

● IMAGING IN NEURAL REGENERATION

Multiple injuries of the ascending reticular activating system in a stroke patient: a diffusion tensor tractography study

Consciousness is mainly controlled by activation of the ascending reticular activating system (ARAS). Diffusion tensor tractography (DTT), which is reconstructed from diffusion tensor imaging (DTI) data, allows reconstruction and evaluation of the ARAS in the live human brain (Yeo et al., 2013; Jang et al., 2014; Jang and Kwon, 2015). Injury of the ARAS in various stroke pathologies including subarachnoid hemorrhage, cerebral infarct, intraventricular hemorrhage, and intracerebral hemorrhage has been investigated in many studies using DTT (Jang and Kim, 2015; Jang et al., 2015a, b, c; Jang and Seo, 2015). However, little is known about how the ARAS is injured when there are multiple stroke pathologies. Nonetheless, given its complicated and extensive neural structure, the ARAS is vulnerable to multiple brain pathologies.

A 58-year-old male was diagnosed with an intraventricular hemorrhage (IVH), a spontaneous subarachnoid hemorrhage (SAH), and an intracerebral hemorrhage (ICH) in the basal forebrain. He underwent clipping for a rupture of the anterior communicating artery aneurysm and frontal extraventricular drainage (EVD) for the IVH (Figure 1A). After 6 weeks from onset, he started rehabilitation at the same university hospital. The patient exhibited impaired alertness, with a Glasgow Coma Scale (GCS) score of 10 (best motor response = 6, best verbal response = 1, and eye opening = 3) and Coma Recovery Scale-Revised score of 13 (arousal = 2, verbal function = 0, visual function = 3, motor function = 5, communication = 0, and auditory function = 1) (Teasdale and Jennett, 1974; Giacino et al., 2004). Brain MR images at 6 weeks after onset showed multiple leukomalactic lesions in both fronto-parietal lobes (Figure 1B). Our institutional review board approved the study protocol, and the patient's wife provided signed informed consent.

Using a 1.5-T Philips Gyroscan Intera, DTI data were acquired at 6 weeks after onset. Sixty-five contiguous slices (total scanning time = 7 minutes and 32 seconds; repetition time = 10,726 ms; echo time = 76 ms; acquisition matrix = 96 × 96; reconstruction matrix = 192 × 192 matrix; number of excitations = 1; thickness = 2.5 mm; $b = 1,000 \text{ s/mm}^2$; and field of view = 240 × 240 mm²) were acquired. DTI data was analyzed using the Oxford Centre for FMRIB Software Library. For fiber tracking of the ARAS, FMRIB Diffusion Software with routines option (0.5 mm step lengths, 5,000 streamline samples, curvature thresholds: 0.2) was employed. Three portions of the ARAS were reconstructed by selection of the following regions of interest (ROIs): the dorsal lower ARAS (seed ROI - the pontine reticular formation (RF), target ROI - the intralaminar thalamic nucleus (ILN)) (Yeo et al., 2013), the ventral lower ARAS (seed ROI the pontine RF, target ROI - the hypothalamus) (Jang and Kwon, 2015), and the upper ARAS (seed ROI - the ILN), the neural connectivity of the ILN to the cerebral cortex (Jang et al., 2014). Each ROIs were drawn manually on $b = 0$ image map by experienced neuroimaging scientist.

On 6-week DTT images, narrowing of the right ventral lower ARAS was observed. In the upper ARAS, the neural connectiv-

ity between the thalamic ILN and the cerebral cortex was decreased in both basal forebrains and prefrontal cortices (Figure 1C).

In this study, using DTT, the three portions of the ARAS were evaluated: the dorsal lower ARAS, ventral lower ARAS, and upper ARAS. We observed narrowing of the right ventral lower ARAS, and decreased neural connectivity from the thalamic ILN to both prefrontal cortices and basal forebrains. The impaired consciousness of this patient appeared to be mainly ascribed to these multiple injuries of the ARAS. This patient had multiple pathologic conditions which could induce injury of the ARAS, including IVH, SAH, ICH, and the procedure for EVD. Considering previous studies (Jang and Kim, 2015; Jang et al., 2015b) on injury of the ARAS, the right ventral lower ARAS appeared to be injured by IVH and SAH, and the upper ARAS appeared to be mainly injured by ICH on the right side and EVD on the left side.

In conclusion, we report on a stroke patient who showed multiple injuries of the ARAS due to multiple brain pathologies. We believe that evaluation of the ARAS using DTT would be useful in elucidating injury of the ARAS and the pathogenetic mechanism of injury of the ARAS, particularly in stroke patients with multiple pathologies. Therefore, studies involving long-term follow-up DTT and clinical data should be encouraged.

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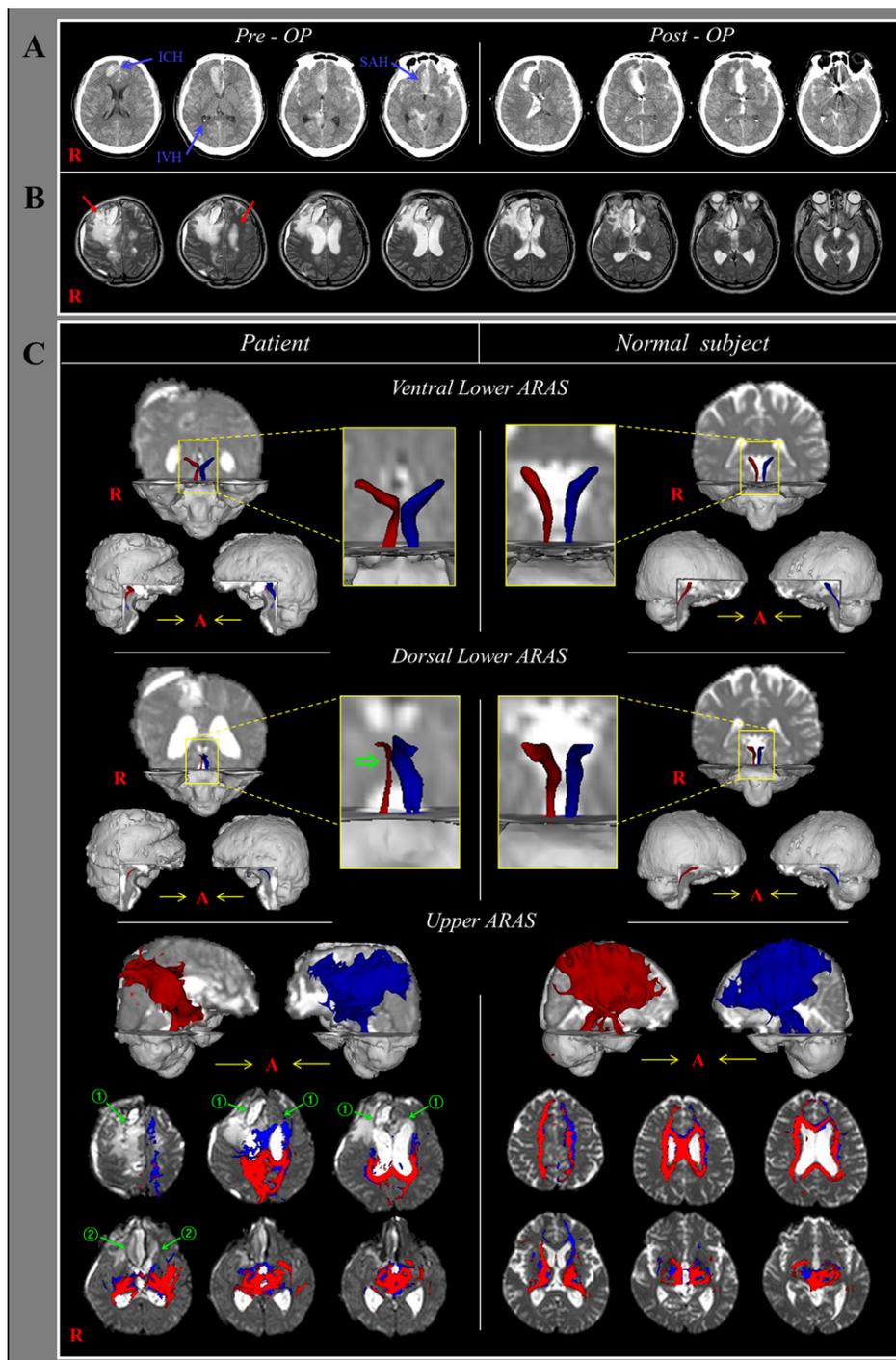


Figure 1 Brain CT, magnetic resonance images and diffusion tensor tractography (DTT) images of a 58-year-old male patient with multiple brain pathologies.

(A) Pre- (Pre-OP) and post-operative (Post-OP) brain CT images at onset show spontaneous subarachnoid hemorrhage, intraventricular hemorrhage, and intracerebral hemorrhage in the basal forebrain (blue arrows). (B) Brain MR images at 6 weeks after onset show multiple leukomalactic lesions (red arrows) in both fronto-parietal lobes. (C) Results of 6-week DTT for the ARAS. Narrowing (green arrow) of the right ventral lower ARAS between the pontine reticular formation and the hypothalamus is observed. In the upper ARAS, the neural connectivity between the thalamic intralaminar thalamic nucleus and the cerebral cortex is decreased (green arrows) in both prefrontal cortices (1) and basal forebrains (2). ARAS: Ascending reticular activating system; ICH: intracerebral hemorrhage; SAH: subarachnoid hemorrhage; IVH: intraventricular hemorrhage; R: right; A: anterior.

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