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Long-term recovery from a minimally responsive state with recovery of an injured ascending reticular activating system

A case report

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Abstract

We report on a patient with hypoxic-ischemic brain injury (HI-BI) who showed recovery from a minimally consciousness state over 6 years concurrent with recovery of an injured ascending reticular activating system (ARAS), which was demonstrated on diffusion tensor tractography (DTT).

A 31-year-old female patient, who suffered from HI-BI, showed impaired consciousness with a minimally conscious state: intermittently obeying simple motor tasks, such as "please grasp my hand." Her consciousness showed recovery with the passage of time; rapid recovery was observed during the recent 2 years.

In the upper ARAS, the neural connectivity to both the basal forebrain and prefrontal cortex had increased on 8-year DTT compared with 1.5-year DTT. In the lower dorsal and ventral ARAS, no significant change was observed between 1.5 and 8 years DTTs.

Recovery of an injured ARAS was demonstrated in a patient who showed recovery from a minimally consciousness state over 6 years following HI-BI. Our results suggest the brain target areas for recovery of impaired awareness in patients with disorders of consciousness.

Abbreviations: ARAS = ascending reticular activating system, CRS-R = Coma Recovery Scale-Revised, DOC = disorders of consciousness, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, FMRIB = Functional Magnetic Resonance Imaging of the Brain, GCS = Glasgow Coma Scale, HI-BI = hypoxic-ischemic brain injury, ROI = region of interest.

Keywords: Ascending reticular activating system, consciousness, diffusion tensor tractography, hypoxic-ischemic brain injury

1. Introduction

Disorders of consciousness (DOC) are ascribed to injury of the ascending reticular activating system (ARAS) following brain injury. Diffusion tensor tractography (DTT), which is reconstructed from diffusion tensor imaging (DTI) data, has enabled three-dimensional reconstruction and estimation of the ARAS in the human brain. Many recent studies using DTT have reported injury of the ARAS in patients with DOC, and a few studies using DTT have reported on recovery of an injured ARAS concurrent with improvement of impaired consciousness, however, it has not been clearly elucidated so far.[1–7]

In the present study, we report on a patient with hypoxic-ischemic brain injury (HI-BI) who showed recovery from a minimally consciousness state over 6 years concurrent with recovery of an injured ARAS, which was demonstrated on DTT.

2. Case report

A 31-year-old female patient who suffered from HI-BI induced by cardiac arrest while sleeping at night underwent cardiopulmonary resuscitation at the emergency room of a university hospital. After 1.5 years from onset, she was admitted to the rehabilitation department of our university hospital for rehabilitation, and no specific lesion was observed on T2-weighted images (Fig. 1A). The patient showed impaired consciousness with a minimally conscious state: intermittently obeying simple motor tasks, such as "please grasp my hand," Glasgow Coma Scale (GCS) score: 10 (eye opening: 3, best verbal response: 1, and best motor response: 6), and Coma Recovery Scale-Revised (CRS-R) score: 11 (auditory function: 2, visual function: 2, motor function: 4, verbal function: 1, communication: 1, and arousal: 1).[8–10] She underwent comprehensive rehabilitative therapy, which included neurotropic drugs (methylphenidate, amantadine, bromocriptine, pramipexole, and levodopa), physical therapy, and

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Editor: Elias Manjarrez.

This work was supported by the Medical Research Center Program (2015R1A5A2009124) through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT, and Future Planning.

The authors have no conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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How to cite this article: Jang SH, Kim SH, Seo JP. Long-term recovery from a minimally responsive state with recovery of an injured ascending reticular activating system: A case report. Medicine 2021;100:9(e23933).

Received: 17 September 2020 / Received in final form: 23 November 2020 / Accepted: 26 November 2020

http://dx.doi.org/10.1097/MD.0000000000023933

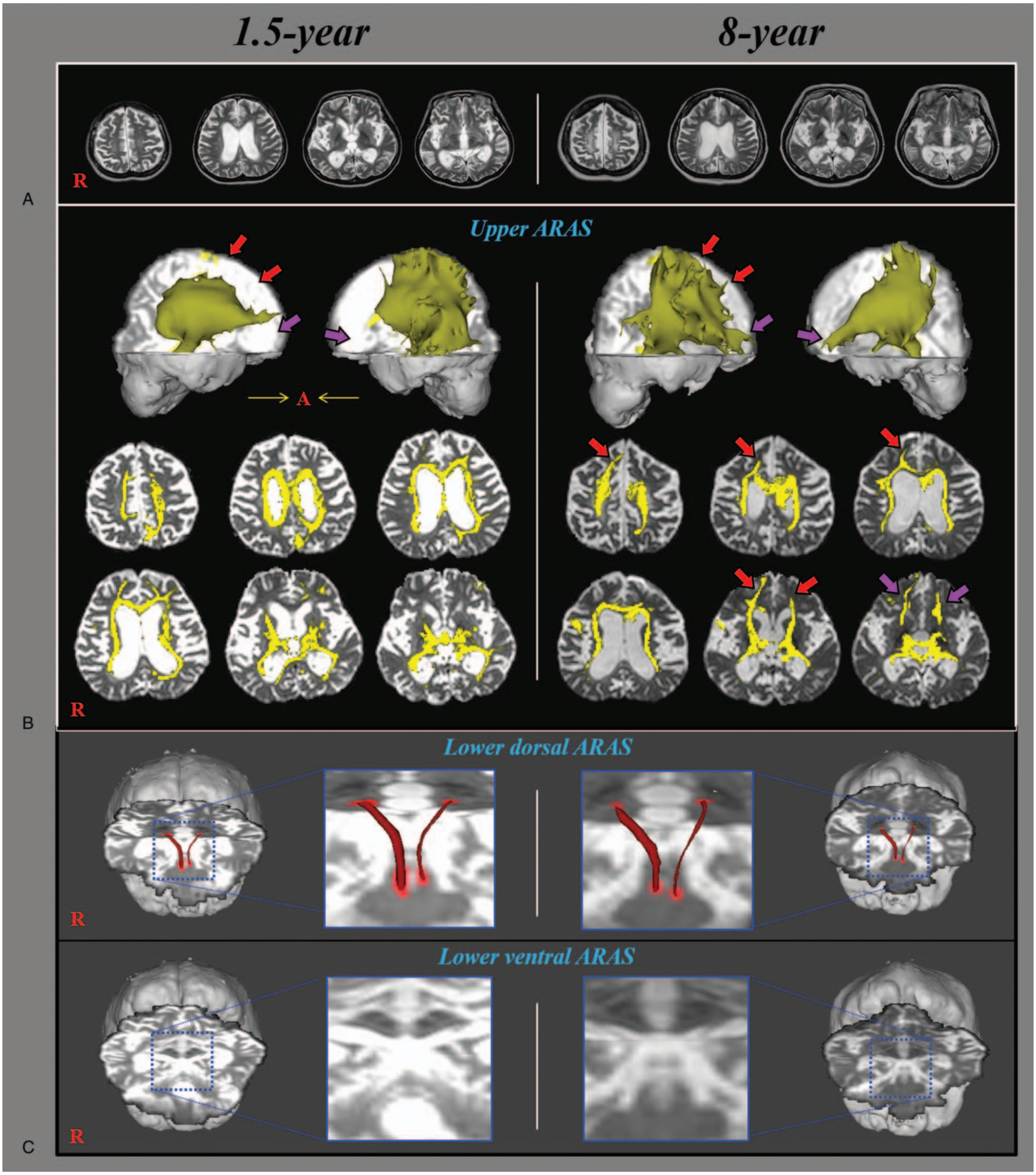

Figure 1. (A) T2-weighted MR images at 1.5 and 8 years after onset show no abnormality. (B) Results of diffusion tensor tractography (DTT). In the upper ascending reticular activating system (ARAS), the neural connectivity to both the basal forebrain (purple arrows) and prefrontal cortex (red arrows) is increased on 8-year DTT compared with 1.5-year DTT. In the lower dorsal and ventral ARAS, no significant change is observed between 1.5- and 8-year DTTs (thinner left lower dorsal ARAS and non-reconstructed both lower ventral ARAS).

occupational therapy for 1 month and continued similar rehabilitation at the outpatient clinic of the same university hospital until 8 years after onset. Her consciousness showed recovery with the passage of time; rapid recovery was observed during the recent 2 years. As a result, she was able to move her arm and leg spontaneously, and raise both hands over her head according to verbal command, and she laughs when her family members speak to her and listens when her family members read books to her. GCS score: 12 (eye opening: 4, best verbal response: 2, and best motor response: 6) with a GRS-R score: 22 (auditory function: 4, visual function: 5, motor function: 6, verbal function: 2, communication: 2, arousal: 3).[8,10] The patient's mother provided signed, informed consent, and the study protocol was approved by our Institutional Review Board.

3. Diffusion tensor imaging

DTI data were acquired two times (1.5 and 8 years after onset) using a 6-channel head coil on a 1.5 T Philips Gyroscan Intera (Philips, Best, Netherlands) with 32 non-collinear diffusion sensitizing gradients by single-shot echo-planar imaging. Sixty-five contiguous slices were acquired parallel to the anterior commissure-posterior commissure line(reconstructed to matrix = 128×128, acquisition matrix = 96×96, field of view = $221 \times 221\,\text{mm}^2$, parallel imaging reduction factor = 2, b = $1000\,\text{s/mm}^2$, EPI factor = 49, TE = 76 ms, TR = 10,726 ms, NEX = 1, and a slice thickness of 2.3 mm. Using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL; www.fmrib.ox.ac.uk/fsl), analysis of DTI data was performed. For the eddy current, Affine multi-scale two-dimensional registration was used for correction of head motion effect and image distortion. A probabilistic tractography method based on a multifiber model was used for the fiber tracking.[11]

For analysis of the connectivity of the upper ARAS, the seed region of interest (ROI) was placed on the thalamic ILN at the level of the inter-commissural plane between the anterior and posterior commissures.[12] For analysis of the lower ARAS, seed and target ROI were as follows: the lower dorsal ARAS (seed ROI—the pontine reticular formation, target ROI—the intralaminar thalamic nucleus), the lower ventral ARAS (seed ROI—the hypothalamus, target ROI—the pontine reticular formation).[13,14] Results for fiber tracking were visualized at a threshold for the ARAS of 2 and for connectivity of the intralaminar nucleus of 15 streamlined through each voxel.[12–14]

In the upper ARAS, the neural connectivity to both the basal forebrain and prefrontal cortex had increased on 8-year DTT compared with 1.5-year DTT (Fig. 1B). In the lower dorsal and ventral ARAS, no significant change was observed between 1.5 and 8 year DTTs (thinner left lower dorsal ARAS and non-reconstructed both lower ventral ARAS) (Fig. 1C).

4. Discussion

In the present study, using DTT, change of the ARAS was evaluated in a patient who had recovered from a minimally conscious state following HI-BI. At 1.5 years after onset, she could obey simple motor tasks intermittently, however, at 8 years after onset, she could respond to other people by movements of limbs and laugh although she could not speak.[9] We attempted to estimate the ARAS according to three portions: the upper ARAS, the lower dorsal ARAS, and the ventral ARAS. We observed significant change in the upper ARAS (increased neural connectivity in both prefrontal cortex and basal forebrain) without change in the lower dorsal and ventral ARAS. As a result, we believe that the clinical recovery of this patient from a minimally conscious state was at least in part attributed to the increased neural connectivity of the prefrontal cortex and basal forebrain. In addition, our results on DTT appeared to coincide with the results of previous studies reporting on the neural structures responsible for the recovery in patients with disorders of consciousness.[4,7,15,16]

In conclusion, recovery of an injured ARAS was demonstrated in a patient who showed recovery from a minimally consciousness state over 6 years following HI-BI. Our results suggest the brain target areas for recovery of impaired awareness in patients with disorders of consciousness. Therefore, further studies to elucidate these target brain areas in large numbers of patients with various brain pathologies and for development of therapeutic strategies to facilitate the brain target areas, and to compare the present findings from the DTT with those of normal subjects should be encouraged. However, limitations of this study should also be considered. Regions of fiber complexity and crossing can prevent full reflection of the underlying fiber architecture by DTT; therefore, DTT may underestimate the fiber tracts.[17]

Author contributions

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Formal analysis: Jeong Pyo Seo.
Methodology: Jeong Pyo Seo.
Supervision: Sung Ho Jang.
Validation: Seong Ho Kim.
Writing – original draft: Jeong Pyo Seo.
Writing – review & editing: Sung Ho Jang.

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