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Mammillothalamic tract in human brain: Diffusion tensor tractography study

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ABSTRACT

The mammillothalamic tract (MTT) is a part of the Papez circuit and connects the mammillary body and anterior thalamus. No studies of the MTT have been performed using diffusion tensor tractography (DTT). In the current study, we attempted to identify the MTT in the human brain using DTT. We recruited 25 healthy volunteers for this study. Diffusion tensor images (DTIs) were scanned using 1.5-T, and the MTT was obtained using FMRIB software. Values of fractional anisotropy (FA), mean diffusicity (MD), and tract volume of the MTT were measured. The location of the highest probability point of the MTT was measured at the bicommissural level. MTTs of all subjects, which originated from the mammillary body, ascended posteriorly to the bicommissural level, along the third ventricle, and then ascended to the anterior thalamus in the antero-lateral direction. Average location of the MTT was 37.15% from the most posterior border of the anterior commissure to the most posterior border of the third ventricle at the bicommissural level. We identified the MTT in the human brain using DTT. These methods and results would be helpful to both clinicians and researchers in this field.

The mammillothalamic tract (MTT) connects the mammillary body and anterior thalamus. As a part of the Papez circuit, it is involved in the episodic memory [1]. Anatomically, the MTT is short and thin. Moreover, it is not easily discriminated from adjacent structures. Several studies have reported on cognitive impairment in patients who showed pathology in the MTT [10,14,15,21]. These studies have been conducted using conventional brain MRI. Therefore, there have been many difficulties in accurate evaluation of the MTT.

Recent developments in diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), allow visualization and localization of neural tracts at the subcortical level in three dimensions [6,9,11–13,18–20]. Although the detailed anatomy of the MTT is already well-known [7,14,15,21], identification of the MTT using DTT can provide useful information for clinicians and researchers in evaluation of the state of the MTT, including the general state of the MTT, and the location and severity of the lesion. However, to our best knowledge, there has been no DTT study of the MTT.

In the current study, we attempted to identify the DTT in the human brain using DTT.

For this study, we recruited 25 right-handed healthy subjects (male: 14, female: 11, mean age: 39.2 ± 14.7 years, range: 22–67 years) with no previous history of neurological, physical or psychiatric illness including alcoholism. All subjects showed full mark (30 points) at the cognitive screening test using Mini-mental state examination (MMSE). All subjects understood the purpose of the study, and provided written, informed consent prior to participation. The study protocol was approved by our local Institutional Research Board.

DTIs were acquired using a sensitivity-encoding head coil on a 1.5-T Philips Gyroscan Intera (Hoffman-LaRoche, Ltd., Best, the Netherlands) with single-shot echo-planar imaging with a navigator echo. Sixty-seven contiguous slices (matrix = 128 × 128 matrix, field of view = 221 mm × 221 mm, repetition time/echo time = 10726/76 ms, b = 1000 s/mm^2, NEX = 1, thickness = 2.3 mm) were acquired for each of the 32 noncollinear diffusion-sensitizing gradients.

Diffusion-weighted imaging data were analyzed 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 multifiber model, and applied in the present study utilizing tractography routines implemented in FMRIB Diffusion (5000 streamline samples, 0.5 mm step lengths, curvature thresholds = 0.2) [2,3,16]. MTTs were determined by selection of fibers passing through three regions of interest (ROIs) (Fig. 1A). Two seed

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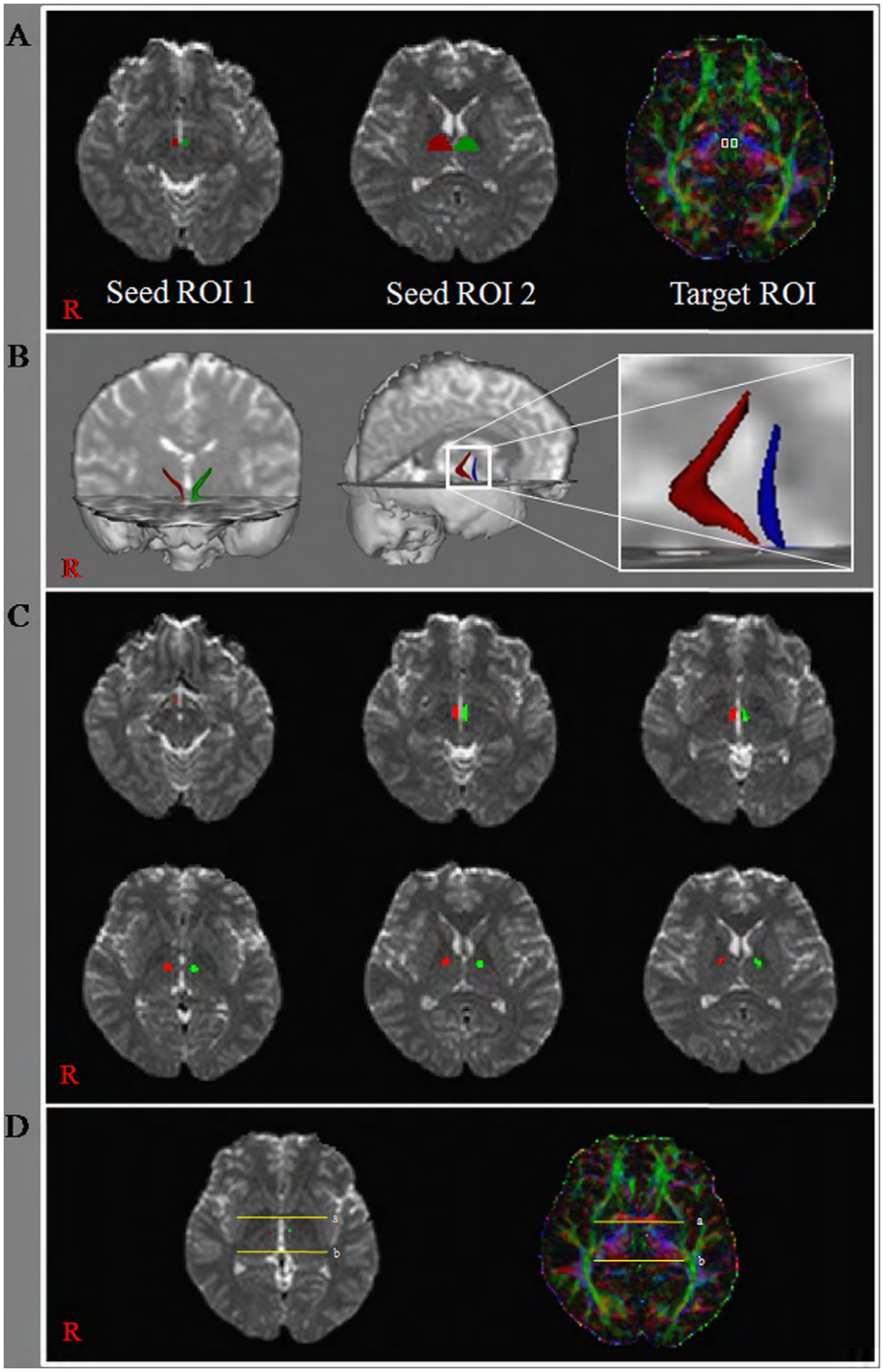

Fig. 1. (A) Seed region of interests are given on the mammillary body (Seed region of interest (ROI) 1) and anterior thalamus (Seed ROI 2). The target ROI (white-lined quadrangle) was given on the isolated MTT area on the color map (posterior to the fornix and anterior to the red nucleus) at the level between the mammillary body and the bicommissural plane. (B) Mammillothalamic tracts (MTTs) were constructed in both hemispheres (right: red color, left: green color) and compared to the column of the fornix (blue color). (C) The pathway of the MTT is shown at each level of the brain. (D) The location of the MTT is shown at the bicommissural level. Landmarks for measurement of the MTT location: (a) the most posterior border of the anterior commissure, (b) the most posterior border of the third ventricle.

ROIs were placed on the location that originated from the mammillary body and anterior thalamus [4,5,8,17]. The target ROI was given on the isolated MTT area on the color map (posterior to the fornix and anterior to the red nucleus) at the level between the mammillary body and bicommissural plane [8]. Out of 5000 samples generated from each seed voxel, results for each contact were visualized threshold at a minimum of 10 streamlines through each voxel for analysis. Values of fractional anisotropy (FA), mean diffusicity (MD), and tract volume of the MTT were measured.

Table 1
Diffusion tensor imaging parameters of the mammillothalamic tract.

Hemisphere	FA	MD	Tract volume	Location
Right	0.38 (0.04)	0.88 (0.07)	60 (27)	38.18 (6.89)
Left	0.37 (0.03)	0.85 (0.1)	59 (29)	36.12 (8.03)
Both	0.37 (0.04)	0.87 (0.08)	59 (27)	37.15 (7.48)

Values represent mean (±standard deviation), FA: fractional anisotropy, MD: mean diffusivity, MD × 10^{-3}(mm^2/s), location (%).

Location and probability of the MTT, which was reconstructed from DTI, were measured for each subject. The location of the highest probability point of the MTT was measured in the anteroposterior direction at the bicommissural level (anterior commissure–posterior commissure). The anterior boundary was set as the most posterior border of the anterior commissure, and the posterior boundary was the most posterior border of the third ventricle (Fig. 1D).

Values of FA, MD, tract volume, and location were used in performance of an independent *t*-test for determination of variances between the right and left hemispheres. We used performance of an independent *t*-test for determination of variances in the value of FA, MD, tract volume and location between male and female. The significant level of the *P* value was set at 0.05.

The MTTs of all subjects, which originated from the mammillary body, ascended posteriorly to the bicommissural level, along the third ventricle, and then ascended to the anterior thalamus in the antero-lateral direction. The MTT curved at or around the bicommissural level (Fig. 1).

Mean values for FA, MD, and tract volume were 0.37, 0.87, and 59, respectively. Average location of the MTT was 37.15% from the anterior boundary at the bicommissural level (Table 1). In terms of FA, MD, tract volume, and location, no significant differences were observed between hemispheres. There were no significant differences in FA, MD, tract volume and location between male and female ($P > 0.05$).

In the current study, we used DTT for identification of the MTT in the human brain. The MTT, which originated from the mammillary body, ascended posteriorly to the bicommussural level, and then changed direction antero-laterally toward the anterior thalamus. For easy clinical application, we measured the location of the MMT at the bicommussural level and found that the MTT was located an average of 37.15% from the most posterior border of the anterior commissure to the most posterior border of the third ventricle. These results are compatible with those of previous MRI studies [7,14,15,21].

Several studies have reported on MTT injury in patients with memory impairment [10,14,15,21]. In 2003, using follow-up volumetric brain MRI, Schott et al. reported on a patient with a left thalamic infarct involving the mamillo-thalamic tract with selective verbal memory impairment [15]. Subsequently, using diffusion and T2 weighted brain MRI, Yoneoka et al. demonstrated lesions of the MTT in patients with Korsakoff syndrome [21]. In 2007, Park et al. reported on a patient who showed ammenia following an infarction of the left MTT [14]. Using functional connectivity MRI, Kim et al. recently demonstrated pathology of the MTT in patients with Wernicke's encephalopathy [10]. However, in terms of the severity of the lesion, integrity of the MTT, general state of the MTT using numerical analysis, and so on, these studies did not provide a detailed estimation of the state of the MTT. Therefore, we think that the methodology used to acquire data in this study of the MTT will be helpful in estimation of the state of the MTT in patients with diseases involving the MTT.

In conclusion, we identified the MTT in the human brain using DTT. As far as we are aware, this is the first DTT study of the MTT in the human brain. These results might be helpful to both clinicians and researchers in this field. We suggest additional studies on clinical correlation, aging and the reliability and validity of the MTT.

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