according to the following inclusion criteria: (1) first-ever stroke, (2) age: 20–80 years, (3) subacute stage of infarct, (4) location of infarction confined to the dorsolateral medulla, and (5) patients with typical central vestibular disorder (vertigo, ataxia, dysarthria, or dysphagia). Patients with severe cognitive problems (Mini-Mental State Examination < 25) were excluded. Data were assembled retrospectively, and the local ethics committee of a Yeungnam University Hospital approved the study protocol.

2.2. Diffusion tensor imaging

Acquisition of DTI data was performed at an average of 14 days (range: 10–21) after symptom onset using a 6-channel head coil on a 1.5 T Philips Gyro Scan Intera (Philips, Best, The Netherlands) and single-shot echo-planar imaging. For each of the 32 non-collinear diffusion sensitizing gradients, 67 contiguous slices were acquired parallel to the anterior commissure/posterior commissure line. The imaging parameters were as follows: acquisition matrix = 96 × 96; reconstructed matrix = 192 × 192; field of view = 240 × 240 mm^2; TR = 10,726 ms; TE = 76 ms; parallel imaging reduction factor (SENSE factor) = 2; EPI factor = 49; b = 1000 s/mm^2; NEX = 1; and slice thickness = 2.5 mm with no gap (acquired voxel size 1.3 × 1.3 × 2.5 mm^3) [15,23].

2.3. Probabilistic fiber tracking

Diffusion-weighted imaging data were analyzed using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL; www.fmrib.ox.ac.uk/fsl). Affine multi-scale two-dimensional registration was used to correct the head motion effect and image distortion due to eddy current. Fiber tracking used a probabilistic tractography method based on a multifiber model, and was applied in the present study with tractography routines implemented in FMRIB Diffusion (5000 streamline samples, 0.5 mm step lengths, curvature thresholds = 0.2).

The core vestibular pathway to the PIVC was determined by selection of fibers passing through the seed region and two target regions of interest (ROIs). To reconstruct the core vestibular pathway to the PIVC, we placed the seed ROI on the vestibular nuclei at the level of the pons corresponding to Schwalbe's nucleus and Deiters' nucleus, and the target ROI on the PIVC, based on a previous study [17]. There were 5000 samples generated from the seed voxel, and the results were visualized at the threshold of 1 streamline through each voxel for analysis. Fractional anisotropy (FA), mean diffusivity (MD), and tract volume of the core vestibular pathway to the PIVC were measured.

2.4. Statistical analysis

SPSS software (Released 2011. IBM SPSS Statistics for Windows, Version 20.0. IBM Corp., Armonk, NY) was used for data analysis. The Kruskal-Wallis with post-hoc Mann-Whitney test was used to determine the differences in values of DTI parameters between patients and normal subjects. Null hypotheses of no difference were rejected if p-values were less than 0.05.

3. Result

A summary of the demographic and clinical characteristics of the patients with lateral medullary syndrome is shown in Table 1. All patients exhibited typical central vestibular signs in subacute stages; vertigo (n = 7, 88%), ataxia (n = 5, 63%), dysarthria (n = 3, 38%) and dysphagia (n = 6, 75%). In the result of DTT, the patient group showed relatively lower connectivity between the vestibular nuclei and the PIVC, compared with normal control group (Fig. 1). The results of statistical comparisons for DTT parameters of the core vestibular pathway to the PIVC are summarized in Table 2. The FA and MD values of the core vestibular pathway to the PIVC did not differ significantly between the patient group and the control group ($p > 0.05$). In contrast, the tract volume of the core vestibular pathway to the PIVC was significantly lower in the patient group compared with the control group ($p < 0.05$).

4. Discussion

In this study, we enrolled eight patients with dorsolateral medullary infarcts who showed signs of typical central vestibular disorder. The tract volume of both core vestibular pathways to the PIVC was lower in patients than in controls. By contrast, the FA and MD value were not different between patients and controls. The neurological meaning of each DTI parameter is as follows: FA, degree of directionality of microstructures; MD, magnitude of water diffusion in tissue; and tract volume, number of voxels contained within a neural tract [2,21]. Therefore, a significant decrement of tract volume of the core vestibular pathway to the PIVC on both sides appeared to indicate interruption of bilateral core vestibular pathways to the PIVC caused by dorsolateral medullary infarcts.

Many previous animal studies revealed the vestibular pathways between the vestibular nuclei and the PIVC. The course of the vestibular pathways is known to form bilateral connections from the vestibular