Quantitative evaluation of the white matter tracts of the limbic system segmented by diffusion tensor tractography: feasibility study of the patients with schizophrenia

H. Yamada[1], S. Aoki[1], H. Yamasue[2], K. Kasai[2], O. Abe[1], M. Yoshida[3], Y. Masutani[1], H. Mori[1], T. Masumoto[1], N. Hayashi[1], T. Okubo[1], K. Ohtomo[1]

[1]Department of Radiology, Graduate School of Medicine, University of Tokyo, Tokyo, Tokyo, Japan, [2]Department of Psychiatry, Graduate School of Medicine, University of Tokyo, Tokyo, Tokyo, Japan, [3]School of Medicine, Kanazawa University, Kanazawa, Ishikawa, Japan

INTRODUCTION

Disruption of a neural circuit has been hypothesized as a mechanism of schizophrenia. Disconnections between the cingulate gyrus and other regions may partly explain some of the symptoms and cognitive dysfunction in schizophrenia. MR diffusion tensor imaging (DTI) is a unique and relatively new technique to visualize and evaluate the cerebral white matter. Quantitative diffusion indices such as fractional anisotropy (FA) have been used for evaluation of normal appearing white matter. Several DTI studies have shown reduced diffusion anisotropy in patients with schizophrenia (1-2). The methods used were region of interest (ROI) analysis of the specific white matter, a normalization technique with statistical parametric map (SPM) or a histogram analysis.

We newly combined diffusion tensor tractography (DTT) and FA analysis for evaluation of the white matter tracts; we used DTT to segment certain white matter tracts and quantitatively analyzed the degree of deterioration of the fibers by measuring FA using semi-automated ROI method. The purpose of this study is to evaluate the clinical feasibility and efficacy of this method in the patients with schizophrenia comparing between the patients and volunteers.

MATERIALS AND METHODS

We studied fourteen patients with schizophrenia (mean 32.8 years old), diagnosed by DSM-IV criteria, and age-matched fifteen normal volunteers (mean 31.2 years old). DTI (TR/TE 6000/78ms, MPG 6 axes, b-value 1000s/mm^2, 128 x 128 pixel matrix, 2 NEX, 5mm thickness/interleave, total acquisition time 5.5 minutes) was performed by 1.5T MR system (Signa Horizon LX ver9.0, General Electric, Milwaukee, U.S.A.). DTT were visualized by the dTV and VOLUME-ONE software (developed by Masutani Y, URL: http://www.ut-radiology.umin.jp/people/masutani/dTV.htm) (3). The study was approved by the institutional review board and written informed consent was obtained from all patients and volunteers.

We investigate the cingulum, fornix, and uncinate fasciculus in this study (**Fig. 1**). DTT of the anterior cingulum (AC) was visualized from the seed-ROI on the inferior portion of the anterior cingulum to the target-ROI on the superior portion of the anterior cingulum. The DTT of the posterior cingulum (PC) was visualized from the seed-ROI on the anterior portion of the horizontal portion of the cingulum above the body of the corpus callosum, to the target-ROI on the posterior portion of the horizontal portion of the cingulum just above the posterior portion of the body of the corpus callosum. DTT of the fornix (FX) was visualized from the seed-ROI on the column of the anterior fornix to the target-ROI on the posterior portion of the fornix just anterior to the crus. DTT of the uncinate fasciculus (UF) was visualized from the seed-ROI on the inferior-posterior portion of the frontal base deep white matter to the target-ROI on the anterior portion of the deep temporal white matter.

Line-tracked DTTs were then volxelized and FA values of the voxels of the tracts on the several slices were measured. FA values of the tracts on the several slices were averaged and statistically analyzed, respectively.

RESULTS

The mean FA values of semi-automatically placed ROIs of the patients with schizophrenia were significantly lower than that of controls in the anterior cingulum, fornix, and uncinate fasciculus. There was no significant difference in the body of cingulum (**Table 1**).

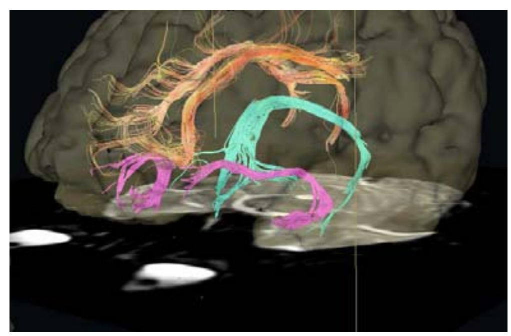

Fig. 1. DTT of the cingulum (orange), fornix (cyan), and uncinate fasciculus (pink)

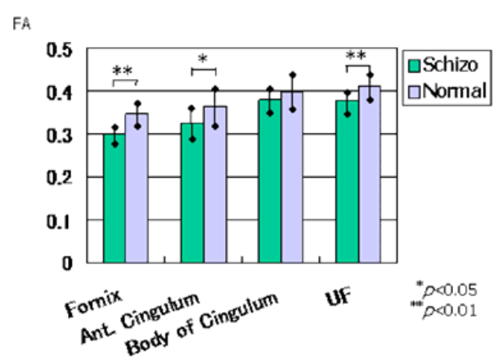

Table. 1. Mean FA of the schizophrenia and normal volunteer

DISCUSSION AND CONCLUSION

Our method, DTT-guided ROI analysis, depicted a subtle FA difference between between patients and controls with high significance. It was relatively objective, because most ROIs were automatically placed on the segmented tract after manually selected the levels of the two representative ROIs, comparing a simple ROI study, in that, ROIs can be set anywhere. Since we segmented the white mater tracts of interest by DTT and evaluated the portion of the segmented tracts selectively, it may be more sensitive than the methods using other anatomical landmarks.

Limbic system and its pathway such as fornix, cingulated, and uncinate fasciculus is considered to have relation with schizophrenia. Our result may reflect reduced diffusion anisotropy of the white matter pathway of the limbic system as decreased FA indices. Manual region-of-interest (ROI) analysis is subjective and difficult to set with anatomical reproducibility. This study suggests that our DTT-guided ROI analysis may be robust enough to perceive changes in diffusion anisotropy in patients with schizophrenia.

In conclusion, DTT can be used for segmentation of the white matter tracts. Mean FA values of the ROIs on the tracts may detect the subtle difference between the schizophrenic patients and the volunteers. Although this method was feasible and promising, further large number studies are necessary to confirm our observation before clinical implementation for the diagnosis of schizophrenia.

REFERENCES

1. Lim KO, et al: Arch Gen Psychiatry **56**: 367-374, 1999.
2. Kubicki M et al: Am J Psychiatry **159**: 813-820, 2002.
3. Masutani Y, et al: Eur J Radiol **46**:53-66, 2003.