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RESEQUENCING OF THE GAP-43 GENE REVEALS SOME RARE GENETIC VARIANTS THAT MAY INCREASE THE GENETIC BURDEN IN SCHIZOPHRENIA

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Objectives: Growth-associated protein 43 (GAP-43) was critical for initial establishment or reorganization of synaptic connections, a process thought to be disrupted in schizophrenia. Abnormal GAP-43 expression has been linked to this disorder in numerous postmortem brain studies. The purpose of this study was to investigate the involvement of the gene encoding GAP-43 in the susceptibility to schizophrenia.
Methods: We searched for genetic variants in the promoter region and 3 exons (including both UTR ends) of the GAP-43 gene using direct sequencing in a sample of Han Chinese schizophrenic patients (n=354) and non-psychotic controls (n=338) from Taiwan, and conducted a case-control association study.
Results: We identified 11 common SNPs in the GAP-43 gene. SNP and haplotype-based analyses showed no association with schizophrenia. Besides, we identified 4 rare variants in 4 out of 354 patients, including 1 variant located at the promoter region, 1 synonymous and 2 missense variants located at exon 2. No rare variants were found in the control subjects. Collectively, these rare variants were significantly overrepresented in the patient group (1.1% v.s 0; p value of Fisher´s exact test = 0.02), suggesting they may increase the genetic burden in schizophrenia.
Conclusion: Although the functional significance of these rare variants remained to be characterized, our study lent support to the hypothesis of multiple rare mutations in schizophrenia, and provided genetic clues to indicate the involvement of neurodevelopment defect in this disorder.

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