● IMAGING IN NEURAL REGENERATION

Reorganization of injured anterior cingulums in a hemorrhagic stroke patient

In this study, we reported on a patient who showed a new neural tract between the injured anterior cingulums and the basal forebrain, as shown by diffusion tensor tractography (DTT).

A 62-year-old female underwent coiling for a ruptured aneurysm in the left middle cerebral artery (M1) and decompressive craniectomy for intracerebral hemorrhage in the left fronto-temporal lobe, intraventricular hemorrhage, and subarachnoid hemorrhage (**Figure 1A, B**). At three weeks after a hemorrhagic stroke, she showed bilateral motor weakness (right side: 2-/5 and left side: 2/5) and severe cognitive impairment (decreased alertness, Mini-Mental State Exam score: uncheckable). She began to recover gradually after two months of rehabilitation.

Diffusion tensor imaging was performed at three weeks after onset using a 6-channel head coil on a 1.5T Philips Gyroscan Intera (Hoffman-LaRoche Ltd, Best, The Netherlands) with single-shot echo-planar imaging and navigator echo. Sixty contiguous slices (acquisition matrix = 96 × 96; reconstruction matrix = 192 × 192; field of view = 240 × 240 mm^2; repetition time = 10,726 ms; echo time = 76 ms, b = 1000 s/mm^2, number of excitations = 1, slice gap = 0 mm and thickness = 2.5 mm) were acquired for each of the 32 non-collinear diffusion-sensitizing gradients. Fiber tracking was performed using the fiber assignment continuous tracking (FACT) algorithm implemented within the diffusion tensor imaging task card software (Philips Extended MR Work Space 2.6.3). For reconstruction of the cingulum, the seed region of interest (ROI) was placed in the middle portion of the cingulum and the target ROI was placed in the posterior portion of the cingulum on the colored coronal images. Termination criteria were fractional anisotropy (FA) < 0.15 and an angle change > 27° (Yoo et al., 2014).

On 3-week DTT images, both cingulums showed discontinuations between the anterior cingulum and the basal forebrain. However, the discontinued right anterior cingulum was connected to the left basal forebrain *via* the genu of the corpus callosum. In addition, the discontinued left anterior cingulum was connected to an unusual neural tract from the right anterior cingulum connected to the left basal forebrain (**Figure 1C**).

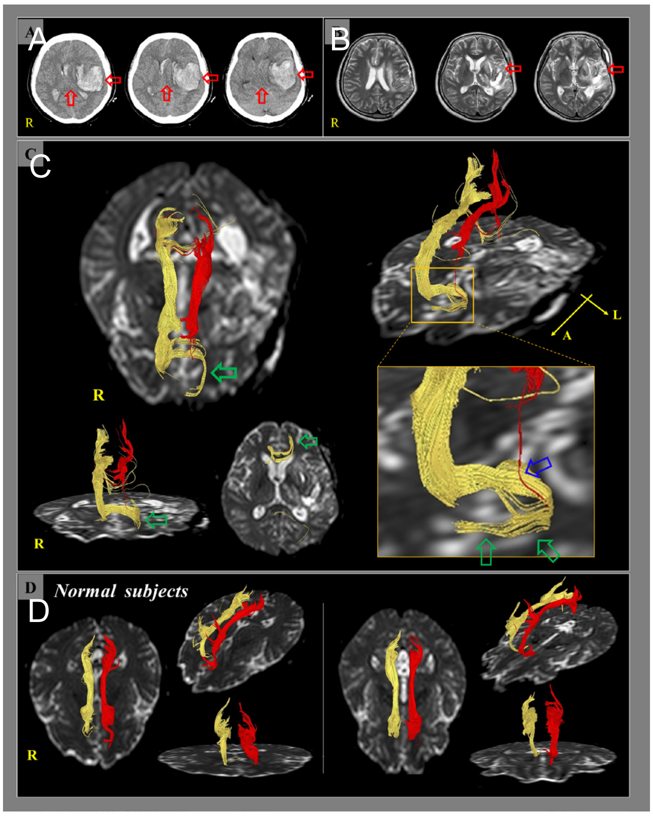

Figure 1 Brain computed tomography (CT), magnetic resonance (MR) imaging, and diffusion tensor tractography (DTT) of a 62-year-old female patient with a hemorrhagic stroke who showed a new neural tract between the injured anterior cingulums and the basal forebrain.

(A) Brain CT images at onset of hemorrhagic stroke show intracerebral hemorrhage in the left fronto-temporal lobe, intraventricular hemorrhage, subarachnoid hemorrhage, and subfalcine herniation (red arrow). (B) Brain MR images at three weeks after a hemorrhagic stroke show a leukomalactic lesion in the left fronto-temporal area (red arrow). (C) DTT of the cingulum. On 3-week DTT images, both cingulums show discontinuations between the anterior cingulums and the basal forebrain. However, the discontinued right anterior cingulum is connected to the left basal forebrain (green arrows) *via* the genu of the corpus callosum. In addition, the discontinued left anterior cingulum is connected to the unusual neural tract (blue arrow) from the right anterior cingulum connected to the left basal forebrain. (D) DTT of the fornix in two normal subjects (60- and 63-year-old females).

In this patient, discontinuations of both anterior cingulums appeared to be ascribed to the left intracerebral hemorrhage and subsequent subfalcine herniation (**Figure 1A, B**). We observed an unusual neural tract between the discontinued right anterior cingulum and the left basal forebrain *via* the genu of the corpus callosum, and the discontinued left anterior cingulum was connected to this unusual neural tract.

The cingulum, which connects the orbitofrontal cortex and the medial temporal lobe, plays an important role in cognition. In particular, it is associated with memory function because the cingulum is the passage of cholinergic innervation from the cholinergic nuclei (the medial septal nucleus [Ch1], the vertical nucleus of the diagonal band [Ch2], and the nucleus basalis of Meynert [Ch4]) in the basal forebrain to the cerebral cortex (Woolf and Butcher, 1986; Selden et al., 1998; Nieuwenhuys et al., 2008; Naidich and Duvernoy, 2009). Therefore, the unusual neural tract between the left basal forebrain and the injured anterior cingulums likely contributes to a compensatory phenomenon to obtain cholinergic innervations from cholinergic nuclei in the left basal forebrain after interruption of cholinergic innervations by complete injury of both anterior cingulums (Woolf and Butcher, 1986; Selden et al., 1998; Nieuwenhuys et al., 2008; Naidich and Duvernoy, 2009).

Discontinuations of both anterior cingulums indicate blockage of cholinergic innervation from the basal forebrain to the cerebral cortex. Therefore, we believe that the development of this unusual neural tract between the basal forebrain and injured cingulums after interruption of cholinergic innervation from the basal forebrain by complete injury of the anterior cingulum might have resulted in the reorganization of cholinergic innervations after stroke (Yeo et al., 2012; Seo and Jang, 2013, 2014; Yoo et al., 2014; Jang et al., 2015).

In conclusion, we reported a stroke patient who showed a new neural tract between the injured anterior cingulums and the basal forebrain. This finding appears to suggest the reorganization of cholinergic innervations after stroke.

Sung Ho Jang, Chul Hoon Chang, Han Do Lee*
Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University, Namku, Daegu, Republic of Korea (Jang SH, Lee HD)
Department of Neurosurgery, College of Medicine, Yeungnam University, Namku, Daegu, Republic of Korea (Chang CH)
Correspondence to: *Han Do Lee, M.S., lhd890221@hanmail.net.*
orcid: *0000-0002-1668-2187 (Han Do Lee)*
Accepted: *2018-01-03*

doi: *10.4103/1673-5374.235308*
Author contributions: *Study conception and design: SHJ, CHC, and HDL; data acquisition: CHC, HDL; data analysis: HDL; paper preparation and writing: SHJ; paper authorization: HDL. All authors approved the final version of this paper for publication.*
Conflicts of interest: *None declared.*
Financial support: *This work was supported by the National Research Foundation (NRF) of Korea Grant funded by the Korean Government (MSIP) (2015R1A2A2A01004073). The funding body played no role in the study conception design, in the collection, analysis and interpretation of data, in the preparation and writing of the report, and in the decision to submit the article for publication.*
Copyright license agreement: *The Copyright License Agreement has been signed by all authors before publication.*
Institutional review board statement: *This study was approved by the Institutional Review Board of Yeungnam University Hospital, Republic of Korea (approval No. YUMC-2017-06-020).*
Data sharing statement: *Datasets analyzed during the current study are available from the corresponding author on reasonable request.*
Plagiarism check: *Checked twice by iThenticate.*
Peer review: *Externally peer reviewed.*

References

Jang SH, Kim SH, Kwon HG (2015) Recovery of injured cingulum in a patient with traumatic brain injury. Neural Regen Res 10:323-324.
Naidich TP, Duvernoy HM (2009) Duvernoy's atlas of the human brain stem and cerebellum: high-field MRI : surface anatomy, internal structure, vascularization and 3D sectional anatomy. Wien; New York: Springer.
Nieuwenhuys R, Voogd J, Huijzen Cv (2008) The human central nervous system, 4th Edition. New York: Springer.
Selden NR, Gitelman DR, Salamon-Murayama N, Parrish TB, Mesulam MM (1998) Trajectories of cholinergic pathways within the cerebral hemispheres of the human brain. Brain 121:2249-2257.
Seo JP, Jang SH (2013) Recovery of injured cingulum in a patient with brain injury: Diffusion tensor tractography study. Neurorehabilitation 33:257-261.
Seo JP, Jang SH (2014) Unusual neural connection between injured cingulum and brainstem in a patient with subarachnoid hemorrhage. Neural Regen Res 9:498-499.
Woolf NJ, Butcher LL (1986) Cholinergic systems in the rat brain: III. Projections from the pontomesencephalic tegmentum to the thalamus, tectum, basal ganglia, and basal forebrain. Brain Res Bull 16:603-637.
Yeo SS, Chang MC, Kim SH, Son S, Jang SH (2012) Neural connection between injured cingulum and pedunculopontine nucleus in a patient with traumatic brain injury. Neurorehabilitation 31:143-146.
Yoo JS, Kim OL, Kim SH, Kim MS, Jang SH (2014) Relation between cognition and neural connection from injured cingulum to brainstem cholinergic nuclei in chronic patients with traumatic brain injury. Brain Inj 28:1257-1261.

(*Copyedited by Li CH, Song LP, Zhao M*)