Functional and Structural Connectivity of Default Mode Network in Patients with Schizophrenia: A Combined Resting-State fMRI and Diffusion Spectrum Imaging Study

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Introduction

Schizophrenia is a complex psychiatric disorder with a wide spectrum of cognitive impairments, and a model of dysconnectivity has been considered to be the psychopathology of this disease [1]. Recent advance in functional MRI (fMRI) and diffusion MRI allows us to evaluate, respectively, functional connectivity (FC) and structural connectivity (SC) in human brain [2-4]. Using resting-state fMRI, investigators have found alteration of FC in the default mode network (DMN) in patients with schizophrenia [5, 6]. Using diffusion MRI, alteration of SC has also been reported [7]. In this study, we combined resting-state fMRI and diffusion spectrum imaging (DSI) to examine the FC and SC of DMN, and further investigated the association of connectivity with neuropsychological data (positive and negative syndrome scale, PANSS) in patients with schizophrenia.

Materials and Methods

Twelve patients with schizophrenia were recruited in the study (five males; age = 26.92 ± 7.35 years; mean Edinburg inventory score = 89.44 ± 18.56, mean PANSS score = 66.25 ± 14.18, mean illness duration = 5.16 ± 5.87; three were drug-naïve). ***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 pulsed-gradient spin-echo diffusion EPI (TR/TE=9100/142 ms, isotropic resolution=2.5 mm, b_{max}=4000 s/mm^2, 102 diffusion gradient vectors). Resting-state fMRI was performed with gradient echo EPI (TR/TE=2000/24 ms, matrix size = 64 x 64, FOV = 256mm, slice thickness = 3mm). ***Data analysis:*** The fluctuations below 0.08 Hz of resting-state fMRI were analyzed. General linear model was applied on whole brain data to reconstruct the activation map of resting-state fMRI. The averaged time series of posterior cingulate cortex and precuneus were used as a paradigm. Six regions within DMN were obtained from the activation maps of individual subjects by one sample *t*-test, including bilateral posterior cingulate gyrus/precuneus (PCCL and PCCR), bilateral medial frontal lobe (MFL and MFR), and bilateral inferior parietal lobe (IPL and IPR). Fifteen nodal pairs in the DMN were determined from those six regions and the FC was derived by calculating the correlation coefficient of time series for each pair. DSI analysis was performed based on the Fourier relationship between the echo signal S(**q**) and the diffusion probability density function P(**r**) [8]. The orientation distribution function was determined by computing the second moment of P(**r**) along each radial direction. Tractography was reconstructed using a streamline-based algorithm adapted for DSI data using in-house software (DSI studio, http://dsi-studio.labsolver.org/). The regions-of-interest (ROIs) obtained from resting-state fMRI were used to select the connecting white matter tracts. Mean generalized fractional anisotropy (GFA) along each tract was calculated to represent the SC for each pair. The Pearson's correlation coefficients were calculated for the following three cases, (1) Clinical PANSS score *vs*. FC, (2) Clinical PANSS *vs*. SC and (3) FC *vs*. SC.

Results

As shown in Fig. 1, significant correlations between PANSS score and FC were found between IPL and IPR (ρ=0.718, *p*=0.009), IPL and PCCR (ρ=0.782, *p*=0.003) and IPR and PCCL (ρ=0.670, *p*=0.017). Moreover, in the pair of IPR and PCCL, there was negative correlation between FC and SC (ρ=-0.740, *p*=0.036) in patients under medication (Fig. 2).

Discussion and Conclusion

With the combined resting-state fMRI and DSI, the relationships between FC, SC and clinical PANSS scores were investigated. In the present study, significant correlations between FC and PANSS scores were found in three pairs of DMN, namely the IPL-IPR, the IPL-PCCR, and the IPR-PCCL pairs. However, the SC showed no significant correlation with PANSS score. Our results suggest that FC of DMN associates with the severity of the clinical symptoms more strongly than SC. Moreover, after excluding three drug-naïve patients, the SC between IPR and PCCL was negatively correlated with FC, implying that alteration of FC might down regulate SC. To clarify this, a longitudinal study is warranted to study the interactions between FC and SC, and their effects on clinical symptoms during the disease course.

References

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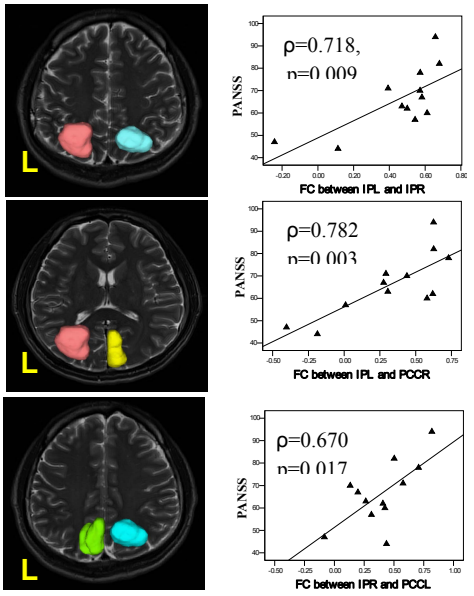

Figure 1 Correlation results between FC and PANSS score of three connection pairs. Three connection pairs were shown with overlapping T2 weighted images in the left column. The functional areas were illustrated in different colors, IPL (red), IPR (blue), PCCR (yellow) and PCCL (green). The scatter plots of PANSS scores (y-axis) against FC (x-axis) were shown in the right column.

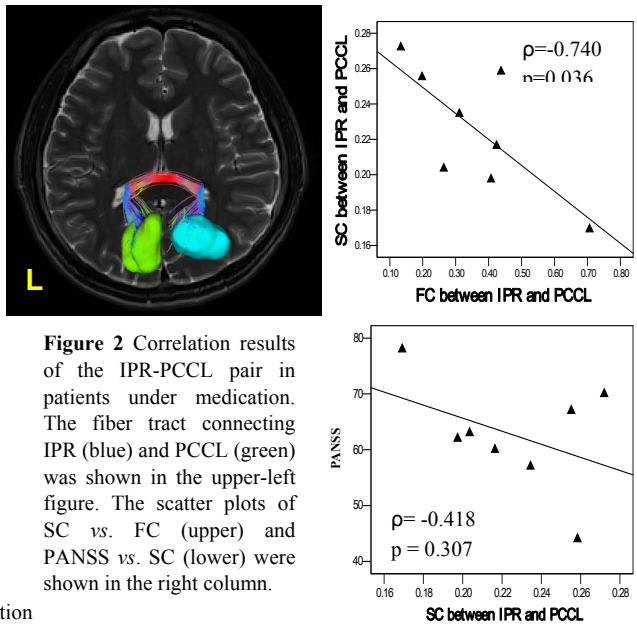

Figure 2 Correlation results of the IPR-PCCL pair in patients under medication. The fiber tract connecting IPR (blue) and PCCL (green) was shown in the upper-left figure. The scatter plots of SC *vs*. FC (upper) and PANSS *vs*. SC (lower) were shown in the right column.