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Neural connectivity of the anterior body of the fornix in the human brain: Diffusion tensor imaging study

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HIGHLIGHTS

- We investigated the neural connectivity of the anterior body of fornix.
- The fornix, part of the Papez circuit, plays a role in episodic memory.
- Anterior body of fornix connected to the cholinergic nuclei and memory function area.

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ABSTRACT

A few studies have reported on the neural connectivity of the fornix in the human brain, however, little is known about the neural connectivity of the anterior body of the fornix. In this study, we used diffusion tensor imaging in investigation of the neural connectivity of the anterior body of the fornix in normal subjects. Forty healthy subjects were recruited for this study. A seed region of interest was placed on the anterior body of the fornix using the FMRIB Software Library. Connectivity was defined as the incidence of connection between the anterior body of the fornix and any neural structure of the brain at the threshold of 5, 25, and 50 streamlines. In all subjects, the anterior body of the fornix showed 100% connectivity to the anterior commissure and hypothalamus at thresholds of 5, 25, and 50. On the other hand, regarding the thresholds of 5, 25, and 50, the anterior body of the fornix showed connectivity to the septal forebrain region (53.8, 23.8, and 15.0%), frontal lobe via anterior commissure (41.3,12.5, and 10.0%), medial temporal lobe (85.0,66.3, and 62.5%), lateral temporal lobe (75.0, 56.3, and 35.0%), occipital lobe (21.3, 5.0, and 1.3%), frontal lobe via septum pellucidum (28.8, 13.8, and 8.8%), tegmentum of midbrain (7.5, 5.0, and 0%), tectum of midbrain (2.5,0, and 0%), and tegmentum of pons (5.0,0, and 0%). The anterior body of the fornix showed high connectivity with the anterior commissure and hypothalamus, and brain areas relevant to cholinergic nuclei (the septal forebrain region and brainstem) and memory function (the medial temporal lobe).

1. Introduction

The fornix is involved in the transfer of information on episodic memory as a part of the Papez circuit between the hippocampus and the mammillary body [5,7,15,18]. Unmasking of latent neural connection is one of the recovery mechanisms after brain injury; therefore, elucidation of the neural connectivity of a neural structure is important in terms of neural control in the normal brain, and brain plasticity in patients with brain injury [1,2]. The fornix is located adjacent to important neural structures such as the anterior commissure and corpus callosum, however, neural connectivity of the fornix has been neglected [8]. That is because research on neural connectivity of the fornix has been difficult using conventional brain CT or MRI [6,16].

Diffusion tensor imaging (DTI) can evaluate white matter, and enables three-dimensional visualization and estimation of the fornix [9,11,14,17]. As a result, a few studies have reported on the neural connectivity of the posterior body of the fornix in the normal brain, and unusual neural connectivity of the anterior and posterior bodies of the fornix in patients with brain injury [8,21,22]. However, no study on neural connectivity of the anterior body of the fornix in the normal human brain has been reported.

In the current study, we used DTI in investigation of the neural connectivity of the anterior body of the fornix in normal subjects.

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2. Methods

2.1. Subjects

Forty healthy subjects (males: 22, females: 18, mean age: 31.8 years, range: 20–50 years) with no previous history of neurological, physical, or psychiatric illness were recruited. All subjects understood the purpose of the study and provided written, informed consent prior to participation. The study protocol was approved by the institutional review board of the Yeungnam university hospital.

2.2. Data acquisition

DTI data were acquired using a 6-channel head coil on a 1.5 T Philips Gyroscan Intera (Philips, Ltd., Best, The Netherlands) with single-shot echo-planar imaging. For each of the 32 non-collinear diffusion sensitizing gradients, we acquired 67 contiguous slices parallel to the anterior commissure-posterior commissure line. Imaging parameters were as follows: acquisition matrix = 96 × 96; reconstructed to matrix = 128 × 128; field of view = 221 × 221 mm^2; TR = 10, 726 ms; TE = 76 ms; parallel imaging reduction factor = 2 (SENSE factor); EPI factor = 59; b = 1000 s/mm^2; NEX = 1; and a slice thickness of 2.3 mm (acquired voxel size 1.73 × 1.73 × 2.3 mm^3).

2.3. Probabilistic fiber tracking

Analysis of diffusion-weighted imaging data was performed using the Oxford Centre for functional magnetic resonance imaging of the brain (FMRIB) software library (FSL; www.fmrib.ox.ac.uk/fsl). Head motion effect and image distortion due to eddy current were corrected by affine multi-scale two-dimensional registration. Fiber tracking was performed using a probabilistic tractography method based on a multi-fiber model, and applied in the current study utilizing tractography routines implemented in FMRIB Diffusion (5000 streamline samples, 0.5 mm step lengths, curvature thresholds = 0.2) [3,4,13]. We used the two regions of interest (ROIs) in order to elucidate the connectivity of the anterior body of the fornix. The first ROI was drawn on the anterior body of the fornix (green color) as a seed mask on the color map with the coronal image. The second ROI was placed on the junction between the body and crus as an exclusion mask on the color map with the coronal image [5]. Out of 5000 samples generated from a seed voxel, results were visualized at the threshold of 5, 25, and 50 streamlines through each voxel for analysis. Connectivity was defined as the incidence of connection between the anterior body of the fornix and any neural structure of the brain.

3. Results

A summary of the connectivity of the anterior body of the fornix is shown in Table 1. In all subjects, the anterior body of the fornix showed 100% connectivity to the anterior commissure and hypothalamus at thresholds of 5, 25, and 50 (Fig. 1).

On the other hand, the anterior body of the fornix was found to be connected to other brain regions via three neural structures: (1) the anterior commissure–to the septal forebrain regions, frontal lobe, medial temporal lobe, lateral temporal lobe, and occipital lobe, (2) the septum pellucidum–to the frontal lobe, and (3) the dorsal longitudinal fasciculus–to the brainstem. Regarding the thresholds of 5, 25, and 50, the anterior body of the fornix showed connectivity to the septal forebrain region (53.8, 23.8, and 15.0%), frontal lobe via anterior commissure (41.3, 12.5, and 10.0%), medial temporal lobe (85.0, 66.3, and 62.5%), lateral temporal lobe (75.0, 56.3, and 35.0%), occipital lobe (21.3, 5.0, and 1.3%), frontal lobe via septum pellucidum (28.8, 13.8, and 8.8%), tegmentum of midbrain (7.5, 5.0, and 0%), tectum of midbrain (2.5, 0, and 0%), and tegmentum of pons (5.0, 0, and 0%).

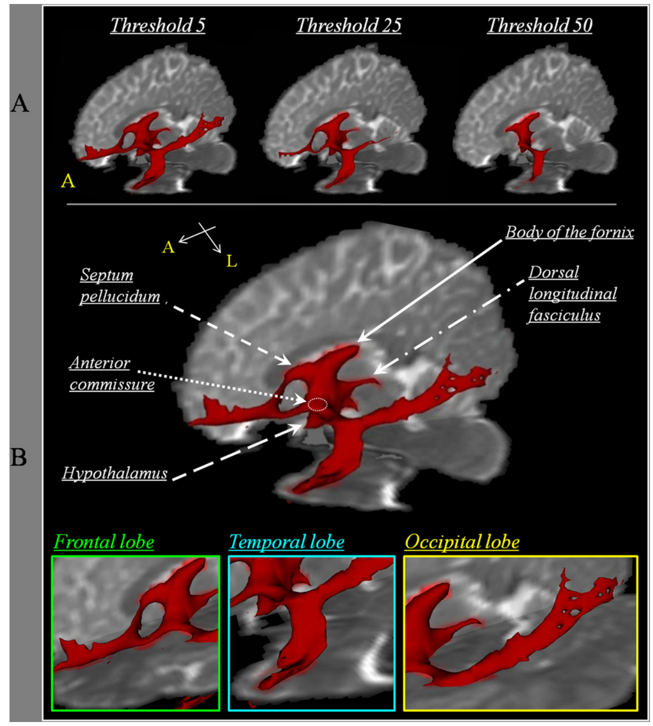

Fig. 1. (A) Neural connectivity of the anterior body of the fornix at a threshold of 5, 25, and 50. (B) Diffusion tensor tractography results regarding connectivity between the anterior body of the fornix and each brain area: the septum pellucidum (broken-lined arrow), the anterior commissure (dotted-lined arrow and dotted circle), the hypothalamus (long broken-lined arrow), the body of the fornix (lined arrow), the dorsal longitudinal fasciculus (broken-dotted-lined arrow), the frontal lobe (green-lined quadrangle)–the anterior body of the fornix connected with the frontal lobe via the anterior commissure and the septum pellucidum, the temporal lobe (skyblue-lined quadrangle)–the anterior body of the fornix connected with the temporal lobe via the anterior commissure and the occipital lobe (yellow-lined quadrangle)–the anterior body of the fornix connected with the occipital lobe via the anterior commissure.

4. Discussion

In the current study, we investigated neural connectivity of the anterior body of the fornix in the normal human brain, using probabilistic tracking. We found the following characteristics of connectivity of the anterior body of the fornix: (1) all subjects showed connectivity with the anterior commissure and the hypothalamus irrespective of thresholds, (2) the anterior body of the fornix showed connectivity with areas known to contain cholinergic neurons: the septal forebrain region and the brainstem, although we could not completely clarify the connectivity to the cholinergic nuclei, and (3) high connectivity to the medial temporal lobe, which contains important structures for memory function, including the hippocampus and the entorhinal cortex.

The fornix is known to be connected to the septal region via the precommissural fornix anteriorly, the mammillary body via the postcommissural fornix anteriorly, and hippocampus via the crus of the fornix posteriorly [5,23]. However, several recent studies using diffusion tensor tractography (DTT) have reported unusual or unknown neural connections of the fornix that had not been previously reported in normal subjects and patients with brain injury [8,21,22]. In 2013, Yeo and Jang reported on a patient who showed an unusual neural connection of an injured fornix following traumatic axonal injury of both fornical crus [21]. In the right fornix, an abnormal neural tract originating from the right crus passed