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COGNITIVE AND MRI BRAIN MORPHOMETRIC CORRELATES WITH COMT GENE VAL158MET POLYMORPHISM IN FIRST-EPISODE TREATMENT-NAÏVE PATIENTS WITH SCHIZOPHRENIA

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Objective: Catechol-O-methyltransferase (COMT) play an important role in modulating cortical dopaminergic catabolism and has been associated with schizophrenia. However, it remains unclear that if the variations in dopamine signaling affect the gray matter (GM) structural maturation in typically developing individuals, and whether such effect are disrupted in schizophrenia patients. This study aims (1) to explore the relationship between the functional polymorphisms Val158Met of COMT gene and GM volume in first-episode treatment-naïve patients with schizophrenia and healthy controls, (2) to investigate the influence of COMT Val158Met on TMT performance, (3) to investigate the relationship among GM volume, cognitive deficit and psychiatric symptoms.

Method: Whole GM volume which was computed by an automated SPM and clinical performances were evaluated in 150 first-episode treatment-naïve patients with schizophrenia and 100 healthy controls. In addition, 2-sample t-tests was used to explore the main effect of diagnostic group, a full factorial model was used to obtain genotype-by-diagnostic interaction in the volume of GM according to genotypes of above the polymorphism, and multiple regression was used to explore the correlation whole GM volume with TMT measurements and clinical syndromes, with age and sex as covariance.

Results: A significant GM volume reduced in the right precentral gyrus [MNI: 37 -16 70], right cerebellum anterior lobe [MNI: 6 -56 26] and left Postcentral gyrus [MNI: -8 -36 80] ($P < .05$, FWE corrected) in schizophrenia. There was also a strong for a group× genotype interaction on the right precuneus ($P < .001$, uncorrected). A significant negative correlation of the GM volume over the cluster located at cerebellum anterior lobe with TMT-A and TMT-B within schizophrenic patients ($P < .05$, FDR corrected). A significant positive correlation of the GM volume over the cluster located at middle frontal gyrus [MNI: 36 60 15] with PANSS subscales for general psychopathological symptoms within schizophrenic patients, the negative correlation of the GM volume over the cluster located at parahippocampa gyrus [MNI: 27 -10 -25] with PANSS subscales for negative symptoms within schizophrenic patients (FDR correction at $p < 0.05$).

Conclusion: These findings suggest that COMT $_{Met}$ variant was associated with disruption of dopaminergic in?eunces on GM maturation and may be the pathogenesis of schizophrenia, and maybe that the abnormal GM structure were association with cognitive function and clinical syndromes.

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