Article: 2653
Topic: 51 - Genetics & Molecular Neurobiology

INFLUENCE OF POLYMORPHISMS IN GENES SLC1A1, GRIN2B AND GRIK2 ON CLOZAPINE-INDUCED OBSESSIVE-COMPULSIVE SYMPTOMS

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Objectives: Clinical observations indicate that atypical antipsychotics, especially clozapine, induce obsessive-compulsive (OC) symptoms in schizophrenic patients. Recent data from neuroimaging and clinical trials suggest a role for altered glutamate neurotransmission in the etiology of OCD. It has been reported that SLC1A1, GRIN2B and GRIK2 regulate glutamate transmission and affect OCD pathophysiology. This study aimed to determine whether SLC1A1, GRIN2B and GRIK2 are associated with clozapine-induced OC symptoms.

Methods: A total of 250 clinically stable schizophrenic patients receiving clozapine treatment and 261 sex- and age-matched controls were recruited. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to evaluate the severity of OC symptoms. Based on the Y-BOCS score, 250 patients were divided into OC group and non-OC group (patients with and without OC symptoms, respectively). Three reported OCD susceptibility polymorphisms SLC1A1 (rs2228622), GRIN2B (rs890) and GRIK2 (rs1556995) were genotyped.

Results: Trends of association with OC symptoms were observed in rs2228622A and rs890T alleles. SLC1A1 and GRIN2B interaction was found in the significant 2-locus, gene-gene interaction model (P=0.0021), using a MDR method. Further analysis showed a significant interaction between SLC1A1 and GRIN2B on the Y-BOCS score ($F_{6,\ 137}$=7.650, P 0.001), and individuals with AA/TT genotypes had a significantly higher mean Y-BOCS score than those with other genotypes, except AG/TT.

Conclusions: These results suggest that SLC1A1, GRIN2B and interactions between the two might confer a susceptibility to OC symptoms in schizophrenic patients receiving clozapine.

https://doi.org/10.1016/S0924-9338(13)77281-X Published online by Cambridge University Press