

# Recovery of consciousness and an injured ascending reticular activating system in a patient who survived cardiac arrest

## A case report

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### Abstract

We report on a patient who survived cardiac arrest and showed recovery of consciousness and an injured ARAS at the early stage of hypoxic-ischemic brain injury (HI-BI) for 3 weeks, which was demonstrated by diffusion tensor tractography (DTT).

A 52-year-old male patient who had suffered cardiac arrest caused by acute coronary syndrome was resuscitated immediately by a layman and paramedics for ~25 minutes. He was then transferred immediately to the emergency room of a local medical center. When starting rehabilitation at 2 weeks after onset, his consciousness was impaired, with a Glasgow Coma Scale (GCS) score of 8 and Coma Recovery Scale-Revised (GRS-R) score of 8. He underwent comprehensive rehabilitative therapy, including drugs for recovery of consciousness. He recovered well and rapidly so that his consciousness had recovered to full scores in terms of GCS:15 and GRS-R:23 at 5 weeks after onset.

The left lower dorsal and right lower ventral ARAS had become thicker on 5-week DTT compared with 2-week DTT (Fig. 1B). Regarding the change of neural connectivity of the thalamic ILN, increased neural connectivity to the basal forebrain and prefrontal cortex was observed in both hemispheres on 5-week DTT compared with 2-week DTT.

Recovery of an injured ARAS was demonstrated in a patient who survived cardiac arrest and his consciousness showed rapid and good recovery for 3 weeks at the early stage of HI-BI.

**Abbreviations:** ARAS = ascending reticular activating system, DTT = diffusion tensor tractography, DTI = diffusion tensor imaging, HI-BI = hypoxic-ischemic brain injury, GCS = Glasgow Coma Scale, GRS-R = Coma Recovery Scale-Revised, ROI = regions of interest, RF = reticular formation, ILN = intralaminar nucleus, FA = fractional anisotropy, TV = tract volume.

**Keywords:** ascending reticular activating system, cardiac arrest, consciousness, diffusion tensor tractography, recovery

## 1. Introduction

Impaired consciousness is caused by injury of the ascending reticular activating system (ARAS). The ARAS is a complicated neural structure which cannot be definitely discriminated from adjacent neural structures on conventional brain MRI. Diffusion

tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), enabled evaluation of the ARAS by 3-dimensional reconstruction in the human brain.<sup>[1-4]</sup> A few studies using DTT have reported on recovery of consciousness and an injured ARAS in chronic patients<sup>[5-7]</sup>; however, little is known about recovery at an early stage of brain injury.

In this study, we report on a patient who survived cardiac arrest and showed recovery of consciousness and an injured ARAS at the early stage of hypoxic-ischemic brain injury (HI-BI) for 3 weeks, which was demonstrated by DTT.

## 2. Case report

A 52-year-old male patient suffered cardiac arrest caused by acute coronary syndrome and was resuscitated immediately by a layman and paramedics for ~25 minutes. He was then transferred immediately to the emergency room of a local medical center. At 2 weeks after onset, he was transferred to the rehabilitation department of a university hospital to undergo rehabilitation. His consciousness was impaired, with a Glasgow Coma Scale (GCS) score of 8 (eye opening: 2, best verbal response: 2, and best motor response: 4) and Coma Recovery Scale-Revised (GRS-R) score of 8 (auditory function: 1, visual function: 1, motor function: 3, verbal function: 2, communication: 1, and arousal: 0).<sup>[8,9]</sup> No abnormal lesion was observed on brain MRI taken at 2 weeks after onset (Fig. 1A). He underwent comprehensive rehabilitative therapy, including drugs for

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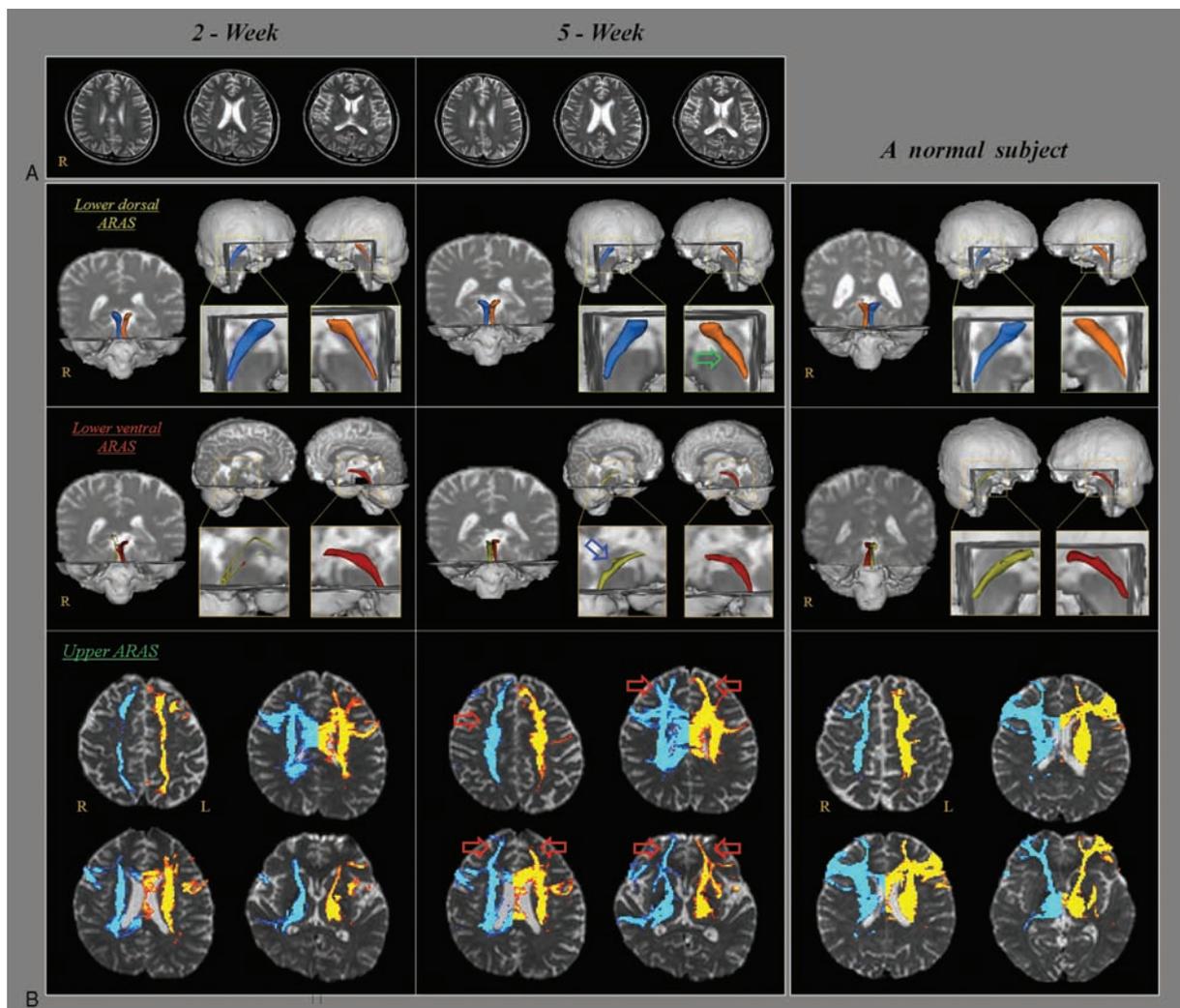
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**Figure 1.** (A) Brain MR images taken at 2 and 5 weeks after onset show no abnormal lesion. (B) Results of diffusion tensor tractography (DTT) of the patient. On 5-week DTT, the left lower dorsal (green arrow) and right lower ventral (blue arrow) ascending reticular activating system had become thicker compared with 2-week DTT. Increased neural connectivity of the thalamic intralaminar nucleus to the basal forebrain and prefrontal cortex (red arrows) was observed in both hemispheres on 5-week DTT compared with 2-week DTT. A normal control subject (53-year-old male).

recovery of consciousness (modafinil, levodopa, ropinirole, amantadine, zolpidem, and donepezil), physical therapy, and occupational therapy.<sup>[10–13]</sup> He recovered well and rapidly so that his consciousness had recovered to full scores in terms of GCS:15 and GRS-R:23 at 5 weeks after onset. Therefore, he was able to walk independently and was evaluated with a score of 9 on the Mini-Mental State Examination (full score: 30).<sup>[14]</sup> The patient's wife provided signed, informed consent, and the study protocol was approved by the Institutional Review Board Yeungnam University hospital.

### 2.1. Diffusion tensor imaging

DTI data were acquired 2 times (2 and 5 weeks after onset) using a 6-channel head coil on a 1.5 T Philips Gyroscan Intera (Philips, Best, Netherlands). Imaging parameters were as follows: echo-planar imaging factor—49; repetition time—10,726 ms; reconstructed matrix— $192 \times 192$ ;  $b$ — $1000 \text{ s/mm}^2$ ; echo time—76 ms; number of excitations—1; and a slice thickness of 2.5 mm with no gap (acquired isotropic voxel size  $1.3 \times 1.3 \times 2.5 \text{ mm}^3$ ).

### 2.2. Probabilistic fiber tracking

The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library was used for the analysis of DTI data. FMRIB Diffusion Software was used for fiber tracking with the following options (step lengths: 0.5 mm, streamline samples: 5000, curvature thresholds: 0.2). Three portions of the ARAS were reconstructed by selection of fibers passing through the following regions of interest (ROIs): the dorsal lower ARAS; the seed ROI: the pontine reticular formation (RF), and the target ROI: the thalamic intralaminar nucleus (ILN). The ventral lower ARAS; the seed ROI: the pontine RF, and the target ROI: the hypothalamus, and the upper ARAS; the seed ROI: the neural connectivity of the ILN to the cerebral cortex was analyzed.<sup>[11]</sup> Out of 5000 samples generated from the seed voxel, results for contact were visualized at a minimum threshold for the lower (dorsal, ventral) ARAS of 2 and for neural connectivity of the ILN of 15 streamlined through each voxel for analysis. DTT parameters (fractional anisotropy [FA] and tract volume [TV]) were measured for the lower dorsal ARAS, lower ventral ARAS and upper ARAS of the patient, and 10 age- and

**Table 1**

**Comparisons of diffusion tensor imaging parameters for the lower dorsal ascending reticular activating system, lower ventral and upper portion of the ascending reticular activating system between the patient and control subjects.**

ARAS		2 weeks		5 weeks		Controls (n = 10)
		Right	Left	Right	Left	
Lower dorsal	FA	0.39	0.40	0.41	0.42	0.41 ± 0.02
	TV	376	202*	381	332	367.52 ± 42.54
Lower ventral	FA	0.41	0.40	0.42	0.41	0.41 ± 0.02
	TV	14*	237	170	225	263.35 ± 60.31
Upper	FA	0.37	0.38	0.37	0.38	0.37 ± 0.02
	TV	6206*	6113*	8736	8331	8393.57 ± 1018.14

ARAS=ascending reticular activating system, FA=fractional anisotropy, TV=tract volume. Values are expressed as mean ± standard deviation.

\*When the diffusion tensor imaging parameters were 2 standard deviations below those of control subjects.

sex-matched normal control subjects (male: 10, mean age: 54.1 years). DTT parameters showing a deviation of >2 standard deviations from normal control values were defined as abnormal.

A summary of the values of FA and TV of the lower dorsal ARAS, lower ventral ARAS, and upper ARAS of the patient and normal control subjects is shown in Table 1. On 2-week DTT, TVs of the left lower dorsal ARAS, right lower ventral ARAS, and both upper ARAS were >2 standard deviations below those of normal control subjects, respectively, whereas on 5-week DTT, these values had increased to within 2 standard deviations of those of normal control subjects. Regarding configuration of DTT, the left lower dorsal and right lower ventral ARAS had become thicker on 5-week DTT compared with 2-week DTT (Fig. 1B). Regarding the change of neural connectivity of the thalamic ILN, increased neural connectivity to the basal forebrain and prefrontal cortex was observed in both hemispheres on 5-week DTT compared with 2-week DTT.

### 3. Discussion

In the present study, using DTT, change of the ARAS was evaluated in a patient who survived cardiac arrest whose consciousness showed rapid and good recovery for 3 weeks at the early stage of HI-BI. The patient's impaired consciousness showed full recovery during 3 week's rehabilitation from 2 weeks (GCS: 8) to 5 weeks (GCS: 15) after onset. The changes of the ARAS were as follows: (1) the narrowed left lower dorsal (TV: 202 → 332) and right ventral ARAS (TV: 14 → 170) observed on 2-week DTT had become thicker on 5-week DTT and (2) the decreased neural connectivity to both basal forebrain and prefrontal cortex (TV: right—6206 → 8736 and left—6113 → 8331) observed on 2-week DTT had increased on 5-week DTT. The FA value indicates the white matter organization and degree of directionality,<sup>[15]</sup> and the TV indicates total number of voxels within a neural tract.<sup>[16]</sup> Therefore, the increment of TV value without change of FA value of the left lower dorsal ARAS, right lower ventral ARAS, and both upper ARAS observed on 5-week DTT appeared to indicate recovery of the injured ARAS.<sup>[15,16]</sup> The narrowing of the lower ARAS and decreased neural connectivity of the upper ARAS indicated neural injury of the ARAS by HI-BI.<sup>[17]</sup> Therefore, thickening of the narrowed lower ARAS and increased connectivity to both basal forebrain and prefrontal cortex, which are important areas of the brain for consciousness, appears to be in agreement with the improved consciousness observed in this patient.<sup>[5-7,12,18,19]</sup> In addition, the changes of the injured ARAS were comparable with those

reported in previous studies on the recovery of consciousness and an injured ARAS.<sup>[5-7]</sup>

In conclusion, recovery of an injured ARAS was demonstrated in a patient who survived cardiac arrest who showed rapid and good recovery of consciousness for 3 weeks at the early stage of HI-BI. A few studies have reported on the recovery of an injured ARAS in patients with brain injury, using follow up DTT.<sup>[5-7]</sup> In 2015, Jang et al reported on a patient with traumatic brain injury who showed recovery of an injured lower dorsal ARAS, by demonstrating changes on DTT at 4- and 40 months after onset.<sup>[5]</sup> Subsequently, Jang and Lee reported on the recovery of an injured ARAS in terms of the configuration of the lower dorsal ARAS, and the neural connectivity of the upper ARAS in a patient with hypoxic ischemic brain injury from 7 months to 45 months after onset.<sup>[6]</sup> Jang et al recently reported on a patient with traumatic brain injury for 2 months from 10 months to 12 months after onset following a shunt operation for hydrocephalus.<sup>[7]</sup> Therefore, this is the first study to demonstrate recovery of the ARAS at the early stage of brain injury in a patient who survived cardiac arrest. However, the limitation of DTT should be considered: DTT may be underestimated due to regions of fiber complexity and crossing.<sup>[20]</sup>

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