Functional genetic polymorphisms in dopaminergic transporters: Association with ADHD traits in the Indian probands

Paramita Ghosh, Subhamita Maitra, Tanusree Saha, Swagata Sinha, Kanchan Mukhopadhyay

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Abstract

Objectives
The dopamine (DAT) and norepinephrine (NET) transporters, encoded by SLC6A3 and SLC6A2 genes, regulate neurotransmitters controlling motor activity, attention, mood swings, and stress induced anxiety, thus becoming targets for therapeutic intervention. We explored contribution of SLC6A3 (rs40184, rs2652511) and SLC6A2 (rs3785143, rs11568324) variants in Attention-deficit hyperactivity disorder associated traits.

Methods
Nuclear families with ADHD probands (N = 200) and ethnically matched controls (N = 180) were recruited based on the DSM-IV-TR. Behavioral traits were assessed by the Conners' Parent Rating Scale-revised. Genomic DNA obtained from peripheral blood leukocytes was subjected to PCR based amplification of target sites followed by restriction fragment length polymorphism and sequencing based analysis. Statistical analysis was performed by population as well as family-based methods.

Results
The control population showed significant difference in allelic and genotypic frequencies for rs40184, rs2652511 and rs11568324 in comparison to other Asian populations. Family-based analysis exhibited preferential transmission of rs3785143 and rs11568324 “C” alleles (P = 0.009 & 0.05). Gene variants showed association with behavioral problems and co-morbid disorders. Multifactor Dimensionality Reduction analysis revealed independent as well as synergistic effects of studied sites and phenotypic traits.

Conclusion
Data obtained for the first time evidenced association of dopamine and norepinephrine transporter gene variants with phenotypic traits and co-morbidity of Indian ADHD probands.