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Correlation between Uncinate Fasciculus and Memory Tasks in Healthy Individual using Diffusion Tensor Tractography*

T. Sato, N. Maruyama, T. Hoshida, K. Minato

Abstract— **Tractography is a procedure that can track and demonstrate the 3D neural tracts of the white matter of the brain. The images of the brain are obtained by analyzing the diffusion tensor, identification of which can provide the anatomical connections of the brain. Studying these connections is integral to the understanding of the brain function. Specifically, the uncinate fasciculus (UF), which is the white matter in the human brain, is said to be related to cognitive function. The UF tractography is calculated using diffusion tensor imaging (DTI) parameter. Studies have shown that the DTI parameter of dementia patients is lower than that of healthy individuals. It is also suggested that the DTI parameter of healthy individuals decreases with age. In addition, the WMS-R score, which is indicative of general memory, verbal memory and other cognitive functions, of the elderly are lower than of the young. However, there is no report yet that has holistically investigated DTI parameter and the memory functions. Thus, in this research, we have calculated the correlation coefficient between the DTI parameter of UF and WMS-R score. Our result shows that the correlation coefficient of diffusivity of the fiber direction and visual memory of a left UF is -0.226 at the maximum. Correlation between DTI measurement and memory performance suggests the relationships between the UF and function in memory tasks lateralization. Our finding matches previous reports on the correlation between FA in the left, or L1 in the right UF, and performance on visual memory.**

I. Introduction

The uncinate fasciculus (UF) is a major white matter tract connecting the anterior temporal and frontal lobes [1]. It is shaped like a curved dumbbell and links the three anterior temporal convolutions and the amygdala with the gyrus rectus, medial retro orbital cortex, and subcallosal area [2]. The UF is important for the formation and retrieval of episodic memories [3, 4].

Diffusion Tensor Imaging (DTI) measures the molecular motion of water in tissue in six or more directions, and characterizes the magnitude and direction of diffusion in every single voxel. Thus, it is used to reveal the microstructure of white matter [5-7]. The integrated white matter tracts measured by DTI are related to individual differences in performance across a wide range of cognitive functions.

The purpose of this study is to investigate the correlation of the degree of DTI parameters with changed memory scores.

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T. Sato, T. Matsuda and K. Minato are with the Nara Institute of Science and Technology, Ikoma, NARA 6300192 JAPAN (phone: +81-743-72-5322; fax: +81-743-72-5329; e-mail: {tsato, kotaro}@is.naist.jp).

N. Maruyama and T. Hoshida are with National Hospital Organization Nara Medical Center, Nara, NARA 6308053 JAPAN (e-mail: {maruyama, hoshida}@wnara.hosp.go.jp).

II. Subjects and Methods

Participants

This study is performed by 41 healthy right-handed individuals (age group: 20-60 years old). The study is approved by the Institutional Review Board of the National Hospital Organization Nara Medical Center, and all subjects have given informed consent prior to the enrollment in the study.

MRI and DTI data acquisition and processing

MR-images are acquired using a 1.5T whole body MR scanner (Toshiba Medical Systems Inc). And then, DTI acquisitions are taken from the subjects. The DTI acquisition consists of axial 2D echo planar imaging (2D EPI) diffusion-weighted sequence with TR/TE = 12000/130 ms, FOV = 24 cm, matrix= 128 × 128, 3-mm contiguous slices without gap, two $\boldsymbol{b}$ values = 0 and 1000 s/mm^2, done in six directions.

The diffusion tensor $\boldsymbol{D}$ is calculated using equation (1),

$$\boldsymbol{S}_b = \boldsymbol{S}_0 \times \exp\left(-\boldsymbol{bD}\right) \qquad (1)$$

where each set of diffusion-weighted images is utilized. $\boldsymbol{S}_b$ is the measured MR signal for a given $\boldsymbol{b}$ value, $\boldsymbol{S}_0$ is the MR signal for $\boldsymbol{b}$ = 0, $\boldsymbol{b}$ value is the diffusion gradient factor along each direction (s/mm^2), the diffusion tensor $\boldsymbol{D}$ describes the molecular mobility and correlation towards these directions. The diffusion tensor $\boldsymbol{D}$ can be diagonalized to the eigenvectors and eigenvalues ($\lambda_1, \lambda_2, \lambda_3$). The eigenvectors describe the major diffusion directions and the eigenvalues are related to their diffusivities. The apparent diffusion coefficient (ADC) can be obtained from the trace of the diagonalized diffusion tensor $(\lambda_1 + \lambda_2 + \lambda_3)/3$. Parametric maps of the ADC and fractional anisotropy (FA) are obtained using these eigenvalues. FA is a scalar value that describes the shape of the diffusion within a given voxel, with a range from 0 to 1. Parametric maps for the axial or parallel, L1 = λ_1, and radial, LT = $(\lambda_2 + \lambda_3)/2$,diffusivities are also defined.

Tractography analysis

DTI Studio software [8] based on the fiber assignment by continuous tracking (FACT) algorithm is used for white matter fiber tracking. Diffusion tensor tractography using multiple regions-of-interest (ROI) are also used to trace the UF bilaterally [9-13]. The tracking method uses fractional anisotropy (FA) threshold of 0.15, and angle threshold of 60 degrees. These thresholds are similar to previous publications [14, 15].

The UF superior and inferior segments traversing the coronal plane is determined as an anatomical landmark as shown in Fig. 1A, ROI. A Boolean "OR" operation on one region combined with an "AND" operation on the other are chosen to construct the UF on each side. On the UF fiber tract, its traced volume and corresponding DTI parameters such as FA, ADC, L1 and LT are recorded in 3D as shown in Fig. 1B.

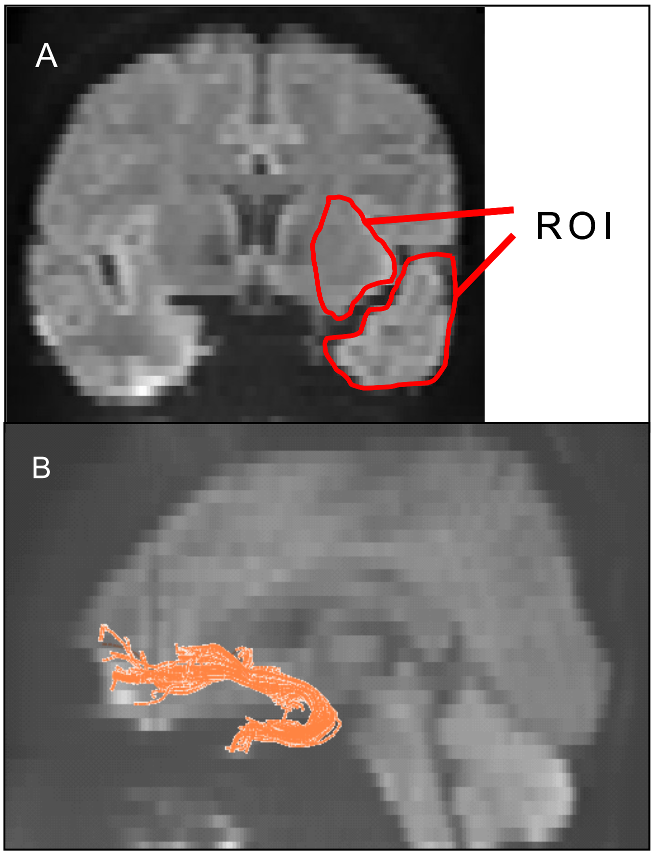

Figure 1. Illustration of the DTI-based fiber tracking of the uncinate fasciculus. (A)The two ROIs. (B) A 3D saggital view of the left UF.

Neuropsychological protocol

All subjects have undergone a comprehensive neuropsychological evaluation. The Wechsler Memory Scale-Revised (WMS-R) is examined as part of the neuropsychological battery. Five memory indices from the WMS-R are used in this study to evaluate memory performance such as *Verbal*, *Visual*, *General*, *Attention/Concentration* and *Delayed Recall Index* are used to assess each memory performance. For the examination of all the memory scores, any age related scaling is not performed.

Analyses

Spearman correlations between DTI and memory scores are obtained.

III. RESULTS

Table 1 shows that the mean FA, ADC, L1 and LT in the left UF are higher than in the right UF. MN denotes the mean values and SD represents standard deviations. Mean ADC in the left UF is significantly higher than in the right UF ($p<0.05$). Mean L1 in the left is also significantly higher in the right ($p < 0.01$). Left and right UF differences are comparable with previous studies [14, 16, 17].

TABLE I. DTI VALUES

FA MN±SD			
	n	***left UF***	***right UF***
Present study	41	0. 374 ± 0. 0228	0. 369 ± 0. 0154
Hasan et al. (2009)	108	0. 436 ± 0. 0246	0. 429 ± 0. 0268
Kiuchi et al. (2009)	16	0. 378 ± 0. 020	0. 383 ± 0. 020
Eluvathingal et al. (2007)	29	0. 432 ± 0. 027	0. 424 ± 0. 023
ADC MN±SD(×1000)(μm²/ms)			
	n	***left UF***	***right UF***
Present study	41	858 ± 44	836 ± 41
Hasan et al. (2009)	108	791	798
Kiuchi et al. (2009)	16	422 ± 20	421 ± 21
Eluvathingal et al. (2007)	29	803 ± 34	807 ± 34
L1 MN±SD(×1000)(μm²/ms)			
	n	***left UF***	***right UF***
Present study	41	1220 ± 52	1182 ± 58
Hasan et al. (2009)	108	1227 ± 40	1209 ± 42
Kiuchi et al. (2009)	16		
Eluvathingal et al. (2007)	29	1232 ± 37	1228 ± 38
LT MN±SD(×1000)(μm²/ms)			
	n	***left UF***	***right UF***
Present study	41	677 ± 44	663 ± 35
Hasan et al. (2009)	108	584 ± 34	582 ± 36
Kiuchi et al. (2009)	16		
Eluvathingal et al. (2007)	29	589 ± 37	569 ± 35

The correlations with DTI measures in the UF are summarized in Table 2. FA in the left UF shows higher correlation in almost all memory indices than in the right UF except in the delayed recall. On the other, ADC, L1 and LT have higher correlations in the right than in the left UF. In Fig. 2 and 3, the representative correlation between FA in the left UF tract, L1 in the right UF, and visual memory score are shown. Significant correlations are not found between DTI measurements and memory scores.

Table II. CORRELATIONS BETWEEN DTI MEASUREMENTS AND MEMORY SCORES

lt UF	**verbal**	**visual**	**general**	**att/con**	**delayed recall**
FA	-0.177	-0.226	-0.202	-0.0877	-0.0963
ADC	-0.0193	-0.0817	-0.0363	-0.0612	-0.115
L1	-0.0692	-0.182	-0.102	-0.0942	-0.14
LT	0.0126	-0.0138	0.00694	-0.0356	-0.0896

rt UF	**verbal**	**visual**	**general**	**att/con**	**delayed recall**
FA	0.113	-0.0674	0.0766	0.0387	0.111
ADC	-0.133	-0.243	-0.17	-0.117	-0.118
L1	-0.101	-0.263	-0.149	-0.101	-0.0852
LT	-0.151	-0.194	-0.177	-0.124	-0.137

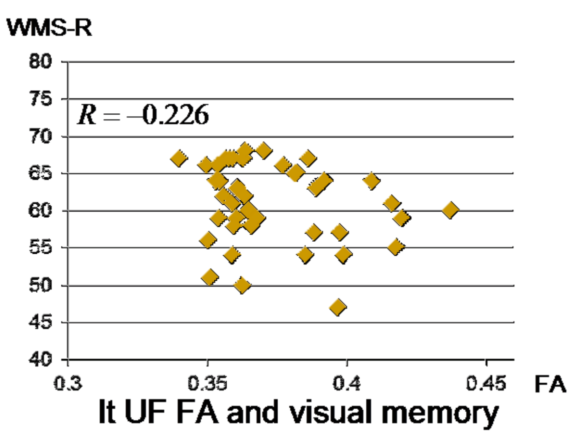

Figure 2. Correlations between FA in the left uncinate fasciculus and visual memory score.

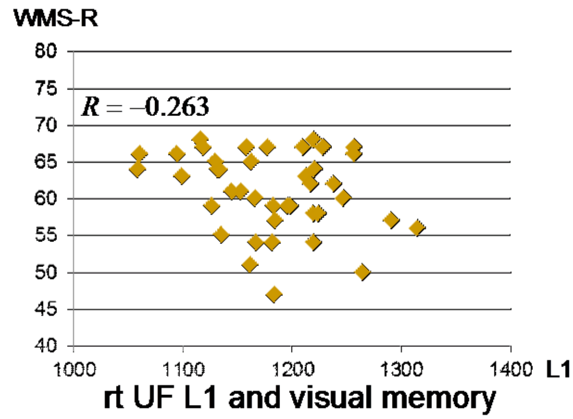

Figure 3. Correlations between L1 in the right uncinate fasciculus and visual memory score.

IV. DISCUSSION

In this study, FA is greater in the left than the right UF with almost symmetrical tract volume. Some studies reported that a left greater than right asymmetry in UF FA [18], but other found that the right UF had higher FA [19]. These discrepancies came from the differences in both the image acquisition and analysis method.

The UF connects the inferior frontal, and anterior and mesial temporal lobes [2]. Mesial temporal and frontal structures are associated with encoding and retrieval of memories. Using fMRI in healthy controls, episodic memory is found to be associated with both mesial temporal and frontal lobe activation [20, 21]. The left medial temporal structures are activated by encoding verbal information, the right is activated by encoding less verbalizable stimuli such as patterns, and both are activated by encoding intermediate verbalizable stimuli such as faces and scenes [21, 22]. The lateralization of memory performance regarding verbal material appears stronger in the left.

Correlation between DTI measures and memory performance suggests the relationship between the UF and function in memory tasks lateralization. In the dominant hemisphere, strong relationships between function and structure have been found in the left hemisphere for both language and memory in a DTI and fMRI studies [23]. Subjects with more lateralized functional activation are likely to have more highly lateralized DTI values.

This correlation between lateralized memory performance and DTI abnormalities has also been observed in diseases. Functions across neuropsychological measures and the relationship between memory performance and DTI measures are found in schizophrenia patients. Lower FA in the right UF is correlated with reduced performance on measures of visual attention [18]. Left UF measurements are also correlated with lower performance on measures of verbal and visual memory [24]. Our finding matches these previous reports on the correlation between FA in the left, or L1 in the right UF, and performance on visual memory.

In this study, neuropsychological measures are available only for the healthy controls. Correlation between memory performance and UF diffusion measures in patients should be compared. However, the correlations between memory performance and integrity of the UF can be found particularly in the dominant hemisphere. Some studies show a right greater than left asymmetry in the stem and the inferior (temporal) part of the UF [19, 25] and a left greater than right asymmetry in the frontal UF. Further study should investigate these two parts of the UF separately.

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