Clinical correlations of fornix are disparate in first episode and chronic patients with schizophrenia: A tract-based diffusion spectrum imaging analysis

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Introduction

Schizophrenia is one of the most disabling and economically catastrophic mental disorders. Altered functional activity and structure of hippocampus and frontal lobe were frequently reported in studies [1]. However, fornix, a main structural pathway communicating the two brain areas, was still not well-studied. How the structure changes of fornix in patients with schizophrenia and how the changes may affect clinical manifestations is still unclear. Observation and comparison of first episode (FE) and chronic patients may provide a glimpse of the disease progression of schizophrenia. Structural connectivity can be evaluated *in vivo* by diffusion spectrum imaging (DSI), a high-angular resolution diffusion imaging (HARDI) MR technique which is capable of solving the crossing fiber problem [2]. Here we employed a novel analysis theme called tract-based automatic analysis (TBAA) which is capable of registering predefined whole brain major white matter tracts from a standard DSI template (NTU-DSI-122) to individual's native brain, and sampling the quantification parameters for white matter property along the tracts [3].

Materials and Methods

Subjects: Fifty-four participants with schizophrenia (29 females; age mean: 31.91 ± 8.68 years) and fifty-four age- and handedness-matched controls (34 females; age mean: 29.76 ± 8.68 years) were recruited in the study. ***MRI Data acquisition:*** All images were acquired on a 3T MRI system with a 32-channel head array (TIM Trio, Siemens, Erlangen, Germany). DSI experiment was performed with a pulsed-gradient spin-echo diffusion EPI (TR/TE = 9100/142 ms, isotropic resolution = 2.5 mm, bmax = 4000 s/mm^2, 102 diffusion gradient vectors). ***MRI Data analysis:*** The flow chart of TBAA was shown in figure 1. The individual DSI images of all the subjects were first co-registered to form a study-specific template (SST) through large deformation diffeomorphic metric mapping (LDDMM), the SST were further normalized onto the NTU-DSI-122 template, a high resolution HARDI template based on 122 healthy individuals [4]. The coordinates of the whole brain 74 major tracts on the NTU-DSI-122 template were transferred to the SST, and then to the individual dataset. The quantification parameter for white matter property, generalized fractional anisotropy (GFA), was sampled in individual's native dataset along the coordinates of the tracts. Each tract was further divided into 100 steps, GFA within the same step were averaged. ***Statistics:*** We applied independent *t*-test on the GFA values of bilateral fornix, using patients/controls as our grouping factor. To find the correlation between the WM properties and clinical manifestation, we applied Spearman's correlation between the GFA value of bilateral fornix and the Positive and Negative Syndrome Scale (PANSS).

Results

The GFA values of bilateral fornix were significantly decreased in patients (Left fornix: p<0.001**, Right fornix: p<0.001**) compared to controls (figure 2). The correlation results showed different patterns in FE and chronic patients. GFA values of the fornix correlated mostly with positive symptoms in FE patients, while in chronic patients the GFA correlated with negative symptoms only (figure 3).

Discussion and Conclusion

In the present study we found that fornix is an important tract when investigating the white matter microstructural changes of schizophrenia. Decreased GFA values of bilateral fornix were found in patients group. Moreover, the correlations of clinical symptoms and GFA of fornix showed entirely different patterns between FE and chronic patients. We hypothesize that the phenomenon may be a complex interaction of medication-related changes and natural disease progress. For future works, we plan to do long term follow-up with detailed medication history of the patients to ascertain the effects of antipsychotic medications.

References

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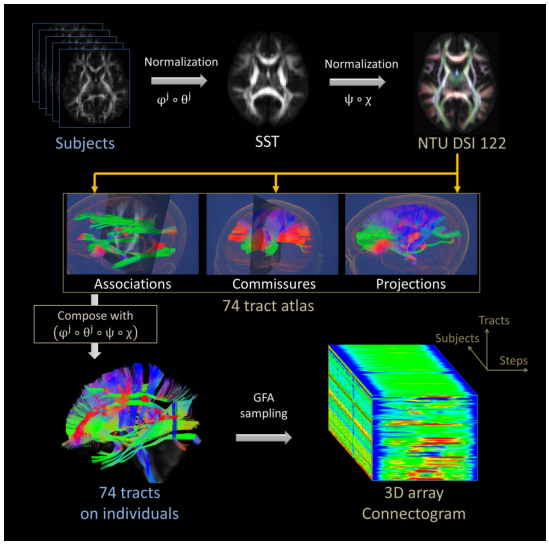

Figure 1 The flowchart of tract-based automatic analysis (TBAA).

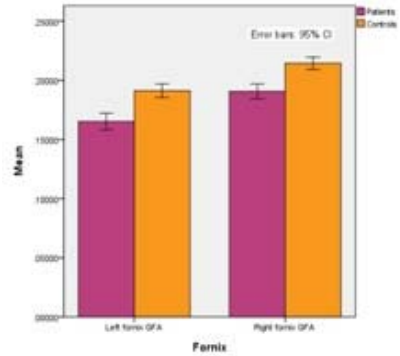

Figure 2. Independent *t*-test of GFA values between patient group and control group in bilateral fornix. The y-axis represents the GFA value; the x-axis consists of two categories: left and right fornix. Patients shown in purple; controls shown in orange. The error bars represent 95% confidence intervals. (Figure 2 is blurry. Please improve it.)

	Positive							Negative						
GFA	1	2	3	4	5	6	7	1	2	3	4	5	6	7
L. For.	-	-	-			-		-	-	-	-		-	
R. For.	-	-	-					-	-	-	-		-	-

Figure 3 Correlation between GFA and positive and negative symptoms of bilateral fornix. Correlations of first episode are shown in blue; chronic in red; purple indicates correlation in both groups. All correlations are negative correlations (shown as "-" in each box).