

Genome-Wide Significant SNPs Proximal to Nicotinic Receptor Genes Impact Cognition in Schizophrenia

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Abstract : Schizophrenia is a psychiatric disorder with symptoms that include cognitive deficits and nicotine has been suggested to have an effect on cognition. In recent years, the advents of Genome-Wide Association Studies (GWAS) has evolved our understanding about the genetic causes of complex disorders such as schizophrenia and studying the role of genome-wide significant genes could potentially lead to the development of new therapeutic agents for treatment of cognitive deficits in schizophrenia. The current study identified six Single Nucleotide Polymorphisms (SNP) from schizophrenia and smoking GWAS that are located on or in close proximity to the nicotinic receptor gene cluster (CHRN) and studied their association with cognition in an Irish sample of 1297 cases and controls using linear regression analysis. Further on, the interaction between CHRN gene cluster and Dopamine receptor D2 gene (DRD2) during working memory was investigated. The effect of these polymorphisms on nicotinic and dopaminergic neurotransmission, which is disrupted in schizophrenia, have been characterized in terms of their effects on memory, attention, social cognition and IQ as measured by a neuropsychological test battery and significant effects in two polymorphisms were found across global IQ domain of the test battery.

Keywords : cognition, dopamine, GWAS, nicotine, schizophrenia, SNPs

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