Diffusion Spectrum Imaging Tractography Study of Ventral and Dorsal Pathways for Language in Schizophrenia

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Introduction Schizophrenia is a mental disorder that goes along with progressively feeble symptoms. The clinical manifestations include auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking with significant social or occupational dysfunction. Abnormalities within language-related brain structures have been associated with clinical symptoms in schizophrenia [1]. Recent functional and anatomical studies suggest that two distinct white matter tracts, called ventral and dorsal pathways provide communication between the two regions that are crucial to language processing [2]. In this study, we used diffusion spectrum imaging tractography to reconstruct the connections involved in the ventral and dorsal pathways for language and to study the alteration of its structural connectivity in schizophrenia.

Materials and Methods The samples consisted of 19 adults with clinical diagnosis of schizophrenia according to the DSM-IV diagnostic criteria and 19 age-, sex- and handedness-matched healthy adult controls. DSI was performed on a 3T magnetic resonance imaging system (TIM Trio, Siemens) using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, image matrix size = 80 x 80, and slice thickness = 2.5 mm. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity bmax = 4000 s/mm^2 were sampled on the grid points in the 3D q-space with $|q| \leq 3.6$ units [3]. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction. The intravoxel fiber orientations were determined by decomposing the original ODF into several constituent ODFs. To reconstruct white matter tracts of the ventral and dorsal pathways [2], we placed regions of interest at bilateral inferior frontal, superior temporal and fusiform gyri (Fig. 1). The mean generalized fractional anisotropy (GFA), an index representing the white matter integrity [4], was measured by calculating the weighted sum of the GFA sampled along each tract bundle. The DSI tractography and tract-specific GFA analysis were performed using DSI studio (http://sites.google.com/a/labsolver.org/dsi-studio/) and an in-house written program in Matlab 7.0, respectively. The two-sample independent Student *t* test was used to compare the fiber integrity of each tract bundle between the two groups. Given their proposed relationship with language processing, linear regression analyses were used to predict patients' scores on the positive, negative and general symptoms of the PANNS, with all connectivity measures entered as predictor variables. Lateralization Index (LI) was calculated using the following formula: LI = (Left GFA - Right GFA) / (Left GFA + Right GFA) [5].

Results Groups did not differ in age at the time of scan (p=0.87), in handedness (all right handed) nor in gender. As compared to the healthy controls, adults with schizophrenia showed a significant decrease in GFA in all the four tracts (Table 1). The linear regression model showed that the right dorsal pathway was significantly predictive of delusions (F=5.559; p=0.031), the left dorsal pathway was significantly predictive of excitement (F=4.845; p=0.042) and general symptoms (F=11.830; p=0.003). Negative partial correlations are observed between the pathways showing significant in regression model and corresponding symptoms. Leftward lateralization of the ventral pathway was found in 57.8% of the patients and 73.6% of the controls; and dorsal pathway was found in 78.9% and 73.6% of the patients and controls, respectively (Fig. 2).

Discussion Using DSI tractography and tract-specific analysis, we are able to map the connectivity of the ventral and dorsal pathways for language and to study their alterations in patients with schizophrenia. Decreased GFA in the ventral and dorsal pathways implies an impaired structural connectivity in schizophrenia. Our results also indicate that the impairment of either side of the dorsal pathway is associated with the severity of delusion (right), excitement (left) and general symptoms (left). Moreover, the decreased percentage of leftward lateralization of the ventral pathway may imply a deviation from the normal pattern [6] of the language processing in schizophrenia.

References [1] L.E. DeLisi, Schizophr Bull. 2001; 27(3):481-96. [2] D. Saur, et al., Proc Natl Acad Sci U S A. 2008 Nov 18;105(46):18035-40. [3] V.J. Wedeen, et al., Magn Reson Med. 2005; 54:1377-86. [4] D.S. Tuch, Magn Reson Med, 2004. [5] D. Qiu, et al., Hum Brain Mapp. 2011 Jan 21. doi: 10.1002/hbm.21168. [6] M. Catani, et al., Proc Natl Acad Sci U S A. 2007 Oct 23; 104(43): 17163-8.

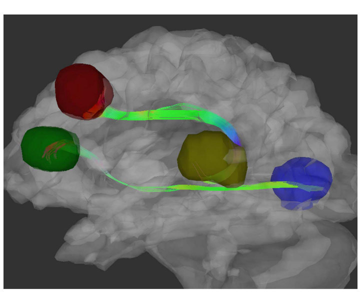

Fig. 1. Connections extracted ventral and dorsal pathways for language by DSI tractography

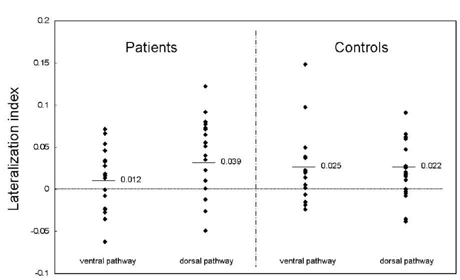

Fig. 2. Distribution and mean values of the lateralization index of patients and controls.

Table 1. Demographics and mean GFA of fiber tracts of the Schizophrenia and control groups

	Schizophrenia	Control	
Sex (M/F)	8/11	8/11	
Age	30.78 ± 6.18	30.47 ± 6.09	
Fiber Tracts	Average ± SD	Average ± SD	*P*
Left ventral pathway	0.2476 ± 0.0310	0.2742 ± 0.0232	0.0239*
Right ventral pathway	0.2411 ± 0.0291	0.2590 ± 0.0312	0.0313*
Left dorsal pathway	0.2505 ± 0.0216	0.2680 ± 0.0203	0.0206*
Right dorsal pathway	0.2318 ± 0.0242	0.2544 ± 0.0228	0.0207*