Cortical Thickness Revealing Cerebral Anatomical Deficits in Drug-naive First-episode Schizophrenia

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Purpose:

Though many previous studies[1] of gray matter volume provided evidences to support the anatomical deficits mainly involving the cortical thalamo-cortical circuits, the results were quite inconsistent. Furthermore, the gray matter volume of a cortical region represents the combination of cortical thickness and surface area, features which are believed to be influenced by different genetic factors related to sulcal patterning and the thickness of the cortical mantle itself. Cortical thickness reflects the size, density and arrangement of neurons, neuroglia and nerve fibers, and thus its measurement could provide important and relatively unique information about disease-specific neuroanatomical changes. However, few studies had explored the deficits of cortical thickness in schizophrenia. Thus the aim of current study was to explore the difference of cortical thickness between 128drug-naïve, first-episode schizophrenia patients and 141 healthy controls.

Methods:

This study was approved by the local ethical committee and written informed consent was obtained from all subjects. 128 antipsychotic-naïve, first-episode schizophrenia patients and 141 healthy comparison subjects were recruited in the present research. Both patients and healthy controls were performed MR examination via a 3-Telsa GE MRI system with an 8 channel phase array head coil. We employed CIVET software (version 1.1.9, Montreal Neurological Institute at McGill University, Montreal, Quebec, Canada) to extract cortical thickness measurements from T1-weighted MRI images. Vertex-based 2-sample t-test was applied to investigate cortical thickness differences between the patient group and the healthy control group with age and sex as covariance. Statistical significance was set at $p<0.05$ with false discovery rate correction for multiple comparisons. Global Assessment of Functioning Scale (GAF) and Positive and Negative Syndrome Scale (PANSS) were used to assess the neuropsychological functioning and clinical symptoms of schizophrenia patients. Besides, correlation analysis between significant difference of cortical thickness in patient group and scale scores was performed to reveal the potential association between the anatomical deficits and clinical symptoms.

Results:

Compared to the control group, schizophrenia patients showed significantly cortical thinning in the bilateral dorsolateral prefrontal cortices (DLPFC), left precentral gyrus, left orbitofrontal cortex (OFC), right precentral and postcentral gyri and thickening in bilateral temporal poles, left medial orbitofrontal cortex (med-OFC), left cuneus and right insula ($P<0.05$)(Figure 1). Meanwhile, the cortical thickness of right DLPFC, bilateral temporal poles, bilateral precentral gyri and left OFC were negatively correlated with the severities of symptoms in patients as identified by PANSS scores for positive symptoms, thought disturbance, activation or depression (Table 1). While positive correlations were found between the cortical thickness of left temporal pole, left cuneus and GAF scores, and between that of right precentral gyrus, left DLPFC and PANSS scores for general psychopathology symptoms as well as depression.

Discussion:

The current studies in the largest sample of drug-naïve, first-episode schizophrenia exhibited significant changes including both thinning and thickening performances of cortical thickness in many cerebral cortices. These obvious alterations of cortices at the very beginning of disease may in some degree facilitate to partly explain the complex neuropathological mechanism of schizophrenia. The cortical thinning, especially, the right DLPFC, may be resulted from neuroprogression characterized by reduced number of neurons or malformation of cortices in schizophrenia. Interestingly, cortical thickening in bilateral temporal poles and other cortices were also revealed and may result from the compensatory mechanism or abnormal neurodevelopment at early stage of schizophrenia. In addition, a strong link between symptoms and cortical thickness displayed a consensus between cerebral structure and clinical manifestations.

Conclusion:

The significant alteration of cortical thickness at the very beginning of antipsychotic-naïve, first-episode patients of schizophrenia provided evidences to support the aberrations in the neurodevelopmental process in schizophrenia[2]. In the further study, longitudinal research about the structural characteristics together with function and clinical symptoms should be performed to investigate the trajectory of disease.

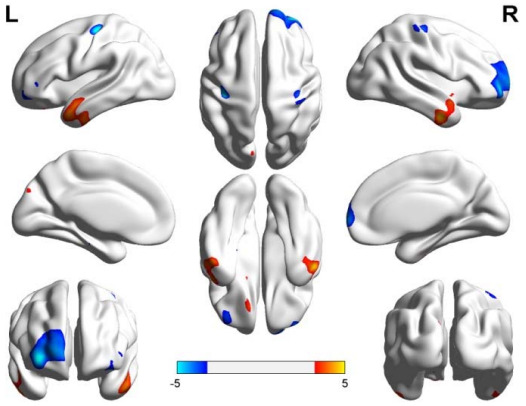

Figure 1. Vertex-based 2-sample t-test analyses of cortical thickness between patients and healthy controls. Thinning (blue): right DLPFC, left precentral gyrus, left OFC, right precentral and postcentral gyri, left DLPFC; Thickening (red): bilateral temporal poles, left med- OFC, left cuneus and right insula.

	Association with cortical thickness clusters(r)							
Clinical measures	DLPFC-R	Temporal-pole-L	Temporal-pole-R	Precentral-L	OFC-L	Precentral-R	Cuneus-L	DLPFC-L
GAF	.082	.272**	.133	.145	.096	-.053	.258*	-.025
PANSS								
Total	.045	-.089	-.086	.068	.054	.119	-.142	.139
Positive	-.232**	-.185*	-.137	-.210*	-.124	-.184*	-.074	-.158
Negative	.100	.038	.043	.078	.020	.043	-.070	.104
General	.109	-.106	-.086	.115	.091	.226*	-.142	.239**
Thought disturbance	-.247**	-.200*	-.149	-.320**	-.181*	-.233**	-.068	-.159
Activation	-.205*	-.092	-.060	-.101	-.151	-.086	-.103	-.069
Paranoid	.004	-.132	-.135	.085	.138	.072	-.117	.044
Depression	.129	-.205*	-.193*	.063	.069	.194*	-.080	.221*

Table 1. Correlation analyses between scores of clinical symptoms and cortical thickness

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

References:

1. Kubota, M., et al., Thalamocortical disconnection in the orbitofrontal region associated with cortical thinning in schizophrenia. Archives of general psychiatry, 2012: p. 1-10.

2. Andreasen, N.C., The lifetime trajectory of schizophrenia and the concept of neurodevelopment. Dialogues in clinical neuroscience, 2010. 12(3): p. 409-415.