Clinical Case Report

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Aggravation of excessive daytime sleepiness concurrent with aggravation of an injured ascending reticular activating system in a patient with mild traumatic brain injury

A case report

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Abstract

Background: We report on a patient who developed aggravation of excessive daytime sleepiness (EDS) concurrent with aggravation of an injured ascending reticular activating system (ARAS) following mild traumatic brain injury (TBI), demonstrated by follow-up diffusion tensor tractographies (DTTs).

Methods: A 42-year-old male patient experienced head trauma resulting from flexion-hyperextension injury after collision with another vehicle from behind while stopped at an intersection. The patient lost consciousness for approximately 10 seconds and experienced no post-traumatic amnesia following the accident. The patient's Glasgow Coma Scale score was 15. No specific lesion was observed on the conventional brain MRI performed at 10 weeks after onset. The patient complained of EDS after the head trauma and aggravation of EDS with passage of time. The Epworth Sleepiness Scale indicated abnormality with a score of 12 at 10 weeks after onset (cut-off: 10 points full mark: 24 score) and it was aggravated with a score of 18 at 16 months.

Results: On 10-week DTT, decreased neural connectivity of the intralaminar thalamic nucleus to the prefrontal cortex and basal forebrain was observed in both hemispheres. However, no significant abnormality was observed in the dorsal and ventral lower ARAS. On 16-month DTT, the upper portion of the left dorsal lower ARAS showed partial tearing and the ventral lower ARAS showed thinning (both sides) and partial tearing (right side).

Conclusions: Aggravation of EDS concurrent with aggravation of an injured ARAS was demonstrated in a patient with mild TBI using DTT.

Abbreviations: ARAS = ascending reticular activating system, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, EDS = excessive daytime sleepiness, ESS = Epworth Sleepiness Scale, ILN = intralaminar thalamic nucleus, ROI = region of interest, TBI = traumatic brain injury.

Keywords: ascending reticular activating system, diffusion tensor tractography, hypersomnia, mild traumatic brain injury

1. Introduction

Excessive daytime sleepiness (EDS) is a common sequela of traumatic brain injury (TBI).[1] Because EDS is related to poor daytime function, elucidation of its pathogenetic mechanism is important.[2] However, the pathogenesis of EDS has not been clearly elucidated. Since the recent development of diffusion tensor tractography (DTT), derived from diffusion tensor imaging (DTI), for the ascending reticular activating system (ARAS), several studies have demonstrated that injury of the ARAS was related to EDS in a few brain pathologies, including TBI, subarachnoid hemorrhage, and intracerebral hemorrhage[3–6]; however, it has not been clearly elucidated so far.

In the present study, we report on a patient who developed aggravation of EDS concurrent with aggravation of an injured ARAS following mild TBI, demonstrated by serial DTTs.

2. Case report

A 42-year-old male patient experienced head trauma resulting from flexion-hyperextension injury after collision with another vehicle from behind while stopping at an intersection in his vehicle. No previous medical history of neurological, physical, or psychiatric illness was noted before head trauma. The patient lost consciousness for approximately 10 seconds and experienced no post-traumatic amnesia at 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 10 weeks after the crash.

Editor: Massimo Tusconi.

The authors have no conflicts of interest to disclose.

This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIP) (NRF-2015R1A2A2A01004073).

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Medicine (2017) 96:4(e5958)

Received: 25 February 2016 / Received in final form: 22 October 2016 / Accepted: 31 December 2016

http://dx.doi.org/10.1097/MD.0000000000005958

Table 1

Epworth Sleepiness Scale for the patient.

No	Situation	Score (0~3)	
		10 wk	16 mo
1	Sitting and reading	2	2
2	Watching TV	2	2
3	Sitting, inactive in a public place (e.g., a theater or a meeting)	2	3
4	As a passenger in a car for an hour without a break	1	2
5	Lying down to rest in the afternoon when circumstances permit	2	3
6	Sitting and talking to someone	0	2
7	Sitting quietly after lunch without alcohol	2	3
8	In a car, while stopped for a few minutes in traffic	1	1
	Total	12	18

The patient complained of EDS after the head trauma and aggravation of EDS with the passage of time. As a result, he frequently felt difficulty in performing activities of daily life because of EDS; working or watching a movie. The Epworth Sleepiness Scale (ESS) indicated abnormality with a score of 12 at 10 weeks after onset (cut-off: 10 points full mark: 24 score), aggravated to a score of 18 at 16 months after onset (Table 1).[7] For treatment, he underwent comprehensive rehabilitative treatment, including administration of neurotrophic drugs (modafinil: 200 mg, ropinirole: 0.25 mg, amantadine: 100 mg, choline aldoscerate; 400 mg, paroxetine HCI: 12.5 mg, alprazolam: 0.25 mg), physical and occupational therapy sessions 5 times per week (60 min/day). The patient signed an informed consent statement and the study protocol was approved by the Yeungnam University hospital Institutional Review Board of a university hospital.

2.1. DTI

DTI data were acquired twice at 10 weeks and 16 months after the head trauma using a 1.5T Philips Gyroscan Intera with 32 non-collinear diffusion sensitizing gradients by single-shot echo-planar imaging. Imaging parameters were as follows: acquisition matrix = 96×96; reconstructed to matrix = 192×192; field of view = $240 \times 240\,mm^2$; TR = 10,398 ms; TE = 72 ms; parallel imaging reduction factor = 2; echo-planar imaging factor = 59; b = $1000\,s/mm^2$; and a slice thickness of 2.5 mm. The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library was used for analysis of DTI data. Affine multiscale 2-dimensional registration was used to correct the head motion effect and image distortion because of the eddy current. FMRIB Diffusion Software with routines option (0.5 mm step lengths, 5000 streamline samples, curvature thresholds = 0.2) was used for fiber tracking. Three portions of the ARAS were reconstructed by selecting fibers passing through regions of interest (ROIs) as follows:[8–10] the dorsal lower ARAS, between the pontine reticular formation (ROI 1) and the intralaminar thalamic nucleus (ILN, ROI 2),[8] the ventral lower ARAS, between the pontine reticular formation (ROI 1) and the hypothalamus (ROI 2),[10] and the upper ARAS, in which the neural connectivity of the ILN (ROI 1) to the cerebral cortex was analyzed.[9]

On 10-week DTT, decreased neural connectivity of the ILN to the prefrontal cortex and basal forebrain was observed in both hemispheres. However, no significant abnormality was observed in the dorsal and ventral lower ARAS. By contrast, on 16-month DTT, the upper portion of the left dorsal lower ARAS showed partial tearing and the ventral lower ARAS showed thinning (both sides) and partial tearing (right side) (Fig. 1).

3. Discussion

According to the international classification of sleep disorders by the American Academy of Sleep Medicine, this patient's diagnosis was posttraumatic EDS because he developed EDS after head trauma and experienced frequent daily sleep episodes.[11] The degree of EDS increased from 12 (ESS score) at 10 weeks to 18 (ESS score) at 16 months after onset. Although only decreased neural connectivity in the prefrontal cortex and basal forebrain was observed on 10-week DTT, aggravation of the left dorsal lower ARAS and both ventral lower ARAS was observed on 16-month DTT. As a result, it appeared that EDS in this patient was at least in part attributable to injury of the ARAS caused by traumatic axonal injury because no specific lesion was observed on the conventional brain MRI.[12] Considering recent studies reporting that injury of the ventral lower ARAS is closely related to hypersomnia, it appeared that the injury of the ventral lower ARAS was the most important contributor to aggravation of EDS in this patient, although injuries of the upper ARAS and lower dorsal lower ARAS were also observed.[3–6] In addition, the aggravation of EDS and delayed appearance of injury of the dorsal and ventral lower ARAS in this patient suggest that the traumatic axonal injury might partially result from secondary injury. In this condition, axons were not damaged at the time of injury, but undergo axonal injury by a sequential process of impaired axoplasmic transport, continued axonal swelling, and subsequent disconnection.[13]

Since the introduction of DTI, several studies using DTT have demonstrated the association of hypersomnia and injury of the ARAS.[3–6] In 2015, Jang et al[3] reported on a patient with narcolepsy who showed injury of the ventral lower ARAS following mild TBI. Subsequently, a study demonstrated recovery from hypersomnia with recovery of injured dorsal and ventral (more recovery than the dorsal lower ARAS) lower ARAS in a patient with subarachnoid hemorrhage.[4] Recently, Jang et al reported on patients with hypersomnia and injury of the dorsal and ventral (more injury than the lower dorsal ARAS) lower ARAS in patients with pontine hemorrhage (1 patient) and mild TBI (2 patients), respectively.[5,6] These studies suggest that injury of the ARAS could be a probable cause for the hypersomnia in patients with brain injury particularly TBI. In addition, analysis of the ARAS using DTT might contribute to understanding the prognosis of EDS. To the best of our knowledge, this is the first study to demonstrate an association between aggravation of EDS and worsening injury of the lower ARAS in patients with brain injury. However, the limitations of this study should be considered. First, because it is a case report, this study is limited; therefore, conduct of further studies comprising a large number of patients is necessary. Second, because regions of fiber complexity and crossing can prevent full reflection of the underlying fiber architecture, DTT may underestimate the neural fiber tracts.[14] Third, we were not able to measure the degree of EDS using an objective measure such as the Multiple Sleep Latency Test.[11] Therefore, conduct of further studies including an objective measure such as the Multiple Sleep Latency Test should be encouraged.

In conclusion, aggravation of EDS concurrent with aggravation of an injured ARAS was demonstrated in a patient with mild TBI using DTT. These results suggest that evaluation of the ARAS

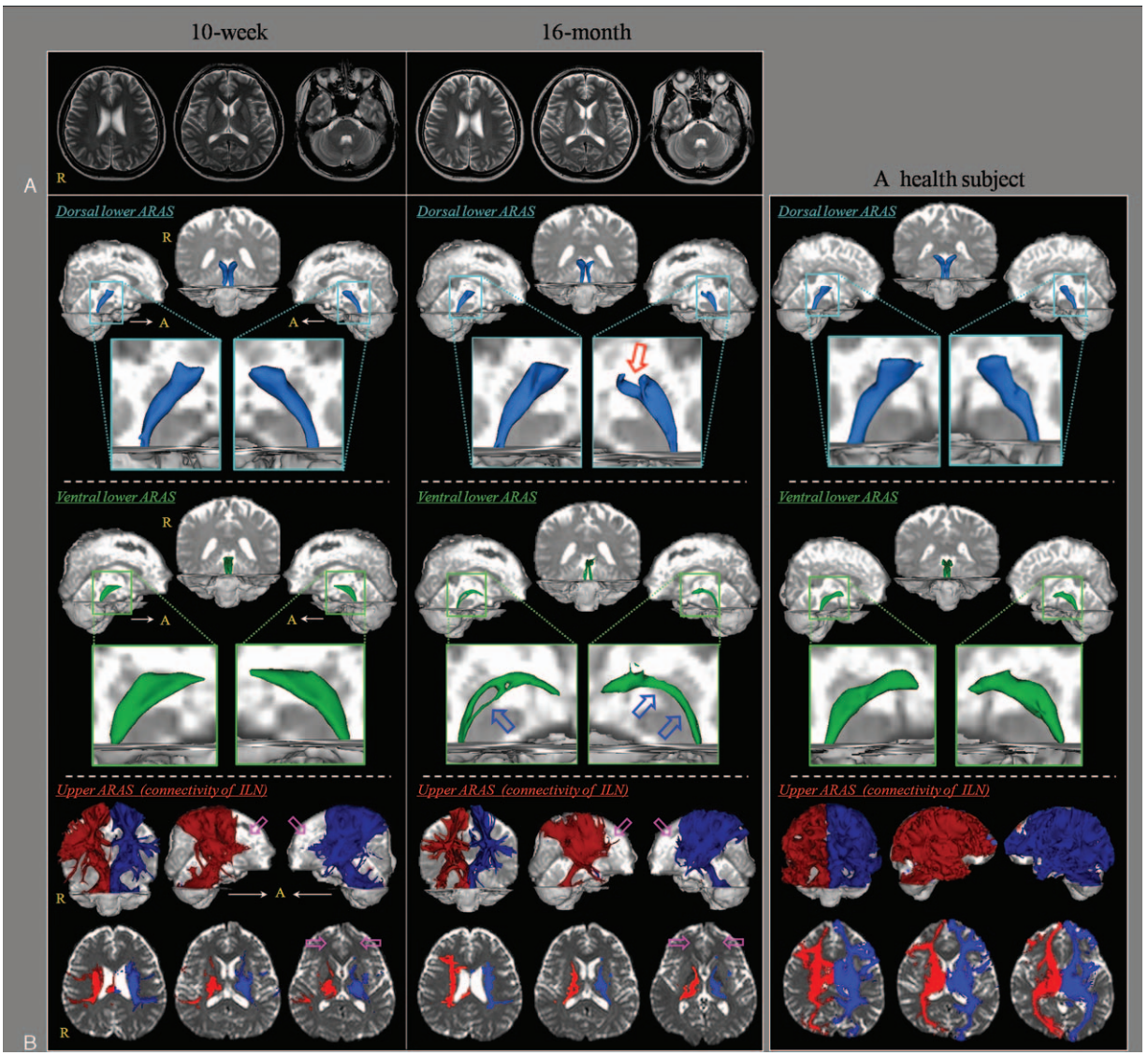

Figure 1. (A) Brain MR images at 10 weeks and 16 months after onset show no abnormal lesions. (B) Results of diffusion tensor tractography (DTT) for the ascending reticular activation system (ARAS). On 10-week DTT, decreased neural connectivity of the intralaminar thalamic nucleus to the prefrontal cortex and basal forebrain is observed in both hemispheres (purple arrows). However, no significant abnormality is observed in the dorsal and ventral lower ARAS. On 16-month DTT, the upper portion of the left dorsal lower ARAS shows partial tearing (red arrow) and the ventral lower ARAS shows thinning in both hemispheres and partial tearing in the right hemisphere (blue arrows). Results of DTT for the ARAS in a health subject (45 year-old male). ARAS = ascending reticular activation system, DTT = diffusion tensor tractography, ILN = intralaminar thalamic nucleus.

using follow-up DTTs might be useful for patients who show change of EDS following brain injury particularly TBI.

Acknowledgements

None.

References

[1] Ouellet MC, Beaulieu-Bonneau S, Morin CM. Sleep-wake disturbances after traumatic brain injury. Lancet Neurol 2015;14:746–57.
[2] Castriotta RJ, Murthy JN. Sleep disorders in patients with traumatic brain injury: a review. CNS Drugs 2011;25:175–85.
[3] Jang SH, Seo WS, Kwon HG. Post-traumatic narcolepsy and injury of the ascending reticular activating system. Sleep Med 2016;17:1–2.
[4] Jang SH, Lee HD, Chang CH, et al. Recovery of hypersomnia concurrent with recovery of an injured ascending reticular activating system in a stroke patient. Medicine 2016;95:e2484.
[5] Jang SH, Chang CH, Jung YJ, et al. Post-stroke hypersomnia. Int J stroke 2016;11:N5–6.
[6] Jang SH, Kwon HG. Injury of the ascending reticular activating system in patients with fatigue and hypersomnia following mild traumatic brain injury: two case report. Medicine (Baltimore) 2016;95: e2628.
[7] Bloch KE, Schoch OD, Zhang JN, et al. German version of the Epworth Sleepiness Scale. Respiration 1999;66:440–7.
[8] Yeo SS, Chang PH, Jang SH. The ascending reticular activating system from pontine reticular formation to the thalamus in the human brain. Front Hum Neurosci 2013;7:416.
[9] Jang SH, Lim HW, Yeo SS. The neural connectivity of the intralaminar thalamic nuclei in the human brain: a diffusion tensor tractography study. Neurosci Lett 2014;579:140–4.

[10] Jang SH, Kwon HG. The ascending reticular activating system from pontine reticular formation to the hypothalamus in the human brain: a diffusion tensor imaging study. Neurosci Lett 2015;590:58–61.
[11] American Academy of Sleep Medicine. The international classification of sleep disorders: diagnostic and coding manual. 2nd edn. American Academy of Sleep Medicine, Westchester, Ill:2005.
[12] Alexander MP. Mild traumatic brain injury: pathophysiology, natura history, and clinical management. Neurology 1995;45:1253–60.
[13] Povlishock JT. Traumatically induced axonal injury: pathogenesis and pathobiological implications. Brain Pathol 1992;2:1–2.
[14] Yamada K, Sakai K, Akazawa K, et al. MR tractography: a review of its clinical applications. Magn Reson Med Sci 2009;8:165–74.